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

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**FORM 10-K**

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(Mark One)

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

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2023

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

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**Regulus Therapeutics Inc.**

(Exact name of registrant as specified in its charter)

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Delaware

(State or Other Jurisdiction of  
Incorporation or Organization)

26-4738379

(I.R.S. Employer  
Identification No.)

4224 Campus Point Court, Suite 210

San Diego

CA

(Address of Principal Executive Offices)

92121

(Zip Code)

(858) 202-6300

(Registrant's Telephone Number, Including Area Code)  
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

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes  No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes  No

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

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

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Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See 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	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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 the registrant has filed a report on and attestation to its management’s assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. Yes  No

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant’s executive officers during the relevant recovery period pursuant to § 240.10D-1(b).

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes  No

As of June 30, 2023, the last business day of the registrant’s most recently completed second fiscal quarter, the aggregate market value of the registrant’s common stock held by non-affiliates of the registrant was approximately \$27.4 million, based on the closing price of the registrant’s common stock on the Nasdaq Stock Market on June 30, 2023 of \$1.47 per share.

The number of outstanding shares of the registrant’s common stock, par value \$0.001 per share, as of March 15, 2024 was 65,465,251.

### DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant’s definitive proxy statement to be filed with the Securities and Exchange Commission pursuant on Schedule 14A in connection with the registrant’s 2024 Annual Meeting of Stockholders, which will be filed subsequent to the date hereof, are incorporated by reference into Part III of this Form 10-K. Such proxy statement will be filed with the Securities and Exchange Commission no later than April 29, 2024.

**REGULUS THERAPEUTICS INC.**  
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**Signatures**

The Regulus Therapeutics logo is a trademark of Regulus Therapeutics Inc. We use “Regulus Therapeutics” as a trademark in the United States and other countries. We have registered this trademark in the United States, the European Union (“EU”) and Switzerland. All other product and company names are trademarks of their respective companies.

## 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 I, Item 1A of this Annual Report and should be carefully considered, together with other information in this Annual 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 we 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 have never generated any revenue from product sales and may never be profitable.
- 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 will depend upon collaborations for the development and eventual commercialization of certain *microRNA* product candidates. If these collaborations are unsuccessful or are terminated, we may be unable to commercialize certain product candidates and we may be unable to generate revenues from our development programs.
- We rely on limited sources of supply for the drug substance of product candidates and any disruption in the chain of supply may cause a delay in developing and commercializing these product candidates.
- Manufacturing issues may arise that could increase product and regulatory approval costs or delay commercialization.
- We rely on third parties to conduct, supervise and monitor our clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.

- If we are unable to obtain or protect intellectual property rights related to our future products and product candidates, we may not be able to compete effectively in our markets.
- We are subject to stringent and evolving laws, regulations, and rules, contractual obligations, industry standards, policies and other obligations related to data privacy and security. Actual or perceived failure by us or the third-party service providers upon which we rely to comply with such obligations could lead to regulatory investigations or actions; litigation (including class actions); fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse business consequences.
- We are subject to stringent and changing obligations related to data privacy and security. Actual or perceived failure by us or the third-party service providers upon which we rely to comply with such obligations could lead to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse business consequences.
- 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 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

### Forward-Looking Statements

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

- the initiation, cost, timing, progress and results of, and our expected ability to undertake certain activities and accomplish certain goals with respect to our research and development activities, preclinical studies and clinical trials;
- our ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations;
- our plans to research, develop and commercialize our product candidates;
- our ability to attract collaborators with relevant development, regulatory and commercialization expertise;
- future activities to be undertaken by any third parties with whom we collaborate or otherwise contract;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our ability to successfully commercialize, and our expectations regarding future therapeutic and commercial potential with respect to our product candidates;

- the rate and degree of market acceptance of our product candidates;
- our ability to develop sales and marketing capabilities, whether alone or with potential future collaborators;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party suppliers and manufacturers;
- the success of competing therapies that are or may become available;
- the loss of key scientific or management personnel;
- our ability to successfully secure and deploy capital;
- our ability to satisfy our debt obligations;
- the accuracy of our estimates regarding future expenses, future revenues, capital requirements and need for additional financing; and
- the risks and other forward-looking statements described under the caption “Risk Factors” under Part I, Item 1A of this Annual Report on Form 10-K.

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.

## Item 1. Business

We are a clinical-stage biopharmaceutical company focused on discovering and developing first-in-class drugs targeting *microRNAs* to treat diseases with significant unmet medical need. We were formed in 2007 when Alnylam Pharmaceuticals, Inc. (“Alnylam”) and Ionis Pharmaceuticals, Inc. (“Ionis”) contributed intellectual property, know-how and financial and human capital to pursue the development of drugs targeting *microRNAs* pursuant to a license and collaboration agreement. We are currently focused on orphan kidney diseases where *microRNA* genetic drivers are implicated and there are clear unmet medical needs. Our product candidate, RGLS8429, an anti-miR next generation oligonucleotide targeting miR-17 for the treatment of autosomal dominant polycystic kidney disease (“ADPKD”), is in Phase 1b clinical development. In June 2022, the U.S. Food and Drug Administration (“FDA”) granted orphan drug designation to RGLS8429 for the treatment of ADPKD.

In addition to this program, we continue to advance and expand our internal discovery pipeline to identify potential product candidates.

*microRNAs* are naturally occurring ribonucleic acid (“RNA”) molecules that play a critical role in regulating key biological pathways. Scientific research has shown that an imbalance, or dysregulation, of *microRNAs* is directly linked to many diseases. Furthermore, many different infectious pathogens interact and bind to host *microRNA* to survive. To date, over 500 *microRNAs* have been identified in humans, each of which can bind to multiple messenger RNAs that control key aspects of cell biology. Since many diseases are multi-factorial, involving multiple targets and pathways, the ability to modulate multiple pathways by targeting a single *microRNA* provides a new therapeutic approach for treating complex diseases.

RNA plays an essential role in the process used by cells to encode and translate genetic information from deoxyribonucleic acid (“DNA”) to proteins. RNA is comprised of subunits called nucleotides and is synthesized from a DNA template by a process known as transcription. Transcription generates different types of RNA, including messenger RNAs that carry the information for proteins in the sequence of their nucleotides. In contrast, *microRNAs* are RNAs that do not code for proteins but rather are responsible for regulating gene expression by modulating the translation and decay of target messenger RNAs. By interacting with many messenger RNAs, a single *microRNA* can regulate the expression of multiple genes involved in the normal function of a biological pathway. Many pathogens, including viruses, bacteria and parasites, also use host *microRNAs* to regulate the cellular environment for survival. In some instances, the host *microRNAs* are essential for the replication and/or survival of the pathogen.

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

- *microRNAs* play a critical role in regulating biological pathways by controlling the translation of many target genes;

- *microRNA* therapeutics regulate disease pathways which may result in more effective treatment of complex multi-factorial diseases;
- many human pathogens, including viruses, bacteria and parasites, use *microRNAs* (host and pathogen encoded) to enable their replication and suppression of host immune responses; and
- *microRNA* therapeutics may be synergistic with other therapies because of their different mechanism of action.

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

Since our inception through December 31, 2023, we have received \$436.1 million from the sale of our equity and convertible debt securities, \$101.8 million from collaborations, principally from upfront payments, research funding and preclinical and clinical milestones, and \$19.8 million in net proceeds from our Term Loan (as defined below). As of December 31, 2023, we had cash and cash equivalents of \$23.8 million.

## **Our strategy**

The key elements of our strategy are to (i) build a meaningful clinical portfolio by advancing our current clinical program and advancing our preclinical programs into clinical development; (ii) focus our resources on developing drugs for indications that represent significant unmet medical needs and where the development activities and commercial opportunities are appropriate for our size and financial resources; (iii) selectively form strategic collaborations to augment our expertise and accelerate development and commercialization; (iv) develop *microRNA* biomarkers to support our therapeutic product candidates; and (v) maintain our scientific and intellectual leadership in the *microRNA* field.

## **Product Candidate**

### **RGLS8429: For Autosomal Dominant Polycystic Kidney Disease**

ADPKD is among the most common human monogenic disorders and a leading cause of end-stage renal disease. It is caused by mutations in the PKD1 or PKD2 genes, that leads to reduced levels of their encoded-proteins polycystin-1 (PC1) and/or polycystin-2 (PC2) causing formation of multiple fluid filled cysts primarily in the kidneys, and to a lesser extent in the liver and other organs. Typical symptoms include flank pain, hematuria, proteinuria, renal colic, urinary tract infection, hypertension, and intracranial aneurysms. Excessive kidney cyst cell proliferation, a central pathological feature, ultimately leads to end-stage renal disease in approximately 50% of ADPKD patients by age 60. Approximately 160,000 individuals are diagnosed with the disease in the United States alone, with an estimated global prevalence of 4 to 7 million.

RGLS8429 is a novel, next generation oligonucleotide for the treatment of ADPKD designed to inhibit miR-17 and to preferentially target the kidney. Administration of RGLS8429 has shown robust data in preclinical models, where clear improvements in kidney function, size, and other measures of disease severity have been demonstrated along with a superior pharmacologic profile in preclinical studies compared to Regulus' first-generation compound, RGLS4326.

In May 2022, the FDA accepted our IND for RGLS8429 for the treatment of ADPKD. The Phase 1 single-ascending dose ("SAD") study in healthy volunteers to assess safety, tolerability and PK of RGLS8429 has been completed. RGLS8429 was well-tolerated with no serious adverse events reported, and plasma exposure was approximately linear across the four doses tested and is similar to the PK data from the first-generation compound. Enrollment and dosing is ongoing in our Phase 1b double-blind, placebo-controlled multiple-ascending dose and an open label fixed dose study ("MAD") in adult patients with ADPKD to assess safety, tolerability and PK of RGLS8429, and to evaluate the efficacy of RGLS8429 treatment across three different dose levels, including changes in polycystins, cystic kidney volume (htTKV), and overall kidney function. The protocol was amended to include a fourth cohort of subjects who will receive an open label fixed dose of RGLS8429 to compare biomarker and safety data to the weight-based dosing.

The first cohort was dosed at 1 mg/kg of RGLS8429 or placebo every other week for three months. In September 2023, we announced positive top-line data from the first cohort of RGLS8429-treated ADPKD patients. Increases in both PC1 and PC2 biomarkers were observed. Statistically significant increases in mean PC1 levels were observed at Day 85 and Day 86 (n=9) compared to baseline (36%-41%). Numeric increases in PC2 were observed during the treatment period, although not statistically significant. These data are consistent with what was observed with our first-generation compound, RGLS4326,

which showed a significant dose response between 0.3mg/kg and 1mg/kg of RGLS4326. Furthermore, the correlation between PK and urinary PC1 response at 1mg/kg is comparable between RGLS4326 and RGLS8429. RGLS8429 was well tolerated by all nine subjects receiving active drug with no safety findings.

In March 2024, we announced positive topline results from the second cohort of patients in our Phase 1b MAD study of RGLS8429 for the treatment of ADPKD. In the second cohort, 14 patients were randomized 3:1 to receive either 2 mg/kg of RGLS8429 or placebo every other week for three months. RGLS8429 was well tolerated with no safety findings of concern. Greater biological activity of RGLS8429 was observed at 2mg/kg based on urinary polycystin levels compared to 1mg/kg and placebo, which was most evident after 3 months of dosing. Exploratory results of imaging-based biomarkers were encouraging, with 3 patients with the highest increases in PC1 and PC2 having reductions in height-adjusted total kidney volume ("htTKV") >4%, with corresponding reductions in total kidney cyst volume ("TKCV"). These data suggest that targeting miR-17 may have a potential impact on htTKV and TKCV in patients with ADPKD, which the Company will further explore at higher doses in cohorts 3 and 4.

The ongoing Phase 1b study is evaluating RGLS8429 dosing at 3 mg/kg in cohort 3, and will explore a 300 mg fixed dose in cohort 4 that will provide higher exposure in a larger number of patients based on anticipated body weight. Based on the results from the second cohort, we plan to amend the protocol to increase the sample size to up to 30 patients in cohort 4. In addition to PC1 and PC2 and safety, imaging biomarkers will also be evaluated.

In October 2023, we announced that we had reviewed all available safety data and have advanced to the third cohort of patients in the MAD study. In January 2024, we announced that we had completed enrollment of the third cohort of patients, with top-line data anticipated in mid-2024. We also completed the 27-week chronic mouse toxicity study for RGLS8429. No RGLS8429-related toxicity, including CNS effects, was observed at any dose level up to the top dose of 300 mg/kg administered every other week.

We recently held a Type D meeting with the FDA to discuss the accelerated approval pathway. The meeting was constructive and confirmed the potential for an accelerated approval pathway based on a single pivotal Phase 2 study of RGLS8429 for the treatment of ADPKD.

## **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.

## **Our *micro*RNA product platform**

We believe we are the leading company in the field of *micro*RNA therapeutics and are uniquely positioned to leverage oligonucleotide technologies developed by us and our founding companies.

We view the following as providing a competitive advantage for our *micro*RNA product platform:

- a mature platform selectively producing multiple development candidates advancing to the clinic;
- scientific advisors who are pioneers in the *micro*RNA field;
- exclusive access to proven RNA therapeutic technologies through our founding companies, such as GalNac conjugation and the corresponding manufacturing rights licensed to us from Alnylam;
- a comprehensive *micro*RNA intellectual property estate with patents and patent applications covering compositions and therapeutic uses related to *micro*RNA and *micro*RNA drug products, as well as access to numerous patents and patent applications relating to RNA technologies, including patent and patent applications relating to chemical modification of oligonucleotides that are useful for *micro*RNA therapeutics; and
- numerous academic collaborations that help us identify new *micro*RNA targets and support our early stage discovery efforts.

The disciplined approach we take for the discovery and development of *micro*RNA therapeutics is as important as the assets assembled to execute our plans and is based on the following four steps:

### *Step 1 - Evaluation of *micro*RNA therapeutic opportunities*

The initiation of our *micro*RNA discovery and development efforts is based on rigorous scientific and business criteria, including:

- existence of significant scientific evidence to support the role of a specific *microRNA* in a disease;
- availability of predictive preclinical disease models to test our *microRNA* development candidates;
- ability to effectively deliver anti-miRs or miR mimics to the diseased cells or tissues; and
- existence of a significant unmet medical need and commercial opportunity.

*Step 2 - Identification of microRNA targets*

We identify *microRNA* targets through bioinformatic analysis of public and proprietary *microRNA* expression profiling data sets from samples of diseased human tissues. The analysis of such data sets can immediately highlight a potential role for specific *microRNAs* in the disease being studied. Further investigation of animal models that are predictive of human diseases in which those same *microRNAs* are also dysregulated provides additional data to support a new program. We have applied this strategy successfully in our existing programs and we believe that this approach will continue to help us identify clinically relevant *microRNA* targets.

*Step 3 - Validation of microRNA targets*

Our validation strategy is based on two distinct steps. First, using genetic tools, we determine whether up-regulation, or overproduction, of the *microRNA* in healthy animals can create the specific disease state and inhibition of the *microRNA* can lead to a therapeutic benefit. Second, using animal models predictive of human diseases, we determine whether pharmacological modulation of the up-regulated *microRNA* target with our anti-miRs can also lead to a therapeutic benefit. This validation process enables us to prioritize *microRNA* targets that appear to be key drivers of disease and not simply correlating markers.

*Step 4 - Optimization of microRNA development candidates*

We have developed a proprietary process that allows us to rapidly generate an optimized development candidate. Unlike traditional drug classes, such as small molecules, in which thousands of compounds must be screened to identify prospective leads, the fact that anti-miRs are complementary to (thereby pairing with) the target *microRNA* allows for a more efficient rational design process. The optimization process incorporates our extensive knowledge base around oligonucleotide chemistry and anti-miR design to efficiently synthesize a starting pool of rationally designed anti-miRs to be evaluated in a series of proven assays and models. We are able to enhance our anti-miRs for distribution in certain tissues, such as the liver and kidney, where the specific *microRNA* target is causing disease.

**Our development candidates**

We are developing single-stranded oligonucleotides, which are chemically synthesized chains of nucleotides that are complementary to (thereby pairing with) the target *microRNA*. We incorporate proprietary chemical modifications to enhance drug properties such as potency, stability and tissue distribution. We refer to these chemically modified oligonucleotides as anti-miRs. Each anti-miR is designed to bind with and inhibit a specific *microRNA* target that is up-regulated in a cell and that is involved in the disease state. In binding to the *microRNA*, anti-miRs correct the dysregulation and return diseased cells to their healthy state.

We have identified and validated several *microRNA* targets across a number of disease categories and are working independently to optimize anti-miR development candidates. We intend to pursue a balanced approach between product candidates that we develop ourselves and those that we develop with partners. We intend to focus our own resources on proprietary product opportunities in therapeutic areas where development and commercialization activities are appropriate for our size and financial resources. In therapeutic areas where costs are more significant, development timelines are longer or markets are too large for our capabilities, we may seek to secure partners with requisite expertise and resources.

## **PIPELINE**



patent term extension is related to the length of time the drug is under regulatory review. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. When possible, depending upon the length of clinical trials and other factors involved in the filing of a new drug application ("NDA") we expect to apply for patent term extensions for patents covering our *microRNA* product candidates and their methods of use.

In some circumstances we rely, and may continue to rely, on trade secrets to protect our technology. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

## **Our Technology Licenses**

### ***Alnylam/Ionis***

In September 2007, we entered into a license and collaboration agreement with Alnylam and Ionis, which we subsequently amended, restated and superseded in January 2009, and further amended in June 2010, October 2011 and August 2013. Under the agreement, we acquired an exclusive, royalty-bearing, worldwide license, with rights to sublicense, to patent rights owned or licensed by Alnylam and Ionis to develop, manufacture and commercialize products covered by the licensed patent rights for use in *microRNA* compounds which are *microRNA* antagonists and *microRNA* therapeutics containing these compounds. In addition, we have certain rights to miR-mimics. Under the agreement, we granted to both Alnylam and Ionis a license to practice our intellectual property developed by us to the extent that it is useful specifically to Alnylam's RNAi programs or Ionis' single-stranded oligonucleotide programs, but not including *microRNA* compounds or therapeutics that are the subject of our exclusive licenses from Alnylam and Ionis.

We are required to use commercially reasonable efforts to develop and commercialize licensed products under the agreement. We are required to notify Alnylam and Ionis when a program reaches development stage (defined as initiation of good laboratory practices ("GLP") toxicology studies) and whether or not we intend to pursue the program. Under the agreement, both Alnylam and Ionis have an option to assume the development and commercialization of product candidates in a program that we do not pursue. If neither Alnylam nor Ionis exercises this option, we are required to use our best efforts to finalize a term sheet with a third party with respect to such program. In the event we are unable to complete a transaction with a third party, both Alnylam and Ionis have a second opt-in option.

If an election is made by either Alnylam or Ionis (but not both) to opt-in, such party will pay us a one-time fixed payment, the amount of which will depend on whether the first or the second opt-in option was exercised, with a higher amount due if the first opt-in option was exercised. Clinical and regulatory milestones are also payable to us in the event the opt-in election is exercised. Such milestones total \$64.0 million in the aggregate if the election is made during the first opt-in period or \$15.7 million in the aggregate if the election is made at the second opt-in period. Tiered royalties are payable to us as a percentage of net sales on all products commercialized by the opt-in party. These royalties range from the low to middle single digits depending upon the volume of sales. The opt-in party is also entitled to sublicense the development program to a third party. In such a case, we are also entitled to receive a percentage of the sublicense income received by the opt-in party. The percentage payable depends upon the point at which the opt-in party sublicenses the program and ranges from the low end of the 10 to 20% range to the high end of the 40 to 50% range. The opt-in party is only required to pay the higher of the clinical and regulatory milestones or the sublicense income received in any calendar quarter. The opt-in party is also responsible for all third-party payments due under other agreements as a result of the development. In the event both Alnylam and Ionis elect to opt-in during either opt-in period, the parties have agreed to work together to amend the development plan to continue development of the project, including funding of such project and assignment of roles and responsibilities.

In the event we or any future collaboration partner continues with the development of a program, each of Alnylam and Ionis are entitled to royalties as a percentage of net sales. For products that we independently commercialize, these royalties will be in the low single digits. For products commercialized by a third-party collaborator, the royalties will be either the same percentage of net sales as described above or, if the sublicense does not provide a specified level of royalties to us or upon our election, a percentage of the sublicense income received by us from the strategic collaboration partner and a modified royalty. The modified royalty would be based upon the lower of the single digit percentage discussed above or one third of the royalty received by us after payments made by us to third parties for development, manufacture and commercialization activities under other agreements. In addition, if we sublicense rights to a collaborator, we will be required to pay to each of Alnylam and Ionis a percentage of our sublicense income in the mid-single digits. We are also responsible for payments due to third parties under

other agreements as a result of our development activities, including payments owed by Alnylam and/or Ionis under their agreements.

Under the October 2011 amendment, Alnylam and Ionis granted us the right to research *micro*RNA mimics under the licensed intellectual property of Alnylam and Ionis. In the event we develop a miR-mimic, we must first obtain approval from Alnylam and/or Ionis, as applicable, and such approval is subject to the consent of applicable third parties, if any. No additional consideration will be owed by us to Alnylam or Ionis for granting approval. We have the right to sublicense our research rights. We granted to both Alnylam and Ionis a fully paid up, worldwide and exclusive license to any intellectual property developed by us and useful to their research programs and which are not *micro*RNA antagonists or approved miR-mimics.

In August 2013, we entered into an amendment to the Amended and Restated License and Collaboration Agreement with Ionis and Alnylam dated January 1, 2009, as amended in June 2010 and October 2011 (as amended, the “Amendment”). Under the terms of the Amendment, the parties agreed to our use of certain Alnylam-controlled intellectual property concerning the use and manufacture of GalNAc conjugates (“GalNAc Process Technology”) on a non-exclusive basis. We will generally not be permitted to sublicense or otherwise transfer the GalNAc Process Technology and other Alnylam licensed intellectual property rights relating to GalNAc conjugate technology without the prior written consent of Alnylam, subject to certain limited exceptions for sublicenses to third party collaboration partners. There were no financial terms related to this Amendment. Amounts included in our operating expenses as a result of costs incurred from services provided under the Agreement or out-of-pocket expenses were zero for the years ended December 31, 2023 and 2022.

In February 2015, we entered into a letter agreement with Alnylam pursuant to which we and Alnylam agreed to the financial terms for certain technology acquired by Alnylam within the licensed patent rights under our Amended and Restated License and Collaboration Agreement (the “Additional Patent Rights”) with Alnylam and Ionis. In addition to any royalties payable by us to Alnylam pursuant to the terms of the Amended and Restated License and Collaboration Agreement, we agreed to pay Alnylam an additional low single-digit royalty on net sales of certain products utilizing the Additional Patent Rights, with the exact royalty percentage payable being dependent on the total amount of net sales during the calendar year. We also agreed to pay Alnylam milestone payments on certain products utilizing the additional patent rights upon the achievement of certain regulatory milestone events. There was no activity under this agreement for the year ended December 31, 2023.

The agreement expires on the earlier of the cessation of development of the potential royalty-bearing products prior to the commercial sale of any such products anywhere in the world or following the first commercial sale of such products, the expiration of royalty obligations determined on a country-by-country and product-by-product basis.

## **Manufacturing**

We contract with third parties to manufacture our product candidates and intend to continue to do so in the future. We do not own or operate, nor do we expect to own or operate, facilities for product manufacturing, storage and distribution, or testing. We have personnel with extensive technical, manufacturing, analytical and quality experience and strong project management discipline to oversee contract manufacturing and testing activities, and to compile manufacturing and quality information for our regulatory submissions.

Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements, which govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. Our systems and contractors are required to be in compliance with these regulations, and this is assessed regularly through monitoring of performance and a formal audit program.

## **Competition**

The biotechnology and pharmaceutical industries are characterized by intense and rapidly changing competition to develop new technologies and proprietary products. While we believe that our intellectual property estate and scientific expertise in the *micro*RNA field provide us with competitive advantages, we face potential competition from many different sources, including larger and better-funded pharmaceutical companies. Any products that we may commercialize will have to compete with existing and new therapies that may become available in the future. In addition, we expect that for each disease category for which we develop and apply our *micro*RNA therapeutics, there are other biotechnology companies that will compete against us by applying marketed products and development programs using technology other than *micro*RNA therapeutics. The key competitive factors that will affect the success of any of our development candidates, if commercialized, are likely to be their efficacy, safety, convenience, price and the availability of reimbursement from government and other third-party payors relative to such competing technologies. Our commercial opportunity could be reduced or eliminated if our competitors have products which are better in one or more of these categories.

Currently, there is one drug approved and several therapies in preclinical and clinical development for the treatment of patients with ADPKD. In 2018, Otsuka Pharmaceutical Co., Ltd. received approval by the FDA to market Jynarque® to slow the kidney function decline in adults at risk of rapidly-progressing ADPKD. Additional therapies reported to be in clinical development include XRx-008 (reformulation of oxypurinol) from Xortx Therapeutics Inc., which completed a bridging pharmacokinetics study and plans to initiate a Phase 3 study in patients with ADPKD and hyperuricemia, tesevatinib from Kadmon Corporation, which completed a Phase 2 study in 2022, and which was recently acquired by Sanofi, and Johnson & Johnson reported the oral small molecule JNJ-0237 had completed a Phase 1 single-ascending dose safety study in healthy volunteers. Vertex recently announced completion of IND-enabling studies of VX-407 for the treatment of a subset of patients with ADPKD with a specific mutation, and anticipate initiating a Phase 1 clinical trial in healthy volunteers in 2024.

Many of our competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, pre-clinical testing, clinical trials, manufacturing, and marketing than we do. Future collaborations and mergers and acquisitions may result in further resource concentration among a smaller number of competitors.

Our commercial potential could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market or make our development more complicated.

### **Government Regulation and Product Approval**

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we are developing. Any product candidate that we develop must be approved by the FDA before it may be legally marketed in the United States and by the appropriate foreign regulatory agency before it may be legally marketed in foreign countries.

#### *U.S. drug development process*

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act ("FDCA") and implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial civil or criminal sanctions. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, debarment, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests, animal studies and formulation studies according to GLP or other applicable regulations;
- submission to the FDA of an application for an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to the FDA's regulations commonly referred to as current good clinical practices ("GCPs") to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA for a new drug;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with the FDA's current good manufacturing practice standards ("cGMP") to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA.

The lengthy process of seeking required approvals and the continuing need for compliance with applicable statutes and regulations require the expenditure of substantial resources and approvals are inherently uncertain.

Before testing any compounds with potential therapeutic value in humans, the drug candidate enters the preclinical study stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the drug candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLP. The sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA imposes a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such trial.

Clinical trials involve the administration of the drug candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's direct control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety. Each protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted in accordance with the FDA's regulations comprising the good clinical practices requirements. Further, each clinical trial must be reviewed and approved by an independent institutional review board ("IRB") at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and provide oversight for the clinical trial until completed.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing may be conducted in patients.
- Phase 2. The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Annual progress reports detailing the results of the clinical trials must be submitted to the FDA and written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events ("AEs") or any finding from tests in laboratory animals that suggests a significant risk for human subjects. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Concurrently with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

*U.S. review and approval processes*

The results of product development, nonclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

In addition, under the Pediatric Research Equity Act ("PREA"), an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

The FDA reviews all NDAs submitted to determine if they are substantially complete before it accepts them for filing. If the FDA determines that an NDA is incomplete or is found to be non-navigable, the filing may be refused and must be re-submitted for consideration. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act ("PDUFA"), the FDA has 10 months from acceptance of filing in which to complete its initial review of a standard NDA and respond to the applicant, and six months from acceptance of filing for a priority NDA. The FDA does not always meet its PDUFA goal dates. The review process and the PDUFA goal date may be extended by three months or longer if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the submission before the PDUFA goal date.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. The FDA may refer applications for novel drug or biological products or drug or biological products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the drug approval process, the FDA also will determine whether a risk evaluation and mitigation strategy ("REMS") is necessary to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA without a REMS, if required.

Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect the sponsor and one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study requirements. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable it will outline the deficiencies in the submission and often will request additional testing or information.

The NDA review and approval process is lengthy and difficult and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. The FDA will issue a complete response letter if the agency decides not to approve the NDA. The complete response letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either submit new information, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require post marketing clinical trials, sometimes referred to as Phase 4 clinical trials, which are designed to further assess a drug safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

### *Orphan drug designation*

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting an NDA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug or biological product as defined by the FDA or if our drug candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. Orphan drug status has similar but not identical benefits in the EU.

### *Expedited development and review programs*

The FDA has several regulatory pathways for expedited development and/or review of products intended to treat serious conditions. These pathways are Fast Track designation, Breakthrough Therapy designation, accelerated approval, and priority review. These programs do not change the standards for approval but may expedite the development or approval process. Products may meet the standards for consideration under one or more of these pathways.

**Fast Track Designation:** The Fast Track program is intended to expedite development or facilitate the process for reviewing new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. In addition to more frequent meetings with the FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval, the FDA will consider for review sections of the NDA on a rolling basis as sections are completed, based on an agreed schedule, and the sponsor pays any required user fees upon submission of the first section of the NDA.

**Breakthrough Therapy Designation:** Breakthrough Therapy designation is a process designed to expedite the development and review of drugs that are intended to treat a serious condition and where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on or more clinically significant endpoint(s). A drug that receives Breakthrough Therapy designation from the FDA is eligible for all Fast Track designation features, plus intensive guidance on an efficient drug development program beginning as early as Phase 1 and organizational commitment involving senior managers.

**Accelerated Approval:** Products may be eligible for accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Accelerated Approval can be granted with restrictions to the marketing and distribution of the product, and the FDA can withdraw marketing approval if the required post-marketing studies fail to show a clinical benefit or if the Sponsor fails to conduct required post-marketing studies.

**Priority Review:** Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a

disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review.

#### *Post-approval requirements*

Any drug products for which we or any future strategic collaboration partners receive FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Failure to comply with FDA requirements can have negative consequences, including adverse publicity, enforcement letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of any products that we may commercialize. Any future strategic collaboration partners may also utilize third parties for some or all of a product we develop with such strategic collaboration partner. Manufacturers of our products are required to comply with applicable FDA manufacturing requirements contained in the FDA's cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA, including withdrawal of the product from the market. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

The FDA also may require post-marketing testing, known as Phase 4 testing, risk evaluation and mitigation strategies and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product.

#### *U.S. patent term restoration and marketing exclusivity*

Depending upon the timing, duration and specifics of the FDA approval of the use of our drug candidates, some of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may intend to apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain applications of other companies seeking to reference another company's NDA. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application ("ANDA") or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were

conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

#### *U.S. Foreign Corrupt Practices Act*

The U.S. Foreign Corrupt Practices Act ("FCPA") prohibits certain individuals and entities, including us, from promising, paying, offering to pay, or authorizing the payment of anything of value to any foreign government official, directly or indirectly, to obtain or retain business or an improper advantage. The U.S. Department of Justice and the U.S. Securities and Exchange Commission ("SEC") have increased their enforcement efforts with respect to the FCPA. Violations of the FCPA may result in large civil and criminal penalties and could result in an adverse effect on a company's reputation, operations, and financial condition. A company may also face collateral consequences such as debarment and the loss of export privileges.

#### *Federal and state healthcare laws and regulations*

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal healthcare laws and regulations have been applied to restrict certain business practices in the biopharmaceutical industry in recent years. These laws include the following:

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or in return for purchasing, leasing, ordering, or arranging for the purchase, lease, or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, formulary managers and other individuals and entities on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exceptions and safe harbors are drawn narrowly, and our practices may not in all cases meet all of the criteria for statutory exceptions or regulatory safe harbor protection. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. The reach of the Anti-Kickback Statute was also broadened by the Patient Protection and Affordable Health Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the "ACA"), which, among other things, amended the intent requirement of the federal Anti-Kickback Statute. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below) or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Federal false claims laws, including the federal civil False Claims Act, prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government. Pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-reimbursable, uses.

Many states also have statutes or regulations similar to the federal Anti-Kickback Statute and civil False Claims Act, which state laws apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Also, the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or

covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

Because of the breadth of these laws, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Such a challenge could have a material adverse effect on our business, financial condition and results of operations.

In addition, we may be subject to data privacy and security regulations by both the U.S. government and the states and other jurisdictions in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH") and their implementing regulations, impose on "covered entities," including certain healthcare providers, healthcare clearinghouses, and health plans, as well as their respective "business associates" that receive or obtain protected health information in connection with providing a service on behalf of a covered entity, relating to the privacy, security, and transmission of personally identifiable health information ("PHI"), as well as their covered subcontractors. HITECH increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, the increase in U.S. state laws (e.g., the California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act of 2020 ("CPRA") (collectively, "CCPA")) governing privacy and security of personal information, including health information, many of which differ from each other in significant ways and may not have the same effect, complicates compliance efforts.

Further, the federal Physician Payments Sunshine Act, enacted as part of the ACA, requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services ("CMS") information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals. Applicable manufacturers and applicable group purchasing organizations must also report annually to CMS ownership and investment interests held by the physicians and their immediate family members.

Other state laws and regulations may also apply, such as those that: require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; require the reporting of information related to drug pricing and/or require the report of information related to transfers of value to healthcare providers or marketing expenditures. Certain state and local laws also require the registration of pharmaceutical sales representatives.

If our operations are found to be in violation of any of the federal and state healthcare laws or regulations described above or any other governmental regulations that apply to us, we may be subject to penalties, including criminal and significant civil monetary penalties, damages, fines, imprisonment, exclusion from government programs, disgorgement, 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 the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our product candidates are ultimately sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

### *Health Reform*

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the United States federal and state levels that seek to reduce healthcare costs.

For example, the ACA includes measures to significantly change the way healthcare is financed by both governmental and private insurers. The ACA, among other things, increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs; required collection of rebates for drugs paid by Medicaid managed care organizations; required manufacturers to participate in a coverage gap discount program, under which they must agree to offer point-of-sale discounts (increased to 70 percent, effective as of January 1, 2019) off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs, implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected expanded the types of entities eligible for the 340B drug discount program; expanded eligibility criteria for Medicaid programs; created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct

comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

There have been judicial and Congressional challenges to certain aspects of the ACA, as well as efforts by the Trump administration to repeal or replace certain aspects of the ACA. For example, President Trump signed several Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Congress has also considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, bills affecting the implementation of certain taxes under the ACA have been signed into law. Legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act ("Tax Act"), includes a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. On June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Further, there have been a number of health reform measures by the Biden administration that have impacted the ACA. For example, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 ("IRA"), into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and by creating a new manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how such challenges and healthcare reform measures of the Biden administration will impact the ACA.

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 until 2032 unless additional Congressional action is taken. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. 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, 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, the Department of Health and Human Services ("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, the IRA, among other things, (i) directs the Secretary of HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare Part B and Medicare Part D, and subjects drug manufacturers to civil monetary penalties and a potential excise tax by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law, and (ii) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions take effect progressively starting in fiscal year 2023. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations, although the Medicare drug price negotiation program is currently subject to legal challenges. In response to the Biden administration's October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. Further, on December 7, 2023, the Biden administration announced an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework. 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. For example, on January 5, 2024, the FDA approved Florida's Section 804 Importation Program (SIP) proposal to import certain drugs from Canada for specific state healthcare programs. It is unclear how this program will be implemented, including which drugs will be chosen, and whether it will be subject to legal challenges in the United States or Canada. Other states have also submitted SIP proposals that are pending review by the FDA. Any such approved importation plans, when implemented, may result in lower drug prices for products covered by those programs.

#### *Pharmaceutical Coverage, Pricing, and Reimbursement*

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we or our collaborators receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage and establish adequate reimbursement levels for such drug products.

In the United States, third-party payors include federal and state healthcare programs, government authorities, private managed care providers, private health insurers and other organizations. Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical drug products and medical services, in addition to questioning their safety and efficacy. Moreover, the process for determining whether a third-party payor will provide coverage for a drug product may be separate from the process for setting the price of a drug product or for establishing the reimbursement rate that such a payor will pay for the drug product. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. 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.

#### *Europe / rest of world government regulation*

In addition to regulations in the United States, we and any future strategic collaboration partners are subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products.

Whether or not we or any future collaborators obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the EU, for example, a clinical trial application ("CTA") must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCPs and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational drug or biological product under EU regulatory systems, we or a strategic collaboration partner must submit a marketing authorization application. The application in the United States is similar to that required in the EU, with the exception of, among other things, country-specific document requirements.

For other countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCPs and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we or any future strategic collaboration partners fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

## Employees

As of December 31, 2023, we had 30 employees, all of which were full-time employees. Of these employees, 22 employees are engaged in research and development activities and 8 employees are engaged in finance, legal, business development, human resources, facilities and general management. As of such date, all our employees were based in the United States. All of our employees are at will employees, which means that each employee can terminate their employment relationship with us and we can terminate our relationship with an employee at any time. We have no collective bargaining agreements with our employees and we have not experienced any work stoppages. We also engage temporary consultants and contractors.

We believe a stable, capable and talented workforce is instrumental to our success. As such, we seek to attract and retain our employees through a competitive base and merit bonus compensation program, high-quality benefits, various health and wellness initiatives and team-building activities. In addition to our overall compensation package, we continually assess our internal talent for further development, training and education in alignment with our organizational needs. Our human resources strategy is managed at the highest levels of our organization, including oversight from the Compensation Committee of the Board of Directors. We believe Regulus is an attractive workplace; however, we are in a highly competitive field and geographic region for life science talent and will continue to face significant competition for talent. We are an Equal Opportunity and Affirmative Action employer in compliance with the requirements of the state and Federal laws.

Our Code of Business Conduct and Ethics serves as a critical tool to help us recognize and report unethical conduct, while preserving and nurturing our core values of respect, business and scientific integrity, and excellence throughout our operations. We provide training on our Code of Business Conduct and Ethics for our all of our employees annually.

## Corporate Information

We were originally formed as a limited liability company under the name Regulus Therapeutics LLC in the State of Delaware in September 2007. In January 2009, we converted Regulus Therapeutics LLC to a Delaware corporation and changed our name to Regulus Therapeutics Inc. Our principal executive offices are located in San Diego, California and our telephone number is (858) 202-6300.

We maintain a website at [www.regulusrx.com](http://www.regulusrx.com), to which we regularly post copies of our press releases as well as additional information about us. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended ("Exchange Act") are available free of charge on our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The SEC maintains an internet site that contains our public filings with the SEC and other information regarding the Company, at [www.sec.gov](http://www.sec.gov). The contents of these websites are not incorporated into this Annual Report. Further, our references to the URLs for these websites are intended to be inactive textual reference only.

The Regulus Therapeutics logo is a trademark of Regulus Therapeutics Inc. We use "Regulus Therapeutics" as a trademark in the United States and other countries. We have registered this trademark in the United States, the EU and Switzerland. This Annual Report contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this Annual Report, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

## Item 1A. Risk Factors

*You should consider carefully the following risk factors, together with all of the other information included in this Annual Report. Each of these risk factors, either alone or taken together, could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our common stock. There may be additional risks that we do not presently know of or that we currently believe are immaterial which could also impair our business and financial position.*

## RISKS RELATED TO THE DISCOVERY AND DEVELOPMENT OF PRODUCT CANDIDATES

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

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

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

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

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

- our research methodology or that of any future 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
- any future collaboration partners may change their development profiles for potential product candidates or abandon a therapeutic area.

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

**Preclinical and clinical studies of our product candidates may not be successful. If we are unable to generate successful results from our preclinical and clinical studies of our product candidates, or experience significant delays in doing so, our business may be materially harmed.**

We have invested a significant portion of our efforts and financial resources in the identification and development of product candidates that target *microRNAs*. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates.

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

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

If we do not, or any future collaboration partners do not, achieve one or more of these factors in a timely manner or at all, we or any future collaboration partners could experience significant delays or an inability to successfully complete the development of, or commercialize, our product candidates, which would materially harm our business. For example, in July 2022, we received notification from Sanofi of its decision to terminate the HERA trial of RG-012 for failure to meet Sanofi's pre-defined futility criteria. In January 2023, we received notification from Sanofi of its decision to terminate the collaboration in its entirety. Preclinical studies, even if successful, may not lead to successful clinical trials and results in early-stage clinical trials may not be predictive of successful results in later stage clinical trials.

**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 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. In October 2021, we announced we would discontinue development of RGLS4326 and would instead prioritize RGLS8429, targeting miR-17.

Additionally, in July 2022, we received notification from Sanofi of its decision to terminate the HERA trial of RG-012 for failure to meet Sanofi's pre-defined futility criteria. In January 2023, we received notification from Sanofi of its decision to terminate the collaboration in its entirety.

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.

If we or any future collaboration partners are required to conduct additional clinical trials or other testing of any product candidates beyond those that are originally 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 any future collaboration partners may:

- be delayed in obtaining marketing approval for our 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 future collaboration partner may develop under an agreement with us, our or any future 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 any future 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 a future collaboration partner fails 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 *microRNA* targets, drug compounds and processes for our development pipeline through acquisitions and in-licenses.**

Presently, we have rights to the intellectual property, through licenses from third parties and under patents that we own, to modulate only a subset of the known *microRNA* targets. Because our programs may involve a range of *microRNA* targets, including targets that require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, our product candidates may require specific 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 December 31, 2023, we had approximately \$23.8 million of cash and cash equivalents and we had \$2.7 million of outstanding debt obligations (which includes \$1.4 million of outstanding principal and \$1.3 million of final payment and loan amendment fees) under our Term Loan with the Lender, which we borrowed under the Loan Agreement. In March 2024, we raised approximately \$94.0 million in net proceeds from the sale of our common stock and non-voting convertible preferred stock in a private placement financing, after deducting placement agent and financial advisor fees and other financing expenses. We believe our existing resources will be sufficient to fund our planned operations and expenditures for at least the next 12 months. We will need to raise additional capital in the future to fund our operations, 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.

For the foreseeable future, we expect to rely primarily on equity and/or debt financings to fund our operations. If there is volatility in the equity markets, it may create additional challenges to raising sufficient additional capital through an equity or equity-linked financing. 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. 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 were comprised of interest only through and including the payment made in December 2022. We resumed making principal payments in January 2023. Under the terms of the Loan Agreement, we are required to maintain a cash balance of no less than \$5.0 million. We are in compliance with all Loan Agreement covenants as of the date of the filing of this Form 10-K.

Amounts outstanding under the Term Loan mature on May 1, 2024.

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, including as a result of a "material adverse change," 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. The definition of "material adverse change" is broad and includes a material impairment in the value of the collateral securing the Term Loan, a material adverse change in our business, operations, or condition (financial or otherwise), and a material impairment of the prospect of repayment of any portion of the Term Loan. Moreover, the determination by the lender as to whether a "material adverse change" has occurred is not within our control. In certain circumstances, procedures by the lenders could result in a loss by us of all of our equipment and inventory, which are included in the collateral granted to the lenders. If any indebtedness under the Loan Agreement were to be accelerated, there can be no assurance that our assets would be sufficient to repay in full that indebtedness. In addition, upon any distribution of assets pursuant to any liquidation, insolvency, dissolution, reorganization or similar proceeding, the holders of secured indebtedness will be entitled to receive payment in full from the proceeds of the collateral securing our secured indebtedness before the holders of other indebtedness or our common stock will be entitled to receive any distribution with respect thereto.

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

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

Since inception, our operations have been primarily limited to acquiring and in-licensing intellectual property rights, developing our *microRNA* product platform, undertaking basic research around microRNA targets and conducting preclinical and clinical studies for our initial programs. We have not yet obtained regulatory approval for any product candidates. Consequently, any predictions about our future success or viability, or any evaluation of our business and prospects, may not be accurate.

We have incurred losses in each year since our inception in September 2007. Our net loss was \$30.0 million and \$28.3 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of \$513.2 million.

We have devoted most of our financial resources to research and development, including our preclinical and clinical development activities. To date, we have financed our operations primarily through the sale of equity securities and convertible debt, through our Term Loan and from revenue received from our former collaboration partners.

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 initiated clinical development of RGLS8429 in the second

quarter of 2022. Even if we or a future 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 any future collaboration agreements; seek to identify additional *microRNA* targets and product candidates; acquire or in-license other products and technologies; continue with clinical development of our product candidates; seek marketing approvals for our product candidates that successfully complete clinical trials; ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval; maintain, expand and protect our intellectual property portfolio; hire additional clinical, regulatory, research and administrative personnel; and create additional infrastructure to support our operations and our product development and planned future commercialization efforts.

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

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

- identifying and validating new *microRNAs* as therapeutic targets;
- completing our research and preclinical development of product candidates;
- initiating and completing clinical trials for product candidates;
- seeking and obtaining marketing approvals for product candidates that successfully complete clinical trials;
- establishing and maintaining supply and manufacturing relationships with third parties;
- launching and commercializing product candidates for which we obtain marketing approval, with a collaboration partner or, if launched independently, successfully establishing a sales force, marketing and distribution infrastructure;
- maintaining, protecting and expanding our intellectual property portfolio; and
- attracting, hiring and retaining qualified personnel.

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

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

**RISKS RELATED TO OUR RELIANCE ON THIRD PARTIES**

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

We may depend upon third party collaboration partners for financial and scientific resources for the clinical development and commercialization of certain of our *microRNA* product candidates. These collaborations will likely provide us with limited control over the course of development of a *microRNA* product candidate, especially once a candidate has reached the stage of clinical development.

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 the collaboration;
- 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.

**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 any future 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; 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 any future 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.

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 rely, and any future collaboration partners may 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 have limited influence over their actual performance. We control only certain aspects of our CROs' activities. Nevertheless, we 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, any future 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 any future 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 licensors or any future collaboration partners. 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 are pursuing development candidates. 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**

**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. 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.

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.

**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 December 31, 2023, we had 30 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 restructuring activities that we may undertake in the future may result in write-offs or other restructuring charges. There can be no assurance that any restructuring activities that we 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 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;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH") and its implementing regulations, which also imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy and security of individually identifiable health information of covered entities subject to the rule, such as health plans, healthcare clearinghouses and certain healthcare providers, as well as their business associates, independent contractors of a covered entity that perform certain services involving the use or disclosure of individually identifiable health information on their behalf and their subcontractors that use, disclose, access, or otherwise process individually identifiable health information;
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services ("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. The Tax Act, includes a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. On June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Further, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 ("IRA") into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and through a newly established manufacturer discount program. 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 and the Consolidated Appropriations Act of 2023, will remain in effect until 2032, unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and federal and state legislative activity designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. For example, 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, the U.S. Department of Health and Human Services ("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. In addition, the IRA, among other things, (1) directs HHS to negotiate the price of certain single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented. These provisions take effect progressively starting in fiscal year 2023. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations, although the Medicare drug price negotiation program is currently subject to legal challenges. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. In response to the Biden administration's October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. Further, on December 7, 2023, the Biden administration announced an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework. 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. For example, on January 5, 2024, the FDA approved Florida's Section 804 Importation Program (SIP) proposal to import certain drugs from Canada for specific state healthcare programs. It is unclear how this program will be implemented, including which drugs will be chosen, and whether it will be subject to legal challenges in the United States or Canada. Other states have also submitted SIP proposals that are pending review by the FDA. Any such approved importation plans, when implemented, may result in lower drug prices for products covered by those programs.

We expect that healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product. Any

reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors.

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

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

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. Certain oligonucleotide therapeutics have shown injection site reactions and pro-inflammatory effects and may also lead to impairment of kidney or liver function. There is a risk that our current and future product candidates may induce similar 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 (including class actions), 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 collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, processing) personal data and other sensitive and confidential information, including proprietary and confidential business data, trade secrets, intellectual property, data we may collect about trial participants in connection with clinical trials, sensitive third-party data, and employee data (collectively, sensitive data). Our data processing activities may subject us to numerous data privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to data privacy and security. 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. For more information regarding risks associated with HIPAA, please refer to the section above that discusses risks associated with federal and state healthcare laws and regulations;

- the European Union’s General Data Protection Regulation (“EU GDPR”) and the United Kingdom GDPR (“UK GDPR”), which contain provisions specifically directed at the processing of health information and, more broadly, imposes significant and complex compliance burdens on processing personal data. Under the EU and UK GDPR, government regulators may impose temporary or definitive bans on data processing, as well as fines of up to 20 million Euros (17.5 million British Pounds under the UK GDPR) or 4% of annual global revenue, whichever is greater; or private litigation related to the processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests. We anticipate that over time we may expand our business operations to include additional operations in the European Economic Area (“EEA”) and the United Kingdom (“UK”), including potentially conducting preclinical and clinical trials and, with such expansion, we would be subject to increased governmental regulation in the European countries in which we might operate, including but not limited to the EU and UK GDPR;
- the California Consumer Privacy Act of 2018 as amended by the California Privacy Rights Act of 2020 (“CPRA”), (collectively, “CCPA”), which requires covered companies to provide new disclosures to California residents, including consumers, business representatives, and employees, and requires businesses to provide specific disclosures in privacy notices and honor requests of California residents to exercise certain privacy rights. The CCPA provides for administrative fines of up to \$7,500 per violation and allows private litigants affected by certain data breaches to recover significant statutory damages. 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, should we become subject to the CCPA in the future. In addition, the CPRA expanded the CCPA’s requirements, including by adding a new right for individuals to correct their personal information and establishing a new regulatory agency to implement and enforce the law. Other states, such as Virginia and Colorado, have also passed comprehensive privacy laws, and similar laws are being considered in several other states, as well as at the federal and local levels. While these states, like the CCPA, also exempt some data processed in the context of clinical trials, these developments further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties upon whom we rely;
- new laws governing the privacy of consumer health data, including Washington’s My Health My Data Act (“MHMD”), broadly define consumer health data, place restrictions on processing consumer health data (including imposing stringent requirements for consents), provide consumers certain rights with respect to their health data, and create a private right of action to allow individuals to sue for violations of the law. Other states are considering and may adopt similar laws; and
- data breach notification laws, personal data privacy laws, consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), and other similar laws (e.g., wiretapping laws) enacted by federal, state, and local governments in the United States.

As our company grows, we may transfer personal data from Europe and other jurisdictions to the United States or other countries. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the EEA and the UK have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it believes are inadequate. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross-border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the United States in compliance with law, such as the EEA and UK’s standard contractual clauses, the UK’s International Data Transfer Agreement / Addendum, and the EU-U.S. Data Privacy Framework and the UK extension thereto (which allows for transfers for relevant U.S.-based organizations who self-certify compliance and participate in the Framework), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the EEA, the UK, or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including 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. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activist groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers out of Europe for allegedly violating the EU GDPR’s cross-border data transfer limitations.

In addition to data privacy and security laws, we are bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. We also publish policies, marketing materials, and other statements regarding data privacy and security and if these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators, or other adverse consequences.

Obligations related to data privacy and security (and individuals' data privacy expectations) are quickly changing, becoming increasingly stringent, and creating uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources, which may necessitate changes to our services, information technologies, systems, and practices and to those of any third parties that process personal data on our behalf. In addition, these obligations may require us to change our business model.

We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. 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 or the third parties upon which we rely fail, or are perceived to have failed, to address or comply with applicable data privacy and security obligations, we could face significant consequences, including but not limited to: government enforcement actions (e.g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class-action claims); additional reporting requirements and/or oversight; bans on processing personal data (including clinical trial 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 regulatory investigations or actions, a material interruption to our operations, including clinical trials, damage to our reputation and/or subject us to costs, fines and penalties or lawsuits.**

In the ordinary course of business, we and the third parties upon which we rely process sensitive data, and, as a result, we and the third parties upon which we rely face a variety of evolving threats, including but not limited to ransomware attacks, which could cause security incidents. Cyberattacks, malicious internet-based activity, online and offline fraud, and other similar activities threaten the confidentiality, integrity, and availability of our sensitive data and information technology systems, and those of the third parties upon which we rely. Such threats are prevalent and continue to rise, are increasingly difficult to detect, and come from a variety of sources, including traditional computer "hackers," threat actors, "hacktivists," organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation-state and nation-state supported actors now engage in attacks (including advanced persistent threat intrusions) for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties upon which we rely may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our services.

We and third parties we rely on may also be the subject of a variety of evolving threats, including but not limited to social-engineering attacks (including through deep fakes, which may be increasingly more difficult to identify as fake, and phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks, credential stuffing, credential harvesting, personnel misconduct or error, ransomware attacks, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, earthquakes, fires, floods, attacks enhanced or facilitated by AI, and other similar threats. Threat actors may continue to develop and use more sophisticated tools and techniques (including AI) that are specifically designed to circumvent security controls, evade detection, and obfuscate forensic evidence, making it more difficult for us to identify, investigate and recover from incidents. In particular, severe ransomware attacks are becoming increasingly prevalent 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. Extortion payments may alleviate the negative impact of a ransomware

attack, but we may be unwilling or unable to make such payments (including, for example, if applicable laws or regulations prohibit such payments).

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 rely upon third-party service providers and technologies to operate critical business systems and process sensitive data 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. If our third-party service providers experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. 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 employees utilize network connections, computers, and devices outside our premises. Additionally, 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. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program.

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. We take steps to detect and remediate vulnerabilities, but we may not be able to detect and remediate all vulnerabilities because the threats and techniques used to exploit the vulnerability change frequently and are often sophisticated in nature. Therefore, such vulnerabilities could be exploited but may not be detected until after a security incident has occurred. These vulnerabilities pose material risks to our business. 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 take steps to detect and remediate vulnerabilities, but 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. Unremediated high risk or critical vulnerabilities pose material risks to our business. Further, we may experience delays in deploying remedial measures designed to address any such identified vulnerabilities.

If we, or a third party upon whom we rely, experience a security incident, or are perceived to have experienced a security incident, we may experience adverse consequences, such as: government enforcement actions that could include investigations, fines, penalties, audits and inspections; additional reporting requirements and/or oversight; restrictions on processing of sensitive data (which could impact our clinical trials or training of our algorithm); litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations (including availability of data); financial loss; and other similar harms. Security incidents and attendant consequences may cause customers to stop using our services, deter new customers from using our services, and negatively impact our ability to grow and operate our business.

Furthermore, our contracts may not contain limitations of liability, and even where they do, 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.

In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position.

**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 war between Russia and Ukraine, the state of war between Israel and Hamas and the risk of a larger conflict arising from either war), and public health issues 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 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 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. Such a health pandemic or epidemic may pose 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. These and similar disruptions in our operations could negatively impact our business, operating results and financial condition.

In addition, our clinical trial may in the future be affected by health pandemics or epidemics. A future pandemic could negatively affect site initiation and create delays in patient enrollment if a pandemic were to 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 an infectious disease, could be delayed or disrupted, which would adversely impact our clinical trial 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. Moreover, the SEC has recently proposed, and may continue to propose, certain mandated ESG reporting requirements, such as the SEC's proposed rules designed to enhance and standardize climate-related disclosures, which, if approved, would significantly increase our compliance and reporting costs and may also result in disclosures that certain investors or other stakeholders deem to negatively impact our reputation and/or that harm our stock price. In addition, we currently do not report our environmental emissions and, absent a legal requirement to do so, we currently do not plan to report our environmental emission. Lack of reporting could result in certain investors declining to invest in our common stock.

**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 existing collaborations or enter into new collaborations;
- failure of any future 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 any future 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;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, any future 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. 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 to regain compliance with the minimum closing bid price requirement. At our 2022 annual meeting of stockholders, our stockholders approved a reverse split of our common stock. In June 2022, we completed a 1-for-10 reverse split of our outstanding common stock and we subsequently regained compliance with the minimum bid price requirement. There can be no assurance that we will be able to 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 December 31, 2023, warrants to exercise an aggregate of 6.2 million shares of our common stock were outstanding at a weighted-average exercise price per share of \$7.76. In addition, as of December 31, 2023, an aggregate of 19.7 million shares were issuable upon conversion of shares of our Class A-1, Class A-2, Class A-3, Class A-4 and Class A-5 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, pursuant to our 2022 Employee Stock Purchase Plan ("ESPP"), our management is authorized to grant stock options and other equity-based awards to our employees. The number of shares available for future grant will automatically increase by a number equal to the lesser of 1% of the total number of shares of Common Stock outstanding on December 31st of the preceding calendar year and 50,000 shares of Common Stock (which number has been adjusted to give effect to the 1-for-10 reverse stock split of the Common Stock, effected on June 28, 2022), subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under the 2019 Plan and the 2022 ESPP 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 1,030,000 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 any lawsuits will be covered or that coverage, if any, will be sufficient. In addition, any future litigation could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, the Tax Act, the Coronavirus Aid, Relief, and Economic Security Act, and the IRA enacted many significant changes to U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to such legislation may affect us, and certain aspects of such legislation could be repealed or modified in future legislation. 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, 2023, we had net operating loss ("NOL") carryforwards for U.S. federal and California state tax purposes of \$389.5 million and \$146.3 million, respectively. A portion of the federal and California state NOL carryforwards will begin to expire, if not utilized, in 2030 and 2033, 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 of \$126.1 million will carry forward indefinitely, but the deductibility of such federal NOLs 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 by "5-percent shareholders" 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, 2023, 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 NOL 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 in the past have experienced, and may in the future experience, extreme volatility and disruptions. 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 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, high inflation, high interest rates, bank failures, 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, exposure to a bank failure, 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 and the two countries are now at war. 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. Additionally, in October 2023, Hamas initiated an attack against Israel, provoking a state of war and the risk of a larger conflict. While we cannot predict the broader consequences, these conflicts 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.

#### **Item 1B. Unresolved Staff Comments**

Not applicable.

#### **Item 1C. Cybersecurity**

##### **Risk management and strategy**

We have implemented and maintain various information security processes designed to identify, assess and manage material risks from cybersecurity threats to our critical computer networks, third party hosted services, communications systems, hardware and software, and our critical data, including intellectual property, confidential information that is proprietary, strategic or competitive in nature (“Information Systems and Data”).

Our legal department, a management committee (composed of our Senior Vice President and General Counsel, our Chief Financial Officer, and our Vice President, Finance and Controller) and a third-party service provider (collectively, the “Cybersecurity Risk Management Team”) help identify, assess and manage the Company’s cybersecurity threats and risks. Our

Cybersecurity Risk Management Team identify and assess risks from cybersecurity threats by monitoring and evaluating our threat environment using various methods including, for example, manual tools, automated tools, conducting scans of the threat environment, evaluating our and our industry's risk profile, evaluating threats reported to us, conducting internal audits, conducting third party threat assessments, and conducting vulnerability assessments to identify vulnerabilities.

Depending on the environment, we implement and maintain various technical, physical, and organizational measures, processes, standards and policies designed to manage and mitigate material risks from cybersecurity threats to our Information Systems and Data, including, for example, a cybersecurity incident response plan, incident detection and response, a disaster recovery and business continuity plan, risk assessments, implementation of security standards, encryption of data, network security controls, data segregation, access controls, physical security, asset management, tracking and disposal, systems monitoring, employee training, penetration testing, cybersecurity insurance, and systems monitoring.

Our assessment and management of material risks from cybersecurity threats are integrated into the Company's overall risk management processes. For example, (1) cybersecurity risk is addressed as a component of the Company's enterprise risk management program; (2) the Cybersecurity Risk Management Team works with management to prioritize our risk management processes and mitigate cybersecurity threats that are more likely to lead to a material impact to our business; (3) our Senior Vice President and General Counsel, our Chief Financial Officer and our Vice President, Finance and Controller evaluate material risks from cybersecurity threats against our overall business objectives and reports to the audit committee of the board of directors, which evaluates our overall enterprise risk.

We use third-party service providers to assist us from time to time to identify, assess, and manage material risks from cybersecurity threats, including for example professional services firms, including legal counsel and cybersecurity consultants.

We use third-party service providers to perform a variety of functions throughout our business, such as hosting companies, contract research organizations, contract manufacturing organizations and supply chain resources. We have a vendor management program to manage cybersecurity risks associated with our use of these providers. The program includes risk assessment for each vendor, system and organization controls reporting, and audits. Depending on the nature of the services provided, the sensitivity of the Information Systems and Data at issue, and the identity of the provider, our vendor management process may involve different levels of assessment designed to help identify cybersecurity risks associated with a provider, as well as contractual obligations related to cybersecurity on the provider.

For a description of the risks from cybersecurity threats that may materially affect the Company and how they may do so, see our risk factors under Part 1. Item 1A. Risk Factors in this Annual Report on Form 10-K, including "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 regulatory investigations or actions, a material interruption to our operations, including clinical trials, damage to our reputation and/or subject us to costs, fines and penalties or lawsuits."

## **Governance**

Our board of directors addresses the Company's cybersecurity risk management as part of its general oversight function. The board of directors' audit committee is responsible for overseeing Company's cybersecurity risk management processes, including oversight and mitigation of risks from cybersecurity threats.

Our cybersecurity risk assessment and management processes are implemented and maintained by certain Company management, including our Senior Vice President and General Counsel, Chief Financial Officer, Vice President, Finance and Controller. Our Senior Vice President and General Counsel has expertise as a Life Sciences executive, has had a key role in information technology and cybersecurity oversight for several years and has completed several cybersecurity trainings. Our Chief Financial Officer has several years of expertise performing audits as a public accountant, including audits over information technology controls, and has also completed several cybersecurity trainings. Our Vice President, Finance and Controller has expertise playing a key role with information technology general controls and control testing for the Company for many years, and has several years of expertise leading and performing audits as a public accountant, including audits over information technology controls. He has also completed several cybersecurity trainings.

These positions are responsible for hiring appropriate personnel, helping to integrate cybersecurity risk considerations into the Company's overall risk management strategy, and communicating key priorities to relevant personnel. They are also responsible for preparing and approving budgets, helping prepare for cybersecurity incidents, approving cybersecurity processes, and reviewing security assessments and other security-related reports.

Our cybersecurity incident response processes are designed to escalate certain cybersecurity incidents to members of management depending on the circumstances, including the Senior Vice President and General Counsel, Chief Financial Officer and Chief Executive Officer. The Cybersecurity Risk Management Team and others work with the Company's incident response team to help the Company mitigate and remediate cybersecurity incidents of which they are notified. In addition, the

Company's incident response processes include reporting to the audit committee of the board of directors for certain cybersecurity incidents.

The audit committee receives periodic reports from the Senior Vice President and General Counsel, Chief Financial Officer, Vice President, Finance and Controller concerning the Company's significant cybersecurity threats and risk and the processes the Company has implemented to address them. The audit committee also receives and has access to various reports, summaries or presentations related to cybersecurity threats, risk and mitigation.

**Item 2. Properties**

On February 11, 2021, we entered into a lease agreement (the "Campus Point Lease") with 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. We are using the Campus Point Premises as our principal executive offices and as a laboratory for research and development, manufacturing and other related uses. The term of the Campus Point Lease ("Campus Point Initial Term") is 60 months, ending April 30, 2026.

We believe that our existing facilities are adequate for our current and future needs.

**Item 3. Legal Proceedings**

We currently are not a party to, and none of our property is the subject of, any material legal proceedings within the meaning of Item 103 of Regulation S-K promulgated under the Securities Act of 1933, as amended.

**Item 4. Mine Safety Disclosures**

Not applicable.

**PART II**

**Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities**

**Market Information**

Our common stock is listed on The Nasdaq Capital Market under the symbol "RGLS."

**Holders of Record**

As of March 15, 2024, there were 36 holders of record of our common stock.

**Dividend Policy**

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant. In addition, our ability to pay cash dividends is currently prohibited by the terms of the Loan Agreement with Oxford.

**Item 6. [Reserved]**

**Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations**

*You should read the following discussion and analysis and our financial statements and related notes included elsewhere in this Annual Report. The following discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those expressed or implied in any forward-looking statements as a result of various factors, including those set forth under the caption "Risk Factors," under Part I, Item 1A of this Annual Report.*

## OVERVIEW

We are a clinical-stage biopharmaceutical company focused on discovering and developing first-in-class drugs targeting *microRNAs* to treat diseases with significant unmet medical need. We were formed in 2007 when Alnylam Pharmaceuticals, Inc. ("Alnylam") and Ionis Pharmaceuticals, Inc. ("Ionis") contributed significant intellectual property, know-how and financial and human capital to pursue the development of drugs targeting *microRNAs* pursuant to a license and collaboration agreement. We are currently focused on orphan kidney diseases where *microRNA* genetic drivers are implicated and there are clear unmet medical needs. Our product candidate, RGLS8429, an anti-miR next generation oligonucleotide targeting miR-17 for the treatment of autosomal dominant polycystic kidney disease ("ADPKD"), is in Phase 1b clinical development. In June 2022, the U.S. Food and Drug Administration ("FDA") granted orphan drug designation to RGLS8429 for the treatment of ADPKD.

In addition to this program, we continue to advance and expand our internal discovery pipeline to identify potential product candidates.

Since our inception through December 31, 2023, we have relied primarily on the sale of our equity to fund company operations. Through December 31, 2023, we have received \$436.1 million in net proceeds from the sale of our equity and convertible debt securities, \$101.8 million from 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 December 31, 2023, we had cash and cash equivalents of approximately \$23.8 million. In March 2024, we sold and issued approximately \$100.0 million of our common stock and non-voting convertible preferred stock in a private placement financing. After deducting placement agent and financial advisor fees and other financing expenses, net proceeds to us from the financing were approximately \$94.0 million.

## FINANCIAL OPERATIONS OVERVIEW

### 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;
- external research and development expenses incurred under arrangements with third parties, such as contract research organizations, or CROs, contract manufacturing organizations, or CMOs, other clinical trial related vendors, consultants and our scientific advisors;
- license fees; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, amortization of leasehold improvements and equipment, and laboratory and other supplies.

We expense research and development costs as incurred. We account for nonrefundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received. Certain of the raw materials used in the process of manufacturing drug product are capitalized upon their acquisition and expensed upon usage, as we have determined these materials have alternative future use.

To date, we have conducted research on many different *microRNAs* with the goal of understanding how they function and identifying those that might be targets for therapeutic modulation. At any given time we are working on multiple targets, primarily within our therapeutic areas of focus. Our organization is structured to allow the rapid deployment and shifting of resources to focus on the most promising targets based on our ongoing research. As a result, in the early phase of our development programs, our research and development costs are not tied to any specific target. However, we are currently spending the vast majority of our research and development resources on our ADPKD program.

Since our inception, we have incurred a total of approximately \$430.7 million in research and development expenses through December 31, 2023.

The process of conducting clinical trials and preclinical studies necessary to obtain regulatory approval is costly and time consuming. We, or any future 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, regulatory developments, 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, intellectual property, legal services and director and officer insurance programs and investor relations costs, 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 ESTIMATES**

The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities, and the revenues and expenses incurred during the reported periods. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

### **Clinical Trial and Preclinical Study Accruals**

We make estimates of our accrued expenses for clinical trial and preclinical study activities based on the facts and circumstances known to us at the 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. 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 by reviewing contracts, vendor agreements and purchase orders, and through discussions with internal clinical and preclinical personnel and external service providers as to the progress or stage of completion of services and the agreed-upon fee to be paid for such services. 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.

Our significant accounting policies are described within "The Business, Basis of Presentation and Summary of Significant Accounting Policies" of our financial statements included elsewhere in this Annual Report.

### **Recent Accounting Pronouncements**

For a discussion of recently issued accounting pronouncements, refer to the section titled "Recent Accounting Pronouncements" within "The Business, Basis of Presentation and Summary of Significant Accounting Policies" of our financial statements included elsewhere in this Annual Report.

## **RESULTS OF OPERATIONS**

### **Comparison of the years ended December 31, 2023 and 2022**

The following table summarizes our results of operations for the years ended December 31, 2023 and 2022 (in thousands):

	Years ended December 31,	
	2023	2022
Research and development expenses	21,152	18,410
General and administrative expenses	9,957	9,829
Interest and other income (expenses), net	1,073	(83)

#### *Research and development expenses*

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

	2023	% of total	2022	% of total	Increase (decrease)	
					\$	%
<b>Research and development</b>						
<i>Personnel and internal expenses</i>	\$ 8,814	41 %	\$ 7,411	40 %	\$ 1,403	19 %
<i>Third-party and outsourced expenses</i>	11,164	53 %	10,309	56 %	855	8 %
<b>Non-cash stock-based compensation</b>	1,029	5 %	594	3 %	435	73 %
<b>Depreciation</b>	145	1 %	96	1 %	49	51 %
<b>Total research and development expenses</b>	<u>\$ 21,152</u>	<u>100 %</u>	<u>\$ 18,410</u>	<u>100 %</u>	<u>\$ 2,742</u>	<u>15 %</u>

Research and development expenses increased by \$2.7 million for the year ended December 31, 2023, compared to the year ended December 31, 2022. The aggregate increase was primarily driven by costs associated with the progression of our clinical trials and preclinical studies, most notably the advancement of RGLS8429 for the treatment of ADPKD in the Phase 1b study.

#### *General and administrative expenses*

General and administrative expenses were \$10.0 million for the year ended December 31, 2023, compared to \$9.8 million for the year ended December 31, 2022. These amounts reflect personnel-related and ongoing general business operating costs.

#### *Interest and other (expenses) income, net*

Net interest and other income was \$1.1 million for the year ended December 31, 2023, compared to net interest and other expense of \$0.1 million for the year ended December 31, 2022. These amounts primarily consisted of interest earned on our cash equivalents and short-term investments, offset by interest charges associated with our outstanding Term Loan.

## **LIQUIDITY AND CAPITAL RESOURCES**

As of December 31, 2023, we had cash and cash equivalents of approximately \$23.8 million. In March 2024, we raised approximately \$94.0 million in net proceeds from the sale of our common stock and non-voting convertible preferred stock in a private placement financing.

If we are unable to maintain sufficient financial resources, our business, financial condition and results of operations will be materially and adversely affected. To fund our operations in both the short term and long term (beyond 12 months), we may seek to raise additional capital through equity and/or debt financings. There can be no assurance that we will be able to obtain the needed financing on acceptable terms or at all. Additionally, equity or debt financings may have a dilutive effect on the holdings of our existing stockholders. We believe our existing resources will fund our planned operations and expenditures for at least the next 12 months.

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

- 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 terms and timing of any strategic collaboration, licensing and other arrangements that we may establish;

- the outcome, timing and cost of regulatory approvals;
- delays that may be caused by changing regulatory requirements;
- the cost and timing of hiring new employees to support our continued growth;
- the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;
- the costs and timing of procuring clinical and commercial supplies of our product candidates;
- the costs and timing of establishing sales, marketing and distribution capabilities, and the pricing and reimbursement for any products for which we may receive regulatory approval;
- the extent to which we acquire or invest in businesses, products or technologies; and
- payments under our Term Loan.

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. There can be no assurance that deterioration in credit and financial markets and confidence in economic conditions will not occur in the future. 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 years ended December 31, 2023 and 2022 (in thousands):

	Years ended December 31,	
	2023	2022
Net cash (used in) provided by:		
Operating activities	\$ (26,768)	\$ (25,526)
Investing activities	14,491	(15,120)
Financing activities	11,816	4,491
Total	<u>\$ (461)</u>	<u>\$ (36,155)</u>

#### *Operating activities*

Net cash used in operating activities increased to \$26.8 million for the year ended December 31, 2023, compared to \$25.5 million for the year ended December 31, 2022. The increase in net cash used in operating activities was primarily attributable to net losses of \$30.0 million and \$28.3 million for the years ended December 31, 2023 and 2022, respectively.

#### *Investing activities*

Net cash provided by investing activities was \$14.5 million for the year ended December 31, 2023, compared to net cash used in investing activities of \$15.1 million for the year ended December 31, 2022. The net cash provided by investing activities for the year ended December 31, 2023 was primarily attributable to sales of \$20.0 million of short-term investments, partially offset by purchases of \$4.9 million of short-term investments. The net cash used in investing activities for the year ended December 31, 2022 was primarily attributable to purchases of \$32.8 million of short-term investments, partially offset by sales of \$18.0 million of short-term investments. The short-term investments purchased and sold in the years ended December 31, 2023 and 2022 were all U.S. Treasury securities.

#### *Financing activities*

Net cash provided by financing activities was \$11.8 million for the year ended December 31, 2023, compared to net cash provided by financing activities of \$4.5 million for the year ended December 31, 2022. Net cash provided by financing activities for the year ended December 31, 2023 was primarily attributable to total net proceeds received from our private placement of common stock and non-voting convertible preferred stock in April 2023 of \$14.0 million and net proceeds from shares sold and settled under the ATM Offering of \$1.1 million, partially offset by \$3.3 million of principal payments made on our Term Loan. Net cash provided by financing activities for the year ended December 31, 2022 was primarily attributable to

net proceeds from the issuance of our common stock sold in our ATM Offering pursuant to our Common Stock Sales Agreement (the "Stock Sales Agreement") with H.C. Wainwright & Co., LLC ("HCW") of \$4.5 million.

## MATERIAL CASH REQUIREMENTS

The following table summarizes our contractual obligations and commitments as of December 31, 2023 that will affect our future liquidity (in thousands):

	<b>Payments due by period</b>				
	<b>Total</b>	<b>&lt;1 year</b>	<b>1-3 years</b>	<b>3-5 years</b>	<b>&gt;5 years</b>
Facility operating lease obligations	\$ 1,901	\$ 800	\$ 1,101	\$ —	\$ —
Term Loan obligations	2,713	2,713	—	—	—
<b>Total</b>	<b>\$ 4,614</b>	<b>\$ 3,513</b>	<b>\$ 1,101</b>	<b>\$ —</b>	<b>\$ —</b>

We enter into contracts in the normal course of business with clinical sites for the conduct of clinical trials, CROs for clinical research studies, professional consultants for expert advice and other vendors for clinical supply manufacturing or other services. These contracts generally provide for termination on notice, and therefore are cancellable contracts and not included in the table of contractual obligations and commitments.

In addition to the contractual obligations above, we also expect to have future material cash requirements related to our preclinical and clinical programs and personnel expenses.

### Item 7A. 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 cash equivalents 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 and U.S. Treasury securities. The primary objectives of our investment activities are to ensure liquidity and to preserve principal while at the same time maximizing the interest 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 December 31, 2023, 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 December 31, 2023 the outstanding principal amount of the Term Loan was \$1.4 million.

The Term Loan bears interest at a floating per annum rate equal to the greater of (a) 8.95% and (b) the sum of (i) the 1-month CME Term Secured Overnight Financing Rate (SOFR) reference rate on the last business day of the month that immediately precedes the month in which the interest will accrue, (ii) 0.10% and (iii) 8.51%.

If a 10% change in interest rates were to have occurred on December 31, 2023, this change would not have had a material effect on our interest expense as of that date.

**Item 8. Financial Statements and Supplementary Data**

**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

To the Stockholders and the Board of Directors of Regulus Therapeutics Inc.

**Opinion on the Financial Statements**

We have audited the accompanying balance sheets of Regulus Therapeutics Inc. (the Company) as of December 31, 2023 and 2022, the related statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2023, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2023, in conformity with U.S. generally accepted accounting principles.

**Basis for Opinion**

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

**Critical Audit Matter**

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

***Accrued research and development expenses***

*Description of the Matter* During 2023, the Company incurred \$21.2 million for research and development expense and, as of December 31, 2023, the Company accrued \$921 thousand for research and development expenses. As described in Note 1 to the financial statements, the Company records accruals for estimated costs of clinical trial and preclinical studies that include services provided by clinical trial investigational sites and contract research organizations and other clinical trial-related activities. Clinical trial and preclinical study activities performed by third parties are accrued and expensed based upon estimates of the time period over which these services will be performed and the level of effort to be expended in each period.

Auditing management’s accounting for clinical trial and preclinical study accruals is especially challenging as evaluating the progress or stage of completion of the activities under the Company’s research and development agreements is dependent on information from third-party service providers and internal clinical personnel, which includes both subjective and qualitative aspects.

*How We Addressed the Matter in Our Audit* To test the Company’s accrued research and development expenses for clinical trial and preclinical study activities, among other procedures, we obtained supporting evidence of the research and development activities performed for significant clinical trials and preclinical studies. We inspected summaries of project status meetings with accounting personnel and clinical and preclinical project managers to corroborate the status of significant research and development activities. To verify the appropriate measurement of clinical trial and preclinical study accruals, we compared the costs for a sample of transactions against the related invoices and contracts and confirmed amounts incurred to-date with third-party service providers. We also examined a sample of subsequent payments to evaluate the completeness of the clinical trial and preclinical study accruals.

/s/ Ernst & Young LLP

We have served as the Company’s auditor since 2007.

San Diego, California

March 21, 2024

## (In thousands, except share and per share data)

	December 31,	
	2023	2022
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 23,767	\$ 24,228
Short-term investments	—	14,932
Restricted cash	62	62
Prepaid materials, net	3,010	3,010
Prepaid expenses and other current assets	1,340	1,847
Total current assets	28,179	44,079
Property and equipment, net	1,061	536
Intangibles, net	33	62
Right of use asset	1,477	2,039
Total assets	<u>\$ 30,750</u>	<u>\$ 46,716</u>
<b>Liabilities and stockholders' equity</b>		
Current liabilities:		
Accounts payable	\$ 204	\$ 175
Accrued liabilities	691	961
Accrued research and development expenses	921	1,252
Accrued compensation	2,979	2,205
Current portion of term loan, less debt issuance costs	1,334	4,511
Other current liabilities	2,379	2,553
Total current liabilities	8,508	11,657
Operating lease liability, less current portion	1,055	1,768
Total liabilities	9,563	13,425
Commitments and Contingencies (Note 8)		
Stockholders' equity (deficit):		
Class A-1 convertible preferred stock, \$0.001 par value; 256,700 shares authorized, issued and outstanding at December 31, 2023 and 2022	—	—
Class A-2 convertible preferred stock, \$0.001 par value; 1,330,832 shares authorized, issued and outstanding at December 31, 2023 and 2022	1	1
Class A-3 convertible preferred stock, \$0.001 par value; 258,707 shares authorized, issued and outstanding at December 31, 2023 and 2022	—	—
Class A-4 convertible preferred stock, \$0.001 par value; 3,725,720 shares authorized, issued and outstanding at December 31, 2023 and 2022	4	4
Class A-5 convertible preferred stock, \$0.001 par value, 140,827 and 0 shares authorized, issued and outstanding at December 31, 2023 and 2022, respectively	—	—
Common stock, \$0.001 par value; 300,000,000 shares authorized at December 31, 2023 and 2022; 20,222,672 and 16,840,261 shares issued and outstanding at December 31, 2023 and 2022, respectively	20	17
Additional paid-in capital	534,375	516,457
Accumulated other comprehensive loss	—	(12)
Accumulated deficit	(513,213)	(483,176)
Total stockholders' equity	<u>21,187</u>	<u>33,291</u>
Total liabilities and stockholders' equity	<u>\$ 30,750</u>	<u>\$ 46,716</u>

See accompanying notes to these financial statements.

**Regulus Therapeutics Inc.**  
**STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS**  
(In thousands, except share and per share data)

	2023	2022
Operating expenses:		
Research and development	21,152	18,410
General and administrative	9,957	9,829
Total operating expenses	31,109	28,239
Loss from operations	(31,109)	(28,239)
Other income (expense):		
Interest and other income	1,677	605
Interest and other expense	(604)	(688)
Loss before income taxes	(30,036)	(28,322)
Income tax expense	(1)	(1)
Net loss	<u>\$ (30,037)</u>	<u>\$ (28,323)</u>
Other comprehensive loss:		
Unrealized loss on short-term investments, net	—	(12)
Comprehensive loss	<u>\$ (30,037)</u>	<u>\$ (28,335)</u>
Net loss per share, basic and diluted	<u>\$ 1.58</u>	<u>\$ 1.86</u>
Weighted average shares used to compute basic and diluted net loss per share	<u>18,960,401</u>	<u>15,259,958</u>

See accompanying notes to these financial statements.

**STATEMENTS OF STOCKHOLDERS' EQUITY**  
(In thousands, except share data)

	Convertible Preferred Stock		Common stock		Additional paid-in capital	Accumulated other comprehensive loss	Accumulated deficit	Total stockholders' equity
	Shares	Amount	Shares	Amount				
<b>Balance at December 31, 2021</b>	5,571,959	\$ 5	14,597,118	\$ 15	\$ 509,791	\$ —	\$ (454,853)	\$ 54,958
Issuance of common stock upon vesting of restricted stock units	—	—	36,300	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	2,177	—	—	2,177
Issuance of common stock under Employee Stock Purchase Plan	—	—	1,743	—	3	—	—	3
Issuance of common stock through ATM	—	—	2,205,100	2	4,486	—	—	4,488
Unrealized loss on short-term investments	—	—	—	—	—	(12)	—	(12)
Net loss	—	—	—	—	—	—	(28,323)	(28,323)
<b>Balance at December 31, 2022</b>	5,571,959	\$ 5	16,840,261	\$ 17	\$ 516,457	\$ (12)	\$ (483,176)	\$ 33,291
Stock-based compensation expense	—	—	—	—	2,801	—	—	2,801
Issuance of common stock and preferred stock from private placement, net of offering costs	140,827	—	2,615,536	2	14,001	—	—	14,003
Issuance of common stock under Employee Stock Purchase Plan	—	—	41,683	—	45	—	—	45
Issuance of common stock through ATM	—	—	725,192	1	1,071	—	—	1,072
Gain on short-term investments	—	—	—	—	—	12	—	12
Net loss	—	—	—	—	—	—	(30,037)	(30,037)
<b>Balance at December 31, 2023</b>	5,712,786	\$ 5	20,222,672	\$ 20	\$ 534,375	\$ —	\$ (513,213)	\$ 21,187

See accompanying notes to these financial statements.

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

	Years ended December 31,	
	2023	2022
<b>Operating activities</b>		
Net loss	\$ (30,037)	\$ (28,323)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and amortization expense	227	122
Stock-based compensation	2,801	2,177
Amortization of premiums and accretion of discounts on investments, net	(157)	(185)
Other	141	133
Change in operating assets and liabilities:		
Prepaid expenses and other assets	507	(67)
Accounts payable	29	(110)
Accrued liabilities	(396)	140
Accrued research and development expenses	(331)	442
Accrued compensation	773	189
Operating lease right-of-use assets and liabilities, net	(87)	(64)
Other liabilities	(238)	20
Net cash used in operating activities	<u>(26,768)</u>	<u>(25,526)</u>
<b>Investing activities</b>		
Purchases of short-term investments	(4,899)	(32,759)
Sales and maturities of short-term investments	20,000	18,000
Purchases of property and equipment	(613)	(361)
Sales of property and equipment	3	—
Net cash provided by (used in) investing activities	<u>14,491</u>	<u>(15,120)</u>
<b>Financing activities</b>		
Proceeds from issuance of securities through private placement, net of issuance costs	14,003	—
Proceeds from issuance of common stock, net	1,117	4,491
Principal payments on term loan	(3,304)	—
Net cash provided by financing activities	<u>11,816</u>	<u>4,491</u>
Net decrease in cash, cash equivalents and restricted cash	(461)	(36,155)
Cash, cash equivalents and restricted cash at beginning of period	24,290	60,445
Cash, cash equivalents and restricted cash at end of period	<u>\$ 23,829</u>	<u>\$ 24,290</u>
<b>Reconciliation of cash, cash equivalents and restricted cash</b>		
Cash and cash equivalents	\$ 23,767	\$ 24,228
Restricted cash	62	62
Total cash, cash equivalents and restricted cash	<u>\$ 23,829</u>	<u>\$ 24,290</u>
<b>Supplemental disclosure of cash flow information</b>		
Interest paid	<u>\$ (447)</u>	<u>\$ (491)</u>
Income taxes paid	<u>\$ (1)</u>	<u>\$ (1)</u>
<b>Supplemental disclosure of non-cash investing and financing activities</b>		
Purchases of property and equipment included in accrued liabilities	<u>\$ 126</u>	<u>\$ 6</u>

See accompanying notes to these financial statements.

**Regulus Therapeutics Inc.**  
**NOTES TO FINANCIAL STATEMENTS**

**1. The Business, Basis of Presentation and Summary of Significant Accounting Policies**

We are a clinical-stage biopharmaceutical company focused on discovering and developing first-in-class drugs targeting *microRNAs* to treat diseases with significant unmet medical need. We were formed in 2007 when Alnylam Pharmaceuticals, Inc. ("Alnylam") and Ionis Pharmaceuticals, Inc. ("Ionis") contributed significant intellectual property, know-how and financial and human capital to pursue the development of drugs targeting *microRNAs* pursuant to a license and collaboration agreement.

**Basis of Presentation**

On June 24, 2022, we filed a Certificate of Amendment of Amended and Restated Certificate of Incorporation with the Secretary of State of the state of Delaware to effect a 1-for-10 reverse stock split of our issued and outstanding common stock. The primary purpose of the reverse stock split was to raise the per share trading price of our common stock to seek to maintain the listing of our common stock on The Nasdaq Capital Market. At the effective time of the reverse stock split, 5:00 p.m. on June 28, 2022, each 10 shares of our issued and outstanding common stock were automatically combined and converted into one issued and outstanding share of common stock. All of our stock options, restricted stock units ("RSUs") and warrants outstanding immediately prior to the reverse stock split, as well as the conversion ratio of our outstanding convertible preferred stock, were proportionately adjusted. All issued and outstanding common stock, options exercisable for common stock, restricted stock units, common stock issuable upon conversion of outstanding convertible preferred stock, warrants and per share amounts contained in these financial statements have been retrospectively adjusted.

**Liquidity**

Through December 31, 2023, we have principally been financed through net 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 \$557.7 million. As of December 31, 2023, we had approximately \$23.8 million of cash and cash equivalents. Based on our operating plans, we believe our cash and cash equivalents will be sufficient to fund our planned operations for at least 12 months following the issuance of these financial statements. As of December 31, 2023, we are in compliance with all loan agreement covenants.

We intend to seek additional capital through equity and/or debt financings, collaborative or other funding arrangements with partners or through other sources of financing. Should we seek additional financing from outside sources, we may not be able to raise such financing on terms acceptable to us or at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to scale back or discontinue the advancement of product candidates, reduce headcount, file for bankruptcy, reorganize, merge with another entity, or cease operations.

If we are unable to raise additional capital when needed, we may have to liquidate our assets, and in doing so might realize significantly less for those assets than the values at which they are carried on our financial statements. Stockholders may lose all or part of their investment in our common stock.

**Use of Estimates**

Our 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.

**Stock-Based Compensation**

We account for stock-based compensation expense related to stock options granted to employees and members of our board of directors by estimating the fair value of each stock option on the date of grant using the Black-Scholes option pricing model. We recognize stock-based compensation expense using the accelerated multiple-option approach. Under the accelerated multiple-option approach (also known as the graded-vesting method), we recognize compensation expense over the requisite service period for each separately vesting tranche of the award as though the award was in substance multiple awards, resulting in accelerated expense recognition over the vesting period. For performance-based awards granted to employees (i) the fair

value of the award is determined on the grant date, (ii) we assess the probability of the individual milestones under the award being achieved and (iii) the fair value of the shares subject to the milestone is expensed over the implicit service period commencing once management believes the performance criteria is probable of being met.

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

### **Clinical Trial and Preclinical Study Accruals**

We make estimates of our accrued expenses for clinical trial and preclinical study activities as of each balance sheet date in our financial statements based on the facts and circumstances known to us at that time. These accruals are based upon estimates of costs incurred and fees that may be associated with services provided by clinical trial investigational sites and CROs and for other clinical trial-related activities. Payments under certain contracts with such parties depend on factors such as successful enrollment of patients, site initiation and progression through the various stages of our clinical trials. In accruing for these services, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If possible, we obtain information regarding unbilled services directly from these service providers. However, we may be required to estimate these services based on other information available to us. If we underestimate or overestimate the activities or fees associated with a study or service at a given point in time, adjustments to research and development expenses may be necessary in future periods. Historically, our estimated accrued liabilities have approximated actual expense incurred. Subsequent changes in estimates may result in a material change in our accruals.

### **Prepaid Materials**

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

### **Research and Development**

Research and development costs are expensed as incurred and consist of costs associated with research activities supporting our drug discovery efforts, compensation and related benefits, non-cash stock-based compensation, license fees, laboratory supplies and associated overhead and facility costs.

### **Income Taxes**

Income taxes are accounted for under the asset and liability method. This approach requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of the differences between the tax basis of assets or liabilities and their carrying amounts in the financial statements using the enacted tax rates and laws that are anticipated to be in effect when the differences are expected to reverse. We provide a valuation allowance against net deferred tax assets if it is more likely than not that these items will either expire before we are able to realize their benefit or if future deductibility is uncertain.

In accordance with the accounting standards for uncertain tax positions, we evaluate the recognition threshold and measurement attribute criteria for the financial statement recognition and measurement of tax positions taken or expected to be taken in a tax return. For those benefits to be recognized, a tax position must be more likely than not to be sustained upon examination by taxing authorities.

### **Cash and Cash Equivalents**

We classify time deposits and other investments that are highly liquid and have maturities of 90 days or less at the date of purchase as cash equivalents. The carrying amounts approximate fair value due to the short maturities of these instruments.

### **Concentrations of Credit Risk**

Financial instruments that potentially subject us to significant concentrations of credit risk consist primarily of cash equivalents and short-term investments. We maintain deposits in federally insured financial institutions in excess of federally

insured limits. We have not experienced any material losses in such accounts and believe we are not exposed to significant risk. We have invested our excess cash primarily in money market funds and U.S. Treasury securities. Additionally, we adhere to established guidelines regarding approved investments and maturities of investments, which are designed to preserve their principal value and maintain liquidity.

### **Property and Equipment**

We carry our property and equipment at cost, which consists of lab equipment, computer equipment and software, furniture and fixtures and leasehold improvements. Property and equipment is depreciated using the straight-line method over the estimated useful lives (generally three to five years). Leasehold improvements are amortized over the lesser of their useful life or the remaining lease term, including any renewal periods that are deemed to be reasonably assured. Repair and maintenance costs that do not improve service potential or extend economic life are expensed as incurred.

### **Impairment of Long-Lived Assets**

We regularly review the carrying amount of our property, equipment and intangible assets to determine whether indicators of impairment may exist which warrant adjustments to carrying values or estimated useful lives. If indications of impairment exist, projected future undiscounted cash flows associated with the asset are compared to the carrying amount to determine whether the asset's value is recoverable. If the carrying value of the asset exceeds such projected undiscounted cash flows, the asset will be written down to its estimated fair value. No impairment charges were recorded during the years ended December 31, 2023 or 2022.

### **Segment Reporting**

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. To date, we have viewed our operations and managed our business as one segment operating primarily within the United States.

### **Comprehensive Loss**

Comprehensive loss is defined as the change in equity during a period from transactions and other events and/or circumstances from non-owner sources. Our only component of other comprehensive loss is unrealized loss on available-for-sale securities. Comprehensive loss has been reflected in the statements of operations and comprehensive loss and as a separate component in the statements of stockholders' equity for all periods presented.

### **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 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.

### **Fair Value of Financial Instruments**

We follow ASC 820-10 issued by the FASB with respect to fair value reporting for financial assets and liabilities. The guidance defines fair value, provides guidance for measuring fair value and requires certain disclosures. The guidance does not apply to measurements related to share-based payments. The guidance discusses valuation techniques such as the market approach (comparable market prices), the income approach (present value of future income or cash flow), and the cost approach (cost to replace the service capacity of an asset or replacement cost). The guidance establishes a fair value hierarchy that prioritizes the inputs to valuation techniques used to measure fair value into three broad levels.

Our financial instruments consist of cash and cash equivalents, contract and other receivables, accounts payable, accrued liabilities, and our Term Loan. Fair value estimates of these instruments are made at each reporting period end based on relevant market information. These estimates may be subjective in nature and involve uncertainties and matters of significant judgment and therefore cannot be determined with precision. The carrying amount of cash, cash equivalents, contract and other receivables, accounts payable, and accrued liabilities are generally considered to be representative of their respective fair values because of the short-term nature of those instruments. We believe that the fair value of the Term Loan approximates its carrying value.

### **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. The adoption of this guidance had no impact 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 expedites 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. On December 21, 2022, the FASB issued ASU No. 2022-06, *Reference Rate Reform (Topic 848): Deferral of the Sunset Date of Topic 848*, which deferred the sunset date in Topic 848 from December 31, 2022 to December 31, 2024. The ASU became effective upon issuance. We adopted this guidance in June 2023, when we entered into an amendment to our loan agreement (see note 9).

## **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, warrants 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) 29,216,399 shares for the year ended December 31, 2023, consisting of convertible preferred stock, warrants, stock options and restricted stock units, and 13,200,906 shares for the year ended December 31, 2022, consisting 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 December 31, 2023, our cash balance was comprised entirely of cash and cash equivalents (money market funds) and there was no unrealized gain or loss.

	Maturity (in years)	Amortized cost	Unrealized		Estimated fair value
			Gains	Losses	
<b>As of December 31, 2022</b>					
U.S. Treasury securities	1 or less	\$ 14,944	\$ —	\$ (12)	\$ 14,932
		<u>\$ 14,944</u>	<u>\$ —</u>	<u>\$ (12)</u>	<u>\$ 14,932</u>

#### 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 December 31, 2023 and 2022 (in thousands):

	Fair value as of December 31, 2023			
	Total	Level 1	Level 2	Level 3
<b>Cash equivalents:</b>				
Money market funds	\$ 23,084	\$ 23,084	\$ —	\$ —
	<u>\$ 23,084</u>	<u>\$ 23,084</u>	<u>\$ —</u>	<u>\$ —</u>

	Fair value as of December 31, 2022			
	Total	Level 1	Level 2	Level 3
<b>Cash equivalents:</b>				
Money market funds	\$ 21,490	\$ 21,490	\$ —	\$ —
U.S. Treasury securities	14,932	14,932	—	—
	<u>\$ 36,422</u>	<u>\$ 36,422</u>	<u>\$ —</u>	<u>\$ —</u>

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

#### 5. Collaborations

## Sanofi

In February 2014, we and Sanofi entered into a second amended and restated collaboration and license agreement (the “Sanofi Agreement”) to discover, develop and commercialize *micro*RNA therapeutics to focus on specific orphan disease and oncology targets. Under the terms of the Sanofi Agreement, Sanofi had opt-in rights to our clinical fibrosis program targeting miR-21 for the treatment of Alport syndrome (which rights were relinquished by Sanofi in November 2018), our preclinical program targeting miR-21 for oncology indications, and our preclinical program targeting miR-221/222 for 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. We were eligible to receive royalties on *micro*RNA therapeutic products commercialized by Sanofi and would have had the right to co-promote these products relating to our preclinical program targeting miR-221/222.

On January 6, 2023, Sanofi delivered to us a written notice of Sanofi’s election to terminate, in its entirety, the Sanofi Agreement. Previously, on July 12, 2022, we received notification from Sanofi of its decision to terminate the Phase 2 clinical study of lademirsen for the treatment of Alport syndrome for failure to meet Sanofi’s pre-defined futility criteria. In accordance with the Sanofi Agreement, the termination became effective on February 5, 2023, which was 30 days following the date of delivery of the notice by Sanofi. As of the effective date of the termination of the Sanofi Agreement, we are no longer eligible to receive any option exercise fees, royalties, or development, clinical, regulatory or commercial milestones from Sanofi.

## 6. Property and Equipment, net

The following table summarizes our major classes of property and equipment (in thousands):

	December 31,	
	2023	2022
Laboratory equipment	\$ 4,687	\$ 4,359
Computer equipment and software	367	470
Furniture and fixtures	12	12
Leasehold improvements	115	115
Construction in progress	126	—
	5,307	4,956
Less accumulated depreciation and amortization	(4,246)	(4,420)
Property and equipment, net	\$ 1,061	\$ 536

Depreciation and amortization of property and equipment of \$0.2 million and \$0.1 million was recorded for the years ended December 31, 2023 and 2022, respectively.

## 7. Intangible Assets, net

The following table summarizes our major classes of intangible assets (in thousands):

	December 31,	
	2023	2022
Patents	\$ 133	\$ 183
Accumulated amortization - Patents	(100)	(121)
Intangibles, net	\$ 33	\$ 62

Intangible asset amortization of less than \$0.1 million was recorded for the years ended December 31, 2023 and 2022. Amortization of intangible assets over the next five years is expected to be less than \$0.1 million per year. The weighted-average period over which the amortization remaining at December 31, 2023 is expected to be recognized is approximately 11.4 years.

## 8. Commitments and Contingencies

### License Agreements

We have license agreements with third parties that require us to make annual license maintenance payments and future payments upon the success of licensed products that include milestones and/or royalties. Minimum future payments over the next five years are not material.

## **Litigation**

From time to time, we may be involved in various lawsuits, legal proceedings, or claims that arise in the ordinary course of business. We believe there are no claims or actions pending against us at December 31, 2023 which will have, individually, or in the aggregate, a material adverse effect on our business, liquidity, financial position or results of operations. Litigation, however, is subject to inherent uncertainties, and an adverse result in such matters may arise from time to time that may harm our business.

## **9. 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 bore 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 June 2023, we entered into an amendment to the Loan Agreement (the "Rate Amendment") pursuant to which, effective July 1, 2023, the Term Loan bears interest at a floating per annum rate equal to the greater of (a) 8.95% and (b) the sum of (i) the 1-month CME Term Secured Overnight Financing Rate ("SOFR") reference rate on the last business day of the month that immediately precedes the month in which the interest will accrue, (ii) 0.10% and (iii) 8.51%.

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 ten times between October 2017 through August 2020. On December 31, 2021, we entered into an eleventh amendment to the Loan Agreement (the "Eleventh Amendment"). Under the terms of the Eleventh Amendment, the maturity date for the Term Loan was extended to May 1, 2024. In addition, under the Eleventh Amendment, our required monthly payments to the Lender were comprised of interest only through and including December 1, 2022.

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-K.

As of December 31, 2023, \$1.4 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 \$1.3 million accrued liability balance is presented in other current liabilities on our balance sheet as of December 31, 2023). We had less than \$0.1 million of debt issuance costs outstanding as of December 31, 2023, 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. All amounts that remained payable under the Term Loan as of December 31, 2023 are due in 2024.

## **10. Stockholders' Equity**

### **Common Stock**

As of December 31, 2023, there were 20,222,672 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.

## **Reverse Stock Split**

On June 24, 2022, we filed a Certificate of Amendment of Amended and Restated Certificate of Incorporation with the Secretary of State of the state of Delaware to effect a 1-for-10 reverse stock split of our issued and outstanding common stock. The primary purpose of the reverse stock split was to raise the per share trading price of our common stock to seek to maintain the listing of our common stock on The Nasdaq Capital Market. At the effective time of the reverse stock split, 5:00 p.m. on June 28, 2022, each 10 shares of our issued and outstanding common stock were automatically combined and converted into one issued and outstanding share of common stock. All of our stock options, RSUs and warrants outstanding immediately prior to the reverse stock split, as well as the conversion ratio of our outstanding convertible preferred stock, were proportionately adjusted. All issued and outstanding common stock, options exercisable for common stock, restricted stock units, common stock issuable upon conversion of outstanding convertible preferred stock, warrants and per share amounts contained in these financial statements have been retrospectively adjusted.

## **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 with the 2009 Plan, the "Prior Plans") that on or after the effective date of the 2019 Plan (i) expire or terminate for any reason prior to exercise or settlement; (ii) are forfeited because of the failure to meet a contingency or condition required to vest such shares or otherwise return to the Company, or (iii) are reacquired, withheld (or not issued) to satisfy a tax withholding obligation in connection with an award or to satisfy the purchase price or exercise price of a stock award. No further grants will be made under the Prior Plans. In addition, on January 22, 2020, an additional 416,686 shares of common stock became available for issuance under the 2019 Plan pursuant to the second closing under our May 2019 securities purchase agreement. Further, on January 1<sup>st</sup> 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. In addition, on June 13, 2023, our stockholders approved an amendment to the 2019 Plan, which authorized an additional 5,000,000 shares of common stock available for issuance thereunder. As of December 31, 2023, 819,459 shares of common stock were available for new equity award grants under the 2019 Plan and 7,348,950 shares of common stock were reserved for issuance pursuant to equity awards outstanding under the 2019 Plan as of December 31, 2023.

## **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 5635I(4) of the Nasdaq Listing Rules. The Inducement Plan initially reserved 200,000 shares of common stock and provides for the grant of non-qualified stock options 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. The authorized number of shares available for grant under the Inducement Plan was subsequently increased in October 2022 to 540,000 shares in the aggregate, and subsequently increased again in December 2023 to 1,030,000 shares in the aggregate.

Under the Inducement Plan, options are 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 December 31, 2023, 500,000 shares of common stock were reserved for future issuance under the Inducement Plan and 530,000 shares of common stock were reserved for future issuance pursuant to equity awards outstanding under the Inducement Plan.

## **2022 Employee Stock Purchase Plan**

In June 2022, our stockholders approved and we adopted the 2022 Employee Stock Purchase Plan (the "2022 Purchase Plan"), which enables participants to contribute up to 15% of such participant's eligible compensation during a defined rolling six-month periods to purchase our common stock. The purchase price of common stock under the 2022 Purchase Plan will be the lesser of: (i) 85% of the fair market value of our common stock at the inception of the enrollment period or (ii) 85% of the fair market value of our common stock at the applicable purchase date. The 2022 Purchase Plan supersedes the 2012 Employee Stock Purchase Plan, and no further offerings will be made under the 2012 Employee Stock Purchase Plan. As of December 31,

2023, a maximum of 137,424 shares of our common stock were reserved for future issuance and have been authorized for purchase under the 2022 Purchase Plan.

### **2023 Private Placement of Common Stock and Non-Voting Preferred Stock**

On April 13, 2023, we entered into a Securities Purchase Agreement (the “April 2023 SPA”) with certain institutional and other accredited investors (the “2023 Purchasers”), pursuant to which we agreed to sell and issue shares of our common stock and shares of our newly designated non-voting convertible preferred stock in a private placement transaction (the “2023 PIPE”).

At the closing under the April 2023 SPA that occurred on April 13, 2023 (the “2023 Closing”), we sold and issued to the 2023 Purchasers (i) 2,615,536 shares of common stock at a purchase price of \$0.9001 per share, and (ii) 140,827 shares of non-voting Class A-5 convertible preferred stock, in lieu of shares of common stock, at a price of \$90.01 per share. Total gross proceeds from the 2023 Closing were approximately \$15.0 million. Each share of non-voting Class A-5 convertible preferred stock is convertible into 100 shares of common stock, subject to certain beneficial ownership conversion limitations. An aggregate of 222,198 shares of common stock were purchased for \$0.2 million by a director of the Company at the 2023 Closing.

We evaluated the non-voting Class A-5 convertible preferred stock sold in the 2023 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.

### **Additional Outstanding Non-Voting Preferred Stock and Warrants**

In May 2019, we sold and issued (i) 973,045 shares of common stock (ii) 415,898 shares of non-voting Class A-1 convertible preferred stock and (iii) accompanying warrants to purchase an aggregate of 1,388,943 shares of common stock. Each share of non-voting Class A-1 convertible preferred stock is convertible into one share 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 \$10.80 per share, subject to proportional adjustments in the event of stock splits or combinations or similar events. The warrants are also exercisable on a net exercise “cashless” basis.

In December 2019, we sold and issued 3,288,390 shares of non-voting Class A-2 convertible preferred stock and accompanying warrants to purchase an aggregate of 3,288,390 shares of common stock. Each share of non-voting Class A-2 convertible preferred stock is convertible into one share 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 \$6.66 per share, subject to proportional adjustments in the event of stock splits or combinations or similar events. The warrants are also exercisable on a net exercise “cashless” basis.

In December 2020, we sold and issued (i) 2,434,152 shares of common stock (ii) 272,970 shares of non-voting Class A-3 convertible preferred stock and (iii) accompanying warrants to purchase an aggregate of 2,030,341 shares of common stock. Each share of non-voting Class A-3 convertible preferred stock is convertible into one share 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 \$7.46 per share, subject to proportional adjustments in the event of stock splits or combinations or similar events. The warrants are also exercisable on a net exercise “cashless” basis.

In November 2021, we sold and issued (i) 5,892,335 shares of common stock and (ii) 3,725,720 shares of non-voting Class A-4 convertible preferred stock. Each share of non-voting Class A-4 convertible preferred stock is convertible into one share of common stock, subject to certain beneficial ownership conversion limitations.

### **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. 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.

A total of 725,192 shares were sold and settled for net proceeds of \$1.1 million (net of less than \$0.1 million in offering costs) under the ATM Offering during the year ended December 31, 2023. A total of 2,205,100 shares were sold and settled for proceeds of \$4.5 million (net of \$0.1 million in offering costs) under the ATM Offering during the year ended December 31, 2022. At December 31, 2023, approximately \$44.2 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 December 31, 2023 (in thousands):

Class A-1 convertible preferred stock outstanding (as-converted)	257
Class A-2 convertible preferred stock outstanding (as-converted)	1,331
Class A-3 convertible preferred stock outstanding (as-converted)	259
Class A-4 convertible preferred stock outstanding (as-converted)	3,726
Class A-5 convertible preferred stock outstanding (as-converted)	14,083
Warrants to purchase Common Stock	6,186
Common stock options outstanding	6,188
RSUs outstanding	1,161
Common stock available for future grant under the 2019 Equity Incentive Plan	819
Common stock available for future grant under the 2021 Inducement Plan	500
2022 Employee Stock Purchase Plan	137
Total common shares reserved for future issuance	<u>34,647</u>

The following table summarizes our stock option activity under all equity incentive plans for the year ended December 31, 2023 (shares and aggregate intrinsic value in thousands):

	Number of options	Weighted average exercise price	Weighted average remaining contractual term	Aggregate intrinsic value
Stock Options outstanding at December 31, 2022	1,372	\$ 7.53		
Granted	5,008	\$ 1.39		
Exercised	—	\$ —		
Canceled/forfeited/expired	(192)	\$ 6.79		
Stock Options outstanding at December 31, 2023	<u>6,188</u>	\$ 2.58	9.0	\$ 7
Vested and exercisable at December 31, 2023	<u>1,510</u>	\$ 5.34	7.9	\$ —

The weighted average grant date fair value per share of employee stock options granted during the years ended December 31, 2023 and 2022 was \$1.09 and \$2.00, respectively.

There were no stock option exercises during the years ended December 31, 2023 or 2022.

The total compensation cost related to stock options not yet recognized was \$3.6 million as of December 31, 2023. The weighted-average period over which this expense is expected to be recognized is approximately 1.6 years.

The following table summarizes our RSU activity under all equity incentive plans for the year ended December 31, 2023 (shares and aggregate intrinsic value in thousands):

	Number of options	Weighted average grant date fair value	Weighted average remaining contractual term	Aggregate intrinsic value
RSUs outstanding at December 31, 2022	70	\$ 2.57		
Granted	1,161	\$ 1.38		
Vested	—	\$ —		
Canceled/forfeited/expired	(70)	\$ 2.57		
RSUs outstanding at December 31, 2023	<u>1,161</u>	\$ 1.38	2.4	\$ 1,486

The total compensation cost related to non-vested RSUs not yet recognized was \$1.4 million as of December 31, 2023. The weighted-average period over which this expense is expected to be recognized is approximately 2.4 years.

### 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 2019 Equity Incentive Plan, 2021 Inducement Plan and the shares purchasable under our Employee Stock Purchase Plans during the periods presented:

	Year ended December 31,	
	2023	2022
<b>Stock options</b>		
Risk-free interest rate	4.1 %	2.0 %
Volatility	96.4 %	96.1 %
Dividend yield	—	—
Expected term (years)	6.1	6.1
<b>Employee stock purchase plan shares</b>		
Risk-free interest rate	4.9 %	1.6 %
Volatility	89.1 %	104.7 %
Dividend yield	—	—
Expected term (years)	0.5	0.5

*Risk-free interest rate* - The risk-free interest rate assumption was based on observed interest rates appropriate for the expected term of the stock option grants.

*Expected dividend yield* - The expected dividend yield assumption was based on the fact that we have never paid cash dividends and have no present intention to pay cash dividends.

*Expected volatility* - The expected volatility assumption was based on the historical volatility of the trading price of our common stock.

*Expected term* - The expected term represents the period of time that options are expected to be outstanding. Because we do not have sufficient historical exercise behavior data, we determine the expected life using the simplified method, which was an average of the contractual term of the option and its ordinary vesting period.

*Forfeitures* - We account for forfeitures as they occur.

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

	Year ended December 31,	
	2023	2022
Research and development	\$ 1,029	\$ 594
General and administrative	1,772	1,583
Total	<u>\$ 2,801</u>	<u>\$ 2,177</u>

### 11. Defined Contribution Plan

In 2009, we established an employee 401(k) salary deferral plan (“401(k) Plan”) covering all eligible employees. Active employees who are at least 18 years old and are not otherwise disqualified under the terms of the 401(k) Plan are eligible to participate. Employees may contribute up to 50% of their compensation per year (subject to a maximum limit prescribed by federal tax law). Under the 401(k) Plan, we may elect to match a discretionary percentage of employee contributions. We elected to match 50% of employees’ contributions up to 6% of the employees’ eligible salary for the periods presented. We made matching contributions of \$0.2 million and \$0.1 million for the years ended December 31, 2023 and 2022, respectively.

### 12. Income Taxes

The following table summarizes the components of our income tax expense (in thousands):

	Year ended December 31,	
	2023	2022
Current:		
Federal	\$ —	\$ —
State	1	1
	<u>1</u>	<u>1</u>
Deferred:		
Federal	—	—
State	—	—
	<u>—</u>	<u>—</u>
Income tax expense	<u>\$ 1</u>	<u>\$ 1</u>

The following is a reconciliation of the expected statutory federal income tax provision to our actual income tax provision (in thousands):

	Year ended December 31,	
	2023	2022
Expected income tax benefit at federal statutory tax rate	\$ (6,308)	\$ (5,948)
State income taxes, net of federal benefit	1	1
Tax credits	(3,022)	(1,850)
Change in valuation allowance	8,081	7,327
Return to provision adjustments	39	(18)
Stock compensation	755	236
Reserve for uncertain tax positions	453	253
Other	2	—
Income tax expense	<u>\$ 1</u>	<u>\$ 1</u>

The following table summarizes the significant components of our deferred tax assets and liabilities (in thousands):

	December 31,	
	2023	2022
Deferred tax assets:		
Net operating loss carryovers	\$ 92,609	\$ 90,085
Research and development and other tax credits	39,532	36,963
Intangibles and property and equipment basis difference	255	496
Section 174 research and development	6,546	3,302
Stock compensation expense	619	818
Lease liability	371	508
Other	748	597
Total deferred tax assets	<u>140,680</u>	<u>132,769</u>
Total deferred tax liabilities	<u>(444)</u>	<u>(611)</u>
Gross deferred tax asset	140,236	132,158
Valuation allowance	(140,236)	(132,158)
Net deferred tax asset	<u>\$ —</u>	<u>\$ —</u>

For all periods presented, we have determined that it is more likely than not that our deferred tax asset will not be realized. Accordingly, we have recorded a valuation allowance to offset the net deferred tax asset of \$140.2 million. The valuation allowance increased by approximately \$8.1 million and \$7.3 million during the years ended December 31, 2023 and 2022, respectively.

As of December 31, 2023, we had NOL carryforwards for U.S. federal and California state tax purposes of \$389.5 million and \$146.3 million, respectively, portions of which begin to expire in 2030 and 2033, respectively. Our federal NOL carryforwards generated in tax years beginning after December 31, 2017 of \$126.1 million will carry forward indefinitely.

As of December 31, 2023, we also had federal research and development tax credits, orphan drug credits and California research and development tax credit carryforwards of \$13.0 million, \$24.3 million and \$10.5 million, respectively. The federal research and development tax credit carryforwards will begin to expire in 2029 and the federal orphan drug credits will begin to expire in 2034. The California research and development tax credit carryforwards are available indefinitely.

Pursuant to Sections 382 and 383, use of the Company's net operating loss and credit carryforwards may be limited if a cumulative change in ownership of more than 50% (by value) occurs within a three-year period. The Company has not performed an analysis through December 31, 2023 to determine whether its net operating loss and research and development credit carryforwards are subject to annual limitation under Sections 382 or 383 of the Code, and these financial statements do not contain any adjustment relating to such potential limitations. However, if the Company experienced an ownership change that resulted in an annual limitation on the Company's net operating loss carryforwards under Section 382 of the Code there would be no material impact to the Company's financial statements.

The following table summarizes the changes in the amount of our unrecognized tax benefits (in thousands):

	Year Ended December 31,	
	2023	2022
Beginning balance of unrecognized tax benefits	\$ 5,785	\$ 16,953
Increase (decrease) for prior year tax positions	16	(11,463)
Increase for current year tax positions	449	295
Total	<u>\$ 6,250</u>	<u>\$ 5,785</u>

Included in unrecognized tax benefits of \$6.3 million at December 31, 2023 was \$5.4 million of tax benefits that, if recognized, would reduce our annual effective tax rate, subject to valuation allowance. We do not expect that there will be a significant change in the unrecognized tax benefits over the next 12 months.

We are subject to taxation in the United States and state jurisdictions where applicable. Our tax years for 2010 and forward are subject to examination by the U.S. and California tax authorities due to carryforward of unutilized net operating losses and research and development credits.

It is our practice to recognize interest and/or penalties related to income tax matters in income tax expense. For the years ended December 31, 2023 and 2022, we have not recognized any interest or penalties related to income taxes.

### 13. Leases

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 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. Under the Campus Point Lease, we were required to maintain a deposit of \$61,591 in a specially designated bank account, which we recorded as restricted cash on our balance sheet at December 31, 2023 and 2022.

The table below summarizes our lease liabilities and corresponding ROU assets as of December 31, 2023 and 2022 (in thousands):

	<u>Year Ended December 31,</u>	
	<u>2023</u>	<u>2022</u>
<b>Assets</b>		
Operating	\$ 1,477	\$ 2,039
Total ROU assets	<u>\$ 1,477</u>	<u>\$ 2,039</u>
<b>Liabilities</b>		
Current:		
Operating	\$ 713	\$ 649
Long-term:		
Operating	1,055	1,768
Total lease liabilities	<u>\$ 1,768</u>	<u>\$ 2,417</u>

The table below summarizes our lease costs from our statement of operations and cash payments from our statement of cash flows during the years ended December 31, 2023 and 2022 (in thousands):

	<u>Year Ended December 31,</u>	
	<u>2023</u>	<u>2022</u>
Lease cost:		
Operating lease cost	\$ 690	\$ 690
Cash payment information:		
Operating cash used for operating leases	\$ 776	\$ 754
Total cash paid for amounts included in the measurement of lease liabilities	\$ 776	\$ 754

The table below summarizes other non-cash information under our operating lease obligations as of December 31, 2023 and 2022 (in thousands, except years and rates):

	Year Ended December 31,	
	2023	2022
Supplemental non-cash information:		
Operating lease liabilities arising from obtaining right-of-use assets	\$ —	\$ —
Weighted-average remaining lease term (years) - operating leases	2.3	3.3
Weighted-average discount rate - operating leases	6.0 %	6.0 %

We did not have any finance lease obligations as of December 31, 2023 or 2022.

Our future lease payments under our operating lease at December 31, 2023 are as follows (in thousands):

	Operating Leases
2024	800
2025	824
2026	277
2027	—
2028	—
Total operating lease payments	\$ 1,901
Less: amount representing interest	(133)
Present value of obligations under operating lease	1,768
Less: current portion	(713)
Long-term operating lease obligations	\$ 1,055

## 14. Subsequent Event

### *Private Placement of Common Stock and Non-Voting Preferred Stock*

On March 11, 2024, the Company entered into a Securities Purchase Agreement (the “Purchase Agreement”) with certain institutional and other accredited investors (the “Purchasers”), pursuant to which the Company sold and issued (i) 45,108,667 shares of common stock, at a purchase price of \$1.60 per share and (ii) 173,915 shares of the Company’s newly designated non-voting Class A-6 convertible preferred stock, par value \$0.001 per share (the “Class A-6 Convertible Preferred Stock”), in lieu of shares of Common Stock, at a purchase price of \$160.00 per share in a private placement transaction (the “Private Placement”), which closed on March 14, 2024. The Company received net proceeds of approximately \$94.0 million in the Private Placement after deducting placement agent and financial advisor fees and other expenses.

Stelios Papadopoulos, Ph.D., the Company’s Chairman of the Board of Directors, is a Purchaser under the Purchase Agreement and purchased 250,000 shares of Common Stock.

Each share of Class A-6 Convertible Preferred Stock is convertible into 100 shares of common stock, subject to certain beneficial ownership conversion limitations. In the event of the Company’s liquidation, dissolution or winding up, holders of Class A-6 Convertible Preferred Stock will participate pari passu with any distribution of proceeds to holders of common stock, holders of the Company’s Class A-1 convertible preferred stock, holders of the Company’s Class A-2 convertible preferred stock, holders of the Company’s Class A-3 convertible preferred stock, holders of the Company’s Class A-4 convertible preferred stock, holders of the Company’s Class A-5 convertible preferred stock and the holders of any series of class of the Company’s preferred stock or other capital stock thereafter created ranking on its terms on parity with the Class A-6 Convertible Preferred Stock or the common stock. Holders of Class A-6 Convertible Preferred Stock are entitled to receive dividends on shares of Class A-6 Convertible Preferred Stock equal (on an as converted to common stock basis) to, and in the same form as, dividends actually paid on the common stock. Shares of Class A-6 Convertible Preferred Stock generally have no voting rights, except as required by law.

### **Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure**

None.

**Item 9A. 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 December 31, 2023, 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 a reasonable assurance level as of December 31, 2023.

**Management's Report on 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 Exchange Act Rule 13a-15(f) and 15(d)-15(f). Internal control over financial reporting is a process designed under the supervision and with the participation of our management, including our principal executive officer and our principal financial officer, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP.

As of December 31, 2023, our management assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control-Integrated Framework (2013 Framework)*. Based on this assessment, our management concluded that, as of December 31, 2023, our internal control over financial reporting was effective based on those criteria.

**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..

**Item 9B. Other Information**

None.

**Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections**

Not applicable.

**PART III**

**Item 10. Directors, Executive Officers and Corporate Governance**

The information required by this item and not set forth below will be set forth in the sections headed “Election of Directors” and “Executive Officers” in our Proxy Statement for our 2024 Annual Meeting of Stockholders (“Proxy Statement”) to be filed with the SEC no later than April 29, 2024, and is incorporated herein by reference.

We have adopted a code of ethics for directors, officers (including our principal executive officer and our principal financial officer) and employees, known as the Code of Business Conduct and Ethics. The Code of Business Conduct and Ethics is available on our website at <http://www.regulusrx.com> under the Corporate Governance section of our Investor Relations page. We will promptly disclose on our website (i) the nature of any amendment to the policy that applies to our principal executive officer, principal financial and accounting officer or persons performing similar functions and (ii) the nature of any waiver, including an implicit waiver, from a provision of the policy that is granted to one of these specified individuals that is required to be disclosed pursuant to SEC rules and regulations, the name of such person who is granted the waiver and the date of the waiver.

*Stelios Papadopoulos, Ph.D.* Chair of the Board, has served on our Board of Directors since our conversion to a corporation in January 2009 and as our Chair since June 2013, and prior to that was a director of Regulus Therapeutics LLC since July 2008. Since December 1994, Dr. Papadopoulos has served as a director and, since 1998, as Chair of the Board for Exelixis, Inc., a publicly held biotechnology company, which he co-founded. From July 2008 until June 2023, Dr. Papadopoulos served as a member of the board of directors of Biogen Inc. (formerly Biogen Idec Inc.), a publicly held biopharmaceutical company, and served as its Chair of the board of directors from June 2014 until June 2023. From August 2020 until June 2023, Dr. Papadopoulos served as Chair of the board of Eucrates Biomedical Acquisition Corp., a special purpose acquisition corporation. From 2000 to 2006, Dr. Papadopoulos served as Vice Chair with Cowen and Co., LLC, an investment banking firm. From 1987 to 2000, Dr. Papadopoulos served in several positions with PaineWebber, Incorporated, most recently as Chair of PaineWebber Development Corp., a PaineWebber subsidiary focusing on biotechnology. Dr. Papadopoulos holds an M.S. in Physics, a Ph.D. in Biophysics and an MBA in Finance from New York University.

*David Baltimore, Ph.D.* has served on our Board of Directors since our conversion to a corporation in January 2009, and prior to that was a director of Regulus Therapeutics LLC since November 2007. Dr. Baltimore is currently President Emeritus and Judge Shirley Hufstедler Distinguished Professor of Biology at the California Institute of Technology (“Caltech”), and before that from 1997 to 2006, Dr. Baltimore served as President of the California Institute of Technology. From 1968 to 1972, Dr. Baltimore served as an associate professor at the Massachusetts Institute of Technology, and from 1972 to 1997 was a professor at the Massachusetts Institute of Technology. From 1990 to 1994, Dr. Baltimore served as professor at The Rockefeller University where he also served as the President from July 1990 to December 1991. Dr. Baltimore served as a director of Amgen Inc., a publicly held biotechnology company from 1997 to May 2018, and also served as a director of Immune Design Corp., a publicly held biotechnology company, from 1997 until its acquisition by Merck & Co., Inc. in February 2019. In 1975, Dr. Baltimore received the Nobel Prize in Medicine as a co-recipient. Dr. Baltimore holds a Ph.D. in Biology from The Rockefeller University and a B.A. with High Honors in Chemistry from Swarthmore College.

*Kathryn J. Collier* has served on our Board of Directors since April 2018. From March 2022 until January 2024, Ms. Collier served as the Senior Vice President of Corporate Finance for Pattern Energy Group LP, a privately-held renewable energy company. From July 2019 to March 2022, Ms. Collier served as the Vice President for Audit Services of Sempra Energy (“Sempra”), a publicly-traded energy services holding company overseeing the internal audit function for Sempra, including the Financial Leadership Program and audit oversight of Sempra’s operating companies. From March 2019 to July 2019, Ms. Collier served as the Chief Strategy and Origination Officer for Sempra LNG, a wholly-owned subsidiary of Sempra. From August 2018 to March 2019, Ms. Collier served as Chief Financial Officer and Chief Administrative Officer for Sempra North America Infrastructure. Ms. Collier also previously served as Vice President and Treasurer for Sempra from April 2012 to August 2018. Prior to joining Sempra in 2012, Ms. Collier held several executive positions within global corporation and investment banking at Bank of America Merrill Lynch. Ms. Collier holds a B.S. in accounting from Valparaiso University.

*Joseph P. Hagan* has served as our Chief Executive Officer and principal executive officer since May 2017. Mr. Hagan previously served as our President and Chief Executive Officer from May 2017 until June 2023 and our Chief Operating Officer, principal financial officer and principal accounting officer from January 2016 to May 2017. From June 2011 through December 2015, Mr. Hagan served as the Executive Vice President, Chief Financial Officer and Chief Business Officer of Orexigen Therapeutics, Inc. (“Orexigen”). From May 2009 to June 2011, Mr. Hagan served as Orexigen’s Senior Vice President, Corporate Development, Strategy and Communications. From September 1998 to April 2008, Mr. Hagan served as Managing Director of Amgen Ventures. Prior to starting the Amgen Ventures Fund, Mr. Hagan served as Head of corporate development for Amgen Inc. (“Amgen”). Before joining Amgen, Mr. Hagan spent five years in the bioengineering labs at Genzyme and Advanced Tissue Sciences. Mr. Hagan served on the board of directors of Aurinia Pharmaceuticals, Inc. from February 2018 to June 2023, and he also previously served on the board of directors of Zosano Pharma Corp., from May 2015 to May 2022. He received an M.B.A. from Northeastern University and a B.S. in Physiology and Neuroscience from the University of California, San Diego.

*Alice S. Huang, Ph.D.* has served on our Board of Directors since January 2021. Dr. Huang is currently Senior Faculty Associate of Biology and Biological Engineering at the California Institute of Technology ("Caltech"), having joined Caltech in July 1997. Previous to her tenure at Caltech she was Dean for Science and Professor of Biology at New York University, Professor of Microbiology and Molecular Genetics at Harvard Medical School and Director, Laboratories of Infectious Disease at Boston Children's Hospital. She also served as director of Virus-Host Interactions in Cancer for 15 years, a training program at Harvard funded by the National Cancer Institute. Dr. Huang has served on the Board of Trustees of the Keck Graduate Institute since 1998 and has previously served on the Board of Trustees of Waksman Foundation for Microbiology, the Rockefeller Foundation, Public Agenda, Johns Hopkins University, the Health Effects Institute, and the University of Massachusetts. Dr. Huang is serving on the advisory boards of the Institute for Basic Biomedical Sciences at Johns Hopkins University School of Medicine since 2008 as well as the Schlesinger Library at Radcliffe Institute since 2018. She has previously served on the advisory boards of the National Foundation for Infectious Diseases, the US Army Medical Research and Development Command and Food and Drug Administration. She has been a fellow of the American Association of Women in Science since 1978, American Academy of Microbiology since 1982, Academia Sinica in Taiwan since July 1990, and the American Association for the Advancement of Science since 2000, serving as its president from 2010 to 2011. Dr. Huang received her B.A., M.A. and Ph.D. degrees from the Johns Hopkins University.

*Preston S. Klassen, M.D.* has served as our President and Head of Research and Development and as a member of our Board of Directors since June 2023. Dr. Klassen previously served as President and Chief Operating Officer of Zura Bio Limited from February to April 2023. From June 2020 to February 2023, Dr. Klassen served as President and Chief Executive Officer and as a member of the Board of Directors of Metacrine, Inc., a biopharmaceutical company. From March 2017 to June 2020, Dr. Klassen served as Executive Vice President, Head of Research and Development and Chief Medical Officer of Arena Pharmaceuticals, Inc., a biopharmaceutical company. From June 2016 to March 2017, he was Chief Medical Officer of Laboratoris Sanifit S.L., a biotechnology company, and prior to that, from November 2009 to May 2016, was Executive Vice President, Head of Global Development at Orexigen Therapeutics, Inc. Dr. Klassen also held several positions of increasing responsibility at Amgen Inc., including Therapeutic Area Head for Nephrology. Before joining Amgen, he was a faculty member in the Division of Nephrology at Duke University Medical Center. From February 2014 to May 2020, Dr. Klassen served on the board of directors of Conatus Pharmaceuticals Inc., a publicly traded biotechnology company that merged with Histogen Inc. in May 2020. Dr. Klassen holds a B.S. in Chemistry from Central University of Iowa. Dr. Klassen received his medical degree from the University of Nebraska College of Medicine and completed his residency in internal medicine, fellowship in nephrology, and Master of Health Sciences degree at Duke University.

*Jake R. Nunn* has served on our Board of Directors since June 2019. Since January 2023, Mr. Nunn has served as a Venture Partner with SR One Capital Management, a venture capital firm. Previously, Mr. Nunn was a venture advisor at New Enterprise Associates, Inc. ("NEA"), a venture capital firm, where he was a partner from June 2006 until January 2019. Prior to joining NEA, he served as a partner and an analyst for the MPM BioEquities Fund, a life sciences fund at MPM Capital, L.P., a private equity firm. Previously, he was a healthcare research analyst and portfolio manager at Franklin Templeton Investments and an investment banker with Alex Brown & Sons. Mr. Nunn has served on the board of directors of Trevena, Inc., a publicly-held biotechnology company focused on the central nervous system since July 2013, Addex Therapeutics Ltd., a publicly-held biopharmaceutical company focused on allosteric modulators for neurological disorders since June 2018. Mr. Nunn served on the board of directors of Oventus Medical Ltd., a publicly-held medical device company from February 2020 until September 2023 and Hexima Limited, a publicly-held biopharmaceutical company focused on novel anti-fungals from September 2021 until June 2022. Mr. Nunn also served on the board of directors of Dermira, Inc., a publicly-held biopharmaceutical company focused on dermatology, from May 2011 until its acquisition by Eli Lilly and Company in February 2020. From 2009 to May 2015, Mr. Nunn served on the board of directors of Hyperion Therapeutics, Inc. and from 2008 to February 2016, Mr. Nunn served on the board of directors of TriVascular Technologies, Inc. Mr. Nunn received his A.B. in economics from Dartmouth College and his M.B.A. from the Stanford Graduate School of Business. He also holds the Chartered Financial Analyst designation and is a member of the CFA Society of San Francisco.

*William H. Rastetter, Ph.D.* has served on our Board of Directors since April 2013. From 2006 to February 2013, Dr. Rastetter served as a partner in the venture capital firm, Venrock. He served as Chief Executive Officer of IDEC Pharmaceuticals Corp. ("IDEC Pharmaceuticals") from December 1986 through November 2003, and as Chair from May 1996 to November 2003. Upon the merger of IDEC Pharmaceuticals and Biogen Inc. in November 2003, Dr. Rastetter served as Executive Chair of Biogen Idec until the end of 2005. Dr. Rastetter served as Chair of the board of Illumina, Inc., a publicly held biotechnology company, from 2005 to January 2016 and served on its board of directors from 1998 to January 2016. He was a founder of Receptos, Inc. in 2009 and served as its Chair until the sale of the publicly held company to Celgene Corporation in 2015. Currently, he has served as the Chair of the board of directors of Fate Therapeutics, Inc., a publicly held biotechnology company, since November 2011; Chair of the board of directors of Neurocrine Biosciences, Inc., a publicly held biotechnology company, since May 2011 and on its board of directors since February 2010; on the board of directors of Grail, Inc., a privately-held company, since January 2016, and as its Chair from August 2017 to November 2018. Dr. Rastetter served on the board of directors of Cerulean Pharma Inc. ("Cerulean"), a publicly held biotechnology company since January 2014, as its lead independent director from April 2014 to June 2016, and as its Chair from June 2016 until July 2017 when Cerulean and Daré Bioscience Inc. completed a reverse merger and he currently serves as Chair of the board of the surviving company, Daré Bioscience Inc., a publicly-traded company. In addition, he serves as an advisor to Illumina Ventures. He is the author of numerous scientific papers and patent applications in the fields of organic and bioorganic chemistry, protein and enzyme engineering, and biotechnology. Dr. Rastetter holds an S.B. in Chemistry from the Massachusetts Institute of Technology and received his M.A. and Ph.D. in Chemistry from Harvard University.

*Hugh Rosen, M.D., Ph.D.* has served on our Board of Directors since June 2016. Since 2002, Dr. Rosen has served as a professor at the Scripps Research Institute of La Jolla (“TSRI”) and, since August 2023, serves as Chair of Molecular and Cellular Biology. From April 2017 until March 2023, Dr. Rosen served as the President and Chair of the Board of ActivX Biosciences, Inc., a wholly owned biopharmaceutical subsidiary of Kyorin Pharmaceutical Co., Ltd. Prior to joining TSRI, Dr. Rosen served in various capacities with Merck Research Laboratories most recently serving as Executive Director in Immunology, Rheumatology and Infectious Diseases and Chair of the Worldwide Business Strategy Team for Antibacterials and Antifungals, reporting to the Management Committee. Dr. Rosen was a scientific founder of Receptos, Inc., now a wholly owned biopharmaceutical subsidiary of Celgene Corporation, and of BlackThorn Therapeutics, now Neumora Therapeutics, Inc., a publicly held biopharmaceutical company. He received his M.D. from the University of Cape Town, South Africa and his Ph.D. in Physiological Sciences from Oxford.

*Pascale Witz, MBA, MSc* has served on our Board of Directors since June 2017. Ms. Witz is the founder and since November 2016, the president of PWH Advisors, a consultancy firm advising management at life science companies and investment firms. From September 2015 through May 2016, Ms. Witz served as the Executive Vice President, Diabetes & Cardiovascular for Sanofi, S.A. (“Sanofi”). Prior to that position, Ms. Witz served as the Executive Vice President, Global Divisions and Strategic Development, commencing in July 2013. During her tenure at Sanofi, she launched multiple medicines across three continents, and strengthened the pipeline through licensing and partnerships. From 2009 to 2013, Ms. Witz served as President and CEO of General Electric’s (“GE”) Pharmaceutical Diagnostics, an integrated Pharmaceutical organization. Ms. Witz joined GE Healthcare in 1996, where she held various positions of increasing responsibilities and lead global businesses based out of the USA, France and the UK. She formerly worked for Becton Dickinson Pharmaceutical Systems from 1991 to 1996. Ms. Witz has served on the board of Fresenius Medical Care AG & Co. KGaA, since May 2016 and Revvity, Inc. (formerly PerkinElmer, Inc.), since October 2017. Ms. Witz also served on the board of Horizon Pharma, from August 2017 until its acquisition by Amgen, Inc. in October 2023, TESARO, Inc., from May 2018 until its acquisition by GlaxoSmithKline plc in January 2019 and from May 2016 to April 2018, served on the board of Savencia SA. Ms. Witz received her MBA from INSEAD, Fontainebleau, France and her M.S. in Biochemistry from the Institut National des Sciences Appliquées (INSA), Lyon, France. She was also a Ph.D. student in Molecular Biology at the Centre National de la Recherche Scientifique, Strasbourg, France.

**Item 11. Executive Compensation**

The information required by this item will be set forth in the sections headed “Executive Compensation” and “Director Compensation” in our Proxy Statement and is incorporated herein by reference.

**Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters**

The information required by this item will be set forth under the heading “Security Ownership of Certain Beneficial Owners and Management” in our Proxy Statement and is incorporated herein by reference.

The information required by Item 201(d) of Regulation S-K will be set forth in the section headed “Equity Compensation Plan Information” in our Proxy Statement and is incorporated herein by reference.

**Item 13. Certain Relationships and Related Transactions and Director Independence**

The information required by this item will be set forth in the section headed “Transactions With Related Persons” and “Independence of the Board of Directors” in our Proxy Statement and is incorporated herein by reference.

**Item 14. Principal Accounting Fees and Services**

The information required by this item will be set forth in the section headed “Ratification of Selection of Independent Registered Public Accounting Firm” in our Proxy Statement and is incorporated herein by reference.

**PART IV**

**Item 15. Exhibits, Financial Statement Schedules**

*Financial Statements.* We have filed the following financial statements with this Annual Report:

	<u>Page Number</u>
Report of Independent Registered Public Accounting Firm (PCAOB ID: 42)	58
Balance Sheets	59
Statements of Operations and Comprehensive Loss	61
Statements of Stockholders' Equity	62
Statements of Cash Flows	63
Notes to Financial Statements	64

*Financial Statement Schedules.* All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

*Exhibits.*

<b>Exhibit Number</b>	<b>Description</b>
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 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 27, 2022).
3.5	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).
3.6	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).
3.7	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).
3.8	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).
3.9	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).
3.10	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).
3.11	Certificate of Designation of Preferences, Rights and Limitations of Class A-5 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 April 13, 2023).

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- 3.12 Certificate of Decrease of Class A-1 Convertible Preferred Stock, Class A-2 Convertible Preferred Stock and Class A-3 Convertible Preferred Stock.
- 3.13 Certificate of Designation of Preferences, Rights and Limitations of Class A-6 Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed with the SEC on March 14, 2024).
- 3.14 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, 3.10, 3.11, 3.12, 3.13 and 3.14.
- 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 August 11, 2022).
- 4.3 Description of Common Stock.
- 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 May 9, 2019).
- 4.5 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\* Form of Indemnity Agreement between the Registrant and its directors and officers (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012).
- 10.2\* Regulus Therapeutics Inc 2012 Equity Incentive Plan and Form of Stock Option Agreement and Form of Stock Option Grant Notice thereunder (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012).
- 10.3\* Non-Employee Director Compensation Policy, as amended (incorporated by reference to Exhibit 10.6 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on November 12, 2019).
- 10.4\* Regulus Therapeutics Inc. 2022 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on August 11, 2022).
- 10.5\* Regulus Therapeutics Inc. 2019 Equity Incentive Plan, as amended (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K (File No. 00135670), filed with the SEC on June 14, 2023).
- 10.6\* Form of Stock Option Grant Notice and Option Agreement under the Regulus Therapeutics Inc. 2019 Equity Incentive Plan (incorporated by reference to Exhibit 99.2 to the Registrant's Registration Statement on Form S-8 (Registration No. 333-233414, filed with the SEC on August 22, 2019).
- 10.7\* Form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement under the Regulus Therapeutics Inc. 2019 Equity Incentive Plan (incorporated by reference to Exhibit 99.3 to the Registrant's Registration Statement on Form S-8 (Registration No. 333-233414, filed with the SEC on August 22, 2019).
- 10.8\* Regulus Therapeutics Inc. 2021 Inducement Plan, as amended (incorporated by reference to Exhibit 99.5 to the Registrant's Registration Statement on Form S-8 (File No. 333-276484, filed with the SEC on January 12, 2024).
- 10.9\* Form of Stock Option Grant Notice, Form of Option Agreement and Notice of Exercise under the Regulus Therapeutics Inc. 2021 Inducement Plan (incorporated by reference to Exhibit 99.6 to the Registrant's Registration Statement on Form S-8 (File No. 333-269184), filed with the SEC on January 11, 2023).

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- 10.10\* Employment Agreement, effective January 1, 2016, by and between the Registrant and Joseph P. Hagan (incorporated by reference to Exhibit 10.10 to the Registrant's Annual Report on Form 10-K (File No. 001-35670), filed with the SEC on February 23, 2016).
- 10.11\* Employment Agreement between the Registrant and Christopher Aker, dated July 24, 2018 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on May 10, 2019).
- 10.12\* Employment Agreement between the Registrant and Cris Calsada, dated August 30, 2019 (incorporated by reference to Exhibit 10.7 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on November 12, 2019).
- 10.13\* Employment Agreement, by and between the Registrant and Preston Klassen, M.D., dated June 12, 2023 (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on August 8, 2023).
- 10.14\* Joseph P. Hagan, Yearly Discretionary Base Salary Increase, effective January 1, 2024.
- 10.15\* Christopher Aker, Yearly Discretionary Base Salary Increase, effective January 1, 2024.
- 10.16\* Cris Calsada, Yearly Discretionary Base Salary Increase, effective January 1, 2024.
- 10.17\* Preston Klassen, Yearly Discretionary Base Salary Increase, effective January 1, 2024.
- 10.18† Amended and Restated License and Collaboration Agreement among the Registrant, Alnylam Pharmaceuticals, Inc. and Ionis Pharmaceuticals, Inc. (formerly known as Isis Pharmaceuticals, Inc.), dated January 1, 2009 (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on May 14, 2021).
- 10.19† Amendment Number One to the Amended and Restated License and Collaboration Agreement among the Registrant, Alnylam Pharmaceuticals, Inc. and Ionis Pharmaceuticals, Inc. (formerly known as Isis Pharmaceuticals, Inc.), dated June 10, 2010 (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on May 14, 2021).
- 10.20† Amendment Number Two to the Amended and Restated License and Collaboration Agreement among the Registrant, Alnylam Pharmaceuticals, Inc. and Ionis Pharmaceuticals, Inc. (formerly known as Isis Pharmaceuticals, Inc.), dated October 25, 2011 (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on May 14, 2021).
- 10.21† Amendment Number Three to the Amended and Restated License and Collaboration Agreement among the Company, Alnylam Pharmaceuticals, Inc. and Isis Pharmaceuticals, Inc., dated August 2, 2013 (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on May 14, 2021).
- 10.22 Assignment Agreement between the Registrant and Ionis Pharmaceuticals, Inc. (formerly known as Isis Pharmaceuticals, Inc.), dated July 13, 2009 (incorporated by reference to Exhibit 10.26 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012).
- 10.23 Loan and Security Agreement, dated June 17, 2016, by and between the Registrant and Oxford Finance LLC (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on August 3, 2016).
- 10.24 First Amendment to Loan and Security Agreement, dated October 4, 2017, by and between the Registrant and Oxford Finance LLC. (incorporated by reference to Exhibit 10.31 to the Registrant's Annual Report on Form 10-K (File No. 001-35670), filed with the SEC on March 8, 2018).
- 10.25†† Second Amendment to Loan and Security Agreement, dated March 6, 2018, by and between the Registrant and Oxford Finance LLC (incorporated by reference to Exhibit 10.30 to the Registrant's Annual Report on Form 10-K (File No. 001-35670), filed with the SEC on March 9, 2021).
- 10.26† Third Amendment to Loan and Security Agreement, dated August 6, 2018, by and between the Registrant and Oxford Finance LLC (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on November 9, 2018).

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10.27	Fourth Amendment to Loan and Security Agreement, dated November 5, 2018, by and between the Registrant and Oxford Finance LLC (incorporated by reference to Exhibit 10.37 to the Registrant's Annual Report on Form 10-K (File No. 001-35670), filed with the SEC on March 18, 2019).
10.28	Fifth Amendment to Loan and Security Agreement, dated January 31, 2019, by and between the Registrant and Oxford Finance LLC (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on February 1, 2019).
10.29	Sixth Amendment to Loan and Security Agreement, dated March 7, 2019, by and between the Registrant and Oxford Finance LLC (incorporated by reference to Exhibit 10.44 to the Registrant's Annual Report on Form 10-K (File No. 001-35670), filed with the SEC on March 18, 2019).
10.30	Seventh Amendment to Loan and Security Agreement, dated April 9, 2019, by and between the Registrant and Oxford Finance LLC (incorporated by reference to Exhibit 10.7 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on May 10, 2019).
10.31	Eighth Amendment to Loan and Security Agreement, dated May 3, 2019, by and between the Registrant and Oxford Finance LLC (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on May 9, 2019).
10.32	Ninth Amendment to Loan and Security Agreement, dated May 1, 2020, by and among the Registrant and Oxford Finance, LLC (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on May 14, 2020).
10.33	Tenth Amendment to Loan and Security Agreement, dated August 25, 2020, by and among the Registrant and Oxford Finance, LLC. (incorporated by reference to Exhibit 10.34 to the Registrant's Annual Report on Form 10-K (File No. 001-35670), filed with the SEC on March 23, 2023).
10.34	Eleventh Amendment to Loan and Security Agreement, dated December 31, 2021, by and between the Company and Oxford Finance LLC (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on January 5, 2022).
10.35	Amendment to Loan and Security Agreement, dated June 19, 2023, by and between the Company and Oxford Finance LLC (incorporated by reference to Exhibit 10.4 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on August 8, 2023).
10.36	Lease Agreement, dated February 11, 2021, by and between the Registrant and ARE-SD Region No. 44 LLC (incorporated by reference to Exhibit 10.44 to the Registrant's Annual Report on Form 10-K (File No. 001-35670), filed with the SEC on March 9, 2021).
10.37	Assignment and Assumption of Lease, dated February 11, 2021, by and between the Registrant and Turning Point Therapeutics, Inc. (incorporated by reference to Exhibit 10.45 to the Registrant's Annual Report on Form 10-K (File No. 001-35670), filed with the SEC on March 9, 2021).
10.38 <sup>Ω</sup>	Securities Purchase Agreement, dated March 11, 2024, by and among the Company and the Purchasers thereto (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed with the SEC on March 14, 2024).
23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney. Reference is made to the signature page hereto.
31.1	Certification of the Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
31.2	Certification of the Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
32.1**	Certification of the Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
97	Incentive Compensation Recoupment Policy.

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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	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibit 101. INS)

† We have received confidential treatment for certain portions of this agreement, which have been omitted and filed separately with the SEC pursuant to Rule 406 under the Securities Act of 1933, as amended, or Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

†† Certain portions of this exhibit (indicated by “[\*\*\*]”) have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

Ω Schedules and exhibits have been omitted pursuant to Item 601(a)(5) of Regulation S-K.

\* Indicates management contract or compensatory plan.

\*\* This certification is being furnished solely to accompany this annual report pursuant to 18 U.S.C. Section 1350, and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934 and is 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.

### **Item 16. Form 10-K Summary**

None.

## **SIGNATURES**

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

Date: March 21, 2024

Regulus Therapeutics Inc.

By: /s/ Joseph P. Hagan  
Joseph P. Hagan  
Chief Executive Officer  
(Principal Executive Officer)

## **POWER OF ATTORNEY**

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Joseph P. Hagan and Cris Calsada as his or her true and lawful attorneys-in-fact, and each of them, with full power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or

could do in person, hereby ratifying and confirming all that said attorneys-in-fact, and either of them, or his or her or their substitute or substitutes may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Joseph P. Hagan</u> Joseph P. Hagan	Chief Executive Officer and Director (Principal Executive Officer)	March 21, 2024
<u>/s/ Cris Calsada</u> Cris Calsada	Chief Financial Officer (Principal Financial Officer)	March 21, 2024
<u>/s/ Daniel J. Penksa</u> Daniel J. Penksa	Vice President, Finance & Controller (Principal Accounting Officer)	March 21, 2024
<u>/s/ Stelios Papadopoulos</u> Stelios Papadopoulos, Ph.D.	Chairman of the Board of Directors	March 21, 2024
<u>/s/ David Baltimore</u> David Baltimore, Ph.D.	Director	March 21, 2024
<u>/s/ Kathryn Collier</u> Kathryn Collier	Director	March 21, 2024
<u>/s/ Alice Huang</u> Alice Huang, Ph.D.	Director	March 21, 2024
<u>/s/ Preston Klassen</u> Preston Klassen, M.D.	Director	March 21, 2024
<u>/s/ Jake R. Nunn</u> Jake R. Nunn	Director	March 21, 2024
<u>/s/ William H. Rastetter</u> William H. Rastetter, Ph.D.	Director	March 21, 2024
<u>/s/ Hugh Rosen</u> Hugh Rosen, M.D., Ph.D.	Director	March 21, 2024
<u>/s/ Pascale Witz</u> Pascale Witz	Director	March 21, 2024