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 MARCH 31, 2022

or

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

FOR THE TRANSITION PERIOD FROM _____ TO _____

Commission file number: 001-35670

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

Delaware	**26-4738379**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
4224 Campus Point Court, Suite 210 San Diego CA	**92121**
(Address of Principal Executive Offices)	**(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 x No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes x No ☐

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

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☐

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

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

As of May 6, 2022, the registrant had 145,981,180 shares of Common Stock ($0.001 par value) outstanding.

REGULUS THERAPEUTICS INC.
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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 to develop our product candidates and implement our operating plans, and if we are unable to do so when needed, we will not be able to complete the development and commercialization of our product candidates.

- 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 *micro*RNA 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.

PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

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

	March 31, 2022	December 31, 2021
	(Unaudited)	
Assets		
Current assets:		
Cash and cash equivalents	$ 53,902	$ 60,383
Restricted cash	62	62
Contract and other receivables	8	—
Prepaid materials, net	3,010	3,010
Prepaid expenses and other current assets	951	1,780
Total current assets	57,933	65,235
Property and equipment, net	394	281
Intangibles, net	74	83
Right of use asset	2,436	2,564
Other assets	148	291
Total assets	$ 60,985	$ 68,454
Liabilities and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 625	$ 285
Accrued liabilities	827	821
Accrued research and development expenses	608	810
Accrued compensation	858	2,016
Current portion of term loan, less debt issuance costs	826	—
Other current liabilities	957	1,295
Total current liabilities	4,701	5,227
Term loan, less debt issuance costs	3,588	4,673
Lease liability, less current portion	2,262	2,417
Other long-term liabilities	1,193	1,179
Total liabilities	11,744	13,496
Commitments and Contingencies	—	—
Stockholders' equity:		
Class A-1 convertible preferred stock, $0.001 par value; 256,700 shares authorized, issued, and outstanding at March 31, 2022 (unaudited) and December 31, 2021	—	—
Class A-2 convertible preferred stock, $0.001 par value; 1,330,832 shares authorized, issued, and outstanding at March 31, 2022 (unaudited) and December 31, 2021	1	1
Class A-3 convertible preferred stock, $0.001 par value; 258,707 shares authorized, issued, and outstanding at March 31, 2022 (unaudited) and December 31, 2021	—	—
Class A-4 convertible preferred stock, $0.001 par value; 3,725,720 shares authorized, issued, and outstanding at March 31, 2022 (unaudited) and December 31, 2021	4	4
Common stock, $0.001 par value; 400,000,000 shares authorized at March 31, 2022 and December 31, 2021; 145,981,180 and 145,971,184 shares issued and outstanding at March 31, 2022 (unaudited) and December 31, 2021, respectively	146	146
Additional paid-in capital	510,662	509,660
Accumulated deficit	(461,572)	(454,853)
Total stockholders' equity	49,241	54,958
Total liabilities and stockholders' equity	$ 60,985	$ 68,454

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 March 31,	
	2022	2021
	(Unaudited)	
Operating expenses:		
Research and development	3,679	3,320
General and administrative	2,890	2,478
Total operating expenses	6,569	5,798
Loss from operations	(6,569)	(5,798)
Other income (expense):		
Interest and other income	6	1
Interest and other expense	(155)	(216)
Loss before income taxes	(6,718)	(6,013)
Income tax expense	(1)	—
Net loss and comprehensive loss	$ (6,719)	$ (6,013)
Net loss per share, basic and diluted	$ (0.05)	$ (0.08)
Weighted average shares used to compute basic and diluted net loss per share	145,973,989	71,290,918

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, 2021	5,571,959	$ 5	145,971,184	$ 146	$ 509,660	$ (454,853)	$ 54,958
Issuance of common stock under Employee Stock Purchase Plan	—	—	9,996	—	2	—	2
Stock-based compensation expense	—	—	—	—	1,000	—	1,000
Net loss	—	—	—	—	—	(6,719)	(6,719)
Balance at March 31, 2022	5,571,959	$ 5	145,981,180	$ 146	$ 510,662	$ (461,572)	$ 49,241
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

See accompanying notes to these condensed financial statements.

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

	Three months ended March 31,	
	2022	2021
	(Unaudited)	
Operating activities		
Net loss	$ (6,719)	$ (6,013)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and amortization expense	26	335
Stock-based compensation	1,000	691
Other	38	10
Change in operating assets and liabilities:		
Contracts and other receivables	(8)	432
Prepaid expenses and other assets	681	356
Accounts payable	340	275
Accrued liabilities	(26)	14
Accrued research and development expenses	(202)	(371)
Accrued compensation	(1,159)	(941)
Operating lease right-of-use assets and liabilities, net	(12)	90
Other liabilities	(340)	(589)
Net cash used in operating activities	(6,381)	(5,711)
Investing activities		
Purchases of property and equipment	(102)	(53)
Net cash used in investing activities	(102)	(53)
Financing activities		
Proceeds from issuance of common stock, net	2	6,382
Proceeds from exercise of common stock options	—	26
Payments on financing leases	—	(72)
Net cash provided by financing activities	2	6,336
Net (decrease) increase in cash and cash equivalents	(6,481)	572
Cash and cash equivalents at beginning of period	60,445	31,087
Cash and cash equivalents at end of period	$ 53,964	$ 31,659
Reconciliation of cash, cash equivalents and restricted cash		
Cash and cash equivalents	$ 53,902	$ 31,597
Restricted cash	62	62
Total cash, cash equivalents and restricted cash	$ 53,964	$ 31,659
Supplemental disclosure of cash flow information		
Interest paid	$ (110)	$ (109)
Income taxes paid	$ (1)	$ —
Supplemental disclosure of non-cash investing and financing activities		
Non-cash acquisition of property and equipment	$ 33	$ 24

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, 2021, from which the balance sheet information herein was derived.

Liquidity

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 $538.0 million. As of March 31, 2022, we had approximately $53.9 million of cash and cash equivalents. 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.

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.

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, and forfeitures are recognized as they occur.

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 these raw materials 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.

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) 131,659,415 for the three months ended March 31, 2022 and 89,859,197 for the three months ended March 31, 2021, and consisted of convertible preferred stock, warrants, 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 March 31, 2022 and December 31, 2021, our cash balance was comprised entirely of cash and cash equivalents (money market funds) and there was no unrealized gain or loss in either period.

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 March 31, 2022 and December 31, 2021 (in thousands):

	Fair value as of March 31, 2022			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents (money market funds)	$ 49,911	$ 49,911	$ —	$ —
	$ 49,911	$ 49,911	$ —	$ —

	Fair value as of December 31, 2021			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents (money market funds)	$ 57,905	$ 57,905	$ —	$ —
	$ 57,905	$ 57,905	$ —	$ —

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, 2024 (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 nine times between October 2017 through May 2020. On August 25, 2020 we entered into a tenth amendment to the Loan Agreement with the Lender (the "Tenth Amendment"). Pursuant to the terms of the Tenth Amendment, we were 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"). 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 were not obligated to make principal payments on the Term Loan until January 1, 2022.

On December 31, 2021, we entered into an eleventh amendment to the Loan Agreement (the "Eleventh Amendment"). Under the terms of the Eleventh Amendment, our required monthly payments to the Lender are to be comprised of interest only through and including (i) December 1, 2022, if the 2022 Equity Event (as defined below) does not occur or (ii) December 1, 2023 if the 2022 Equity Event occurs. The "2022 Equity Event" means the receipt by us, during the calendar year 2022, of unrestricted net cash proceeds of at least $20.0 million from the sale and issuance of our equity securities. In addition, the maturity date for the Term Loan was extended to May 1, 2024.

If the 2022 Equity Event does not occur, then commencing on January 1, 2023 and continuing on each successive payment date thereafter through and including the maturity date of May 1, 2024, we will be required to make consecutive equal monthly payments of principal, together with applicable interest, in arrears, to the Lender.

If the 2022 Equity Event does occur, then commencing on January 1, 2024 and continuing on each successive payment date thereafter through and including the maturity date of May 1, 2024, we will be required to make consecutive equal monthly payments of principal, together with applicable interest, in arrears, to the Lender.

The Eleventh Amendment also provides that we are required to maintain a minimum cash balance of $5.0 million. As consideration for the Lender's entry into the Eleventh Amendment, we made a payment of $0.3 million to the Lender.

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. 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. We are in compliance with all Loan Agreement covenants as of the date of the filing of this Form 10-Q.

As of March 31, 2022, $4.7 million of principal was outstanding under the Term Loan. An additional $1.3 million is also payable at the conclusion of the Term Loan (the related $1.2 million accrued liability balance is presented in other long-term liabilities on our balance sheet at March 31, 2022). We had less than $0.1 million of debt issuance costs outstanding as of March 31, 2022, 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 March 31, 2022, future principal payments for the Term Loan due under the Loan Agreement are as follows (in thousands):

2022	$ —
2023	3,304
2024	1,377
	$ 4,681

Paycheck Protection Program Loan

On April 23, 2020, we received proceeds in the amount of approximately $0.7 million (the "PPP Loan") from Silicon Valley Bank, as lender, pursuant to the Paycheck Protection Program of the Coronavirus Aid, Relief, and Economic Security 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.

We 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 nine months ended September 30, 2021.

6. Stockholders' Equity

Common Stock

As of March 31, 2022, there were 145,981,180 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 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 the with 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 March 31, 2022, 4,452,863 shares of common stock were available for new equity award grants under the 2019 Plan and 13,871,693 shares of common stock were reserved for issuance pursuant to equity awards outstanding under the 2019 Plan as of March 31, 2022.

2021 Inducement Plan

On November 23, 2021, our Board of Directors adopted the 2021 Inducement Plan (the "Inducement Plan"), which became effective immediately. Stockholder approval of the Inducement Plan was not required pursuant to Rule 5635(c)(4) of the Nasdaq Listing Rules. The Inducement Plan initially reserved 2,000,000 shares of common stock and provides for the grant of NSOs that was used exclusively for grants to individuals that were not previously employees or directors of the Company, as an inducement material to the individual's entry into employment with the Company.

Under the Inducement Plan, options were granted with varying vesting terms, but typically vested over four years, with 25% of the total grant vesting on the first anniversary of the effective date of the option grant and the remaining grant vesting monthly thereafter over the following 36 months.

As of March 31, 2022, 1,800,000 shares of common stock were reserved for future issuance under the Inducement Plan and 200,000 shares of common stock were reserved for future issuance pursuant to equity awards outstanding under the Inducement Plan.

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.

At a second closing under the May 2019 SPA that occurred on December 24, 2019 (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 may be exercised 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 $0.7464 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.

On November 24, 2021, we entered into a Securities Purchase Agreement (the "November 2021 SPA") with certain institutional and other accredited investors, including one of the Company's directors (the “2021 Purchasers”), pursuant to which we agreed to sell and issue shares of our common stock and shares of newly designated non-voting convertible preferred stock (the “2021 PIPE”).

At the closing under the November 2021 SPA that occurred on November 30, 2021 (the “2021 Closing”), we sold and issued to the 2021 Purchasers (i) 58,923,352 shares of common stock at a purchase price of $0.36 per share, and (ii) 3,725,720 shares of non-voting Class A-4 convertible preferred stock, in lieu of shares of common stock, at a price of $3.60 per share. Total gross proceeds from the 2021 Closing were approximately $34.6 million. Each share of non-voting Class A-4 convertible preferred stock is convertible into 10 shares of common stock, subject to certain beneficial ownership conversion limitations. An aggregate of 2,222,222 shares of common stock were purchased for $0.8 million by a director of the Company at the 2021 Closing.

We evaluated the non-voting Class A-4 convertible preferred stock sold in the 2021 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 May 2019 SPA, the December 2020 SPA and the November 2021 SPA for the three months ended March 31, 2022 and 2021 (in thousands):

	Class A-1 Convertible Preferred Stock	Class A-2 Convertible Preferred Stock	Class A-3 Convertible Preferred Stock	Class A-4 Convertible Preferred Stock	Warrants	Common Stock
Balance at December 31, 2021	257	1,331	259	3,726	61,868	
Conversions/Exercises	—	—	—	—	—	
Balance at March 31, 2022	257	1,331	259	3,726	61,868	
Balance at December 31, 2020	257	1,416	259	—	66,038	
Conversions/Exercises	—	(78)	—	—	(3,920)	3,199
Balance at March 31, 2021	257	1,338	259	—	62,118	

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 that 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. No shares were sold under the ATM Offering during the three months ended March 31, 2022. A total of 4,009,585 shares were sold and settled for proceeds of $5.8 million (net of $0.2 million in offering costs) under the Stock Sales Agreement during the three months ended March 31, 2021. On August 10, 2021, we increased the amount of common stock available for sale in the ATM Offering under the Stock Sales Agreement to $50.0 million. At March 31, 2022, approximately $50.0 million remained eligible to be sold in the ATM Offering, subject to compliance with the rules applicable to sales on Form S-3.

Shares Reserved for Future Issuance

The following shares of common stock were reserved for future issuance as of March 31, 2022 (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
Class A-4 convertible preferred stock outstanding (as-converted)	37,257
2019 PIPE Initial Closing warrants	12,778
2019 PIPE Milestone Closing warrants	30,595
2020 PIPE warrants	18,495
Common stock options outstanding	12,846
RSUs outstanding	1,226
Common stock available for future grant under the 2019 Equity Incentive Plan	4,453
Common stock available for future grant under the 2021 Inducement Plan	1,800
Employee Stock Purchase Plan	291
Total common shares reserved for future issuance	138,203

The following table summarizes our stock option and RSU (together Stock Awards) activity under all equity incentive plans for the three months ended March 31, 2022 (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, 2021	8,661	$ 1.17	401	$ 0.95
Granted	4,357	$ 0.26	848	$ 0.26
Canceled/forfeited/expired	(172)	$ 0.90	(23)	$ 0.95
Stock Awards outstanding at March 31, 2022	12,846	$ 0.87	1,226	$ 0.47

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, 2021 Inducement Plan and the shares purchasable under our Employee Stock Purchase Plan during the periods presented:

	Three months ended March 31,	
	2022	2021
Stock options		
Risk-free interest rate	1.7 %	0.9 %
Volatility	95.7 %	95.7 %
Dividend yield	—	—
Expected term (years)	6.1	6.1
Performance stock options		
Risk-free interest rate	—	1.0 %
Volatility	—	95.7 %
Dividend yield	—	—
Expected term (years)	0.0	6.1
Employee stock purchase plan shares		
Risk-free interest rate	0.3 %	0.1 %
Volatility	97.8 %	101.3 %
Dividend yield	—	—
Expected term (years)	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 March 31,	
	2022	2021
Research and development	$ 270	$ 181
General and administrative	730	510
Total	$ 1,000	$ 691

7. Collaborations

Revenue recognized from our strategic collaborations was zero for the three months ended March 31, 2022 and 2021.

Sanofi

In July 2012, we amended and restated our collaboration and license agreement with Sanofi to expand the potential therapeutic applications of the *micro*RNA alliance targets to be developed under such agreement. The following elements were delivered as part of the strategic collaboration with Sanofi: (1) a license for up to four *micro*RNA 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 *micro*RNA programs and we were granted the exclusive right to negotiate with Sanofi for co-development and commercialization of certain miR-21 anti-miRs in oncology and Alport syndrome.

In 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 *micro*RNA 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 *micro*RNA 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 March 31, 2022, 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 at inception 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. 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 assigned all rights, title, and interest under the Prior Lease to Assignee and delivered the Prior 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 March 31, 2022 are as follows (in thousands):

	Operating Leases
Remaining 2022	$ 569
2023	776
2024	800
2025	824
2026	277
Total operating lease payments	$ 3,246
Less: amount representing interest	(380)
Present value of obligations under operating leases	2,866
Less: current portion	(604)
Long-term operating lease obligations	$ 2,262

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, 2021 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, 2021, or Annual Report, filed with the Securities and Exchange Commission on March 10, 2022. 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 *micro*RNAs 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 *micro*RNAs pursuant to a license and collaboration agreement. Our lead product candidates are RG-012 and RGLS8429. 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. RGLS8429, an anti-miR targeting miR-17, is our next-generation compound for the treatment of autosomal dominant polycystic kidney disease ("ADPKD"). In May 2022, the U.S. Food and Drug Administration ("FDA") accepted our Investigational New Drug application ("IND") for RGLS8429. We plan to initiate a Phase 1 study for RGLS8429 in the second quarter of 2022. In addition to these programs, we continue to develop a pipeline of other preclinical drug product candidates.

*micro*RNAs 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 *micro*RNAs is directly linked to many diseases. Furthermore, many different infectious pathogens interact and bind to host *micro*RNA to survive. To date, over 500 *micro*RNAs have been identified in humans, each of which can bind to multiple messenger RNAs that control key aspects of cell biology. Since many diseases are multi-factorial, involving multiple targets and pathways, the ability to modulate multiple pathways by targeting a single *micro*RNA provides a new therapeutic approach for treating complex diseases.

RNA plays an essential role in the process used by cells to encode and translate genetic information from 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, *micro*RNAs are RNAs that do not code for proteins but rather are responsible for regulating gene expression by modulating the translation and decay of target messenger RNAs. By interacting with many messenger RNAs, a single *micro*RNA can regulate the expression of multiple genes involved in the normal function of a biological pathway. Many pathogens, including viruses, bacteria and parasites, also use host *micro*RNAs to regulate the cellular environment for survival. In some instances, the host *micro*RNAs are essential for the replication and/or survival of the pathogen. For example, miR-122 is a *micro*RNA expressed in human hepatocytes and is a key factor for the replication of the hepatitis C virus ("HCV").

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

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

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

We believe that *micro*RNA biomarkers may be used to select optimal patient segments in clinical trials and to monitor disease progression or relapse. We believe these *micro*RNA biomarkers can be applied toward drugs that we develop and drugs developed by other companies with which we partner or collaborate.

Since our inception through March 31, 2022, we have received $416.4 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 March 31, 2022, we had cash and cash equivalents of $53.9 million.

Lead Product Candidates

We currently have two lead product candidates.

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, 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 IND, were completed in the second quarter of 2019. Sanofi has completed enrollment of patients into a Phase 2 clinical trial evaluating Lademirsen (RG-012) for the treatment of adult patients with Alport Syndrome, with final data expected in the first half of 2023.

RGLS8429: RGLS8429, an anti-miR oligonuceotide targeting miR-17, is our next-generation compound for the treatment of ADPKD. In October 2021, we announced that we would discontinue further development of RGLS4326, our first generation compound for the treatment of ADPKD, based on discussions with the FDA and data from the second cohort of patients in the Phase 1b trial of RGLS4326. We believe RGLS8429 has a superior pharmacologic profile compared with RGLS4326. In both in vitro and in vivo efficacy studies, RGLS8429 exhibits equal potency for its molecular target (miR-17) as RGLS4326. Further, in recently-completed IND-enabling 13-week toxicity studies, RGLS8429 was well tolerated at dose levels higher than those that resulted in off-target central nervous system effects in the chronic toxicity studies of RGLS4326.

In May 2022, the FDA accepted our IND for RGLS8429 for the treatment of ADPKD. We plan to initiate a Phase 1 single-ascending dose ("SAD") study in healthy volunteers to assess safety, tolerability and PK of RGLS8429. Following the SAD study, we plan to initiate a Phase 1b MAD study in adult patients with ADPKD to assess safety, tolerability and PK of RGLS8429, and to evaluate the dose response of RGLS8429 treatment on ADPKD biomarkers including polycystins, cystic kidney volume (htTKV), and overall kidney function. Top-line data from the healthy volunteer portion of the study are expected in the second half of 2022, and top-line biomarker data for the first cohort of RGLS8429-treated patients with ADPKD are expected in the first half of 2023.

Preclinical Pipeline

A major focus of our preclinical research has historically targeted dysregulated *micro*RNAs implicated in diseases of high unmet medical need where we know we can effectively deliver to the target tissue or organ, such as the liver, kidney and central nervous system ("CNS"). Furthermore, we are investigating the potential for target organ-selective delivery strategies.

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 *micro*RNAs with the goal of understanding how they function and identifying those that might be targets for therapeutic modulation. At any given time we are working on multiple targets, primarily within our therapeutic areas of focus. Our organization is structured to allow the rapid deployment and shifting of resources to focus on the 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 ADPKD program.

Since our inception, we have incurred a total of approximately $394.9 million in research and development expenses through March 31, 2022.

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. 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, 2021. 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 months ended March 31, 2022 and 2021

The following table summarizes our results of operations for the three months ended March 31, 2022 and 2021 (in thousands):

	Three months ended March 31,	
	2022	2021
Revenue under collaborations	$ —	$ —
Research and development expenses	3,679	3,320
General and administrative expenses	2,890	2,478
Interest and other expenses, net	(149)	(215)

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 the three months ended March 31, 2022 and 2021.

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 March 31, 2022	% of total	Three months ended March 31, 2021	% of total	Increase (decrease)	
					$	%
Research and development						
Personnel and internal expenses	$ 1,715	47 %	$ 1,520	46 %	$ 195	13 %
Third-party and outsourced expenses	1,674	45 %	1,288	39 %	386	30 %
Non-cash stock-based compensation	270	7 %	181	5 %	89	49 %
Depreciation	20	1 %	331	10 %	(311)	(94)%
Total research and development expenses	$ 3,679	100 %	$ 3,320	100 %	$ 359	11 %

Research and development expenses were $3.7 million for the three months ended March 31, 2022, compared to $3.3 million for the three months ended March 31, 2021. These amounts reflect the internal and external costs associated with advancing our clinical and preclinical pipeline. The aggregate increase for the three months ended March 31, 2022, as compared to the three months ended March 31, 2021, was primarily attributable to an increase in external research and development expenses, which were primarily driven by an increase in spend on IND-related activities (most notably, third-party drug manufacturing) for our RGLS8429 product candidate.

General and administrative expenses

General and administrative expenses were $2.9 million for the three months ended March 31, 2022, compared to $2.5 million for the three months ended March 31, 2021. The increase for the three months ended March 31, 2022, as compared to the three months ended March 31, 2021, was attributable to a general increase in personnel-related and ongoing general business operating costs.

Interest and other expenses, net

Net interest and other expenses were $0.1 million for the three months ended March 31, 2022, compared to net interest and other expenses of $0.2 million for the three months ended March 31, 2021. These amounts were primarily related to interest charges associated with our outstanding Term Loan.

LIQUIDITY AND CAPITAL RESOURCES

As of March 31, 2022, we had cash and cash equivalents of $53.9 million. We believe that our existing cash and cash equivalents will be sufficient to fund our anticipated and operating capital expenditure requirements into the fourth quarter of 2023. If we are unable to maintain sufficient financial resources, our business, financial condition and results of operations will be materially and adversely affected. We will need to raise additional capital to develop our product candidates and implement our operating plans. There can be no assurance that we will be able to obtain this 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.

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

- the terms and timing of any 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;
- whether and when we achieve any milestones under our collaboration and license agreement with Sanofi; and
- payments under our Term Loan.

To date, we have funded our operations primarily through the sale of equity, and to a lesser extent, through convertible debt, up-front payments, research funding and milestone payments under collaborative arrangements. Since inception, we have primarily devoted our resources to funding research and development, including discovery research, and preclinical and clinical development activities. To fund future operations, we will likely need to raise additional capital. We anticipate that we will seek to fund our operations through public or private equity or debt financings or other sources, such as potential collaboration agreements. We cannot make assurances that anticipated additional financing will be available to us on favorable terms, or at all. Although we have previously been successful in obtaining financing through our equity securities offerings, there can be no assurance that we will be able to do so in the future. As a result of the COVID-19 pandemic and actions taken to slow its spread, as well as the recent military action initiated by Russia against Ukraine (and responses taken by the global community, including sanctions and trade restrictions), the global credit and financial markets have experienced extreme volatility, including in liquidity and credit availability, declines in consumer confidence, declines in economic growth, and uncertainty about economic stability. There can be no assurance that deterioration in credit and financial markets and confidence in economic conditions will not occur. If equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult to obtain, more costly and/or more dilutive.

The following table shows a summary of our cash flows for the three months ended March 31, 2022 and 2021 (in thousands):

	Three months ended March 31,	
	2022	2021
	(unaudited)	
Net cash (used in) provided by:		
Operating activities	$ (6,381)	$ (5,711)
Investing activities	(102)	(53)
Financing activities	2	6,336
Total	$ (6,481)	$ 572

Operating activities

Net cash used in operating activities was $6.4 million for the three months ended March 31, 2022, compared to $5.7 million for the three months ended March 31, 2021. The increase in net cash used in operating activities for the three months

ended March 31, 2022, as compared to the three months ended March 31, 2021, was attributable to a $0.7 million increase in net loss for the three months ended March 31, 2022 as compared to the same period in 2021.

Investing activities

Net cash used in investing activities was $0.1 million for the three months ended March 31, 2022 and 2021.

Financing activities

Net cash provided by financing activities was less than $0.1 million for the three months ended March 31, 2022, compared to $6.3 million for the three months ended March 31, 2021. Net cash provided by financing activities for the three months ended March 31, 2021 was primarily attributable to proceeds from the issuance of our common stock pursuant to our Common Stock Sales Agreement with H.C. Wainwright & Co., LLC.

MATERIAL CASH REQUIREMENTS

As of March 31, 2022, there have been no material changes, outside of the ordinary course of business, in our outstanding contractual obligations from those disclosed under the subheading Material Cash Requirements in our Annual Report.

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 March 31, 2022, 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 March 31, 2022, 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%.

In July 2017, the Chief Executive of the United Kingdom Financial Conduct Authority ("FCA") announced that the FCA intends to phase out the use of LIBOR. On March 5, 2021, the FCA announced that all LIBOR settings will either cease to be provided by any administrator or no longer be representative: (a) immediately after December 31, 2021, in the case of the one week and two-month U.S. dollar settings; and (b) immediately after June 30, 2023, in the case of the remaining U.S. dollar settings. The United States Federal Reserve has also advised banks to cease entering into new contracts that use USD LIBOR as a reference rate. The Alternative Reference Rate Committee has identified the Secured Overnight Financing Rate ("SOFR") as its preferred alternative rate for LIBOR. At this time, we are not able to predict when LIBOR will cease to be available and how markets will respond to SOFR or other alternative reference rates as the transition away from the LIBOR benchmarks is anticipated in coming years. Accordingly, the outcome of these reforms is uncertain and any changes in the methods by which LIBOR is determined or regulatory activity related to LIBOR's phaseout could cause LIBOR to perform differently than in the past or cease to exist. 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.

If a 10% change in interest rates were to have occurred on March 31, 2022, 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 March 31, 2022, 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 March 31, 2022.

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 (*) were not included as a separate risk factor in, or contain changes to the similarly titled risk factors included in, Item 1A of our Annual Report. If any of the following risks actually occurs, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline.

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

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

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

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

- our research methodology or that of 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 *micro*RNAs. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates.

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

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

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

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 were 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 the FDA that included the results from the planned 13-week interim analysis of the then 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, the 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 were outlined in two parts. In order to resume the MAD study, the FDA requested the final reports from the chronic toxicity studies in both mice and non-human primates and satisfactory related analyses to ensure subjects could 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 the FDA lifted the partial clinical hold of the MAD study. We recommenced the MAD study in February 2020. Following the completion of the MAD study in healthy volunteers, we initiated a Phase 1b study in patients with ADPKD to evaluate RGLS4326 for safety, PK, and changes in levels of polycystin 1 and polycystin 2. We then met with the FDA in a Type A meeting and, based on the FDA's likely limitations on dose and duration of therapy and data from the second cohort of patients in the Phase 1b trial of RGLS4326 in ADPKD, we believe that a strategic prioritization of our next-generation compound, RGLS8429, represents a more judicious use of our resources, rather than continuing the development of RGLS4326, our first generation compound. In October 2021, we announced we would discontinue development of RGLS4326 and would instead prioritize RGLS8429, targeting miR-17. We may be incorrect in our expectation that the development work for RGLS4326 will benefit the development of RGLS8429.

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. COVID-19 has impacted, and may continue to impact, our future clinical activities and/or the activities of our partnered programs.

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 ("AEs") or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance.

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 GMP 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, we may have to pursue collaboration agreements for the development and commercialization of our programs and potential product candidates in indications with potentially large commercial markets, 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 smaller 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 to develop our product candidates and implement our operating plans, and if we are unable to do so when needed, we will not be able to complete the development and commercialization of our product candidates.*

As of March 31, 2022, we had approximately $53.9 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 ("Term Loan") with Oxford Finance LLC ("Oxford" or the "Lender"), which we borrowed under a loan and security agreement with Oxford dated June 2016 (as amended, the "Loan Agreement"). 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 *micro*RNA 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 2022, with an extension of the interest only period through and including the

payment to be made in December 2023 should we secure at least $20.0 million in cash proceeds from an equity financing transaction at any point during 2022. Under the terms of the Loan Agreement, we are required to maintain a cash balance of no less than $5.0 million. 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, 2024.

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 FCA, which regulates LIBOR, announced that the FCA intends to phase out the use of LIBOR. On March 5, 2021, the FCA announced that all LIBOR settings will either cease to be provided by any administrator or no longer be representative: (a) immediately after December 31, 2021, in the case of the one week and two-month U.S. dollar settings; and (b) immediately after June 30, 2023, in the case of the remaining U.S. dollar settings. The United States Federal Reserve has also advised banks to cease entering into new contracts that use USD LIBOR as a reference rate. The Alternative Reference Rate Committee, a committee convened by the Federal Reserve that includes major market participants, has identified the SOFR, a new index calculated by short-term repurchase agreements, backed by Treasury securities, as its preferred alternative rate for LIBOR. At this time, we are not able to predict when LIBOR will cease to be available and how markets will respond to SOFR or other alternative reference rates as the transition away from the LIBOR benchmarks is anticipated in coming years. Accordingly, the outcome of these reforms is uncertain and any changes in the methods by which LIBOR is determined or regulatory activity related to LIBOR's phaseout could cause LIBOR to perform differently than in the past or cease to exist. 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. Furthermore, we cannot predict or quantify the time, effort and cost required to transition to the use of new benchmark rates, including with respect to negotiating and implementing any necessary changes to existing contractual agreements, and implementing changes to our systems and processes. 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 *micro*RNA product platform, undertaking basic research around microRNA targets and conducting preclinical

and clinical studies for our initial programs. We have not yet obtained regulatory approval for any product candidates. Consequently, any predictions about our future success or viability, or any evaluation of our business and prospects, may not be accurate.

We have incurred losses in each year since our inception in September 2007. Our net losses were $6.7 million and $6.0 million for the three months ended March 31, 2022 and 2021, respectively. As of March 31, 2022, we had an accumulated deficit of $461.6 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 plan to initiate clinical development of RGLS8429 in the second quarter of 2022. 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 *micro*RNA targets and product candidates; acquire or in-license other products and technologies; continue with clinical development of our product candidates; seek marketing approvals for our product candidates that successfully complete clinical trials; ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval; maintain, expand and protect our intellectual property portfolio; hire additional clinical, regulatory, research and administrative personnel; and create additional infrastructure to support our operations and our product development and planned future commercialization efforts.

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

Our ability to generate revenue and achieve profitability depends on our ability, alone or with 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 *micro*RNAs as therapeutic targets;
- completing our research and preclinical development of product candidates;
- initiating and completing clinical trials for product candidates;
- seeking and obtaining marketing approvals for product candidates that successfully complete clinical trials;
- establishing and maintaining supply and manufacturing relationships with third parties;
- launching and commercializing product candidates for which we obtain marketing approval, with 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 *micro*RNA 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 *micro*RNA product candidates. These collaborations will likely provide us with limited control over the course of development of a *micro*RNA product candidate, especially once a candidate has reached the stage of clinical development. For example, in our 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 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 *micro*RNA therapeutics space, including patents and patent applications related to targeting *micro*RNAs, such as miR-122, for the treatment of disease. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable

patents, or until such patents expire. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

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

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

We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. For example, 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 *micro*RNA product candidates. Assuming sole responsibility for further development will increase our expenditures and may mean we will need to limit the size and scope of one or more of our programs, seek additional funding and/or choose to stop work altogether on one or more of the affected product candidates. This could result in a limited potential to generate future revenue from such *micro*RNA product candidates and our business could be materially and adversely affected. Further, under certain circumstances, we may owe Sanofi royalties on any product candidate that we may successfully commercialize.

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

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

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

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

The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize. We will not achieve our business plan if the acceptance of any of these products is inhibited by price competition or the reluctance of physicians to switch from existing drug products to our products, or if physicians switch to other new drug products or choose to reserve our future products for use in limited circumstances. The

inability to compete with existing or subsequently introduced drug products would have a material adverse impact on our business, financial condition and prospects.

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

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

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

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

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. Even if favorable coverage and reimbursement status is attained for one or more products for which we or our collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

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 March 31, 2022, 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 information security laws and other privacy and information security laws. If we are unable to comply, or have not fully complied or are perceived to 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. The laws and regulations that may affect our ability to operate include, but may not be limited to:

- 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;
- 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 CMS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners), 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; 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; and state and local laws that require the registration of pharmaceutical sales representatives, 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 (or perceived 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 of 2010, 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, 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 remained 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, including the Infrastructure Investment and Jobs Act, will remain in effect through 2031, except for a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic, unless additional Congressional action is taken. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. 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 concurrently released a final rule and guidance in September 2020 implementing a portion of the importation executive order providing pathways for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, the 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 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 the rule has been delayed by the Biden administration until January 1, 2026. 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. As a result of litigation challenging the Most Favored Nation model, on August 10, 2021, CMS published a final rule that rescinded the Most Favored Nation Model interim final rule. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. In addition, Congress is considering drug pricing as part of the budget reconciliation process. 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 AEs. 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.

We are subject to stringent and evolving U.S. and foreign laws, regulations, rules, contractual obligations, policies and other obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation, fines and penalties, a disruption of our business operations; reputational harm, loss of revenue or profits, and other adverse business consequences.*

In the ordinary course of business we process personal data and other sensitive and confidential information, including patient data. Our data processing activities may subject us to numerous data privacy and security obligations, such as various laws and regulations by the federal government and by the U.S. states and foreign jurisdictions in which we conduct our business. Data privacy and security obligations are stringent and changing, with new data privacy and security laws being proposed or enacted. Preparing for and complying with these obligations requires significant resources and may necessitate changes to our information technologies, systems, and practices and to those of any third parties that process personal data on our behalf. The laws and regulations that may affect our ability to operate include, but may not be limited to:

- HIPAA, as amended by HITECH, and their implementing regulations, which imposes certain requirements on certain types of individuals and entities relating to the privacy, security and transmission of certain individually identifiable health information;

- the European Union's General Data Protection Regulation ("GDPR") adopted 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. Under the GDPR, government regulators may impose temporary or definitive bans on data processing, as well as fines of up to 20 million euros or 4% of annual global revenue, whichever is greater. Further, individuals may initiate litigation related to processing of their personal data. 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 of 2018 ("CCPA"), which 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 ("CPRA"), effective January 1, 2023, will expand the CCPA. The CPRA establishes a new California Privacy Protection Agency to implement and enforce the CPRA, which could increase the risk of enforcement. 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; and

- Certain jurisdictions have enacted data localization laws and cross-border personal data transfer laws, which could make it more difficult to transfer information across jurisdictions (such as transferring or receiving personal data that originates in the EU or in other foreign jurisdictions). Existing mechanisms that facilitate cross-border personal data transfers may change or be invalidated. For example, absent appropriate safeguards or other circumstances, the EU GDPR generally restricts the transfer of personal data to countries outside of the European Economic Area ("EEA") that the European Commission does not consider to provide an adequate level of data privacy and security, such as the United States. The European Commission released a set of "Standard Contractual Clauses" ("SCCs") that are designed to be a valid mechanism to facilitate personal data transfers out of the EEA to these jurisdictions. Currently, these SCCs are a valid mechanism to transfer personal data outside of the EEA, but there exists some uncertainty regarding whether the SCCs will remain a valid mechanism. Additionally, the SCCs impose additional compliance burdens, such as conducting transfer impact assessments to determine whether additional security measures are necessary to protect the at-issue personal data. In addition, Switzerland and the UK similarly restrict personal data transfers outside of those jurisdictions to countries such as the United States that do not provide an adequate level of personal data protection, and certain countries outside Europe (e.g. Russia, China, Brazil) have also passed or are considering laws requiring local data residency or otherwise impeding the transfer of personal data across borders, any of which could increase the cost and complexity of doing business. If we cannot implement a valid compliance mechanism for cross-border data transfers, we may face increased exposure to regulatory actions, substantial fines, and injunctions against processing or transferring personal data from Europe or other foreign jurisdictions. The inability to

import personal data to the United States could significantly and negatively impact our business operations, including by limiting our ability to conduct clinical trial activities in Europe and elsewhere; limiting our ability to collaborate with parties that are subject to such cross-border data transfer or localization laws; or requiring us to increase our personal data processing capabilities and infrastructure in foreign jurisdictions at significant expense.

Although we endeavor to comply with all applicable data privacy and security obligations, we may at times fail (or be perceived to have failed) to do so. Moreover, despite our efforts, our personnel or third parties upon whom we rely may fail to comply with such obligations, which could negatively impact our business operations and compliance posture. For example, any failure by a third-party processor to comply with applicable law, regulations, or contractual obligations could result in adverse effects, including inability to or interruption in our ability to operate our business and proceedings against us by governmental entities or others. If we fail, or are perceived to have failed, to address or comply with data privacy and security obligations, we could face significant consequences. These consequences may include, but are not limited to, government enforcement actions (e.g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class-related claims); additional reporting requirements and/or oversight; bans on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials.

Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; interruptions or stoppages in our business operations (including, as relevant, clinical trials); inability to process personal data or to operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or revision or restructuring of our operations.

Cybersecurity risks and the failure to maintain the security, confidentiality, integrity, and availability of our information technology systems or data, 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. We may rely upon third-party service providers and technologies to operate critical business systems to process sensitive information in a variety of contexts, including, without limitation, third-party providers of cloud-based infrastructure, encryption and authentication technology, employee email, content delivery to customers, and other functions. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place.

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 and we cannot guarantee that third parties and infrastructure in our supply chain or our third-party partners' supply chains have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach of or disruption to our information technology systems or the third-party information technology systems that support us and our services. Despite security controls we have in place, such attacks are difficult to avoid. Our remote workforce poses increased risks to our information technology systems and data, as some of our employees work from home, utilizing network connections outside our premises. Future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies.

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 is increasingly demanding and continues to evolve. Maintaining compliance with applicable information security and privacy obligations 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 the 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.

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 other geopolitical events (such as the Russia-initiated military action against Ukraine), 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. For example, the COVID-19 pandemic 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 in the future, 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 trial has been, and may in the future be, affected by the ongoing COVID-19 pandemic. If there is a rise in the number of severe COVID-19 cases that require hospitalization, due to a new variant or otherwise, 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 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. Our common stock did 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. Therefore, we requested and were granted an additional 180-day period during which we must regain compliance with the minimum closing bid price requirement. Pursuant to our definitive proxy statement filed with the SEC on April 27, 2022, we are seeking approval from our stockholders at our 2022 annual meeting of the approval of a reverse split of our common stock. There can be no assurance that the foregoing reverse stock split proposal will be approved, or 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.

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 clinical trial and preclinical study accruals, 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 March 31, 2022, 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 March 31, 2022, an aggregate of 55.7 million shares were issuable upon conversion of shares of our Class A-1, Class A-2, Class A-3 and Class A-4 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"). Currently, we plan to register the increased number of shares available for issuance under the 2019 Plan each year.

In addition, we adopted an Inducement Plan in 2021 (the “Inducement Plan”) pursuant to which our management has the ability to grant stock options exercisable for up to an aggregate of 2,000,000 shares of our common stock to new employees as inducements material to such new employees entering into employment with us. The number of shares which may be granted under the Inducement Plan may be increased in the future by our board of directors. In the event we increase the number of shares which may be granted under the Inducement Plan, or adopt another inducement plan for which no stockholder approval is required under applicable rules and regulations, and grant options pursuant to such plan, our stockholders may experience additional dilution, which could cause our stock price to fall.

We may be 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 and certain of our current and former executive officers 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 Biden administration and Congress have proposed various U.S. federal tax law changes, which if enacted could have a material adverse impact on our business, cash flow, financial condition, or results of operations. In addition, it is uncertain if and to what extent various states will conform to federal tax legislation. Future tax 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, 2021, we had net operating loss ("NOL") carryforwards for U.S. federal and California state tax purposes of $366.8 million and $276.0 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 current law, 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 federal tax laws. 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 or 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, 2021, 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. 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.

General Risk Factors

Unstable market, economic and geopolitical conditions may have serious adverse consequences on our business, financial condition and stock price.*

The global credit and financial markets have experienced extreme volatility and disruptions in the past. These disruptions can result in severely diminished liquidity and credit availability, increases in inflation, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment, higher inflation, or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary

financing in a timely manner and on favorable terms could have a material adverse effect on our operations, growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive an economic downturn or rising inflation, which could directly affect our ability to attain our operating goals on schedule and on budget.

Other international and geo-political events could also have a serious adverse impact on our business. For instance, in February 2022, Russia initiated military action against Ukraine. In response, the United States and certain other countries imposed significant sanctions and trade actions against Russia and could impose further sanctions, trade restrictions, and other retaliatory actions. While we cannot predict the broader consequences, the conflict and retaliatory and counter-retaliatory actions could materially adversely affect global trade, currency exchange rates, inflation, regional economies, and the global economy, which in turn may increase our costs, disrupt our supply chain, impair our ability to raise or access additional capital when needed on acceptable terms, if at all, or otherwise adversely affect our business, financial condition, and results of operations.

Our business could be negatively impacted by environmental, social and corporate governance (ESG) matters or our reporting of such matters.*

There is an increasing focus from certain investors, employees, partners, and other stakeholders concerning ESG matters. We may be, or be perceived to be, not acting responsibly in connection with these matters, which could negatively impact us. For instance, the SEC has recently proposed climate change and ESG reporting requirements, which, if approved, would significantly increase our costs. In addition, we currently do not report our environmental emissions, and lack of reporting or future reporting could result in certain investors from declining to invest in our common stock.

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

None.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

None.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

None.

ITEM 6. EXHIBITS

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on August 3, 2016).
3.2	Certificate of Amendment of Amended and Restated Certificate of Incorporation of 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).
3.3	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).
3.4	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).
3.5	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).
3.6	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).
3.7	Certificate of Designation of Preferences, Rights and Limitations of Class A-4 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 November 30, 2021).
3.8	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).
3.9	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).
3.10	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on June 8, 2016).
4.1	Reference is made to Exhibits 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9 and 3.10.
4.2	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).
4.3	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).
4.4	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).

10.1*	Joseph P. Hagan, Yearly Discretionary Base Salary Increase, effective January 1, 2022 (incorporated by reference to Exhibit 10.14 to the Registrant's Annual Report on Form 10-K (File No. 001-35670), filed with the SEC on March 11, 2022).
10.2*	Christopher Aker, Yearly Discretionary Base Salary Increase, effective January 1, 2022 (incorporated by reference to Exhibit 10.15 to the Registrant's Annual Report on Form 10-K (File No. 001-35670), filed with the SEC on March 11, 2022).
10.3*	Cris Calsada, Yearly Discretionary Base Salary Increase, effective January 1, 2022 (incorporated by reference to Exhibit 10.16 to the Registrant's Annual Report on Form 10-K (File No. 001-35670), filed with the SEC on March 11, 2022).
10.4*	Denis Drygin, Yearly Discretionary Base Salary Increase, effective January 1, 2022 (incorporated by reference to Exhibit 10.17 to the Registrant's Annual Report on Form 10-K (File No. 001-35670), filed with the SEC on March 11, 2022).
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	Inline XBRL Instance Document.
101.SCH	Inline XBRL Taxonomy Extension Schema Document.
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	Inline 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.

* Indicates management contract or compensatory plan.

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

SIGNATURES

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

Regulus Therapeutics Inc.

Date: May 12, 2022 By: /s/ Joseph P. Hagan

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

Date: May 12, 2022 By: /s/ Cris Calsada

Cris Calsada
Chief Financial Officer
(Principal Financial Officer)

Exhibit 31.1

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

I, Joseph P. Hagan, certify that:

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

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

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

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

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

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

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

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

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

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

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

May 12, 2022

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

Exhibit 31.2

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

I, 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.

May 12, 2022

/s/ Cris Calsada
Cris Calsada
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

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

In connection with the quarterly report of Regulus Therapeutics Inc. (the "Company") on Form 10-Q for the quarter ended March 31, 2022 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.

May 12, 2022

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

May 12, 2022

/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.