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

FORM 10-K

(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, 2019

or

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

FOR THE TRANSITION PERIOD FROM _____ TO _____

Commission file number: 001-35670

Regulus Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)

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

10628 Science Center Drive, Suite 225
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 ☐

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

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

As of June 28, 2019, 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 \$24.3 million, based on the closing price of the registrant’s common stock on the Nasdaq Stock Market on June 28, 2019 of \$1.25 per share.

The number of outstanding shares of the registrant’s common stock, par value \$0.001 per share, as of March 6, 2020 was 21,040,118.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant’s proxy statement to be filed with the Securities and Exchange Commission pursuant on Schedule 14A in connection with the registrant’s 2020 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 not later than April 29, 2020.

**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 and Switzerland. We use “microMarkers” as a service mark in the United States and other countries. We have registered this service mark in the United States. All other product and company names are trademarks of their respective companies.

PART I

Forward-Looking Statements

This Annual Report on Form 10-K and the documents incorporated by reference herein may contain “forward-looking statements” within the meaning of the federal securities laws made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth below under Part 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;
- the potential election of any strategic collaboration partner to pursue development and commercialization of any programs or product candidates that are subject to a collaboration with such partner;
- our ability to attract collaborators with relevant development, regulatory and commercialization expertise;
- future activities to be undertaken by our strategic collaboration partners, collaborators and other third parties;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our ability to successfully commercialize, and our expectations regarding future therapeutic and commercial potential with respect to, our product candidates;
- the rate and degree of market acceptance of our product candidates;
- our ability to develop sales and marketing capabilities, whether alone or with potential future collaborators;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party suppliers and manufacturers;
- the success of competing therapies that are or may become available;
- the loss of key scientific or management personnel;
- our ability to successfully secure and deploy capital;
- our ability to satisfy our debt obligations;
- the accuracy of our estimates regarding future expenses, future revenues, capital requirements and need for additional financing; 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

Overview

We are a clinical-stage biopharmaceutical company focused on discovering and developing first-in-class drugs targeting *micro*RNAs to treat diseases with significant unmet medical need. We were formed in 2007 when Alnylam Pharmaceuticals, Inc. (“Alnylam”) and Ionis Pharmaceuticals, Inc. (“Ionis”) contributed significant intellectual property, know-how and financial and human capital to pursue the development of drugs targeting *micro*RNAs pursuant to a license and collaboration agreement. Our most advanced product candidates are RG-012 and RGLS4326. RG-012 is an anti-miR targeting miR-21 for the treatment of Alport syndrome, a life-threatening kidney disease with no approved therapy available. In November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program, to Sanofi. As a result, Sanofi became responsible for all costs incurred in the development of our miR

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programs. The transition activities were completed in the second quarter of 2019. RGLS4326 is an anti-miR targeting miR-17 for the treatment of autosomal dominant polycystic kidney disease ("ADPKD"). In addition to these clinical programs, we continue to develop a pipeline of preclinical drug product candidates.

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

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

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

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

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

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

Since our inception through December 31, 2019, we have received \$342.5 million from the sale of our equity and convertible debt securities, \$91.8 million from our collaborations, principally from upfront payments, research funding and preclinical and clinical milestones, and \$19.8 million in net proceeds from our Term Loan. As of December 31, 2019, we had cash and cash equivalents of \$34.1 million.

Development Stage Pipeline

We currently have two programs in clinical development.

RG-012: In May 2017, we completed a Phase 1 multiple-ascending dose ("MAD") clinical trial in 24 healthy volunteers (six-week repeat dosing) to determine safety, tolerability and pharmacokinetics ("PK") of RG-012 prior to chronic dosing in patients. In Phase 1 clinical trials to date, RG-012 was well-tolerated, and there were no serious adverse events ("SAEs") reported. In the third quarter of 2017, we initiated HERA, a Phase 2 randomized (1:1), double-blinded, placebo-controlled clinical trial evaluating the safety and efficacy of RG-012 in 40 Alport syndrome patients. In parallel, a renal biopsy study was

also initiated in the third quarter of 2017 to evaluate RG-012 renal tissue PK, target engagement and downstream effects on genomic disease biomarkers. In December 2017, we concluded our global ATHENA natural history of disease study. Kidney tissue concentrations were achieved in biopsy patients that would be predictive of therapeutic benefit based on animal disease models. In addition, modulation of the target, miR-21, was observed. RG-012 has received orphan designation in both the United States and Europe. In November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program to Sanofi. As a result, Sanofi became responsible for all costs incurred in the development of these miR-21 programs. The transition activities, including the transfer of the investigational new drug application ("IND"), were completed in the second quarter of 2019. Sanofi is currently enrolling patients into a Phase 2 clinical trial.

RGLS4326: RGLS4326 is a novel oligonucleotide designed to inhibit miR-17 using a unique chemistry designed to preferentially deliver to the kidney. Preclinical studies with RGLS4326 have demonstrated a reduction in kidney cyst formation, improved kidney weight/body weight ratio, decreased cyst cell proliferation and preserved kidney function in mouse models of ADPKD. In March 2018, we completed dose escalation of a Phase 1 single ascending dose ("SAD") clinical trial in healthy volunteers and found RGLS4326 was well tolerated and no SAEs were reported. In April 2018, we initiated a Phase 1 randomized, double-blind, placebo-controlled, MAD clinical trial in healthy volunteers designed to characterize the safety, tolerability, PK and pharmacodynamics of multiple doses of RGLS4326. In July 2018, we voluntarily paused this study due to unexpected observations in our 27-week mouse chronic toxicity study, which was designed to support the Phase 2 proof-of-concept clinical trial in ADPKD previously planned to start in mid-2019. The observations in the mouse chronic toxicity study were unexpected, given the favorable safety profile of RGLS4326 in previous 7-week non-GLP and GLP toxicity studies in mouse and non-human primates required for Phase 1 testing, which had no significant findings across similar dose levels and frequencies. In September 2018, we initiated a new mouse chronic toxicity study with several changes believed to address the unexpected findings in the earlier terminated chronic mouse toxicity study. In January 2019, we announced data from a planned interim analysis of this study after 13 weeks of dosing in which no adverse or other significant findings across the range of doses tested were shown.

In January 2019, we submitted a comprehensive data package for RGLS4326 to the U.S. Food and Drug Administration ("FDA") that included the results from the planned 13-week interim analysis of the ongoing repeat mouse chronic toxicity study, as well as results from additional investigations, analytical testing, additional data from the previously terminated mouse chronic toxicity study, data from the completed Phase 1 SAD study and data from the first cohort of the Phase 1 MAD study to support our plan to resume the Phase 1 MAD study. In July 2019, FDA notified us of additional nonclinical data requirements and placed the IND on a partial clinical hold, formalizing the specific requirements to re-initiate the MAD study and further proceed into studies of extended duration. The additional data requirements were outlined in two parts. In order to resume the MAD study, FDA requested the final reports from the chronic toxicity studies in both mice and non-human primates and satisfactory related analyses to ensure subjects can be safely dosed. In November 2019, we submitted a complete response to the partial clinical hold in order to be able to resume the MAD study and in December 2019, FDA lifted the partial clinical hold on the MAD study. We recommenced the MAD study in February 2020. We remain on partial clinical hold with FDA with respect to RGLS4326 extended duration studies. Information from the clinical studies, together with information from additional nonclinical studies, will be used to address the requirements to support studies of extended duration. In addition to the MAD study in healthy volunteers, we plan to conduct a Phase 1b study in patients with ADPKD in the second half of 2020 to evaluate RGLS4326 for safety, PK, and biomarkers of pharmacodynamic activity.

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 and kidney. We also have early discovery programs investigating additional *micro*RNA targets for infectious diseases, immunology and indications for which there is *micro*RNA dysregulation or in disease settings where the host *micro*RNAs are essential for the replication and/or survival of the pathogen.

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

Glioblastoma multiforme program: In January 2019, we announced RGLS5579 as a clinical candidate in our glioblastoma multiforme ("GBM") program. RGLS5579, which targets *micro*RNA-10b, demonstrated statistically significant improvements in survival as both a monotherapy as well as in combination with temozolamide ("TMZ") in an orthotopic GBM animal model. In combination with TMZ, the addition of a single dose of anti-mir-10b, delivered intracranially, led to a more than two-fold improvement in survival compared to TMZ alone. These, and additional survival data on RGLS5579, were

presented in November 2018 at the Society for Neuro-Oncology Meeting in New Orleans, Louisiana. We plan to seek a partner to further advance development of RGLS5579.

Hepatitis B virus program: We have determined that advancing our preclinical programs targeting the Hepatitis B virus ("HBV") represents an attractive opportunity in our pipeline for investment, affecting an estimated 250 million people worldwide. We have identified several microRNA targets that serve as host factors for the virus. Our lead compound directed to one of the host microRNAs has demonstrated sub-nanomolar potency against HBV DNA replication and more than 95% reduction in Hepatitis B surface antigen in *in vitro* studies. Additionally, we have demonstrated reduction of both HBV DNA and surface antigen in an *in vivo* efficacy model. We believe that targeting a host factor in the liver represents a unique mechanism of action for treatment of the virus compared to other programs in development and holds the potential for achieving a functional cure.

Non-Alcoholic Steatohepatitis program: Across multiple animal models of non-alcoholic steatohepatitis ("NASH"), our lead candidate has demonstrated improvement in key endpoints, including NAFLD Activity Score (NAS), liver transaminases, hyperglycemia, and disease-related gene expression. In the diet-induced NASH mouse model (Amylin model) after two to four weekly doses, early onset of improvement across multiple disease parameters including liver triglycerides and blood levels of transaminases was observed. After nine weeks of treatment, there was evidence of sustained benefit with significant improvement of liver fibrosis and hyperglycemia compared to control-treated animals. We believe that targeting dysregulated *microRNA* in a complex disease like NASH may offer a unique mechanism of action from other programs in development. We plan to seek a partner to further advance its development.

Our *microRNA* product platform

We believe we are the leading company in the field of *microRNA* 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 *microRNA* product platform:

- a mature platform selectively producing multiple development candidates advancing to the clinic;
- scientific advisors who are pioneers in the *microRNA* 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 *microRNA* intellectual property estate with patents and patent applications covering compositions and therapeutic uses related to *microRNA* and *microRNA* 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 *microRNA* therapeutics;
- development expertise and financial resources provided by our strategic collaboration with Sanofi; and
- numerous academic collaborations that help us identify new *microRNA* targets and support our early stage discovery efforts.

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

Step 1 - Evaluation of microRNA therapeutic opportunities

The initiation of our *microRNA* 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 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 demonstrated the therapeutic benefit of inhibiting *microRNA*-122 in humans with RG-101 in HCV patients. In addition to these human proof-of-concept results, we have demonstrated therapeutic benefits of our anti-miRs in over 20 different preclinical models of human diseases.

We have identified and validated several *microRNA* targets across a number of disease categories and are working independently and with our strategic collaboration partner 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.



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Our strategy

The key elements of our strategy are to (i) build a meaningful clinical portfolio by advancing our current clinical programs and advancing our preclinical programs into clinical development; (ii) focus our resources on developing drugs for indications that represent significant unmet medical need and where the development and commercialization activities 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.

Strategic Collaboration

- In June 2010, we formed a strategic collaboration with Sanofi to discover and develop *microRNA* therapeutics for fibrotic diseases. In July 2012, we expanded the collaboration to include potential *microRNA* therapeutics in oncology. The original research term for this strategic collaboration expired in June 2013, upon which we and Sanofi entered into an option agreement pursuant to which we granted Sanofi an exclusive right to negotiate the co-development and commercialization of certain of our unencumbered *microRNA* programs, for which Sanofi paid us an upfront option fee of \$2.5 million. In addition, Sanofi granted us an exclusive option to negotiate the co-development and commercialization of miR-21. In February 2014, we and Sanofi extended our strategic collaboration and Sanofi concurrently made a \$10.0 million investment in our common stock. Under those terms of our extended collaboration, Sanofi had opt-in rights to our RG-012 clinical fibrosis program targeting miR-21 for the treatment of Alport syndrome, our preclinical program targeting miR-21 for hepatocellular carcinoma ("HCC") and kidney fibrosis, and has opt-in rights to our preclinical programs targeting miR-221/222 for oncology indications.

In November 2018, we amended our collaboration and license agreement with Sanofi. Under the terms of the amendment, we granted Sanofi a worldwide, royalty-free, fee-bearing, exclusive license, with the right to sublicense, under our know-how and patents to develop and commercialize miR-21 compounds and products, including RG-012, for all indications, including Alport syndrome. Pursuant to the terms of the amended agreement, Sanofi agreed to assume all responsibilities and obligations for developing and commercializing each of our miR-21 programs, including RG-012, which is currently enrolling in Phase 2 for Alport syndrome, including our obligations regarding the administration and expense of clinical trials and all other costs, including in-license royalties and other in-license payments, related to our miR-21 programs. We have received approximately \$6.8 million in upfront payments and payment for program-related materials. We are also eligible to receive up to \$40.0 million in development milestone payments, including a \$10.0 million payment for an interim enrollment milestone. In addition, Sanofi agreed to reimburse us for certain out-of-pocket expenses associated with transition activities and assume our upstream license royalty obligations.

- We will continue to be responsible for our preclinical program targeting miR-221/222 for oncology indications. If Sanofi chooses to exercise its option on the miR-221/222 program, Sanofi will reimburse us for a significant portion of our preclinical and clinical development costs and will also pay us an option exercise fee for any such program, provided that \$1.25 million of the \$2.5 million upfront option fee paid to us by Sanofi in connection with the June 2013 option agreement will be creditable against such option exercise fee. In addition, we will be eligible to receive clinical and regulatory milestone payments under this program and potentially commercial milestone payments. We will also be eligible to receive royalties on miR-221/222 products commercialized by Sanofi and have the right to co-promote these products. Under our collaboration and license agreement with Sanofi, we are eligible to receive up to approximately \$209.0 million in aggregate milestone payments upon successful commercialization of *microRNA* therapeutics, in addition to royalties on net sales for the miR-221/222 program. These payments include up to \$79.0 million upon achievement of preclinical and clinical development milestones, up to \$70.0 million upon achievement of regulatory milestones and up to \$60.0 million upon achievement of commercialization milestones.

For additional information, see Note 5 to our financial statements under Item 8 of Part II of this Annual Report.

Our Intellectual Property and Technology Licenses

Intellectual property

We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking and maintaining patents intended to cover our products and compositions, their methods of use and any other

inventions that are important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Our objective is to continue to expand our intellectual property estate through our multiple layer approach in order to protect our *microRNA* therapeutics and to maintain our leading position in the *microRNA* therapeutics field.

We believe that we have a leading intellectual property position relating to the development and commercialization of *microRNA* therapeutics, composed of:

- approximately 145 patents and patent applications that we own or have in-licensed from academic institutions related to *microRNA* and *microRNA* drug products; and
- numerous patents and patent applications exclusively licensed from our founding companies, Alnylam and Ionis, related to RNA technologies, including patent and patent applications relating to chemical modification of oligonucleotides that are useful for *microRNA* therapeutics, including chemical modifications incorporated into our clinical candidates.

Our portfolio of exclusively and jointly owned patent and patent applications is currently composed of approximately 145 U.S. and foreign patents and patent applications with claims to compositions-of-matter or methods related to our *microRNA* drug products and *microRNA* product platform. Based on the patents and patents that may issue from pending applications within our portfolio, patent protection for our *microRNA* drug products and their methods of use is currently expected to expire between 2024 and 2039.

Our founding companies, Alnylam and Ionis, each own or otherwise have rights to numerous patents and patent applications concerning oligonucleotide technologies and a substantial number of these patents and applications have been exclusively licensed to us for use in the *microRNA* field. The technologies covered in these patents and applications include various chemical modifications that are applicable to *microRNA* therapeutics. Due to patent expiration and strategic patent portfolio decisions, the total number licensed to us will fluctuate from year to year. Among the licensed patents or patent applications, those covering key chemical modifications for use in *microRNA* drug products are currently expected to expire in 2023, 2027 and 2029.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing the non-provisional application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office ("U.S. PTO") in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent.

The term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration of a U.S. patent as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the 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 *micro*RNA 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 one of our collaboration partners 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, 2019 and 2018.

In February 2015, we entered into a letter agreement with Alnylam Pharmaceuticals, Inc. ("Alnylam") pursuant to which we and Alnylam agreed to the financial terms for certain technology acquired by Alnylam within the licensed patent rights under our Amended and Restated License and Collaboration Agreement (the "Additional Patent Rights") with Alnylam and

Ionis. In addition to any royalties payable by us to Alnylam pursuant to the terms of the Amended and Restated License and Collaboration Agreement, we agreed to pay Alnylam an additional low single-digit royalty on net sales of certain products utilizing the Additional Patent Rights, with the exact royalty percentage payable being dependent on the total amount of net sales during the calendar year. We also agreed to pay Alnylam milestone payments on certain products utilizing the additional patent rights of up to \$33.0 million per product upon the achievement of certain regulatory milestone events. There was no activity under this agreement for the year ended December 31, 2019.

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.

Other Licenses

We also previously held technology licenses with Max Planck related to various targets and with the University of Würzburg, which encompassed the use of anti-miR therapeutics targeting miR-21 for the treatment of fibrosis, including kidney, liver, lung and cardiac fibrosis. As part of our amendment with Sanofi in November 2018, these licenses were assigned to Sanofi and we no longer consider the technology licenses to be material to our business.

We also previously held an exclusive license from Stanford University to patent rights concerning the use of anti-miR therapeutics targeting miR-122 for the treatment of HCV infection, and an exclusive license from ETH Zürich to patent rights related to the use of anti-miR therapeutics targeting miR-103/107 for the treatment of metabolic disorders, including type 2 diabetes. These licenses were terminated in 2019 and we no longer consider the licensed patent rights to be material to our business.

Manufacturing

We contract with third parties to manufacture our compounds 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 *microRNA* field provide us with competitive advantages, we face potential competition from many different sources, including larger and better-funded pharmaceutical companies. Not only must we compete with other companies that are focused on *microRNA* therapeutics, but 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 *microRNA* therapeutics, there are other biotechnology companies that will compete against us by applying marketed products and development programs using technology other than *microRNA* 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.

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 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. For example, our RG-012 drug candidate to treat Alport syndrome has received orphan drug designation in both the United States and Europe. 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 European Union.

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.

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 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.

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.

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 our 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. Our strategic collaboration partners may also utilize third parties for some or all of a product we are developing 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:

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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. Other 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 and the narrowness of the federal Anti-Kickback Statute’s exceptions and safe harbors, 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 regulation by both the federal government and the states 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 individually identifiable health information. 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, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. The recently adopted European General Data Protection Regulation (“GDPR”) contains new provisions specifically directed at the processing of health information, higher sanctions and extra-territoriality measures that are intended to bring non-EU companies under the data security and privacy legal framework specified in the regulation. We anticipate that over time we may expand our business operations to include operations in the EU, including potentially conducting preclinical and clinical trials. With such expansion, we would be subject to increased governmental regulation in the EU countries in which we might operate, including the GDPR.

Additionally, California recently enacted legislation that has been dubbed the first “GDPR-like” law in the United States. Known as the California Consumer Privacy Act (“CCPA”), it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of

consumers or households. The CCPA, which went into effect on January 1, 2020, requires covered companies to provide new disclosures to California consumers, provides such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. The CCPA may impact (possibly significantly) our business activities and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information.

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, as defined by such law, 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.

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. Among the provisions of the ACA of greatest importance to the pharmaceutical and biotechnology industry are the following:

- implemented an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- increased the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- created a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts to 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;
- extended manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expanded the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- implemented a requirement to annually report drug samples that manufacturers and distributors provide to physicians;
- created a licensure framework for follow-on biologic products;
- 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 & Medicaid 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. Since January 2017, President Trump has signed two 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. Concurrently, Congress has considered legislation that would repeal or 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 eliminates the health insurer tax. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace the ACA 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, will remain in effect through 2029 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and federal and state legislative activity designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. For example, at the federal level, the Trump administration's budget proposal for fiscal year 2020 contains further drug price control measures that could be enacted during the budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. In addition, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services ("HHS") has solicited feedback on some of these measures and, at the same, has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. While some of these and other measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing.

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 our 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 our 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 European Union, 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 European Union regulatory systems, we or our strategic collaboration partners must submit a marketing authorization application. The application in the United States is similar to that required in the European Union, with the exception of, among other things, country-specific document requirements.

For other countries outside of the European Union, 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 our 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, 2019, we had 21 employees, all of which were full-time employees. Of these employees, 14 employees are engaged in research and development activities and 7 employees are engaged in finance, legal, human resources, facilities and general management. We have no collective bargaining agreements with our employees and we have not experienced any work stoppages.

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

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

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

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

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

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

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

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

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

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

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

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of product candidates, we or a collaboration partner must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical trials are expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for their products.

Events which may result in a delay or unsuccessful completion of clinical development include:

- delays in reaching an agreement with the FDA or other regulatory authorities on final trial design;
- imposition of a clinical hold of our clinical trial operations or trial sites by the FDA or other regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- our inability to adhere to clinical trial requirements directly or with third parties such as CROs;
- delays in obtaining required institutional review board approval at each clinical trial site;
- delays in recruiting suitable patients to participate in a trial;
- delays in the testing, validation, manufacturing and delivery of the product candidates to the clinical sites;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- delays caused by patients dropping out of a trial due to protocol procedures or requirements, product side effects or disease progression;
- clinical sites dropping out of a trial to the detriment of enrollment;
- time required to add new clinical sites; or
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials.

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

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

- be delayed in obtaining marketing approval for our future product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as originally intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

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

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

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

If AEs are observed in any clinical trials of our product candidates, including those that a collaboration partner may develop under an agreement with us, our or our collaboration partners' ability to obtain regulatory approval for product candidates may be negatively impacted.

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

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

Any of these events could prevent us or our collaboration partners from achieving or maintaining market acceptance of the affected product and could substantially increase the costs of commercializing our future products and impair our ability to generate revenues from the commercialization of these products either on our own or with a collaboration partner.

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

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

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

Even if we obtain regulatory approval in the United States, the FDA may still impose significant restrictions on the indicated uses or marketing of our product candidates, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. The holder of an approved NDA is obligated to monitor and report AEs and any failure of a product to meet the specifications in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

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

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

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

Moreover, the FDA closely regulates the marketing, labeling, advertising and promotion of pharmaceutical products. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. Companies may also share truthful and not misleading information that is otherwise consistent with the labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in significant civil, criminal and administrative penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. 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, our existing strategy is to pursue collaboration agreements for the development and commercialization of our programs and potential product candidates in indications with potentially large commercial markets such as ADPKD, HCC, fibrosis, HCV, and HBV, while focusing our internal development resources and any internal sales and marketing organization that we may establish on research programs and product candidates for selected markets, such as orphan diseases. As a result, we may forego or delay pursuit of opportunities with other programs or product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

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

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

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

RISKS RELATED TO OUR FINANCIAL CONDITION AND NEED FOR ADDITIONAL CAPITAL

We will need to raise additional capital, and if we are unable to do so when needed, we will not be able to continue as a going concern.

This Form 10-K includes disclosures regarding management's assessment of our ability to continue as a going concern as our current liquidity position and recurring losses from operations since inception and negative cash flows from operating activities raise substantial doubt about our ability to continue as a going concern. As of December 31, 2019, we had approximately \$34.1 million of cash and cash equivalents and we had \$16.5 million of outstanding debt obligations (which includes \$14.6 million of outstanding principal and \$1.9 million of final payment and loan amendment fees) under our \$20.0 million term loan ("Term Loan") with Oxford Finance, LLC ("Oxford" or the "Lender"), which we borrowed under a loan and security agreement with Oxford dated June 2016 (as amended, the "Loan Agreement"). We will need to raise additional capital to fund our operations and service our debt obligations, and if we are unable to raise additional capital when needed, we will not be able to continue as a going concern.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. We expect our research and development expenses to substantially increase in connection with our ongoing activities, particularly as we advance our product candidates towards or through clinical trials. We will need to raise additional capital to fund our operations and such funding may not be available to us on acceptable terms, or at all.

Additionally, our collaboration partners may not elect to pursue the development and commercialization of any of our *microRNA* product candidates that are subject to their respective collaboration agreements with us. Any of these events may increase our development costs more than we expect. In November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program, to Sanofi, which will be responsible for all costs incurred in the development of our miR-21 programs. As a result, we will not receive royalties in the event our miR-21 programs are eventually commercialized and will also receive significantly reduced milestones for these programs. We may need to raise additional capital or otherwise obtain funding through additional collaborations if we choose to initiate clinical trials for new product candidates other than programs currently partnered. In any event, we will require additional capital to obtain regulatory approval for, and to commercialize, future product candidates.

For the foreseeable future, we expect to rely primarily on equity and/or debt financings to fund our operations. Raising additional capital through the sale of securities could cause significant dilution to our stockholders. For example, in May 2019, we completed the initial closing of a private placement under a Securities Purchase Agreement between us and various investors (the "May 2019 SPA"), pursuant to which we sold and issued (i) 9,730,534 shares of common stock and accompanying warrants to purchase up to an aggregate of 9,730,534 shares of common stock at a combined purchase price of \$1.205 per share, and (ii) 415,898 shares of non-voting Class A-1 convertible preferred stock, in lieu of shares of common stock, at a price of \$10.80 per share, and accompanying warrants to purchase an aggregate of 4,158,980 shares of common stock at a price of \$0.125 for each share of common stock underlying such warrants. Each share of non-voting Class A-1 convertible preferred stock is convertible into 10 shares of common stock, subject to certain beneficial ownership conversion limitations. The warrants are exercisable for a period of five years following the date of issuance and have an exercise price of

\$1.08 per share, subject to proportional adjustments in the event of stock splits or combinations or similar events. In December 2019, following our announcement of our plan to recommence our Phase 1 MAD clinical trial of RGLS4326 in the first quarter of 2020, we completed a second and final closing under the May 2019 SPA (the “Milestone Closing”), pursuant to which we sold and issued (i) 3,288,390 shares of non-voting Class A-2 convertible preferred stock, in lieu of shares of common stock, at a price of \$6.66 per share, and accompanying warrants to purchase an aggregate of 32,883,900 shares of common stock at a price of \$0.125 for each share of common stock underlying such warrants. Each share of the non-voting Class A-2 convertible preferred stock is convertible into 10 shares of common stock, subject to certain beneficial ownership conversion limitations. The warrants are exercisable for a period of five years following the date of issuance and have an exercise price of \$0.666 per share, pursuant to proportional adjustments in the event of stock splits or combinations or similar events. Current stockholders may be diluted by the exercise of the warrants and/or the conversion of the convertible preferred stock issued under the May 2019 SPA. 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 and security agreement with Oxford (the “Loan Agreement”). Under the terms of the Loan Agreement, Oxford provided us with a term loan of \$20.0 million (“Term Loan”). Our obligations under the Loan Agreement are secured by a first priority security interest in substantially all of our current and future assets, except for the assets that were licensed, assigned and transferred to Sanofi pursuant to a November 2018 amendment (the “2018 Sanofi Amendment”) to our collaboration and license agreement with Sanofi dated February 4, 2014 (the “Sanofi License Agreement”) that modify the parties’ rights and obligations with respect to our miR-21 programs, including our RG-012 program, provided that Oxford will continue to have liens on all proceeds received by us pursuant to the Sanofi License Agreement. We have also agreed not to encumber our intellectual property assets, except as permitted by the Loan Agreement.

As a result of our completion of the Milestone Closing under the May 2019 SPA, our required monthly payments to the Lender are comprised of interest only through and including the payment to be made in April 2021. Commencing in May 2021, and continuing on each successive payment date thereafter, we are required to make consecutive equal monthly payments of principal, together with applicable interest, in arrears, to the Lender. In the event we receive the \$10.0 million first development milestone payment (the “Milestone Payment”) under the 2018 Sanofi Amendment, we will be required to use 100% of the Milestone Payment to partially prepay the Term Loan. Upon payment of the Milestone Payment to the Lender, we will no longer be required to maintain cash in a collateral account controlled by Lender and the lien on our intellectual property will be released.

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

Under the Term Loan, our interest rate on borrowed amounts is dependent on LIBOR. LIBOR, which is the basic rate of interest used in lending between banks on the London interbank market and is widely used as a reference for setting the interest rate on loans globally, is currently scheduled to be phased out in 2021. Before LIBOR is phased out, we may need to renegotiate the Term Loan to replace LIBOR with a new standard, which has yet to be established. The consequences of these

developments cannot be entirely predicted, but could result in higher interest rates on our outstanding principal amount under the Term Loan. We cannot provide assurance that future interest rate changes will not have a material negative impact on our business, financial position, or operating results.

The Loan Agreement requires us, and any debt arrangements we may enter into in the future may require us, to comply with various covenants that limit our ability to, among other things:

- dispose of assets;
- complete mergers or acquisitions;
- incur indebtedness;
- encumber assets;
- pay dividends or make other distributions to holders of our capital stock;
- make specified investments; and
- engage in transactions with our affiliates.

These restrictions could inhibit our ability to pursue our business strategies. If we default under our obligations under the Loan Agreement, the lender could proceed against the collateral granted to it to secure our indebtedness or declare all obligation under the Loan Agreement to be due and payable. In certain circumstances, procedures by the lenders could result in a loss by us of all of our equipment and inventory, which are included in the collateral granted to the lenders. If any indebtedness under the Loan Agreement were to be accelerated, there can be no assurance that our assets would be sufficient to repay in full that indebtedness. In addition, upon any distribution of assets pursuant to any liquidation, insolvency, dissolution, reorganization or similar proceeding, the holders of secured indebtedness will be entitled to receive payment in full from the proceeds of the collateral securing our secured indebtedness before the holders of other indebtedness or our common stock will be entitled to receive any distribution with respect thereto.

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

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

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

We have incurred losses in each year since our inception in September 2007. Our net losses were \$18.6 million and \$48.7 million for the years ended December 31, 2019 and 2018, respectively. As of December 31, 2019, we had an accumulated deficit of \$411.3 million.

We have devoted most of our financial resources to research and development, including our preclinical and clinical development activities. To date, we have financed our operations primarily through the sale of equity securities and convertible debt, through our Term Loan and from revenue received from our collaboration partners. We have a collaboration with Sanofi relating to the development of our miR-221/222 program for oncology indications. Under our collaboration and license agreement with Sanofi, Sanofi has an option to obtain exclusive worldwide licenses for the development, manufacture and commercialization of our preclinical program targeting miR-221/222 for HCC. If Sanofi exercises its option, it will assume responsibility for funding and conducting further clinical development and commercialization activities for such product candidate. However, if Sanofi does not exercise its option, we will be responsible for funding further development of the applicable product candidate and may not have the resources to do so unless we are able to enter into another collaboration for such product candidate. Pursuant to the 2018 Sanofi Amendment, we completed the transition of further development activities of our miR-21 programs, including our RG-012 program, to Sanofi, in the second quarter of 2019. As a result, Sanofi became responsible for all costs incurred in the development of our miR-21 programs.

The size of our future net losses will depend, in part, on the rate of future expenditures and our ability to obtain funding through equity or debt financings, collaborations or grants. We re-initiated clinical development of RGLS4326 for the treatment of ADPKD. We had also initiated clinical development of RG-012, which we subsequently transferred to Sanofi, and it will be several years, if ever, before Sanofi has a product candidate ready for commercialization. Even if we or a collaboration partner successfully obtains regulatory approval to market a product candidate, our revenues will also depend upon the size of any markets in which our product candidates have received market approval, and our ability to achieve sufficient market acceptance and adequate market share for our products.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we: continue our research and preclinical and clinical development of our product candidates, both independently and under our collaboration agreements; seek to identify additional *micro*RNA targets and product candidates; acquire or in-license other products and technologies; continue with clinical development of our product candidates; seek marketing approvals for our product candidates that successfully complete clinical trials; ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval; maintain, expand and protect our intellectual property portfolio; hire additional clinical, regulatory, research and administrative personnel; and create additional infrastructure to support our operations and our product development and planned future commercialization efforts.

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

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

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

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

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

RISKS RELATED TO OUR RELIANCE ON THIRD PARTIES

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

We are likely to depend upon third party collaboration partners for financial and scientific resources for the clinical development and commercialization of certain of our *micro*RNA product candidates. These collaborations will likely provide us with limited control over the course of development of a *micro*RNA product candidate, especially once a candidate has reached the stage of clinical development. For example, in our strategic collaboration with Sanofi, Sanofi has the option to obtain an exclusive worldwide license to develop, manufacture and commercialize our preclinical program targeting miR-221/222 for

HCC upon the achievement of relevant endpoints in clinical trials. However, Sanofi is not under any obligation to exercise this option. While Sanofi has development obligations with respect to programs that it may elect to pursue under our agreement, our ability to ultimately recognize revenue from this and future relationships will depend upon the ability and willingness of our collaboration partners to successfully meet their respective responsibilities under our agreements with them. In November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program, to Sanofi. As a result, Sanofi became responsible for all costs incurred in the development of our miR-21 program, but we will not receive royalties in the event our miR-21 programs are eventually commercialized, and the milestone payments we are eligible to receive for these programs has been significantly reduced.

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

- a collaboration partner may shift its priorities and resources away from our programs due to a change in business strategies, or a merger, acquisition, sale or downsizing of its company or business unit;
- a collaboration partner may cease development in therapeutic areas which are the subject of our collaborations;
- a collaboration partner may change the success criteria for a particular program or potential product candidate thereby delaying or ceasing development of such program or candidate;
- a significant delay in initiation of certain development activities by a collaboration partner will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- a collaboration partner could develop a product that competes, either directly or indirectly, with a collaboration product;
- a collaboration partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- a collaboration partner with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- a collaboration partner may exercise its rights under the agreement to terminate the collaboration;
- a dispute may arise between us and a collaboration partner concerning the research, development or commercialization of a program or product candidate resulting in a delay in milestones, royalty payments or termination of a program and possibly resulting in costly litigation or arbitration which may divert management attention and resources; and
- a collaboration partner may use our proprietary information or intellectual property in such a way as to invite litigation from a third party or fail to maintain or prosecute intellectual property rights such that our rights in such property are jeopardized.

Specifically, with respect to termination rights, Sanofi may terminate the entire collaboration or its current collaboration target program for any or no reason upon 30 days' written notice to us. The agreement with Sanofi may also be terminated by either party for material breach by the other party, including a failure to comply with such party's diligence obligations that remains uncured after 120 days. Depending on the timing of any such termination, we may not be entitled to receive the option exercise fees or milestone payments, as these payments terminate with termination of the respective program or agreement.

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

- under certain circumstances, we may owe Sanofi royalties with respect to product candidates covered by our agreement with Sanofi that we elect to continue to commercialize, depending upon the stage of development at which such product commercialization rights reverted back to us, or additional payments if we license such product candidates to third parties;
- product candidates subject to the Sanofi agreement, as applicable, may be terminated or significantly delayed;
- our cash expenditures could increase significantly if it is necessary for us to hire additional employees and allocate scarce resources to the development and commercialization of product candidates that were previously funded by Sanofi;
- we would bear all of the risks and costs related to the further development and commercialization of product candidates that were previously the subject of the Sanofi agreement, including the reimbursement of third parties; and

- in order to fund further development and commercialization, we may need to seek out and establish alternative collaborations with third-party partners; this may not be possible, or we may not be able to do so on terms which are acceptable to us, in which case it may be necessary for us to limit the size or scope of one or more of our programs or increase our expenditures and seek additional funding by other means.

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

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

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

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

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

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

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

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

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

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

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

In addition, if our collaboration partners elect to pursue the development and commercialization of certain programs, we will lose control over the manufacturing of the product candidate subject to the agreement. For example, in November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program, to Sanofi, who is responsible for all costs incurred in the development of our miR-21 programs. As a result, we will no longer be involved in the development or commercialization of our miR-21 programs. Sanofi will be free to use a manufacturer of its own choosing or manufacture the product candidates in its own manufacturing facilities. In such a case, we will have no control over Sanofi's processes or supply chains to ensure the timely manufacture and supply of the product candidates. In addition, we will not be able to ensure that the product candidates will be manufactured under the correct conditions to permit the product candidates to be used in such clinical trials.

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

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

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

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

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

We, our collaboration partners and our CROs are required to comply with the FDA's or other regulatory agency's good clinical practices ("GCPs") for conducting, recording and reporting the results of IND-enabling studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA and non-U.S. regulatory agencies enforce these GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or applicable non-U.S. regulatory agency may require us to perform additional clinical trials before approving any marketing applications for the relevant jurisdiction. Upon

inspection, the FDA or applicable non-U.S. regulatory agency may determine that our clinical trials did not comply with GCPs. In addition, our clinical trials will require a sufficiently large number of test subjects to evaluate the safety and effectiveness of a potential drug product. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process.

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

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

RISKS RELATED TO OUR INTELLECTUAL PROPERTY

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

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

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

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

In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available however the life of a patent, and the protection it affords, is limited. Once the patent life has expired for a product, we may be open to competition from generic medications. Further, if we encounter

delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although each of our employees agrees to assign their inventions to us through an employee inventions agreement, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. In addition, others may independently discover our trade secrets and proprietary information.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

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

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

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

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

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

We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. For example, our exclusive license agreements with our founding companies, Alnylam and Ionis, provide us with rights to nucleotide technologies in the field of *micro*RNA therapeutics based on oligonucleotides that modulate *micro*RNAs. Some of these technologies, such as intellectual property relating to the chemical modification of oligonucleotides, are relevant to our product candidate development programs. If our license agreements with Alnylam or Ionis are terminated, or our business relationships with either of these companies or our other licensors are disrupted by events that may include the acquisition of either company, our access to critical intellectual property rights will be materially and adversely affected.

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

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

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

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

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

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

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

RISKS RELATED TO COMMERCIALIZATION OF PRODUCT CANDIDATES

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

In November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program, to Sanofi. The transition activities were completed in the second quarter of 2019. As a result, we have no influence and/or control over their approaches to development and commercialization of our miR-21 programs. If Sanofi or any potential future collaboration partners do not perform in the manner that we expect or fail to fulfill their responsibilities in a timely manner, or at all, the clinical development, regulatory approval and commercialization efforts related to product

candidates we have licensed to such collaboration partners could be delayed or terminated. If we terminate any of our collaborations or any program thereunder due to a material breach by Sanofi, and except in the case of RG-012, we have the right to assume the responsibility at our own expense for the development of the applicable *microRNA* product candidates. Assuming sole responsibility for further development will increase our expenditures and may mean we will need to limit the size and scope of one or more of our programs, seek additional funding and/or choose to stop work altogether on one or more of the affected product candidates. This could result in a limited potential to generate future revenue from such *microRNA* product candidates and our business could be materially and adversely affected. Further, under certain circumstances, we may owe Sanofi royalties on any product candidate that we may successfully commercialize.

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

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

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

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

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

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

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

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

- demonstration of clinical safety and efficacy compared to other products;
- the relative convenience, ease of administration and acceptance by physicians, patients and healthcare payors;
- the prevalence and severity of any AEs;

- limitations or warnings contained in the FDA-approved label for such products;
- availability of alternative treatments;
- pricing and cost-effectiveness;
- the effectiveness of our or any collaborators' sales and marketing strategies;
- our ability to obtain hospital formulary approval;
- our ability to obtain and maintain sufficient third party coverage and adequate reimbursement; and
- the willingness of patients to pay out-of-pocket in the absence of third party coverage.

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

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

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

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

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

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

If any product candidates that we develop are approved for commercialization, we may also enter into agreements with third parties to market them on a worldwide basis or in more limited geographical regions. We expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- different payor reimbursement regimes, governmental payors or patient self-pay systems and price controls;

- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

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

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

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

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

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

RISKS RELATED TO OUR BUSINESS OPERATIONS AND INDUSTRY

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

We are highly dependent on principal members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any

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

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

In July 2018, we implemented a corporate restructuring which involved a reduction in our total workforce by approximately 60%. The workforce reduction was substantially completed in July 2018. As of December 31, 2019, we had 21 employees, all of which were full-time employees. In the future, we may need to expand our organization.

Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. Moreover, if our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

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

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

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

From time to time we may undertake internal restructuring activities as we continue to evaluate and attempt to optimize our cost and operating structure in light of developments in our business strategy and long-term operating plans. For example, we initiated a corporate restructuring in May 2017 and in July 2018, each of which resulted in a reduction in our workforce. Any such restructuring activities may result in write-offs or other restructuring charges. There can be no assurance that any restructuring activities that we have undertaken or undertake in the future will achieve the cost savings, operating efficiencies or other benefits that we may initially expect. Restructuring activities may also result in a loss of continuity, accumulated knowledge and inefficiency during transitional periods and thereafter. In addition, internal restructurings can require a significant amount of time and focus from management and other employees, which may divert attention from commercial operations. If any internal restructuring activities we have undertaken or undertake in the future fail to achieve some or all of the expected benefits therefrom, our business, results of operations and financial condition could be materially and adversely affected.

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

Our operations may be directly, or indirectly through our relationships with customers, third party payors, healthcare providers, and others subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by the federal government and by the U.S. states and foreign jurisdictions in which we conduct our business. The healthcare laws and regulations that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, either the referral of an individual, or the purchase or recommendation of an item or service for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment to the federal government, including Medicare or Medicaid, that are false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created additional federal criminal statutes that prohibit, among other things, executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- HIPAA, as amended by HITECH, and their implementing regulations, which imposes certain requirements on certain types of individuals and entities relating to the privacy, security and transmission of individually identifiable health information;
- the European General Data Protection Regulation ("GDPR") adopted by the European Union ("EU") in May 2018, which contains provisions specifically directed at the processing of health information, higher sanctions and extra-territoriality measures intended to bring non-EU companies under the regulation; we anticipate that over time we may expand our business operations to include additional operations in the EU, including potentially conducting preclinical and clinical trials and, with such expansion, we would be subject to increased governmental regulation in the EU countries in which we might operate, including the GDPR;
- California recently enacted legislation that has been dubbed the first "GDPR-like" law in the United States. Known as the California Consumer Privacy Act ("CCPA"), it has created new individual privacy rights for consumers (as that word is broadly defined in the law) and placed increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA, which went into effect on January 1, 2020, requires covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allows for a new cause of action for data breaches. The CCPA may impact (possibly significantly) our business activities and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information;
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services ("CMS") information related to payments or other transfers of value made to physicians, as defined by such law, 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; state and local laws that require the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, 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 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 ACA was passed and includes measures to significantly change the way healthcare is financed by both governmental and private insurers. There remain 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. Since January 2017, President Trump has signed two 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. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act includes a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate”. In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated “Cadillac” tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the “individual mandate” was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA and our business.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2029 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and federal and state legislative activity designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. For example, at the federal level, the Trump administration’s budget proposal for fiscal year 2020 contained further drug price control measures that could be enacted during the budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. In addition, the Trump administration released a “Blueprint” to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services (“HHS”) has solicited feedback on some of

these measures and, at the same, has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. While some of these and other measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing.

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

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

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

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

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

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

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

Our business requires manipulating, analyzing and storing large amounts of data. In addition, we rely on a global enterprise software system to operate and manage our business. We also maintain personally identifiable information about our employees. Our business therefore depends on the continuous, effective, reliable, and secure operation of our computer hardware, software, networks, Internet servers, and related infrastructure. To the extent that our hardware or software malfunctions or access to our data by internal research personnel is interrupted, our business could suffer. The integrity and

protection of our employee and company data is critical to our business and employees have a high expectation that we will adequately protect their personal information. The regulatory environment governing information, security and privacy laws is increasingly demanding and continues to evolve. Maintaining compliance with applicable security and privacy regulations may increase our operating costs. Although our computer and communications hardware is protected through physical and software safeguards, it is still vulnerable to fire, storm, flood, power loss, earthquakes, telecommunications failures, physical or software break-ins, software viruses, and similar events. These events could lead to the unauthorized access, disclosure and use of non-public information. The techniques used by criminal elements to attack computer systems are sophisticated, change frequently and may originate from less regulated and remote areas of the world. As a result, we may not be able to address these techniques proactively or implement adequate preventative measures. If our computer systems are compromised, we could be subject to fines, damages, litigation and enforcement actions, and we could lose trade secrets, the occurrence of which could harm our business. In addition, any sustained disruption in internet access provided by other companies could harm our business.

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

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

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

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

Following the result of a referendum in 2016, the United Kingdom left the European Union on January 31, 2020, commonly referred to as “Brexit.” Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom will be subject to a transition period until December 31, 2020, or the Transition Period, during which EU rules will continue to apply. Negotiations between the United Kingdom and the European Union are expected to continue in relation to the customs and trading relationship between the United Kingdom and the European Union following the expiry of the Transition Period.

Since a significant proportion of the regulatory framework in the United Kingdom applicable to our business and our product candidates is derived from EU directives and regulations, Brexit, following the Transition Period, could materially impact the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the United Kingdom or the European Union. For example, as a result of the uncertainty surrounding Brexit, the EMA relocated to Amsterdam from London. Following the Transition Period, the United Kingdom will no longer be covered by the centralized procedures for obtaining EU-wide marketing authorization from the EMA and, unless a specific agreement is entered into, a separate process for authorization of drug products, including our product candidates, will be required in the United Kingdom, the potential process for which is currently unclear. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. In addition, we may be required to pay taxes or duties or be subjected to other hurdles in connection with the importation of our product candidates into the European Union, or we may incur expenses in establishing a manufacturing facility in the European Union in order to circumvent such hurdles. If any of these outcomes occur, we may be forced to restrict

or delay efforts to seek regulatory approval in the United Kingdom or the European Union for our product candidates, or incur significant additional expenses to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the United Kingdom.

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

Our headquarters are located in San Diego County. We are vulnerable to natural disasters such as earthquakes and wild fires, as well as other events that could disrupt our operations. We do not carry insurance for earthquakes or other natural disasters and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our business operations. In addition, natural disasters or other catastrophic events in various parts of the world, including interruptions in the supply of natural resources, political and governmental changes, disruption in transportation networks or delivery services, severe weather conditions, wildfires and other fires, explosions, actions of animal rights activists, terrorist attacks, earthquakes, wars and public health issues 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 epidemics, including the novel coronavirus (COVID-19) pandemic, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations. In addition, the COVID-19 pandemic could materially affect our operations globally, including at our headquarters in San Diego. If the COVID-19 pandemic continues to spread, we may need to limit operations or implement limitations, including work from home policies. In particular, port closures and other restrictions resulting from the coronavirus pandemic may disrupt our supply chain or limit our ability to obtain sufficient materials for our product candidates. In addition, our clinical trials may be affected by the COVID-19 pandemic as site initiation and patient enrollment may be delayed due to prioritization of hospital resources toward the COVID-19 pandemic and it may delay enrollment in our clinical trials and/or clinical trials undertaken by our collaboration partner. The ultimate impact of the COVID-19 pandemic or other health epidemics is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material impact on our operations.

RISKS RELATED TO OUR COMMON STOCK

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

Our stock price has historically been, and is expected to continue to be, highly volatile.

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

- adverse results or delays in preclinical studies or clinical trials;
- inability to obtain additional funding;
- any delay in filing an IND or NDA for any of our product candidates and any adverse development or perceived adverse development with respect to the FDA's review of that IND or NDA;
- failure to maintain our existing collaborations or enter into new collaborations;
- failure of our collaboration partners to elect to develop and commercialize product candidates under our collaboration agreements or the termination of any programs under our collaboration agreements;
- failure by us or our licensors and collaboration partners to prosecute, maintain or enforce our intellectual property rights;
- failure to successfully develop and commercialize our product candidates;
- changes in laws or regulations applicable to our preclinical and clinical development activities, product candidates or future products;
- inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;

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- 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;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our collaboration partners or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

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

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. In May 2014, the FASB issued Accounting Standards Update ("ASU") No. 2014-09, *Revenue from Contracts with Customers (Topic 606)*, which requires an entity to recognize the amount of revenue when promised goods or services are transferred to customers. The standard requires a company to recognize revenue to depict the transfer of goods or services to customers in the amount that reflects the consideration it expects to be entitled to receive in exchange for those goods or services. The FASB subsequently issued amendments to ASU No. 2014-09 that have the same effective date and transition date. These new standards became effective for us on January 1, 2018 and were adopted using the modified retrospective method through a cumulative-effect adjustment directly to accumulated deficit of \$1.8 million.

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

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

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

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

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. For example, on May 7, 2019, we completed the initial closing of the private placement under the May 2019 SPA, pursuant to which we sold and issued (i) 9,730,534 shares of common stock and accompanying warrants to purchase up to an aggregate of 9,730,534 shares of common stock at a combined purchase price of \$1.205 per share, and (ii) 415,898 shares of non-voting Class A-1 convertible preferred stock, in lieu of shares of common stock, at a price of \$10.80 per share, and accompanying warrants to purchase an aggregate of 4,158,980 shares of common stock at a price of \$0.125 for each share of common stock underlying such warrants. Each share of non-voting Class A-1 convertible preferred stock is convertible into 10 shares of common stock, subject to certain beneficial ownership conversion limitations. The warrants will be exercisable for a period of five years following the date of issuance and will have an exercise price of \$1.08 per share, subject to proportional adjustments in the event of stock splits or combinations or similar events. In December 2019 following our announcement of resumption of our Phase 1 MAD clinical trial of RGLS4326, we completed the Milestone Closing under the May 2019 SPA, pursuant to which we sold and issued (i) 3,288,390 shares of non-voting Class A-2 convertible preferred stock, in lieu of shares of common stock, at a price of \$6.66 per share, and accompanying warrants to purchase an aggregate of 32,883,900 shares of common stock at a price of \$0.125 for each share of common stock underlying such warrants. Each share of the non-voting Class A-2 convertible preferred stock is convertible into 10 shares of common stock, subject to certain beneficial ownership conversion limitations. The warrants are exercisable for a period of five years following the date of issuance and have an exercise price of \$0.666 per share, pursuant to proportional adjustments in the event of stock splits or combinations or similar events. Current stockholders may be diluted by the exercise of the warrants issued in the Private Placement.

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. Commencing in January 2021, the number of shares available for future grant under the 2019 Plan will automatically increase each year by up to 5% of all shares of our capital stock outstanding as of December 31st of the preceding calendar year, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. Furthermore, we may grant or provide for the grant of rights to purchase shares of our common stock pursuant to our 2012 Employee Stock Purchase Plan ("the ESPP"). The number of shares of our common stock reserved for issuance under the ESPP will automatically increase on January 1 of each calendar year by the lesser of 1% of the total number of shares of our common stock outstanding on December 31st of the preceding calendar year and 41,666 shares, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under the 2019 Plan and the ESPP each year.

In addition, we previously adopted an Inducement Plan in 2015 (the "Inducement Plan") pursuant to which our management had the ability to grant stock options exercisable for up to an aggregate of 83,333 shares of our common stock to new employees as inducements material to such new employees entering into employment with us. Upon approval of our 2019 Plan by our stockholders, we also reduced the shares available under the Inducement Plan to zero. However, the number of shares which may be granted under the Inducement Plan may be increased in the future by our board of directors. In the event we increase the number of shares which may be granted under the Inducement Plan, or adopt another inducement plan for which no stockholder approval is required under applicable rules and regulations, and grant options pursuant to such plan, our stockholders may experience additional dilution, which could cause our stock price to fall.

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

Our common stock is currently listed on The Nasdaq Capital Market. Prior to January 11, 2019, our common stock was listed on The Nasdaq Global 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. In December 2017, April 2018 and September 2019, we received a letter from The Nasdaq Stock Market advising us in each case 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 Stock Market, and therefore we could become subject to delisting if our common stock did not meet the \$1.00 minimum bid price for 10 consecutive trading days within the 180-day period following the date of the letter. The bid price of our common stock closed above \$1.00 for 10 consecutive trading days within the 180-day compliance periods following the December 2017 letter and the September 2019 letter, and therefore regained compliance in each of those cases with Nasdaq's \$1.00 minimum bid price requirement for continued listing. As a result of the April 2018 letter, we effected a 1-for-12 reverse stock split of our issued and outstanding common stock in October 2018 in order to regain compliance with Nasdaq's \$1.00 minimum bid price requirement for continued listing.

On November 13, 2018, we were notified by The Nasdaq Stock Market that we failed to comply with the listing rules of The Nasdaq Global Market as we did not maintain a minimum of \$10 million in stockholder equity and therefore could be subject to delisting. In December 2018, we submitted a plan to The Nasdaq Global Market to regain compliance with the Nasdaq Listing Rules, which included, among other specific measures, transferring our listing to The Nasdaq Capital Market, which has a lower minimum stockholders' equity requirement of \$2.5 million. On January 11, 2019, our transfer to The Nasdaq Capital Market became effective. Based upon the transfer to The Nasdaq Capital Market, and the other specific measures outlined in our plan, Nasdaq approved our plan and provided us with an extension to May 13, 2019 to comply with the trading rules of The Nasdaq Capital Market. We regained compliance with the minimum stockholders' equity requirement in May 2019 as a result of our completion of the initial closing of the private placement under the May 2019 SPA, pursuant to which we raised net proceeds of approximately \$15.7 million. On November 13, 2018, we were again notified by The Nasdaq Stock Market that we failed to comply with the minimum stockholders' equity requirement and therefore could be subject to delisting. In December 2019, due to the Milestone Closing under the May 2019 SPA, we regained compliance with the minimum stockholders' equity requirement.

There can be no assurance that we will continue to maintain compliance with the \$1.00 minimum bid price requirement or the minimum stockholders' equity requirement, or continuously satisfy Nasdaq's other continued listing standards in the future. In the future, if we are ultimately not able to maintain or timely regain compliance with Nasdaq's continued listing requirements, our common stock will be subject to delisting. In the event that our common stock is delisted from Nasdaq and is not eligible for quotation or listing on another market or exchange, trading of our common stock could be conducted only in the over-the-counter market or on an electronic bulletin board established for unlisted securities such as the Pink Sheets or the OTC Bulletin Board. In such event, it could become more difficult to dispose of, or obtain accurate price quotations for our common stock and there would likely also be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further. In addition, the delisting of our common stock from The Nasdaq Capital Market would constitute an event of default under our Loan Agreement with Oxford.

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

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. On January 31, 2017, a putative class action complaint was filed in the United States District Court for the Southern District of California against us, Paul C. Grint (our former Chief Executive Officer) and Joseph P. Hagan (then our Chief Operating Officer and currently our President and Chief Executive Officer). The complaint includes claims asserted, on behalf of certain purchasers of our securities, under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended. In general, the complaint alleges that between January 21, 2016, and June 27, 2016, the defendants violated the federal securities laws by making materially false and misleading statements regarding our business and the prospects for RG-101, thereby artificially inflating the price of our securities. A second action has subsequently been filed making the same allegations but extending the period of alleged violations to January 27, 2017 and also naming our former Chief Research & Development Officer, Timothy M. Wright, as a defendant. These actions were consolidated and on December 22, 2017, lead plaintiffs filed a consolidated complaint against the Company, Dr. Grint, Mr. Hagan, and Michael Huang (our former Vice President of Clinical Development). The consolidated complaint alleges that between February 17, 2016 and June 12, 2017, the Defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, by making materially false and misleading statements regarding RG-101. The consolidated complaint seeks unspecified monetary damages and an award of attorneys' fees and costs. On February 6, 2018, defendants filed a motion to dismiss the consolidated complaint. On March 23, 2018, plaintiff filed their opposition to the motion and on April 24, 2018, defendants filed their response. On September 5, 2019, the court granted the defendants' motion to dismiss with leave to amend. The plaintiffs filed their amended complaint on October 1, 2019. Subsequent to the filing of the amended complaint, counsel for the parties

engaged in negotiations to resolve the case. On November 4, 2019, the parties agreed in principle to settle the case for \$0.9 million, with approximately \$0.3 million to be paid by us and the balance to be paid by our D&O insurance carrier. On December 11, 2019, the parties entered into a stipulation and agreement of settlement, which was amended on February 6, 2020. On February 7, 2020, plaintiffs filed a motion for preliminary approval of the settlement. The settlement is contingent upon court approval. There can be no assurance that the case will be settled for the amount agreed to in principle, or at all. We are not able to predict or reasonably estimate the ultimate outcome or possible losses relating to these claims. It is possible that additional lawsuits will be filed, or allegations made by stockholders, with respect to these same or other matters and also naming us and/or our officers and directors as defendants. While we carry liability insurance, there is no assurance that any losses we incur in connection with the current lawsuits or any future lawsuits will be covered or that coverage, if any, will be sufficient. In addition, the current lawsuits and similar future litigation could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, the Tax Act enacted many significant changes to the U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Act may affect us, and certain aspects of the Tax Act could be repealed or modified in future legislation. In addition, it is uncertain if and to what extent various states will conform to the Tax Act or any newly enacted federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses under the Tax Act or future reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense.

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

As of December 31, 2019, we had net operating loss ("NOL") carryforwards for U.S. federal and California state tax purposes of \$326.6 million and \$274.6 million, respectively. A portion of the federal and California state NOL carryforwards will begin to expire, if not utilized, in 2030 and 2031, respectively. NOLs that expire unused will be unavailable to offset future income tax liabilities. Under the Tax Cuts and Jobs Act, federal NOLs incurred in taxable years ending after December 31, 2017 may be carried forward indefinitely, but the deductibility of federal NOLs generated in tax years beginning after December 31, 2017 is limited. It is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "Code"), and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income 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 again in July 2015, May 2019 and December 2019. 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.

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

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

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

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

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

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

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

On June 19, 2019, we entered into a lease agreement (the “Lease”) with ARE SD Region No. 44 LLC for the lease of approximately 8,727 square feet of rentable area of the building located at 10628 Science Center Drive, Suite 225, San Diego, California 92121 (the “Premises”). The commencement date of the Lease was July 1, 2019. We are using the Premises as our principal executive offices and as a laboratory for research and development and other related uses. The term of the Lease is two years, six months, ending December 31, 2021. All lease agreements for buildings previously occupied by us have terminated.

We believe that our existing facilities are adequate and our new facilities will be adequate for our current needs.

Item 3. Legal Proceedings

On January 31, 2017, a putative class action complaint was filed by Baran Polat in the United States District Court for the Southern District of California, or District Court, against us, Paul C. Grint (our former Chief Executive Officer), and Joseph P. Hagan (then our Chief Operating Officer and currently our President and Chief Executive Officer). The complaint includes claims asserted, on behalf of certain purchasers of our securities, under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended. In general, the complaint alleges that, between January 21, 2016, and June 27, 2016, the defendants violated the federal securities laws by making materially false and misleading statements regarding our business and the prospects for RG-101, thereby artificially inflating the price of our securities. The plaintiff seeks unspecified monetary damages and other relief. On February 10, 2017, a second putative class action complaint was filed by Li Jin in the District Court against the Company, Mr. Hagan, Dr. Grint, and Timothy Wright, the Company’s former Chief Research and Development Officer. The Complaint alleges claims similar to those asserted by Mr. Polat. The actions have been related. On February 17, 2017, the District Court entered an order stating that defendants need not answer, or otherwise respond, until the District Court enters an order appointing, pursuant to the Private Securities Litigation Reform Act of 1995, lead plaintiff and lead counsel, and the parties then submit a schedule to the District Court for the filing of an amended or consolidated complaint and the timing of defendants’ answer or response. On April 3, 2017, two motions for consolidation of the two actions, appointment of lead plaintiff and approval of counsel were filed in the actions. On October 26, 2017, the District Court entered an order

consolidating the cases, appointing lead plaintiffs, and appointing lead counsel for lead plaintiffs. On December 22, 2017, lead plaintiffs filed a consolidated complaint against the Company, Dr. Grint, Mr. Hagan, and Michael Huang (our former Vice President of Clinical Development). The consolidated complaint alleges that between February 17, 2016 and June 12, 2017, the defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, by making materially false and misleading statements regarding RG-101. The consolidated complaint seeks unspecified monetary damages and an award of attorneys' fees and costs. On February 6, 2018, defendants filed a motion to dismiss the consolidated complaint. On March 23, 2018, plaintiff filed their opposition to the motion and on April 24, 2018, defendants filed their response. On September 5, 2019, the court granted the defendants' motion to dismiss with leave to amend. Plaintiffs filed their amended complaint on October 1, 2019. Subsequent to the filing of the amended complaint, counsel for the parties engaged in negotiations to resolve the case. On November 4, 2019, the parties agreed in principle to settle the case for \$0.9 million, with approximately \$0.3 million to be paid by us and the balance to be paid by our D&O insurance carrier. On December 11, 2019, the parties entered into a stipulation and agreement of settlement, which was amended on February 6, 2020. On February 7, 2020, plaintiffs filed a motion for preliminary approval of the settlement. The settlement is contingent upon court approval. There can be no assurance that the case will be settled for the amount agreed to in principle, or at all. We are not able to predict or reasonably estimate the ultimate outcome or possible losses relating to these claims.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock was listed on The Nasdaq Global Market under the symbol "RGLS" from October 4, 2012 through January 10, 2019. Since January 11, 2019, our common stock has been listed on The Nasdaq Capital Market.

Holders of Record

As of March 6, 2020, there were 7 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.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

Item 6. Selected Financial Data

The selected financial data set forth below is derived from our audited financial statements, including the balance sheets at December 31, 2019 and 2018 and the related statements of operations for each of the years ended December 31, 2019 and 2018 and related notes appearing elsewhere in this Annual Report. The balance sheet data as of December 31, 2017, 2016 and 2015 and the statement of operations data for the years ended December 31, 2017, 2016 and 2015 are derived from our audited financial statements that are not included in this Annual Report. The following selected financial data should be read in conjunction with the financial statements and notes thereto and Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this Annual Report. The selected financial data in this section are

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not intended to replace our financial statements and the related notes. Our historical results are not necessarily indicative of our future results. Amounts are in thousands, except per share data.

| Statement of operations data | Year ended December 31, | | | | |
|---------------------------------------|--------------------------------|-------------|-------------|-------------|-------------|
| | 2019 | 2018 | 2017 | 2016 | 2015 |
| Revenue under collaborations | \$ 6,832 | \$ 72 | \$ 72 | \$ 1,194 | \$ 20,759 |
| Loss from operations | (16,834) | (46,763) | (70,131) | (81,502) | (54,758) |
| Net loss | \$ (18,592) | \$ (48,709) | \$ (71,905) | \$ (81,836) | \$ (55,748) |
| Net loss per share, basic and diluted | \$ (1.08) | \$ (5.59) | \$ (11.47) | \$ (18.59) | \$ (12.98) |

| Balance sheet data | As of December 31, | | | | |
|---|---------------------------|-------------|-------------|-------------|--------------|
| | 2019 | 2018 | 2017 | 2016 | 2015 |
| Cash, cash equivalents and short-term investments | \$ 34,121 | \$ 13,935 | \$ 60,074 | \$ 76,111 | * \$ 115,319 |
| Working capital (deficit) | 18,809 | (7,351) | 34,136 | 73,667 | 121,626 |
| Total assets | 42,081 | 27,927 | 77,809 | 100,661 | 141,083 |
| Term loan | 14,631 | 16,575 | 19,859 | 19,802 | — |
| Accumulated deficit | (411,315) | (392,723) | (345,858) | (273,351) | (191,515) |
| Total stockholders' equity (deficit) | 20,015 | (5,854) | 35,216 | 56,075 | 124,078 |

*Includes \$1.3 million of restricted cash as of December 31, 2015.

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

You should read the following discussion and analysis together with “Item 6. Selected Financial Data” 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 “Item 1A. Risk Factors.”

OVERVIEW

We are a clinical-stage biopharmaceutical company focused on discovering and developing first-in-class drugs targeting *micro*RNAs to treat diseases with significant unmet medical need. We were formed in 2007 when Alnylam and Ionis contributed significant intellectual property, know-how and financial and human capital to pursue the development of drugs targeting *micro*RNAs pursuant to a license and collaboration agreement. Our most advanced product candidates are RG-012 and RGLS4326. RG-012 is an anti-miR targeting miR-21 for the treatment of Alport syndrome, a life-threatening kidney disease with no approved therapy available. In November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program, to Sanofi. As a result, Sanofi became responsible for all costs incurred in the development of our miR programs. The transition activities were completed in the second quarter of 2019. RGLS4326 is an anti-miR targeting miR-17 for the treatment of ADPKD. In addition to these clinical programs, we continue to develop a pipeline of preclinical drug product candidates.

Since our inception through December 31, 2019, we have relied primarily on the sale of our equity and convertible debt securities to fund company operations. We have received \$342.5 million from the sale of our equity and convertible debt securities, \$91.8 million from our collaborations, principally from upfront payments, research funding and preclinical and clinical milestones, and \$19.8 million in net proceeds from our Term Loan. As of December 31, 2019, we had cash and cash equivalents of approximately \$34.1 million.

FINANCIAL OPERATIONS OVERVIEW

Revenue

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

In the future, we may generate revenue from a combination of license fees and other upfront payments, payments for research and development services, milestone payments, product sales and royalties in connection with licenses and collaborations. We expect that any revenue we generate will fluctuate from quarter-to-quarter as a result of the timing of our achievement of preclinical, clinical, regulatory and commercialization milestones, if at all, the timing and amount of payments relating to such milestones and the extent to which any of our products are approved and successfully commercialized by us or our collaboration partners. If our current or future collaboration partners do not elect or otherwise agree to fund our development costs pursuant to our current or future license and collaboration agreements, or we or our collaboration partner fails to develop product candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenues, and our results of operations and financial position would be adversely affected.

Research and development expenses

Research and development expenses consist of costs associated with our research activities, including our drug discovery efforts and the development of our therapeutic programs. Our research and development expenses include:

- employee-related expenses, including salaries, benefits, travel and stock-based compensation expense;
- external research and development expenses incurred under arrangements with third parties, such as contract research organizations ("CRO"), contract manufacturing organizations ("CMOs"), other clinical trial related vendors, consultants and our scientific advisors;
- license fees; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, amortization of leasehold improvements and equipment, and laboratory and other supplies.

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

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

Since our inception, we have spent a total of approximately \$358.0 million in research and development expenses through December 31, 2019.

The process of conducting clinical trials and preclinical studies necessary to obtain regulatory approval is costly and time consuming. We, or our collaboration partners, may never succeed in achieving marketing approval for any of our product candidates. The probability of success for each product candidate may be affected by numerous factors, including preclinical data, clinical data, competition, manufacturing capability and commercial viability.

Successful development of future product candidates is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each future product candidate and are difficult to predict. We anticipate we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to our ability to maintain or enter into new collaborations with respect to each program or potential product candidate, the scientific and clinical success of each future product candidate, as well as ongoing assessments as to each future product candidate's commercial potential. We will need to raise additional capital and may seek additional collaborations in the future in order to advance our various programs.

General and administrative expenses

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

Other income (expense), net

Other income (expense) consists primarily of interest income and expense, and various income or expense items of a non-recurring nature. We earn interest income from interest-bearing accounts and money market funds for cash and cash equivalents and marketable securities, such as interest-bearing bonds, for our short-term investments. Interest expense is primarily attributable to interest charges associated with borrowings under our secured Term Loan.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

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.

While our significant accounting policies are described in the notes to our financial statements appearing elsewhere in this Annual Report, we believe that the following critical accounting policies are most important to understanding and evaluating our reported financial results.

Revenue Recognition

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

Effective January 1, 2018, we adopted Accounting Standards Update (“ASU”) 2014-09, *Revenue from Contracts with Customers* (Topic 606) (“Topic 606”) using the modified retrospective method which consisted of applying and recognizing the cumulative effect of Topic 606 at the date of initial application. Topic 606 supersedes the revenue recognition requirements in Accounting Standards Codification (“ASC”) Topic 605, *Revenue Recognition* (“Topic 605”). All periods prior to the adoption date of Topic 606 have not been restated to reflect the impact of the adoption of Topic 606, but are accounted for and presented under Topic 605. The following paragraphs in this section describe our revenue recognition accounting policies under Topic 606 upon adoption on January 1, 2018. Refer to Note 1 to the financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2017 for revenue recognition accounting policies under Topic 605.

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

Collaborative Arrangements

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

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

License Fees

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

Milestone Payments

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

Royalties

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

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, CROs and for other clinical trial-related activities. Payments under certain contracts with such parties depend on factors such as successful enrollment of patients, site initiation and the completion of clinical trial milestones. In accruing for these services, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If possible, we obtain information regarding unbilled services directly from these service providers. However, we may be required to estimate these services based on other information available to us. If we underestimate or overestimate the activities or fees associated with a study or service at a given point in time, adjustments to research and development expenses may be necessary in future periods. Historically, our estimated accrued liabilities have approximated actual expense incurred. Subsequent changes in estimates may result in a material change in our accruals.

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, 2019 and 2018

The following table summarizes our results of operations for the years ended December 31, 2019 and 2018 (in thousands):

| | Years ended December 31, | |
|-------------------------------------|-----------------------------|---------|
| | 2019 | 2018 |
| Revenue under collaborations | \$ 6,832 | \$ 72 |
| Research and development expenses | 12,349 | 33,975 |
| General and administrative expenses | 11,317 | 12,860 |
| Interest and other expenses, net | (1,757) | (1,884) |

Revenue under collaborations

Our revenues are generated from ongoing collaborations, and generally consist of upfront payments for licenses or options to obtain licenses in the future, milestone payments and payments for other research services. Revenue under collaborations was \$6.8 million for the year ended December 31, 2019, compared to less than \$0.1 million for the year ended December 31, 2018. The increase was attributable to recognition of the Upfront Amendment Payments under the 2018 Sanofi Amendment as revenue during the year ended December 31, 2019.

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):

| | 2019 | % of total | 2018 | % of total | Increase (decrease) | |
|--|------------------|-------------|------------------|-------------|---------------------|--------------|
| | | | | | \$ | % |
| Research and development | | | | | | |
| <i>Personnel and internal expenses</i> | \$ 6,669 | 54% | \$ 15,790 | 46% | \$ (9,121) | (58)% |
| <i>Third-party and outsourced expenses</i> | 4,799 | 38% | 15,053 | 44% | (10,254) | (68)% |
| Non-cash stock-based compensation | 309 | 3% | 2,256 | 7% | (1,947) | (86)% |
| Depreciation | 572 | 5% | 876 | 3% | (304) | (35)% |
| Total research and development expenses | <u>\$ 12,349</u> | <u>100%</u> | <u>\$ 33,975</u> | <u>100%</u> | <u>\$ (21,626)</u> | <u>(64)%</u> |

Research and development expenses decreased by \$21.6 million for the year ended December 31, 2019 compared to the year ended December 31, 2018. The aggregate decrease was driven by a \$10.3 million decrease in external development expenses, primarily attributable to the voluntary pause of the RGLS4326 Phase 1 MAD clinical study in the third quarter of 2018 (and subsequent FDA partial clinical hold of the RGLS4326 Phase 1 MAD clinical study in the third quarter of 2019) and commencement of the transfer of the RG-012 program to Sanofi under the 2018 Sanofi Amendment in the fourth quarter of 2018. Additionally, the decrease for the year ended December 31, 2019 compared to the year ended December 31, 2018 was attributable to a \$9.1 million reduction in personnel and internal expenses, driven by a reduction in costs subsequent to our corporate restructuring in the third quarter of 2018. Non-cash stock-based compensation decreased by \$1.9 million for the year ended December 31, 2019 compared to the year ended December 31, 2018, primarily attributable to a reduction in personnel over the periods under comparison.

General and administrative expenses

General and administrative expenses were \$11.3 million for the year ended December 31, 2019 compared to \$12.9 million for the year ended December 31, 2018. These amounts reflect personnel-related and ongoing general business operating costs. The decrease during the year ended December 31, 2019, as compared to the year ended December 31, 2018, is primarily attributable to a reduction in costs subsequent to our corporate restructuring in the third quarter of 2018.

Interest and other expenses, net

Net interest and other expenses were \$1.8 million for the year ended December 31, 2019 compared to \$1.9 million for the year ended December 31, 2018. These amounts are primarily related to interest charges associated with our outstanding Term Loan.

LIQUIDITY AND CAPITAL RESOURCES

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

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

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

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

The following table shows a summary of our cash flows for the years ended December 31, 2019 and 2018 (in thousands):

| | Years ended December 31, | |
|---------------------------------|-----------------------------|---------------|
| | 2019 | 2018 |
| Net cash (used in) provided by: | | |
| Operating activities | \$ (19,821) | \$ (43,273) |
| Investing activities | 74 | 46,519 |
| Financing activities | 39,933 | (2,830) |
| Total | <u>\$ 20,186</u> | <u>\$ 416</u> |

Operating activities

Net cash used in operating activities decreased to \$19.8 million for the year ended December 31, 2019, compared to \$43.3 million for the year ended December 31, 2018. Net cash used in operating activities were primarily attributable to net losses of \$18.6 million and \$48.7 million for the years ended December 31, 2019 and 2018, respectively. Adjustments for non-cash charges, including stock-based compensation, decreased to \$5.4 million for the year ended December 31, 2019, compared to \$8.6 million for the year ended December 31, 2018. Changes in working capital resulted in net cash used in operating activities of \$6.6 million for the year ended December 31, 2019, compared to net cash used in operating activities of \$3.2 million for the year ended December 31, 2018.

Investing activities

Net cash provided by investing activities for the year ended December 31, 2019 was primarily attributable to net sales of property and equipment. Net cash provided by investing activities for the year ended December 31, 2018 was primarily related to the net of purchases, sales and maturities of investments. Net sales and maturities of investments was \$46.5 million for the year ended December 31, 2018.

Financing activities

Net cash provided by financing activities was \$39.9 million for the year ended December 31, 2019, compared to net cash used in financing activities of \$2.8 million for the year ended December 31, 2018. Net cash provided by financing activities for the year ended December 31, 2019 was attributable to total net proceeds received from our private placement of common stock, warrants to purchase common stock and non-voting convertible preferred stock in May 2019 and December 2019 of \$40.1 million. Our 2018 financing activities primarily related to \$3.3 million of principal payments on our Term Loan.

CONTRACTUAL OBLIGATIONS AND COMMITMENTS

The following is a summary of our long-term contractual obligations as of December 31, 2019 (in thousands):

| | Payments due by period | | | | |
|--|------------------------|---------------|------------------|--------------|--------------|
| | Total | <1 year | 1-3 years | 3-5 years | >5 years |
| Operating lease obligations relating to facility | \$ 871 | \$ 429 | \$ 442 | \$ — | \$ — |
| Outstanding secured Term Loan | 14,681 | — | 14,681 | — | — |
| Annual maintenance fees for license agreements | 140 | 18 | 35 | 35 | 52 |
| Total | <u>\$ 15,692</u> | <u>\$ 447</u> | <u>\$ 15,158</u> | <u>\$ 35</u> | <u>\$ 52</u> |

Off-Balance Sheet Arrangements

As of December 31, 2019, we did not have any off-balance sheet arrangements.

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 the short-term investments to fluctuate. Financial instruments that potentially subject us to significant concentrations of credit risk consist primarily of cash and cash equivalents. We invest our excess cash primarily in debt instruments of U.S. government-sponsored agencies and the U.S. Treasury. The primary objectives of our investment activities are to ensure liquidity and to preserve principal while at the same time maximizing the income we receive from our 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, 2019, 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, 2019, the outstanding principal amount of the term loan was \$14.7 million. The Term Loan bears interest at a floating per annum rate equal to (i) 8.51% plus (ii) the greater of (a) the 30 day U.S. Dollar LIBOR rate reported in The Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue and (b) 0.44%. Changes in the U.S. Dollar LIBOR rate may therefore affect our interest expense associated with the Term Loan. LIBOR is currently scheduled to be phased out in 2021. Before LIBOR is phased out, we may need to renegotiate the Term Loan to replace LIBOR with a new standard, which has yet to be established. The consequences of these developments cannot be entirely predicted, but could result in higher interest rates on the principal amount of the Term Loan.

If a 10% change in interest rates were to have occurred on December 31, 2019, 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

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Regulus Therapeutics Inc. (the Company) as of December 31, 2019 and 2018, the related statements of operations and comprehensive loss, stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2019, 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, 2019 and 2018, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2019, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

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 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.

/s/ Ernst & Young LLP

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

San Diego, California
March 12, 2020

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

| | December 31, | |
|--|------------------|------------------|
| | 2019 | 2018 |
| Assets | | |
| Current assets: | | |
| Cash and cash equivalents | \$ 34,121 | \$ 13,935 |
| Contract and other receivables | 1,141 | 26 |
| Prepaid materials, net | 3,924 | 4,194 |
| Prepaid expenses and other current assets | 1,221 | 1,140 |
| Total current assets | 40,407 | 19,295 |
| Property and equipment, net | 921 | 7,806 |
| Intangibles, net | 266 | 500 |
| Other assets | 487 | 326 |
| Total assets | <u>\$ 42,081</u> | <u>\$ 27,927</u> |
| Liabilities and stockholders' equity (deficit) | | |
| Current liabilities: | | |
| Accounts payable | \$ 1,321 | \$ 1,714 |
| Accrued liabilities | 917 | 1,625 |
| Accrued compensation | 1,676 | 1,601 |
| Current portion of term loan, less debt issuance costs | 14,631 | 16,575 |
| Current portion of contract liabilities | 6 | 2,572 |
| Other current liabilities | 3,047 | 2,559 |
| Total current liabilities | 21,598 | 26,646 |
| Contract liabilities, less current portion | — | 6 |
| Deferred rent, less current portion | — | 6,820 |
| Other long-term liabilities | 468 | 309 |
| Total liabilities | 22,066 | 33,781 |
| Stockholders' equity (deficit): | | |
| Class A-1 convertible preferred stock, \$0.001 par value; 415,898 shares authorized, issued and outstanding at December 31, 2019; 0 shares authorized, issued and outstanding at December 31, 2018 | 1 | — |
| Class A-2 convertible preferred stock, \$0.001 par value; 3,288,390 shares authorized, issued and outstanding at December 31, 2019; 0 shares authorized, issued and outstanding at December 31, 2018 | 3 | — |
| Common stock, \$0.001 par value; 200,000,000 shares authorized, 21,018,663 and 8,818,019 shares issued and outstanding at December 31, 2019 and 2018, respectively | 21 | 9 |
| Additional paid-in capital | 431,305 | 386,860 |
| Accumulated deficit | (411,315) | (392,723) |
| Total stockholders' equity (deficit) | 20,015 | (5,854) |
| Total liabilities and stockholders' equity (deficit) | <u>\$ 42,081</u> | <u>\$ 27,927</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)

| | 2019 | 2018 |
|--|-------------|-------------|
| Revenues: | | |
| Revenue under collaborations | \$ 6,832 | \$ 72 |
| Total revenues | 6,832 | 72 |
| Operating expenses: | | |
| Research and development | 12,349 | 33,975 |
| General and administrative | 11,317 | 12,860 |
| Total operating expenses | 23,666 | 46,835 |
| Loss from operations | (16,834) | (46,763) |
| Other income (expense): | | |
| Interest and other income | 374 | 459 |
| Interest and other expense | (2,131) | (2,343) |
| Loss before income taxes | (18,591) | (48,647) |
| Income tax expense | (1) | (62) |
| Net loss and comprehensive net loss | \$ (18,592) | \$ (48,709) |
| Net loss per share, basic and diluted | \$ (1.08) | \$ (5.59) |
| Weighted average shares used to compute basic and diluted net loss per share | 17,260,176 | 8,718,563 |

See accompanying notes to these financial statements.

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

| | Convertible Preferred Stock | | Common stock | | Additional paid-in capital | Accumulated other comprehensive income (loss) | Accumulated deficit | Total stockholders' equity (deficit) |
|--|--------------------------------|--------|--------------|--------|----------------------------------|--|------------------------|---|
| | Shares | Amount | Shares | Amount | | | | |
| Balance at December 31, 2017 | — | \$ — | 8,662,435 | \$ 9 | \$ 381,199 | \$ (134) | \$ (345,858) | \$ 35,216 |
| Issuance of common stock upon exercise of options | — | — | 328 | — | 1 | — | — | 1 |
| Issuance of common stock upon vesting of restricted stock units | — | — | 128,840 | — | — | — | — | — |
| Stock-based compensation expense | — | — | — | — | 5,441 | — | — | 5,441 |
| Issuance of common stock under Employee Stock Purchase Plan | — | — | 26,416 | — | 219 | — | — | 219 |
| Unrealized gain on short-term investments | — | — | — | — | — | 134 | — | 134 |
| Cumulative effect of accounting change (ASU 2014-09) | — | — | — | — | — | — | 1,844 | 1,844 |
| Net loss | — | — | — | — | — | — | (48,709) | (48,709) |
| Balance at December 31, 2018 | — | \$ — | 8,818,019 | \$ 9 | \$ 386,860 | \$ — | \$ (392,723) | \$ (5,854) |
| Issuance of common stock upon exercise of options | — | — | 2,750 | — | 3 | — | — | 3 |
| Issuance of common stock upon vesting of restricted stock units | — | — | 559,445 | — | — | — | — | — |
| Issuance of common stock, preferred stock and warrants from private placement, net of offering costs | 3,704,288 | 4 | 9,730,534 | 10 | 40,070 | — | — | 40,084 |
| Stock-based compensation expense | — | — | — | — | 2,288 | — | — | 2,288 |
| Issuance of common stock under Employee Stock Purchase Plan | — | — | 4,035 | — | 3 | — | — | 3 |
| Issuance of common stock through ATM | — | — | 1,903,880 | 2 | 2,081 | — | — | 2,083 |
| Net loss | — | — | — | — | — | — | (18,592) | (18,592) |
| Balance at December 31, 2019 | 3,704,288 | \$ 4 | 21,018,663 | \$ 21 | \$ 431,305 | \$ — | \$ (411,315) | \$ 20,015 |

See accompanying notes to these financial statements.

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

| | Years ended December 31, | |
|---|--------------------------|-------------|
| | 2019 | 2018 |
| Operating activities | | |
| Net loss | \$ (18,592) | \$ (48,709) |
| Adjustments to reconcile net loss to net cash used in operating activities | | |
| Depreciation and amortization expense | 931 | 2,262 |
| Stock-based compensation | 2,288 | 5,441 |
| Amortization of premium on investments, net | — | 148 |
| Gain on reduction of lease liability | 1,839 | — |
| Other | 293 | 756 |
| Change in operating assets and liabilities: | | |
| Contracts and other receivables | (1,115) | 347 |
| Prepaid materials | 270 | 134 |
| Prepaid expenses and other assets | (242) | 630 |
| Accounts payable | (393) | (4,029) |
| Accrued liabilities | (708) | (1,370) |
| Accrued compensation | 75 | (384) |
| Contract liabilities | (2,572) | 2,428 |
| Deferred rent | — | (1,252) |
| Other liabilities | (1,895) | 325 |
| Net cash used in operating activities | (19,821) | (43,273) |
| Investing activities | | |
| Purchases of short-term investments | — | — |
| Sales and maturities of short-term investments | — | 46,541 |
| Purchases of property and equipment | (221) | (22) |
| Sales of property and equipment | 318 | — |
| Acquisition of intangibles | (23) | — |
| Net cash provided by investing activities | 74 | 46,519 |
| Financing activities | | |
| Proceeds from issuance of securities through private placement, net of issuance costs | 40,084 | — |
| Proceeds from issuance of common stock, net | 2,086 | 219 |
| Proceeds from exercise of common stock options | 3 | 1 |
| Proceeds from financing leases | — | 492 |
| Payments on financing leases | (263) | (200) |
| Principal payments on term loan | (1,977) | (3,342) |
| Net cash provided by (used in) financing activities | 39,933 | (2,830) |
| Net increase in cash and cash equivalents | 20,186 | 416 |
| Cash and cash equivalents at beginning of period | 13,935 | 13,519 |
| Cash and cash equivalents at end of period | \$ 34,121 | \$ 13,935 |
| Supplemental disclosure of cash flow information | | |
| Interest paid | \$ (1,655) | \$ (2,073) |
| Income taxes paid | \$ (1) | \$ (1) |
| Supplemental disclosure of non-cash investing and financing activities | | |

| | | |
|--|------|------|
| Non-cash acquisition of property and equipment | \$ 3 | \$ — |
|--|------|------|

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 biopharmaceutical company focused on discovering and developing first-in-class drugs that target microRNAs to treat a broad range of diseases. We were formed in 2007 when Alnylam and 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. Regulus Therapeutics Inc. was converted to a Delaware corporation on January 2, 2009. As used in this report, unless the context suggests otherwise, “the Company,” “our,” “us” and “we” means Regulus Therapeutics Inc.

Liquidity

The accompanying financial statements have been prepared on a basis which assumes we are a going concern, and does not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classifications of liabilities that may result from any uncertainty related to our ability to continue as a going concern. Through the date of the issuance of these financial statements, we have principally been financed through proceeds received from the sale of our common stock and other equity securities, debt financings, up-front payments and milestones received from collaboration agreements, totaling \$454.1 million. As of December 31, 2019, we had approximately \$34.1 million of cash and cash equivalents. Based on our operating plans, we believe our cash and cash equivalents may not be sufficient to fund our operations for the period one year following the issuance of these financial statements. As a result, there is substantial doubt about our ability to continue as a going concern. All amounts due under the Term Loan (see note 9) have been classified as a current liability as of December 31, 2019 and 2018 due to the considerations discussed above and the assessment that the material adverse change clause under the Term Loan is not within the Company's control. We have not been notified, by the Lender, of an event of default as of the date of the filing of this Form 10-K.

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

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

Use of Estimates

Our financial statements are prepared in accordance with U.S. generally accepted accounting principles ("GAAP"), which requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements and accompanying notes. An estimated loss contingency is accrued in our financial statements if it is probable that a liability has been incurred and the amount of the loss can be reasonably estimated. Although these estimates are based on our knowledge of current events and actions we may undertake in the future, actual results may ultimately differ from these estimates and assumptions.

Revenue Recognition

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

Effective January 1, 2018, we adopted Accounting Standards Update (“ASU”) 2014-09, Revenue from Contracts with Customers (Topic 606) (“Topic 606”) using the modified retrospective method which consisted of applying and recognizing the cumulative effect of Topic 606 at the date of initial application. Topic 606 supersedes the revenue recognition requirements in Accounting Standards Codification (“ASC”) Topic 605, Revenue Recognition (“Topic 605”). The following paragraphs in this section describe our revenue recognition accounting policies under Topic 606 upon adoption on January 1, 2018. Refer to Note 1 to the financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2017 for revenue recognition accounting policies under Topic 605.

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

Collaborative Arrangements

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

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

License Fees

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

Milestone Payments

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

Royalties

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

Stock-Based Compensation

We account for stock-based compensation expense related to stock options granted to employees and members of our board of directors by estimating the fair value of each stock option on the date of grant using the Black-Scholes option pricing model. We recognize stock-based compensation expense using the accelerated multiple-option approach. Under the accelerated multiple-option approach (also known as the graded-vesting method), we recognize compensation expense over the requisite service period for each separately vesting tranche of the award as though the award was in substance multiple awards, resulting in accelerated expense recognition over the vesting period. For performance-based awards granted to employees (i) the fair value of the award is determined on the grant date, (ii) we assess the probability of the individual milestones under the award being achieved and (iii) the fair value of the shares subject to the milestone is expensed over the implicit service period commencing once management believes the performance criteria is probable of being met.

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

Clinical Trial and Preclinical Study Accruals

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

Prepaid Materials

We capitalize the purchase of certain raw materials and related supplies for use in the manufacturing of drug product in our preclinical and clinical development programs, as we have determined that these materials have alternative future use. We can use these raw materials and related supplies in multiple clinical drug products, and therefore have future use independent of the development status of any particular drug program until it is utilized in the manufacturing process. We expense the cost of materials when used. We periodically review these capitalized materials for continued alternative future use and write down the asset to its net realizable value in the period in which an impairment is identified.

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 maintain our cash equivalents with two highly accredited financial institutions. We have historically invested our excess cash primarily in certificates of deposit and debt instruments of financial institutions and corporations, United States Treasury securities and United States government-sponsored enterprise 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.

Intangibles

We capitalize costs which consist principally of outside legal costs and filing fees related to obtaining patents. We review our capitalized patent costs periodically to determine that they include costs for patent applications that have future value and an alternative future use. We evaluate costs related to patents that we are not actively pursuing and write off these costs. We amortize patent costs over their patent lives, beginning with the date the patents are issued. The weighted average remaining life of the issued patents was approximately 7 years at December 31, 2019.

We obtain licenses from third parties and capitalize the costs related to exclusive licenses that have alternative future use within multiple potential programs. We amortize capitalized licenses over their estimated useful life or term of the agreement. We did not have any licenses capitalized on our balance sheet at December 31, 2019 and 2018.

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, 2019 or 2018.

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 losses on available-for-sale securities. Comprehensive losses have 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.

Corporate Restructuring

In July 2018, we implemented corporate restructurings to streamline our operations, reduce our operating expenses, extend our cash runway and focus our resources on our most promising programs.

In connection with our July 2018 restructuring, we reduced our workforce by approximately 60%. We recorded net charges of approximately \$0.8 million for employee severance and other related termination benefits and less than \$0.1 million in net one-time, non-cash stock-based compensation charges due to the acceleration of outstanding stock options, in accordance with executive employment agreements, partially offset by the reversal of expense previously recognized for stock options that were cancelled upon termination. All payments associated with the corporate restructuring were paid in full by the end of the third quarter of 2018.

Recent Accounting Pronouncements

As disclosed above, effective January 1, 2018, we adopted Topic 606. Since ASU 2014-09 was issued, several additional ASUs have been issued and incorporated within Topic 606 to clarify various elements of the guidance. As part of our adoption efforts, we have completed the assessment of our collaboration and license agreements under Topic 606. We adopted Topic 606 in the first quarter of 2018 using the modified retrospective method which consists of applying and recognizing the cumulative effect of Topic 606 at the date of initial application and providing certain additional disclosures as defined per Topic 606. On January 1, 2018, we recorded a cumulative adjustment to decrease deferred revenue and accumulated deficit by approximately \$1.8 million to reflect the impact of the adoption of Topic 606. The cumulative adjustment relates primarily to our agreement with Sanofi which is described further in Note 5.

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

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

There was no impact on revenue recognized in 2019 or 2018 as a result of the adoption of Topic 606.

In February 2016, the FASB issued ASU No. 2016-02, *Leases*, which increases transparency and comparability among organizations by requiring recognition of lease assets and lease liabilities on the balance sheet and disclosure of key information about leasing arrangements. Since ASU 2016-02 was issued, several additional ASUs have been issued to clarify various elements of the guidance. The standard is effective for annual reporting periods beginning after December 15, 2018, including interim periods within those annual reporting periods. We adopted the new lease standard on January 1, 2019, using the alternative modified transition method provided by the standard and did not retrospectively apply to prior periods. We elected the “package of practical expedients” (excluding the hindsight practical expedient) permitted under the transition guidance which allows us to not reassess our historical assessment of whether existing contracts are or contain a lease and the classification of existing lease arrangements. As a result of the adoption of the new standard, we recognized operating lease right-of-use assets (“ROU assets”) of \$3.3 million and operating lease liabilities of \$11.3 million on our balance sheet as of January 1, 2019. Operating lease ROU assets are recorded within our balance sheets as other assets and operating lease liabilities are recorded within our balance sheets as other current liabilities and other long-term liabilities. There was no change upon adoption to our capital leases, referred to as finance leases under the new lease standard. Our finance lease ROU asset and liability balances were each \$0.6 million as of January 1, 2019. Finance lease ROU assets are recorded in property and equipment, net and current and non-current finance lease liabilities are recorded in other current liabilities and other long-term liabilities, respectively, in our balance sheets. The adoption of the new lease standard had no impact on our accumulated deficit and also had no impact on our results of operations and cash flows. See Note 13, *Leases*, for further detail.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. The amendments in this update replace the incurred loss impairment methodology in current GAAP with a methodology that reflects expected credit losses and requires consideration of a broader range of reasonable and supportable information to inform credit loss estimates. Entities will apply the new guidance as a cumulative-effect adjustment to retained earnings as of the beginning of the first reporting period in which the guidance is adopted. This update is effective for annual periods beginning after December 15, 2019, and interim periods within those periods. Early adoption is permitted. The adoption of this guidance is not anticipated to have an impact on our financial statements.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation - Stock Compensation: Improvements to Nonemployee Share-Based Payment Accounting*, which aligns the measurement and classification guidance for share-based payment to non-employees with the guidance for share-based payments to employees. Under the new guidance, the measurement period for equity-classified non-employee awards will be fixed at the grant date. This update is effective for annual periods beginning

after December 15, 2018, and interim periods within those periods. The adoption of this guidance had no impact on our financial statements.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement: Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement*, which updates and modifies the disclosure requirements on fair value measurements in Topic 820, primarily in relation to Level 3 fair value measurements. This update is effective for annual periods beginning after December 15, 2019, and interim periods within those periods. Early adoption is permitted. The adoption of this guidance is not anticipated to have an impact on our financial statements.

In November 2018, the FASB issued ASU No. 2018-18, *Collaborative Arrangements*, which clarifies the interaction between Topic 808, *Collaborative Arrangements* and *Topic 606*, including clarification around certain transactions between collaborative arrangement participants and adding unit-of-account guidance to Topic 808. This update is effective for annual periods beginning after December 15, 2019, and interim periods within those periods. Early adoption is permitted. The adoption of this guidance is not anticipated to have an impact on our financial statements.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes - Simplifying the Accounting for Income Taxes* (“ASU 2019-12”). The guidance removes exceptions to the general principles in *Income Taxes (Topic 740)* for allocating tax expense between financial statement components, accounting basis differences stemming from an ownership change in foreign investments and interim period income tax accounting for year-to-date losses that exceed projected losses. The guidance becomes effective for annual reporting periods beginning after December 15, 2020 and interim periods within those fiscal years with early adoption permitted. The Company plans to adopt ASU 2019-12 effective January 1, 2020 and does not expect this adoption to have a material impact on our financial statements.

2. Net Loss Per Share

Basic net loss per share is calculated by dividing net loss by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by dividing net loss by the weighted-average number of common share equivalents outstanding for the period determined using the treasury stock method for stock options outstanding under our stock options plans and the if-converted method for convertible preferred stock. Dilutive common stock equivalents are comprised of stock options outstanding under our stock option plans, restricted stock units and convertible preferred stock. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted net loss per share.

Potentially dilutive securities not included in the calculation of diluted net loss per share because to do so would be anti-dilutive consisted of 3,342,533 shares attributable to convertible preferred stock for the year ended December 31, 2019 and zero shares attributable to common stock options and restricted stock units for the year ended December 31, 2018.

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 until to maturity and do not sell our investments before we have recovered our amortized cost basis. As of December 31, 2019 and 2018, our cash balance was comprised entirely of cash and cash equivalents (money market funds) and there was no unrealized gain or loss in either period.

4. Fair Value Measurements

We have certain financial assets recorded at fair value which have been classified as Level 1, 2, or 3 within the fair value hierarchy as described in the accounting standards for fair value measurements.

Accounting standards define fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants as of the measurement date. Market participants are buyers and sellers in the principal market that are (i) independent, (ii) knowledgeable, (iii) able to transact, and (iv) willing to transact. The accounting standards provide an established hierarchy for inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the most observable inputs be used when available. Observable inputs are inputs that market participants would use in valuing the asset or liability and are developed based on market data obtained from independent sources. Unobservable inputs are inputs that reflect our assumptions about the factors that market participants would use in valuing the asset or liability. The accounting standards prioritize the inputs used in measuring the fair value into the following hierarchy:

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- 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, 2019 and 2018 (in thousands):

| | Fair value as of December 31, 2019 | | | |
|------------------|------------------------------------|------------------|-------------|-------------|
| | Total | Level 1 | Level 2 | Level 3 |
| Assets: | | | | |
| Cash equivalents | \$ 8,909 | \$ 8,909 | \$ — | \$ — |
| | <u>\$ 8,909</u> | <u>\$ 8,909</u> | <u>\$ —</u> | <u>\$ —</u> |
| | | | | |
| | Fair value as of December 31, 2018 | | | |
| | Total | Level 1 | Level 2 | Level 3 |
| Assets: | | | | |
| Cash equivalents | \$ 11,173 | \$ 11,173 | \$ — | \$ — |
| | <u>\$ 11,173</u> | <u>\$ 11,173</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

Revenue recognized from our strategic collaborations was \$6.8 million for the year ended December 31, 2019 and less than \$0.1 million for the year ended December 31, 2018.

Sanofi

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

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

In February 2014, we and Sanofi entered into a second amended and restated collaboration and license agreement (the “2014 Sanofi Amendment”) to renew our strategic collaboration to discover, develop and commercialize *micro*RNA therapeutics to focus on specific orphan disease and oncology targets. Under the terms of the 2014 Sanofi Amendment, Sanofi had opt-in rights to our clinical fibrosis program targeting miR-21 for the treatment of Alport syndrome, our preclinical program targeting miR-21 for oncology indications, and our preclinical program targeting miR-221/222 for HCC. We were responsible for developing each of these programs to proof-of-concept, at which time Sanofi had an exclusive option on each program. If Sanofi chose to exercise its option on any of these programs, Sanofi would reimburse us for a significant portion of our preclinical and clinical development costs and would also pay us an option exercise fee for any such program, provided that \$1.25 million of the \$2.5 million upfront option fee paid to us by Sanofi in connection with the June 2013 option agreement would be creditable against such option exercise fee. We are eligible to receive royalties on *micro*RNA therapeutic products commercialized by Sanofi and will have the right to co-promote these products relating to our preclinical program targeting miR-221/222. As indicated below, we entered into an additional amendment with Sanofi in November 2018, under which Sanofi's opt-in rights to our miR-21 programs under the 2014 Sanofi Amendment were relinquished. Sanofi's opt-in rights with regard to our miR-221/222 preclinical program under the 2014 Sanofi Amendment remained unchanged.

In connection with the 2014 Sanofi Amendment, we entered into a Common Stock Purchase Agreement (the “Sanofi Purchase Agreement”), pursuant to which we sold 108,648 shares of our common stock to Aventisub LLC (“Aventis”), an entity affiliated with Sanofi, in a private placement at a price per share of \$92.04 (as adjusted for the reverse stock split effected in October 2018) for an aggregate purchase price of \$10.0 million. Under the terms of the Sanofi Purchase Agreement, Aventis was not permitted to sell, transfer, make any short sale of, or grant any option for the sale of any common stock for the 12-month period following its effective date. The Sanofi Purchase Agreement and the 2014 Sanofi Amendment were negotiated concurrently and were therefore evaluated as a single agreement. Based upon restricted stock studies of similar duration and a Black-Scholes valuation to measure the discount for lack of marketability, approximately \$0.4 million of the proceeds from the Sanofi Purchase Agreement was attributed to the 2014 Sanofi Amendment, and represents consideration for the value of the program targeting miR-221/222 for HCC. We are recognizing the \$0.4 million allocated consideration into revenue ratably over the estimated period of performance of the miR-221/222 program. As of December 31, 2019, contract liability associated with the Purchase Agreement and the 2014 Sanofi Amendment was less than \$0.1 million, which we are expecting to recognize over the remaining estimated period of performance of less than one year.

We are eligible to receive milestone payments of up to \$38.8 million for proof-of-concept option exercise fees (net of \$1.25 million creditable, as noted above), \$40.0 million for clinical milestones and up to \$130.0 million for regulatory and commercial milestones. In addition, we are entitled to receive royalties based on a percentage of net sales of any products from the miR-221/222 program which, in the case of sales in the United States, will be in the middle of the 10 to 20% range, and, in the case of sales outside of the United States, will range from the low end to the middle of the 10 to 20% range, depending upon the volume of sales. If we exercise our option to co-promote a miR-221/222 product, we will continue to be eligible to receive royalties on net sales of each product in the United States at the same rate, unless we elect to share a portion of Sanofi's profits from sales of such product in the United States in lieu of royalties.

In November 2018, we entered into an amendment to the 2014 Sanofi Amendment with Sanofi to modify the parties' rights and obligations with respect to our miR-21 programs, including our RG-012 program (the “2018 Sanofi Amendment”). Under the terms of the 2018 Sanofi Amendment, we have granted Sanofi a worldwide, royalty-free, fee-bearing, exclusive license, with the right to grant sublicenses, under our know-how and patents to develop and commercialize miR-21 compounds and products for all indications, including Alport Syndrome. Sanofi will control and will assume all responsibilities and obligations for developing and commercializing each of our miR-21 programs, including our obligations regarding the administration and expense of clinical trials and all other costs, including in-license royalties and other in-license payments, related to our miR-21 programs. Under the terms of the 2018 Sanofi Amendment, we have assigned to Sanofi certain agreements, product-specific patents and all materials directed to miR-21 or to any miR-21 compound or product and are required to provide reasonable technical assistance to Sanofi for a period of 24 months after the date of the 2018 Sanofi Amendment. Under the terms of the 2018 Sanofi Amendment, we are eligible to receive approximately \$6.8 million in upfront payments for the license and for miR-21 program-related materials (collectively, the “Upfront Amendment Payments”). We are also eligible to receive up to \$40.0 million in development milestone payments. In addition, Sanofi has agreed to reimburse us for certain out-of-pocket transition activities and assume our upstream license royalty obligations. We and Sanofi also agreed to a general release of claims against each other for any claims that arose at any time prior to the date of the 2018 Sanofi Amendment, or that thereafter could arise based on anything that occurred prior to the date of the 2018 Sanofi Amendment. As of December 31, 2018, we had received \$2.5 million of the approximately \$6.8 million in Upfront Amendment Payments under the 2018 Sanofi Amendment. We determined the amount constituted a contract liability as of December 31, 2018 under Topic 606, as the performance obligation conditions had not been satisfied as of that date. We completed the performance obligations under the 2018 Sanofi Amendment, received the remaining cash proceeds and recognized the \$6.8 million of Upfront Amendment Payments in 2019. As of December 31, 2019, the \$40.0 million in development milestone payments (variable

consideration) are fully constrained and therefore, do not meet the criteria for revenue recognition.

6. Property and Equipment, net

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

| | December 31, | |
|--|--------------|----------|
| | 2019 | 2018 |
| Laboratory equipment | \$ 4,967 | \$ 8,163 |
| Computer equipment and software | 281 | 281 |
| Furniture and fixtures | — | 706 |
| Leasehold improvements | 83 | 8,550 |
| | 5,331 | 17,700 |
| Less accumulated depreciation and amortization | (4,410) | (9,894) |
| Property and equipment, net | \$ 921 | \$ 7,806 |

Depreciation and amortization of property and equipment of \$0.9 million and \$2.3 million was recorded for the years ended December 31, 2019 and 2018, respectively.

7. Intangible Assets, net

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

| | December 31, | |
|------------------------------------|--------------|--------|
| | 2019 | 2018 |
| Patents | \$ 465 | \$ 721 |
| Accumulated amortization - Patents | (199) | (221) |
| Intangibles, net | \$ 266 | \$ 500 |

Intangible asset amortization of less than \$0.1 million was recorded for the year ended December 31, 2019, compared to \$0.1 million for the year ended December 31, 2018. 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, 2019 is expected to be recognized is approximately 14.9 years.

8. Commitments and Contingencies

Federal Securities Litigation

On January 31, 2017, a putative class action complaint was filed by Baran Polat in the United States District Court for the Southern District of California (“District Court”) against the Company, its then-Chief Executive Officer Paul C. Grint, and its then-Chief Operating Officer Joseph P. Hagan (currently the Company’s Chief Executive Officer). The complaint includes claims asserted, on behalf of certain purchasers of the Company’s securities, under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended. In general, the complaint alleges that, between January 21, 2016, and June 27, 2016, the defendants violated the federal securities laws by making materially false and misleading statements regarding the Company’s business and the prospects for RG-101, thereby artificially inflating the price of the Company’s securities. The plaintiff seeks unspecified monetary damages and other relief. On February 10, 2017, a second putative class action complaint was filed by Li Jin in the District Court against the Company, Mr. Hagan, Dr. Grint, and Timothy Wright, the Company’s Chief Research and Development Officer. The Complaint alleges claims similar to those asserted by Mr. Polat. The actions have been related. On February 17, 2017, the District Court entered an order stating that defendants need not answer, or otherwise respond, until the District Court enters an order appointing, pursuant to the Private Securities Litigation Reform Act of 1995, lead plaintiff and lead counsel, and the parties then submit a schedule to the District Court for the filing of an amended or consolidated complaint and the timing of defendants’ answer or response. On April 3, 2017, two motions for consolidation of the two actions, appointment of lead plaintiff, and approval of counsel were filed in the action (“Motions to Consolidate”). On October 26, 2017, the District Court entered an order consolidating the cases, appointing Mark Appel and Michael Spitters to serve as co-lead plaintiffs, and appointing Levi & Korsinsky LLP to serve as lead counsel. On December 22, 2017, lead

plaintiffs filed a consolidated complaint against the Company, Dr. Grint, Mr. Hagan, and Michael Huang (the Company's former Vice President of Clinical Development). The consolidated complaint alleges that between February 17, 2016 and June 12, 2017, the

defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, by making materially false and misleading statements regarding RG-101. The consolidated complaint seeks unspecified monetary damages and an award of attorneys' fees and costs. On February 6, 2018, the defendants filed a motion to dismiss the consolidated complaint. On March 23, 2018, lead plaintiffs filed their opposition to the motion to dismiss. On April 24, 2018, the defendants filed their reply in support of the motion to dismiss. On September 5, 2019, the court granted defendants' motion to dismiss with leave to amend. Plaintiffs filed their amended complaint on October 1, 2019. Subsequent to the filing of the amended complaint, counsel for the parties engaged in negotiations to resolve the case. On November 4, 2019, the parties agreed in principle to settle the case for \$0.9 million, with approximately \$0.3 million to be paid by us and the balance to be paid by our D&O insurance carrier. On December 11, 2019, the parties entered into a stipulation and agreement of settlement, which was amended on February 6, 2020. On February 7, 2020, plaintiffs filed a motion for preliminary approval of the settlement. The settlement is contingent upon court approval. In connection with the proposed settlement and in accordance with authoritative guidance, we recorded the \$0.9 million loss contingency as a current liability on our balance sheet at December 31, 2019, and recorded the \$0.6 million of expected insurance proceeds from our D&O insurance carrier as a current receivable on our balance sheet at December 31, 2019. The \$0.3 million settlement amount payable by the Company was recorded to the statement of operations and comprehensive loss for the year ended December 31, 2019. The settlement is contingent upon both the parties' entry into a definitive settlement agreement and court approval.

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.

9. Term Loan

On June 17, 2016, we entered into a loan and security agreement ("Loan Agreement") with Oxford Finance, LLC, ("Oxford" or sometimes referred to as the "Lender"), pursuant to which Oxford agreed to lend us up to \$30.0 million, issuable in two separate term loans of \$20.0 million (the "Term A Loan") and \$10.0 million (the "Term B Loan"). On June 22, 2016, we received \$20.0 million in proceeds from the Term A Loan, net of debt issuance costs. The ability to borrow on the Term B Loan expired on March 31, 2017, and no amounts were borrowed under the Term B Loan. We refer to all amounts outstanding under the Loan Agreement as the Term Loan.

The outstanding Term Loan will mature on May 1, 2022 (the "Maturity Date") and bears interest at a floating per annum rate equal to (i) 8.51% plus (ii) the greater of (a) the 30 day U.S. Dollar LIBOR rate reported in *The Wall Street Journal* on the last business day of the month that immediately precedes the month in which the interest will accrue and (b) 0.44%. Under the original Loan Agreement, we were required to make interest-only payments through June 1, 2018, followed by 24 equal monthly payments of principal and unpaid accrued interest.

In August 2018, we and Oxford entered into an amendment to our Loan Agreement, providing for a modification of the loan amortization period. Under the terms of the amendment, principal amortization and repayment was deferred between August 2018 through October 2018, and during this period, we were required to make payments of interest-only. Amortization payments recommenced in November 2018. Pursuant to the amendment, we granted the Lender a security interest in our intellectual property as additional collateral for the repayment of the Term Loan.

In November 2018, and in connection with the 2018 Sanofi Amendment, we entered into a fourth amendment to the Loan Agreement with the Lender (the "Fourth Amendment"). Under the terms of the Fourth Amendment, the Lender consented to the 2018 Sanofi Amendment and our license, assignment and transfer to Sanofi of certain of our intellectual property, as required to be delivered to Sanofi under the 2018 Sanofi Amendment (the "Assigned Assets"), which previously served as collateral under the Loan Agreement, and released its liens in the Assigned Assets, provided that the Lender will continue to have liens on all proceeds received by us pursuant to our collaboration and license agreement with Sanofi dated February 4, 2014 (the "Sanofi License Agreement"). Under the terms of the Fourth Amendment, we have the option to prepay part of the Term Loan at any time and in any amount after 10 days' prior written notice. We are also required to prepay a portion of the Term Loan with 25% of certain payments we receive under the 2018 Sanofi Amendment, which payments consist of the Upfront Amendment Payments and the first development milestone payment in the amount of \$10.0 million. In accordance with this term, we prepaid \$0.6 million pursuant to our receipt of \$2.5 million in Upfront Amendment Payments in November 2018. Additionally, we prepaid \$0.4 million pursuant to our receipt of \$1.8 million in Upfront Amendment Payments in March 2019. We are required to pay the applicable 5.5% final payment fee related to each such 2018 Sanofi Amendment prepayment.

On January 31, 2019, we entered into a fifth amendment to the Loan Agreement with the Lender (the "Fifth Amendment"). Under the terms of the Fifth Amendment, our required monthly payment to the Lender for the month of

February 2019 was comprised of interest only. On March 7, 2019, we entered into a sixth amendment to the Loan Agreement with the Lender (the "Sixth Amendment"). Under the terms of the Sixth Amendment, our required monthly payment to the Lender for the month of March 2019 was comprised of interest only.

On April 9, 2019 we entered into a seventh amendment to the Loan Agreement with the Lender (the "Seventh Amendment"). Under the terms of the Seventh Amendment, our required monthly payments to the Lender were to be comprised of interest only through and including the payment date immediately preceding the following date (the "Second Amortization Date"): (i) April 1, 2019, if we did not receive unrestricted gross cash proceeds of not less than \$10 million on or before April 30, 2019 from (a) the issuance and sale of our unsecured subordinated convertible debt and/or equity securities and/or (b) "up front" or milestone payments in connection with a joint venture, collaboration or other partnering transaction other than pursuant to the Sanofi License Agreement (the receipt of such net proceeds, the "Seventh Amendment Capital Event"), and (ii) May 1, 2019, if the Seventh Amendment Capital Event occurs. The Seventh Amendment Capital event did not occur on or before April 30, 2019.

Commencing on the Second Amortization Date, and continuing on each successive payment date thereafter, we were to be required to make consecutive equal monthly payments of principal, together with applicable interest, in arrears, to the Lender; provided, however, that we were required to make the monthly principal payment due April 1, 2019 on May 1, 2019 (in addition to all other payments due on May 1, 2019) if the Seventh Amendment Capital Event did not occur. The Seventh Amendment also provided that we can irrevocably elect to increase the prepayment percentage for the funds that we are required to prepay under the Term Loan in the event we receive \$10.0 million from the first development milestone under the 2018 Sanofi Amendment (the "Milestone Payment") from 25% to 75% (the "Applicable Sanofi Percentage"). Under the Seventh Amendment, we are required to maintain cash in a collateral account controlled by the Lender of (i) \$10.0 million if the Applicable Sanofi Percentage is 25% and if we had not prepaid an aggregate of \$5 million under the Term Loan (which amount shall not include any Sanofi License Agreement prepayments) on or before April 30, 2019 (such prepayment, the "Principal Paydown Event"), (ii) \$5.0 million if the Applicable Sanofi Percentage is 75% and the Principal Paydown Event had not occurred and (iii) zero if the Principal Paydown Event had occurred.

On May 3, 2019, concurrently with our Securities Purchase Agreement dated May 2019 (the "Purchase Agreement") (as described in further detail in Note 10), we entered into an eighth amendment to the Loan Agreement with the Lender (the "Eighth Amendment"). Pursuant to the terms of the Eighth Amendment and as a result of the completion of the initial closing under the Purchase Agreement, our required monthly payments to the Lender were comprised of interest only from May 2019 through and including the payment to be made in April 2020, in exchange for an interest-only period extension fee of \$0.1 million. Additionally, under the Eighth Amendment, the Term Loan maturity date was extended from June 2020 to May 2022, in exchange for a maturity date extension fee of \$0.7 million. Pursuant to the Eighth Amendment, as a result of our receipt of over \$20.0 million in capital in December 2019 under the second and final closing (the "Milestone Closing") under the Purchase Agreement (the "Eighth Amendment Capital Event"), our required monthly payments to the Lender are comprised of interest only through and including the payment to be made in April 2021. Commencing in May 2021, and continuing on each successive payment date thereafter, we are required to make consecutive equal monthly payments of principal, together with applicable interest, in arrears, to the Lender. The Eighth Amendment also provides for an increase in the prepayment percentage for the funds that we are required to prepay under the Term Loan, in the event that we receive the \$10.0 million Milestone Payment, from 75% to 100% of the Milestone Payment. Upon payment of the Milestone Payment to the Lender, we will no longer be required to maintain cash in a collateral account controlled by Lender and the positive lien on our intellectual property will be released.

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 Oxford currently has a positive lien, and certain assets under capital lease obligations. We have also agreed not to encumber our intellectual property assets, except as permitted by the Loan Agreement. The Loan Agreement includes customary events of default, including instances of a material adverse change in our operations, that may require prepayment of the outstanding Term Loan. As of December 31, 2019 we were in compliance with all covenants under the Loan Agreement.

As of December 31, 2019, \$14.7 million was outstanding under the Term Loan, with an additional \$1.9 million payable at the conclusion of the Term Loan. We had approximately \$0.1 million of debt issuance costs outstanding as of December 31, 2019, which are being accreted to interest expense over the life of the Term Loan. In connection with the Term Loan, the debt issuance costs have been recorded as a debt discount in our balance sheets, which are being accreted to interest expense over the life of the Term Loan using an effective interest rate of 8.98%. The exit fees are being accrued over the life of the Term Loan through interest expense.

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

| | | |
|------|----|---------------|
| 2020 | \$ | — |
| 2021 | | 9,035 |
| 2022 | | 5,646 |
| | \$ | <u>14,681</u> |

10. Common Stock and Stockholders' Equity

Common Stock

As of December 31, 2019, there were 21,018,663 shares of common stock outstanding. Each share of common stock is entitled to one vote. The holders of the common stock are also entitled to receive dividends whenever funds are legally available and when declared by our Board of Directors.

2019 Equity Incentive Plan

On June 15, 2019 the Company's board of directors approved, and on August 1, 2019 the Company's stockholders approved, the Company's 2019 Equity Incentive Plan (the "2019 Plan"). The 2019 Plan is intended as the successor to and continuation of the Company's 2012 Equity Incentive Plan. As of December 31, 2019, 403,939 shares of common stock were available for new equity award grants under the 2019 Plan and 3,226,804 shares of common stock are reserved for issuance pursuant to equity awards outstanding as of December 31, 2019. The number of shares authorized for issuance under the 2019 Plan may be increased by (a) the shares subject to outstanding stock awards granted under the Company's 2009 Equity Incentive Plan (the "2009 Plan") and the Company's 2012 Equity Incentive Plan (together with the 2009 Plan, the "Prior Plans") that on or after the effective date of the 2019 Plan (i) expire or terminate for any reason prior to exercise or settlement; (ii) are forfeited because of the failure to meet a contingency or condition required to vest such shares or otherwise return to the Company, or (iii) are reacquired, withheld (or not issued) to satisfy a tax withholding obligation in connection with an award or to satisfy the purchase price or exercise price of a stock award. No further grants will be made under the Prior Plans. In addition, on January 22, 2020, an additional 4,166,860 shares of common stock became available for issuance under the 2019 Plan pursuant to the Milestone Closing of the May 2019 SPA. Further, on January 1st of each year, for a period of not more than ten years, beginning on January 1, 2021 and continuing through January 1, 2029, the number of shares authorized for issuance under the 2019 Plan will increase by 5.0% of the total number of shares of our capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as may be determined by our Board of Directors.

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

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

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

Pursuant to the May 2019 SPA, in the event our Board of Directors unanimously resolves to recommence our Phase 1 multiple ascending dose clinical trial of our RGLS4326 product candidate for the treatment of ADPKD (the "Phase 1 Trial") based on correspondence from the U.S. Food and Drug Administration's Division of Cardiovascular and Renal Products, and thereafter but on or before December 31, 2019 we make a public announcement of our plan to recommence the Phase 1 Trial (the "Public

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

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

Exchange Offer

On October 15, 2018, we filed a tender offer statement on Schedule TO with the Securities and Exchange Commission related to an offer by us to certain eligible optionholders, subject to specified conditions, to exchange some or all of their outstanding options to purchase shares of our common stock for new RSUs (the “Exchange Offer”).

The exchange ratio for each option eligible for exchange was determined using the Black-Scholes option pricing model and was based on, among other things, the fair market value of a share of our common stock, the volatility of our common stock, U.S. treasury rates, the exercise prices of such options, the remaining terms of such options and the term of the new RSUs. There were a total of 915,009 options eligible for exchange in the Exchange Offer by 31 eligible optionholders, all of which were exchanged for 603,058 RSUs. Of the 603,058 RSUs issued in the Exchange Offer, 514,955 contain certain performance conditions requisite for vesting commencement. Incremental stock-based compensation cost associated with the Exchange Offer was \$0.4 million.

ATM Offering

On December 12, 2018, we entered into a Common Stock Sales Agreement (the “Stock Sales Agreement”) with H.C. Wainwright & Co., LLC (“HCW”), pursuant to which we may sell and issue shares of our common stock from time to time through HCW, as our sales agent (the “ATM Offering”). We have no obligation to sell any shares of common stock in the ATM Offering, and may at any time suspend offers under the Stock Sales Agreement or terminate the Stock Sales Agreement. Subject to the terms and conditions of the Stock Sales Agreement, HCW will use its commercially reasonable efforts to sell shares of our common stock from time to time based upon our instructions (including any price, time or size limits or other parameters or conditions the we may impose, subject to certain restrictions). We pay HCW a commission of 3.0% of the gross sales price of any shares sold under the Stock Sales Agreement. A total of 1,903,880 shares were sold for proceeds of \$2.1 million (net of approximately \$0.1 million in commissions) under the ATM Offering during the year ended December 31, 2019. No shares were sold during the year ended December 31, 2018.

Shares Reserved for Future Issuance

The following shares of common stock were reserved for future issuance as of December 31, 2019 (in thousands):

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| | |
|--|---------------|
| Class A-1 convertible preferred stock outstanding (as-converted) | 4,159 |
| Class A-2 convertible preferred stock outstanding (as-converted) | 32,884 |
| Initial Closing warrants | 13,890 |
| Milestone Closing warrants | 32,884 |
| Common stock options outstanding | 3,098 |
| RSUs outstanding | 129 |
| Common stock available for future grant under the 2019 Equity Incentive Plan | 404 |
| Employee Stock Purchase Plan | 192 |
| Total common shares reserved for future issuance | <u>87,640</u> |

The following table summarizes our stock option activity under all equity incentive plans for the year ended December 31, 2019 (shares and aggregate intrinsic value in thousands):

| | Number of options | Weighted average exercise price | Weighted average remaining contractual term | Aggregate intrinsic value |
|--|-------------------|---------------------------------|---|---------------------------|
| Options outstanding at December 31, 2018 | 59 | \$ 45.60 | | |
| Granted | 3,224 | \$ 0.68 | | |
| Exercised | (3) | \$ 0.95 | | |
| Canceled/forfeited/expired | (182) | \$ 6.81 | | |
| Options outstanding at December 31, 2019 | <u>3,098</u> | \$ 1.17 | 9.6 | \$ 703 |
| Exercisable at December 31, 2019 | <u>237</u> | \$ 6.78 | 8.5 | \$ 35 |

The weighted average grant date fair value per share of employee stock options granted during the years ended December 31, 2019 and 2018 was \$0.52 and \$8.63, respectively.

The total intrinsic value of stock options exercised was less than \$0.1 million for the years ended December 31, 2019, and 2018. Cash received from the exercise of stock options was less than \$0.1 million for the years ended December 31, 2019 and 2018.

The total compensation cost related to stock options not yet recognized was \$1.2 million as of December 31, 2019. The weighted-average period over which this expense is expected to be recognized is approximately 1.7 years.

The following table summarizes our RSU activity under all equity incentive plans for the year ended December 31, 2019 (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, 2018 | 601 | \$ 1.50 | | |
| Granted | 287 | \$ 0.95 | | |
| Vested | (559) | \$ 1.27 | | |
| Canceled/forfeited/expired | (200) | \$ 1.34 | | |
| RSUs outstanding at December 31, 2019 | <u>129</u> | \$ 1.50 | 0.8 | \$ 115 |

The total compensation cost related to non-vested RSUs not yet recognized was \$0.4 million as of December 31, 2019. The weighted-average period over which this expense is expected to be recognized is approximately 0.8 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 2012 Equity Incentive Plan, 2015 Inducement Plan, 2019 Equity Incentive

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

| | Year ended December 31, | |
|--|-------------------------|--------|
| | 2019 | 2018 |
| Stock options | | |
| Risk-free interest rate | 1.7% | 2.7% |
| Volatility | 94.6% | 87.8% |
| Dividend yield | — | — |
| Expected term (years) | 6.1 | 6.1 |
| Performance stock options | | |
| Risk-free interest rate | 2.6% | 2.7% |
| Volatility | 93.8% | 87.4% |
| Dividend yield | — | — |
| Expected term (years) | 6.1 | 5.7 |
| Employee stock purchase plan shares | | |
| Risk-free interest rate | 2.3% | 1.9% |
| Volatility | 110.5% | 100.6% |
| 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, | |
|----------------------------|-------------------------|----------|
| | 2019 | 2018 |
| Research and development | \$ 309 | \$ 2,256 |
| General and administrative | 1,979 | 3,184 |
| Total | \$ 2,288 | \$ 5,440 |

Employee Stock Purchase Plan

In October 2012, we adopted the 2012 Employee Stock Purchase Plan (“2012 Purchase Plan”), which enables participants to contribute up to 15% of such participant’s eligible compensation during a defined six-month period to purchase our common stock. The purchase price of common stock under the 2012 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. As of December 31, 2019, 91,948 shares of our common stock had been issued under the 2012 Purchase Plan, with 4,035 shares of common stock issued for the year ended December 31, 2019. Under the 2012 Purchase Plan, 192,687 shares of our common stock were reserved for future issuance and have been authorized for purchase as of December 31, 2019.

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 \$0.1 million for the years ended December 31, 2019 and 2018.

12. Income Taxes

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

| | Year ended December 31, | |
|--------------------|-------------------------|--------------|
| | 2019 | 2018 |
| Current: | | |
| Federal | \$ (13) | \$ (26) |
| State | 1 | 1 |
| | (12) | (25) |
| Deferred: | | |
| Federal | 13 | 87 |
| State | — | — |
| | 13 | 87 |
| Income tax expense | <u>\$ 1</u> | <u>\$ 62</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, | |
|---|-------------------------|--------------|
| | 2019 | 2018 |
| Expected income tax benefit at federal statutory tax rate | \$ (3,904) | \$ (10,216) |
| State income taxes, net of federal benefit | (1,390) | (3,005) |
| Tax credits | (374) | (3,666) |
| Change in valuation allowance | 603 | 12,706 |
| Return to provision adjustments | (358) | 441 |
| Stock compensation | 3,934 | 251 |
| Reserve for uncertain tax positions | 1,444 | 3,596 |
| Other | 46 | (45) |
| Income tax expense | <u>\$ 1</u> | <u>\$ 62</u> |

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

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| | December 31, | |
|---|--------------|-----------|
| | 2019 | 2018 |
| Deferred tax assets: | | |
| Net operating loss carryovers | \$ 79,675 | \$ 74,965 |
| Research and development and other tax credits | 33,429 | 33,121 |
| Deferred revenue | 1 | 16 |
| Intangibles and property and equipment basis difference | 782 | — |
| Stock compensation expense | 1,389 | 5,033 |
| Lease liability | 164 | — |
| Other | 461 | 2,027 |
| Total deferred tax assets | 115,901 | 115,162 |
| Total deferred tax liabilities | (325) | (176) |
| Net deferred tax asset | 115,576 | 114,986 |
| Valuation allowance | (115,564) | (114,960) |
| Net deferred tax asset | \$ 12 | \$ 26 |

For all periods presented, we have determined that it is more likely than not that our deferred tax asset will not be realized, with the exception of the refundable AMT tax credit. Accordingly, we have recorded a valuation allowance to offset the net deferred tax asset of \$115.6 million.

As of December 31, 2019, we had NOL carryforwards for U.S. federal and California state tax purposes of \$328.0 million and \$276.0 million, respectively, which begin to expire in 2030 and 2031, respectively. The federal NOL generated after 2017 of \$64.6 million will carry forward indefinitely and be available to offset up to 80% of future taxable income each year. As of December 31, 2019, we also had federal and California research and development tax credit carryforwards of \$31.1 million and \$9.1 million, respectively. The federal research and development tax credit carryforwards will begin to expire in 2029. 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, 2019 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, | |
|--|-------------------------|-----------|
| | 2019 | 2018 |
| Beginning balance of unrecognized tax benefits | \$ 14,700 | \$ 4,421 |
| (Decrease) increase for prior year tax positions | (7) | 5,961 |
| Increase for current year tax positions | 1,880 | 4,318 |
| Total | \$ 16,573 | \$ 14,700 |

Included in unrecognized tax benefits of \$16.6 million at December 31, 2019 was \$13.3 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 2009 and forward are subject to examination by the U.S. tax authorities and our tax years for 2010 and forward are subject to examination by the 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, 2019 and 2018, we have not recognized any interest or penalties related to income taxes.

13. 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 ROU assets and operating lease liabilities based on the present value of lease payments over the lease term at the commencement date. Operating lease ROU assets are comprised of the lease liability plus any lease payments made and excludes lease incentives. Lease terms include options to renew or terminate the lease when we are reasonably certain that the renewal option will be exercised or when it is reasonably certain that the termination option will not be exercised. For our operating leases, we generally cannot determine the interest rate implicit in the lease, in which case we use our incremental borrowing rate as the discount rate for the lease. We estimate our incremental borrowing rate for our operating leases based on what we would normally pay to borrow on a collateralized basis over a similar term for an amount equal to the lease payments. Operating lease expense is recognized on a straight-line basis over the lease term. Leases with a lease term of 12 months or less are not recorded on the 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.

In July 2015, we entered into an operating lease agreement (the "Prior Lease") for approximately 59,248 square feet of office and laboratory facility space located at 10614 Science Center Drive, San Diego, California 92121. The lease term was 96 months from the lease commencement date, and we moved our headquarters into this facility in May 2016. In conjunction with the lease, we received \$1.4 million of lease incentives and \$8.2 million of tenant improvement allowance, which was to be used for non-structural leasehold improvements. The lease incentives and tenant improvement allowance were included within deferred rent. Our deferred rent balance as of December 31, 2018 was \$8.0 million. The Prior Lease agreement was with ARE SD Region No. 44 LLC ("Landlord").

On February 19, 2019, we entered into an agreement, the ("Space Swap Agreement"), with Nitto Biopharma, Inc. ("Nitto"), pursuant to which we agreed, contingent upon the execution of a new lease agreement (the "February Lease") for Nitto's space with Landlord and the termination of the Prior Lease, to, among other things, (i) swap buildings with Nitto, and (ii) sell, convey and transfer all right, title and interest in certain furniture, fixtures and equipment to Nitto, as set forth in the Space Swap Agreement. Under the Space Swap Agreement, we paid Nitto (a) a relocation assistance payment in the amount of \$0.1 million; (b) \$0.2 million representing the difference between the security deposits under the Prior Lease and Nitto's prior lease, and (c) \$1.3 million as reimbursement for the six monthly installments of base monthly rent due pursuant to the new lease between Nitto and Landlord, subject to certain adjustments, which reimbursements are to be paid as rent comes due for Nitto under its new lease.

On February 25, 2019, we and Landlord entered into a second amendment (the "Prior Lease Amendment") to the Prior Lease. Under the terms of the Prior Lease Amendment, the expiration date of the Prior Lease was accelerated from April 30, 2024 to March 31, 2019 and the Prior Lease terminated on April 1, 2019. The Prior Lease Amendment eliminated all further cash payments due under the Prior Lease, including aggregate base rent over its remaining term of approximately \$14.4 million.

On February 25, 2019, we entered into the February Lease with Landlord, for the lease of approximately 24,562 square feet of rentable area of the building located at 10628 Science Center Drive, San Diego, California, 92121 (the "Premises"), which Premises were previously occupied by Nitto. The commencement date of the February Lease was April 1, 2019 (the "Commencement Date"). The Premises served as our new principal executive offices and as a laboratory for research and development, manufacturing and other related uses. The term of the February Lease ("Initial Term") was 51 months, ending June 30, 2023. The aggregate base rent due over the Initial Term was approximately \$4.8 million. We were also responsible for the payment of additional rent to cover our share of the annual operating expenses, the annual tax expenses and the annual utilities costs related to the February Lease. The base rent payments due were: \$0.6 million in 2019, \$1.2 million in 2020, \$1.2 million in 2021, \$1.2 million in 2022, and \$0.6 million in 2023.

The execution of the February Lease and Prior Lease Amendment resulted in a modification which was not accounted for as a separate contract. Rather, we accounted for the two contracts with Landlord in combination as they were entered into at the same time and negotiated as a package to achieve the same commercial objective. The leasehold improvements under the Prior Lease were accounted for as non-cash consideration of \$5.6 million paid by us upon termination of the Prior Lease to the Landlord. We accounted for a \$1.3 million portion of the reduction in the lease liability for the Prior Lease as a non-cash gain in the statement of operations due to the reduction in lease term and leased space with Landlord and a \$0.9 million portion of the reduction of the lease liability as a deferred credit that is amortized as a reduction to rent expense over the term of the Lease. The \$1.6 million obligation to reimburse Nitto for six monthly installments of base rent of the Prior Lease and certain other costs were accounted for as cost of terminating the Prior Lease in the statement of operations. The net impact of the

modification was a \$0.4 million charge in the statement of operations. Our payment obligations to Nitto under the Space Swap Agreement were fully satisfied as of September 2019 and no assets or liabilities remained with respect to the Prior Lease as of December 31, 2019. The commencement date of the February Lease did not occur until April 1, 2019 and therefore, as of March 31, 2019, the lease liability for the February Lease was zero. On April 1, 2019, we recorded a \$3.8 million lease liability for the February Lease, which was calculated as the present value of future lease payments to be made under the February Lease. A \$2.9 million ROU asset was also recorded on April 1, 2019, which represents the difference between the lease liability and the \$0.9 million deferred credit for the reduction of the lease liability under the Prior Lease.

On June 19, 2019, we entered into a lease agreement (the “New Lease”) with Landlord for the lease of approximately 8,727 square feet of rentable area of the building located at 10628 Science Center Drive, Suite 225, San Diego, California 92121 (the “New Premises”). The commencement date of the New Lease was July 1, 2019 (the “New Commencement Date”). We are using the New Premises as our new principal executive offices and as a laboratory for research and development and other related uses. The term of the New Lease (the “New Initial Term”) is two years, six months, ending December 31, 2021. The base rent payments due for the New Premises are: \$0.1 million in 2019, \$0.4 million in 2020 and \$0.4 million in 2021, net of certain rent abatement terms. We will also be responsible for the payment of additional rent to cover our share of the annual operating expenses of the building, the annual tax expenses of the building and the annual utilities cost of the building.

On June 19, 2019, we entered into a first amendment to the February Lease with Landlord (the “February Lease Amendment”). Under the terms of the February Lease Amendment, the expiration date of the February Lease was accelerated from June 30, 2023 to June 30, 2019 and the February Lease terminated upon the Commencement Date of the New Lease. The February Lease Amendment eliminated all further rents due under the February Lease, including aggregate base rent over its remaining term of approximately \$4.8 million.

The execution of the New Lease and February Lease Amendment resulted in a modification which was not accounted for as a separate contract. Rather, we accounted for the two contracts with Landlord in combination as they were entered into at the same time and negotiated as a package to achieve the same commercial objective. We accounted for a \$0.5 million portion of the reduction in the lease liability for the February Lease as a non-cash gain in the statement of operations due to the reduction in lease term and leased space with Landlord and a \$0.2 million portion of the reduction of the lease liability as a deferred credit that is amortized as a reduction to rent expense over the term of the New Lease. No other assets or liabilities remained with respect to the February Lease as of December 31, 2019. The commencement date of the New Lease did not occur until July 1, 2019 and therefore, as of June 30, 2019, the lease liability for the New Lease was zero. On July 1, 2019, we recorded a \$0.8 million lease liability for the New Lease, which was calculated as the present value of future lease payments to be made under the New Lease. A \$0.6 million ROU asset was also recorded on July 1, 2019, which represents the difference between the lease liability and the remaining \$0.2 million deferred credit for the reduction of the lease liability under the February Lease.

The table below summarizes our lease liabilities and corresponding ROU assets as of December 31, 2019 (in thousands):

Assets

| | | |
|------------------|----|-----|
| Operating | \$ | 464 |
| Financing | | 466 |
| Total ROU assets | \$ | 930 |

Liabilities

Current:

| | | |
|-----------|----|-----|
| Operating | \$ | 361 |
| Financing | | 277 |

Long-term:

| | | |
|-----------|--|-----|
| Operating | | 417 |
| Financing | | 56 |

| | | |
|-------------------------|----|-------|
| Total lease liabilities | \$ | 1,111 |
|-------------------------|----|-------|

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Rent expense for the years ended December 31, 2019 and 2018 was \$0.7 million and \$1.3 million, respectively.

The table below summarizes our lease costs from our statement of operations and cash payments from our statement of cash flows during the year ended December 31, 2019 (in thousands):

| | Year ended December 31, 2019 |
|--|---------------------------------|
| Lease cost: | |
| Operating lease cost | \$ 715 |
| Finance lease cost: | |
| Amortization of right-of-use assets | 182 |
| Interest expense on lease liabilities | 5 |
| Total lease cost | \$ 902 |
| Cash payment information: | |
| Operating cash used for operating leases | \$ 756 |
| Operating cash used for finance leases | 24 |
| Financing cash used for finance leases | 263 |
| Total cash paid for amounts included in the measurement of lease liabilities | \$ 1,043 |

The table below summarizes other non-cash information under our operating and financing lease obligations as of December 31, 2019 (in thousands, except years and rates):

| | |
|--|--------|
| Supplemental non-cash information: | |
| Operating lease liabilities arising from obtaining right-of-use assets | \$ 778 |
| Weighted-average remaining lease term (years) - operating leases | 2.0 |
| Weighted-average remaining lease term (years) - finance leases | 1.2 |
| Weighted-average discount rate - operating leases | 10.9% |
| Weighted-average discount rate - finance leases | 4.9% |

Our future lease payments under operating and finance leases at December 31, 2019 are as follows (in thousands):

| | Operating Leases | Finance Leases |
|---|------------------|----------------|
| 2020 | 429 | 287 |
| 2021 | 442 | 57 |
| Total lease payments | \$ 871 | \$ 344 |
| Less: amount representing interest | (93) | (11) |
| Present value of obligations under leases | 778 | 333 |
| Less: current portion | (361) | (277) |
| Long-term lease obligations | \$ 417 | \$ 56 |

As of December 31, 2018, prior to the adoption of the new leases standard, aggregate future annual minimum lease payments for the Company's operating lease were as follows: \$2.7 million in 2019 and 2020, \$2.8 million in 2021, \$2.9 million in 2022, \$3.0 million in 2023 and \$1.0 million thereafter.

14. Selected Quarterly Financial Data (Unaudited)

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The following financial information reflects all normal recurring adjustments, which are, in the opinion of management, necessary for a fair statement of the results of the interim periods. Summarized quarterly data for 2019 and 2018 are as follows (in thousands, except per share data):

| | For the quarters ending | | | |
|---|-------------------------|-----------|--------------|-------------|
| | March 31 | June 30 | September 30 | December 31 |
| 2019 | | | | |
| Total revenues | \$ 6,778 | \$ 18 | \$ 18 | \$ 18 |
| Total operating expenses | (9,516) | (4,686) | (5,011) | (4,453) |
| Net loss | (3,260) | (5,016) | (5,423) | (4,893) |
| Net loss per share, basic and diluted (1) | \$ (0.31) | \$ (0.30) | \$ (0.26) | \$ (0.23) |
| 2018 | | | | |
| Total revenues | \$ 18 | \$ 18 | \$ 18 | \$ 18 |
| Total operating expenses | (15,601) | (13,362) | (9,872) | (8,000) |
| Net loss | (16,025) | (13,847) | (10,273) | (8,563) |
| Net loss per share, basic and diluted (1) | \$ (1.85) | \$ (1.59) | \$ (1.18) | \$ (0.98) |

(1) Net loss per share is computed independently for each of the quarters presented. Therefore, the sum of the quarterly per-share calculations will not necessarily equal the annual per share calculation.

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, 2019, we carried out an evaluation, under the supervision and with the participation of our management, including our principal executive officer and our principal financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended. Based on this evaluation, our principal executive officer and our principal financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2019.

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, 2019, 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, 2019, 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.

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 section headed “Election of Directors” and “Executive Officers” in our Proxy Statement for our 2020 Annual Meeting of Stockholders ("Proxy Statement") to be filed with the SEC no later than April 29, 2020, 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.

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” 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:

| | Page Number |
|---|--------------------|
| Report of Independent Registered Public Accounting Firm | 58 |
| Balance Sheets | 59 |
| Statements of Operations and Comprehensive Loss | 60 |
| Statements of Stockholders' Equity | 61 |
| Statements of Cash Flows | 62 |
| 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.

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| Exhibit Number | <u>Description</u> |
|-----------------------|---|
| 3.1 | <u>Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on August 3, 2016.</u> |
| 3.2 | <u>Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on October 2, 2018).</u> |
| 3.3 | <u>Certificate of Designation of Preferences, Rights and Limitations of Class A-1 Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on May 9, 2019).</u> |
| 3.4 | <u>Certificate of Designation of Preferences, Rights and Limitations of Class A-2 Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on December 26, 2019).</u> |
| 3.5 | <u>Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on June 8, 2016).</u> |
| 4.1 | Reference is made to Exhibits <u>3.1</u> , <u>3.2</u> , <u>3.3</u> , <u>3.4</u> and <u>3.5</u> . |
| 4.2 | <u>Form of Common Stock Certificate of the Registrant (incorporated by reference to Exhibit 4.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on November 9, 2018).</u> |
| 4.3 | <u>Description of Common Stock.</u> |
| 4.4 | <u>Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on May 9, 2019).</u> |
| 10.1* | <u>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).</u> |
| 10.2* | <u>Regulus Therapeutics Inc. 2009 Equity Incentive Plan, as amended, and Form of Stock Option Grant Notice, Option Agreement and Form of Notice of Exercise (incorporated by reference to Exhibit 10.2 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).</u> |
| 10.3* | <u>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).</u> |
| 10.4* | <u>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).</u> |
| 10.5* | <u>2012 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1, as amended, originally filed with the SEC on August 17, 2012).</u> |
| 10.6 | <u>Regulus Therapeutics Inc. Inducement Plan and Form of Stock Option Grant Notice, Form of Stock Option Agreement and Notice of Exercise thereunder (incorporated by reference to Exhibit 99.1 to the Company's Registration Statement on Form S-8 (File No. 333-206511), filed with the SEC on August 21, 2015).</u> |
| 10.7* | <u>Regulus Therapeutics Inc. 2019 Equity Incentive Plan (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on August 6, 2019).</u> |

10.8*

[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 \(Registration No. 333-233414, filed with the SEC on August 22, 2019\).](#)

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- 10.9* [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 \(Registration No. 333-233414, filed with the SEC on August 22, 2019\).](#)
- 10.10* [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* [Joseph P. Hagan, Base Salary and Target Bonus Increase, effective May 4, 2017 \(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 2, 2017\).](#)
- 10.12* [Joseph P. Hagan, Yearly Discretionary Base Salary Increase, effective January 1, 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, 2018\).](#)
- 10.13* [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\).](#)
- 10.14* [Offer Letter Agreement, dated July 29, 2019, by and between the Registrant and Cris Calsada \(incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K \(File No. 001-35670, filed with the SEC on July 30, 2019\).](#)
- 10.15* [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\).](#)
- 10.16* [Consulting agreement, dated July 26, 2019, by and between the Registrant and Daniel R. Chevallard \(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 August 8, 2019\).](#)
- 10.17† [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 10.17 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\).](#)
- 10.18† [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 10.18 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\).](#)
- 10.19† [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 10.19 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\).](#)
- 10.20† [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 99.1 to the Registrant's Current Report on Form 8-K \(File No. 001-35670\), filed with the SEC on August 7, 2013\).](#)
- 10.21 [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\).](#)
- 10.22† [Non-Exclusive Technology Alliance and Option Agreement between the Registrant and Sanofi, dated June 21, 2010 \(incorporated by reference to Exhibit 10.32 to the Registrant's Registration Statement on Form S-1, as amended \(File](#)

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- 10.23† [Second Amended and Restated Collaboration and License Agreement dated February 4, 2014 between the Registrant and Sanofi \(incorporated by reference to Exhibit 10.52 to the Registrant's Annual Report on Form 10-K \(File No. 001-35670\), filed with the SEC on February 28, 2014\).](#)
- 10.24† [First Amendment to Second Amended and Restated Collaboration and License Agreement, dated November 5, 2018, by and between the Registrant and Sanofi \(incorporated by reference to Exhibit 10.38 to the Registrant's Annual Report on Form 10-K \(File No. 001-35670\), filed with the SEC on March 18, 2019\).](#)
- 10.25 [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\).](#)
- 10.26 [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\).](#)
- 10.27† [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 10.32 to the Registrant's Annual Report on Form 10-K \(File No. 001-35670\), filed with the SEC on March 8, 2018\).](#)
- 10.28† [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\).](#)
- 10.29 [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\).](#)
- 10.30 [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\).](#)
- 10.31 [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\).](#)
- 10.32 [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\).](#)
- 10.33 [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\).](#)
- 10.34 [Lease Agreement, dated February 25, 2019, by and between the Registrant and ARE-SD Region No. 44 LLC. \(incorporated by reference to Exhibit 10.41 to the Registrant's Annual Report on Form 10-K \(File No. 001-35670\), filed with the SEC on March 18, 2019\).](#)
- 10.35 [Agreement, dated February 19, 2019, by and between the Registrant and Nitto Biopharma, Inc. \(incorporated by reference to Exhibit 10.42 to the Registrant's Annual Report on Form 10-K \(File No. 001-35670\), filed with the SEC on March 18, 2019\).](#)
- 10.36 [Second Amendment to Lease Agreement, dated February 25, 2019, by and between the Registrant and ARE-SD Region No. 44 LLC Agreement \(incorporated by reference to Exhibit 10.43 to the Registrant's Annual Report on Form 10-K \(File No. 001-35670\), filed with the SEC on March 18, 2019\).](#)

- 10.37 [Lease Agreement, dated June 19, 2019, by and between the Registrant and ARE-SD Region No. 44 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, 2019\).](#)
- 10.38 [First Amendment to Lease, dated June 19, 2019, by and between the Registrant and ARE-SD Region No. 44 LLC \(incorporated by reference to Exhibit 10.5 to the Registrant's Quarterly Report on Form 10-Q \(File No. 001-35670\), filed with the SEC on August 8, 2019\).](#)

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|---------|--|
| 10.39 | <u>Common Stock Sales Agreement, dated December 12, 2018, by and between the Registrant and H.C. Wainwright & Co., 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 December 12, 2018).</u> |
| 10.40 | <u>Securities Purchase Agreement, dated May 3, 2019, by and among the Registrant and the Purchasers listed on Exhibit A thereto (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 May 9, 2019).</u> |
| 23.1 | <u>Consent of Independent Registered Public Accounting Firm.</u> |
| 24.1 | <u>Power of Attorney. Reference is made to the signature page hereto.</u> |
| 31.1 | <u>Certification of the Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.</u> |
| 31.2 | <u>Certification of the Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.</u> |
| 32.1** | <u>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.</u> |
| 101.INS | XBRL Instance Document. |
| 101.SCH | XBRL Taxonomy Extension Schema Document. |
| 101.CAL | XBRL Taxonomy Extension Calculation Linkbase Document. |
| 101.DEF | XBRL Taxonomy Extension Definition Linkbase Document. |
| 101.LAB | XBRL Taxonomy Extension Label Linkbase Document. |
| 101.PRE | XBRL Taxonomy Extension Presentation Linkbase Document. |

† We have 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.

* 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 12, 2020

Regulus Therapeutics Inc.

By: /s/ Joseph P. Hagan

Joseph P. Hagan

President and 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.

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| <u>Signature</u> | <u>Title</u> | <u>Date</u> |
|--|---|--------------------|
| <u>/s/ Joseph P. Hagan</u> Joseph P. Hagan | President & Chief Executive Officer and Director (Principal Executive Officer) | March 12, 2020 |
| <u>/s/ Cris Calsada</u> Cris Calsada | Chief Financial Officer (Principal Financial Officer) | March 12, 2020 |
| <u>/s/ Daniel J. Penksa</u> Daniel J. Penksa | Controller (Principal Accounting Officer) | March 12, 2020 |
| <u>/s/ Stelios Papadopoulos</u> Stelios Papadopoulos, Ph.D. | Chairman of the Board of Directors | March 12, 2020 |
| <u>/s/ David Baltimore</u> David Baltimore, Ph.D. | Director | March 12, 2020 |
| <u>/s/ Kathryn Collier</u> Kathryn Collier | Director | March 12, 2020 |
| <u>/s/ Jake R. Nunn</u> Jake R. Nunn | Director | March 12, 2020 |
| <u>/s/ William H. Rastetter</u> William H. Rastetter, Ph.D. | Director | March 12, 2020 |
| <u>/s/ Hugh Rosen</u> Hugh Rosen, M.D., Ph.D. | Director | March 12, 2020 |
| <u>/s/ Simos Simeonidis</u> Simos Simeonidis, Ph.D. | Director | March 12, 2020 |
| <u>/s/ Pascale Witz</u> Pascale Witz | Director | March 12, 2020 |