Table of Contents

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, 2020

or

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

FOR THE TRANSITION PERIOD FROM _____ TO _____

Commission file number: 001-35670

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

Delaware	**26-4738379**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
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 ☐

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

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

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

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

As of June 30, 2020, 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 $22.5 million, based on the closing price of the registrant's common stock on the Nasdaq Stock Market on June 30, 2020 of $0.68 per share.

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of March 5, 2021 was 72,504,772.

REGULUS THERAPEUTICS INC.
TABLE OF CONTENTS

Risk Factor Summary

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

- The approach we are taking to discover and develop drugs is novel and may never lead to marketable products.
- We may not be successful in our efforts to identify or discover potential product candidates.
- Preclinical and clinical studies of our product candidates may not be successful. If we are unable to generate successful results from our preclinical and clinical studies of our product candidates, or experience significant delays in doing so, our business may be materially harmed.
- If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- Any of our product candidates may cause adverse effects or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance.
- Even if we complete the necessary preclinical studies and clinical trials, we cannot predict whether or when we will obtain regulatory approval to commercialize a product candidate and we cannot, therefore, predict the timing of any revenue from a future product.
- We will need to raise additional capital, and if we are unable to do so when needed, we will not be able to continue as a going concern.
- Payments under the instruments governing our indebtedness may reduce our working capital. In addition, a default under our loan and security agreement could cause a material adverse effect on our financial position.
- We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.
- We have never generated any revenue from product sales and may never be profitable.
- We will depend upon collaborations for the development and eventual commercialization of certain *micro*RNA product candidates. If these collaborations are unsuccessful or are terminated, we may be unable to commercialize certain product candidates and we may be unable to generate revenues from our development programs.
- We rely on limited sources of supply for the drug substance of product candidates and any disruption in the chain of supply may cause a delay in developing and commercializing these product candidates.
- Manufacturing issues may arise that could increase product and regulatory approval costs or delay commercialization.
- We rely on third parties to conduct, supervise and monitor our clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.
- If we are unable to obtain or protect intellectual property rights related to our future products and product candidates, we may not be able to compete effectively in our markets.

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

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

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

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

PART I

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;
- the potential impact of the COVID-19 pandemic on our business; and
- the risks and other forward-looking statements described under the caption “Risk Factors” under Part I, Item 1A of this Annual Report on Form 10-K.

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

Item 1. Business

We are a clinical-stage biopharmaceutical company focused on discovering and developing first-in-class drugs targeting *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 RG-012 and any other miR-21 programs. The transition activities were completed in the second quarter of 2019. RGLS4326, an anti-miR targeting miR-17, is in Phase 1 development for the treatment of autosomal dominant polycystic kidney disease ("ADPKD"). In addition to these clinical programs, we continue to develop a pipeline of preclinical drug product candidates.

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

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

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

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

We have assembled significant expertise in the *micro*RNA field, including expertise in *micro*RNA biology and oligonucleotide chemistry, a broad intellectual property estate, relationships with key opinion leaders and a disciplined drug

discovery and development process. We are using our *micro*RNA expertise to develop chemically modified, single-stranded oligonucleotides that we call anti-miRs to modulate *micro*RNAs and address underlying disease. We believe *micro*RNAs may play a critical role in complex disease and that targeting them with anti-miRs may become a source of a new and major class of drugs with broad therapeutic application, much like small molecules, biologics and monoclonal antibodies.

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

Since our inception through December 31, 2020, we have received $361.8 million from the sale of our equity and convertible debt securities, $101.8 million from our strategic collaborations, principally from upfront payments, research funding and preclinical and clinical milestones, and $19.8 million in net proceeds from a Term Loan. As of December 31, 2020, we had cash and cash equivalents of $31.1 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. Kidney tissue concentrations were achieved in biopsy patients that would be predictive of therapeutic benefit based on animal disease models. In addition, modulation of the target, miR-21, was observed. In December 2017, we concluded our global ATHENA natural history of disease study. RG-012 has received orphan designation in both the United States and Europe. In November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program to Sanofi. As a result, Sanofi became responsible for all costs incurred in the development of these miR-21 programs. The transition activities, including the transfer of the investigational new drug application ("IND"), were completed in the second quarter of 2019. While Sanofi is currently enrolling patients into a Phase 2 clinical trial, with sites in the United States, Europe, Australia and China, we believe new site initiation and patient enrollment has been, and will continue to be, impacted by the COVID-19 pandemic.

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

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

up. RGLS4326 was well-tolerated with no serious adverse events reported. Results show that plasma exposure is dose proportional.

In October 2020, we commenced dosing in a Phase 1b adaptive design, open-label, short-term, multiple dose study in patients with ADPKD. The study will enroll up to three cohorts of patients with ADPKD to evaluate safety, PK, and changes in levels of polycystin 1 (PC1) and polycystin 2 (PC2). Patients with ADPKD, due to the mutation in the polycystic kidney gene, have been reported to have low levels of PC1 and PC2, the proteins encoded by the PKD1 and PKD2 genes, respectively. This study is designed to evaluate whether different dose levels of RGLS4326 can increase levels of PC1 and PC2, in ADPKD patients. The first cohort enrolled nine patients who will receive RGLS4326 every two weeks over a six week period. We anticipate availability of results from the first cohort in the second quarter of 2021. Additional non-clinical studies initiated last year in mice and non-human primates to further characterize the PK properties of RGLS4326 have also been recently completed. The RGLS4326 IND is currently on a partial clinical hold for treatment of extended duration beyond the current Phase 1b study until the second set of requirements outlined by FDA have been satisfactorily addressed. Information from the Phase 1 clinical studies, together with information from the recently completed additional nonclinical studies, will be used to address the second set of requirements to support studies of extended duration. In July 2020, the FDA granted orphan drug designation to RGLS4326 for the treatment of ADPKD.

Preclinical Pipeline

A major focus of our preclinical research has historically targeted dysregulated *micro*RNAs implicated in diseases of high unmet medical need where we know we can effectively deliver to the target tissue or organ, such as the liver 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. 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. We are currently optimizing our development candidate for HBV.

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 *micro*RNA in a complex disease like NASH may offer a unique mechanism of action from other programs in development. We are seeking a partner to further advance its development.

Cell Therapies program: Cell therapies have been approved to treat a variety of hematological malignancies. Targeting solid tumors, however, has proven challenging for cell therapies due to various factors including the immune-suppressive effect of the tumor microenvironment ("TME"). We believe that ex vivo modulation of microRNA may enable cell therapy approaches to overcome the effects of the TME and address other challenges faced by cell therapies. We have demonstrated that targeting microRNA ex vivo can improve certain characteristics of engineered cells including improved in vitro expansion, effector function, cytokine production, as well as resistance to exhaustion induced by tonic signaling. We are pursuing multiple applications of microRNA technology in a variety of cell therapies.

Our *micro*RNA product platform

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

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

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

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

Step 1 - Evaluation of microRNA therapeutic opportunities

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

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

Step 2 - Identification of microRNA targets

We identify *micro*RNA targets through bioinformatic analysis of public and proprietary *micro*RNA expression profiling data sets from samples of diseased human tissues. The analysis of such data sets can immediately highlight a potential role for specific *micro*RNAs in the disease being studied. Further investigation of animal models that are predictive of human diseases in which those same *micro*RNAs 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 *micro*RNA 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 *micro*RNA in healthy animals can create the specific disease state and inhibition of the *micro*RNA can lead to a therapeutic benefit. Second, using animal models predictive of human diseases, we determine whether pharmacological modulation of the up-regulated *micro*RNA target with our anti-miRs can also lead to a therapeutic benefit. This validation process enables us to prioritize *micro*RNA 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 *micro*RNA 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 *micro*RNA 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 *micro*RNA. 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 *micro*RNA target that is up-regulated in a cell and that is involved in the disease state. In binding to the *micro*RNA, anti-miRs correct the dysregulation and return diseased cells to their healthy state.

We have identified and validated several *micro*RNA 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.

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 *micro*RNA biomarkers to support our therapeutic product candidates; and (v) maintain our scientific and intellectual leadership in the *micro*RNA field.

Strategic Collaboration

- In June 2010, we formed a strategic collaboration with Sanofi to discover and develop *micro*RNA therapeutics for fibrotic diseases. In July 2012, we expanded the collaboration to include potential *micro*RNA 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 *micro*RNA 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 $16.8 million in upfront payments and payment for program-related materials and interim milestone payments. We are also eligible to receive a $25.0 million development milestone payment. 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 $193.8 million in aggregate milestone payments upon successful commercialization of *micro*RNA therapeutics, in addition to royalties on net sales for the miR-221/222 program. These payments include up to $63.8 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 *micro*RNA therapeutics and to maintain our leading position in the *micro*RNA therapeutics field.

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

- approximately 145 patents and patent applications that we own or have in-licensed from academic institutions related to *micro*RNA and *micro*RNA 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 *micro*RNA 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 *micro*RNA drug products and *micro*RNA product platform. Based on the patents and patents that may issue from pending applications within our portfolio, patent protection for our *micro*RNA 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 *micro*RNA field. The technologies covered in these patents and applications include various chemical modifications that are applicable to *micro*RNA 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 *micro*RNA 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 *micro*RNA 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 *micro*RNA compounds which are *micro*RNA antagonists and *micro*RNA 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, 2020 and 2019.

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 upon the achievement of certain regulatory milestone events. There was no activity under this agreement for the year ended December 31, 2020.

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

Manufacturing

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

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. 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:

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

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

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

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

In addition, we may be subject to data privacy and security 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 (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), 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. Beginning in 2022, applicable manufacturers also will be required to report such information regarding its payments and other transfers of value to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year.

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

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

Health Reform

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

For example, the ACA includes measures to significantly change the way healthcare is financed by both governmental and private insurers. 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. For example, President Trump signed several Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Congress has also considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, bills affecting the implementation of certain taxes under the ACA have been signed into law. Legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act ("Tax Act"), includes a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. On 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. The U.S. Supreme Court is currently reviewing this case, but it is unknown when a decision will be reached. Although the U.S. Supreme Court has yet ruled on the constitutionality of the ACA, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how the Supreme Court rule, other such litigation, and healthcare reform measures of the Biden administration will impact the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in

2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030 unless additional Congressional action is taken. However, COVID-19 relief support legislation suspended the 2% Medicare sequester from May 1, 2020 through March 31, 2021. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and federal and state legislative activity designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. For example, at the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. On July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that attempt to implement several of the administration's proposals. The FDA also released a final rule, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed pending review by the Biden administration until March 22, 2021. On November 20, 2020, CMS issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. However, it is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. 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, 2020, we had 24 employees, all of which were full-time employees. Of these employees, 16 employees are engaged in research and development activities and 8 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 "*micro*Markers" 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

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 and have completed all dosing. Information from the clinical studies, together with information from additional nonclinical studies, will be used to address the requirements to support studies of extended duration. In addition to the MAD study in healthy volunteers, we have initiated a Phase 1b study in patients with ADPKD to evaluate RGLS4326 for safety, PK, and changes in levels of PC1 and PC2. We cannot be certain that we will be able to satisfy the requirements to initiate studies of extended duration in a timely manner, or at all.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

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

Because we have limited financial and human resources, our existing strategy is to pursue collaboration agreements for the development and commercialization of our programs and potential product candidates in indications with potentially large commercial markets such as ADPKD, HCC, fibrosis, 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, 2020, we had approximately $31.1 million of cash and cash equivalents and we had $6.0 million of outstanding debt obligations (which includes $4.7 million of outstanding principal and $1.3 million of final payment and loan amendment fees) under our $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"). Additionally, we had $0.7 million of debt obligations outstanding from amounts received under the Paycheck Protection Program of the CARES Act ("PPP Loan"). We will need to raise additional capital to fund our operations and service our debt obligations, and if we are unable to raise additional capital when needed, we will not be able to continue as a going concern.

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

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

For the foreseeable future, we expect to rely primarily on equity and/or debt financings to fund our operations. Raising additional capital through the sale of securities could cause significant dilution to our stockholders.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. Our ability to raise additional funds will depend, in part, on the success of our preclinical studies and clinical trials and other product development activities, regulatory events, our ability to identify and enter into licensing or other strategic arrangements, and other events or conditions that may affect our value or prospects, as well as factors

related to financial, economic and market conditions, many of which are beyond our control. There can be no assurances that sufficient funds will be available to us when required or on acceptable terms, if at all.

If we are unable to raise additional capital when required or on acceptable terms, we may be required to:

- significantly delay, scale back or discontinue the development or commercialization of any future product candidates;
- seek collaborations, or amend existing collaborations, for research and development programs at an earlier stage than otherwise would be desirable or for the development of programs that we otherwise would have sought to develop independently, or on terms that are less favorable than might otherwise be available;
- dispose of technology assets, or relinquish or license on unfavorable terms, our rights to technologies or any future product candidates that we otherwise would seek to develop or commercialize ourselves;
- pursue the sale of our company to a third party at a price that may result in a loss on investment for our stockholders; or
- file for bankruptcy or cease operations altogether.

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

Payments under the instruments governing our indebtedness may reduce our working capital. In addition, a default under our loan and security agreement could cause a material adverse effect on our financial position.

In June 2016, we entered into a loan 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. Our required monthly payments to the Lender are comprised of interest only through and including the payment to be made in December 2021. We are required to maintain $3.0 million in cash in a collateral account.

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

Under the Term Loan, our interest rate on borrowed amounts is dependent on LIBOR. LIBOR is the basic rate of interest used in lending between banks on the London interbank market and is widely used as a reference for setting the interest rate on loans globally. In July 2017, the Chief Executive of the United Kingdom Financial Conduct Authority (“FCA”), which regulates LIBOR, announced that the FCA intends to phase out the use of LIBOR by the end of 2021. In addition, the U.S. Federal Reserve, in conjunction with the Alternative Reference Rates Committee, a steering committee comprised of large U.S. financial institutions, is considering replacing U.S. dollar LIBOR with the Secured Overnight Financing Rate (“SOFR”), a new index calculated by short-term repurchase agreements, backed by Treasury securities. Although there have been certain issuances utilizing SOFR, it is unknown whether this or any other alternative reference rate will attain market acceptance as a replacement for LIBOR. The consequences of these developments cannot be entirely predicted, but could result in higher interest rates on our outstanding principal amount under the Term Loan. We cannot provide assurance that future interest rate changes will not have a material negative impact on our business, financial position, or operating results.

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

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

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

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

In addition, in April 2020 we received proceeds of approximately $0.7 million from a PPP Loan, all or a portion of which may be forgiven, which we have used to retain employees, maintain payroll and make lease and utility payments. The PPP Loan matures on April 23, 2022 and bears interest at a rate of 1.00% per annum. We have used all proceeds from the PPP Loan to retain employees and maintain payroll and are seeking forgiveness in accordance with the program. Under the CARES Act and PPP Flexibility Act, loan forgiveness is available for the sum of documented payroll costs, covered mortgage interest, covered rent payments and covered utilities during the 24 week period beginning on the date of loan disbursement. Not more than 40% of the forgiven amount may be for non-payroll costs. The amount of the PPP Loan eligible to be forgiven will be reduced if our full-time headcount declined during the covered period as compared to specified reference periods, or if salaries and wages for employees with salaries of $100,000 or less annually were reduced by more than 25%, unless certain safe harbors were met. We believe the entire $0.7 million in proceeds from the PPP Loan was used for allowable payroll-related costs. We will be required to repay any portion of the outstanding principal that is not forgiven, along with accrued interest, in accordance with the amortization schedule described above, and we cannot provide any assurance that we will be eligible for loan forgiveness or that any amount of the PPP Loan will ultimately be forgiven by the U.S Small Business Administration ("SBA").

If we are found to be in violation of any of the laws or governmental regulations that apply to us in connection with the PPP Loan, including the False Claims Act, or it is otherwise determined that we were not eligible to receive the PPP Loan, we may be subject to penalties, including significant civil, criminal and administrative penalties and could be required to repay the PPP Loan in its entirety. In addition, our receipt of the PPP Loan may result in adverse publicity and damage to our reputation, and a review or audit by the SBA or other government entity or claims under the False Claims Act could consume significant financial and management resources.

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

Since inception, our operations have been primarily limited to acquiring and in-licensing intellectual property rights, developing our *micro*RNA product platform, undertaking basic research around *micro*RNA 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 $15.7 million and $18.6 million for years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $427.0 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;

- disruptions caused by man-made or natural disasters or public health pandemics or epidemics or other business interruptions, including, for example, the COVID-19 pandemic; and

- the failure to deliver products under specified storage conditions and in a timely manner.

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

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

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

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

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

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

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

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

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

We, our collaboration partners and our CROs are required to comply with the FDA's or other regulatory agency's good clinical practices ("GCPs") for conducting, recording and reporting the results of IND-enabling studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA and non-U.S. regulatory agencies enforce these GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data

generated in our clinical trials may be deemed unreliable and the FDA or applicable non-U.S. regulatory agency may require us to perform additional clinical trials before approving any marketing applications for the relevant jurisdiction. Upon inspection, the FDA or applicable non-U.S. regulatory agency may determine that our clinical trials did not comply with GCPs. In addition, our clinical trials will require a sufficiently large number of test subjects to evaluate the safety and effectiveness of a potential drug product. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process.

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

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

RISKS RELATED TO OUR INTELLECTUAL PROPERTY

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

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

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

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

In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available however the life of a patent, and the protection it affords, is limited. Once

the patent life has expired for a product, we may be open to competition from generic medications. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

RISKS RELATED TO COMMERCIALIZATION OF PRODUCT CANDIDATES

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, natural disasters, including earthquakes, typhoons, floods and fires, public health pandemics or epidemics or other business interruptions, including, for example, the COVID-19 pandemic

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

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

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

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

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

RISKS RELATED TO OUR BUSINESS OPERATIONS AND INDUSTRY

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

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

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

As of December 31, 2020, we had 24 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 significant penalties, including criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Our operations may be directly, or indirectly through our relationships with customers, third party payors, healthcare providers, and others subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation 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 (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), and teaching hospitals, and further requires applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report such information regarding its payment and other transfers of value to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year; and

- state and foreign law equivalents of each of the above federal laws, such as: anti-kickback and false claims laws which may apply to items or services reimbursed by any third party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state laws that require the reporting of information related to drug pricing; state and local laws that require the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information 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 Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the "ACA") was passed and includes measures to significantly change the way healthcare is financed by both governmental and private insurers. There 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. For example, President Trump signed Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Congress has also considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Act includes a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. On 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. The U.S. Supreme Court is currently reviewing this case, but it is unknown when a decision will be reached. Although the U.S. Supreme Court has yet ruled on the constitutionality of the ACA, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how the Supreme Court ruling, other such litigation, and healthcare reform measures of the Biden administration will impact the ACA and our business.

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

centers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and federal and state legislative activity designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. For example, at the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, President Trump announced several executive orders related to prescription drug pricing that attempt to implement several of the Trump administration proposals. The FDA also recently released a final rule, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed pending review by the Biden administration until March 22, 2021. On November 20, 2020, CMS issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. However, it is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing.

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

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

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

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

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

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

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

Cybersecurity risks and the failure to maintain the 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, public health pandemics or epidemics (including, for example, the COVID-19 pandemic), terrorism, war, 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 was subject to a transition period that ended December 31, 2020, or the Transition Period, during which EU rules continued to apply. A trade and cooperation agreement, or the Trade and Cooperation Agreement, that outlines the future trading relationship between the United Kingdom and the European Union was agreed in December 2020.

Since a significant proportion of the regulatory framework in the United Kingdom applicable to our business and our product candidates is derived from EU directives and regulations, Brexit has had, and may continue to have, a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the United Kingdom or the European Union. For example, Great Britain is no longer covered by the centralized procedures for obtaining EU-wide marketing authorization from the EMA and a separate marketing authorization will be required to market our product candidates in Great Britain. It is currently unclear whether the Medicines & Healthcare products Regulatory Agency ("MHRA"), in the U.K. is sufficiently prepared to handle the increased volume of marketing authorization applications that it is likely to receive. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom or the European Union and restrict our ability to generate revenue and achieve and sustain profitability.
While the Trade and Cooperation Agreement provides for the tariff-free trade of medicinal products between the UK and the EU there may be additional non-tariff costs to such trade which did not exist prior to the end of the Transition Period. Further, should the UK diverge from the EU from a regulatory perspective in relation to medicinal products, tariffs could be put into place in the future. We could therefore, both now and in the future, face significant additional expenses (when compared to the position prior to the end of the Transition Period) to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the UK It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the EU These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the United Kingdom.

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

Our headquarters are located in San Diego County. We are vulnerable to natural disasters such as earthquakes and wild fires, as well as other events that could disrupt our operations. We do not carry insurance for earthquakes or other natural disasters and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our business operations. In addition, natural disasters or other catastrophic events in various parts of the world, including interruptions in the supply of natural resources, political and governmental changes, disruption in transportation networks or delivery services, severe weather conditions, wildfires and other fires, explosions, actions of animal rights activists, terrorist attacks, earthquakes, wars and public health issues (including, for example, the COVID-19 pandemic) could disrupt our operations or those of our collaborators, contractors and vendors or contribute to unfavorable economic or other conditions that could adversely impact us.

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

Our business may be adversely affected by the effects of health pandemics or epidemics, including the COVID-19 pandemic, which was declared by the World Health Organization as a global pandemic, and is resulting in travel and other restrictions to reduce the spread of the disease, including a California executive order and several other state and local orders across the country, which, among other things, direct individuals to shelter at their places of residence, direct businesses and governmental agencies to cease non-essential operations at physical locations, prohibit certain non-essential gatherings, and order cessation of non-essential travel. As a result of these recent developments, we have implemented work-from-home policies for most of our employees. The effects of the state executive order, government-imposed quarantines and our work-from-home policies may negatively impact productivity, disrupt our business and delay our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. These and similar, and perhaps more severe, disruptions in our operations could negatively impact our business, operating results and financial condition.

Quarantines, shelter-in-place and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases could impact personnel at third-party manufacturing facilities in the United States and other countries, or the availability or cost of materials, which would disrupt our supply chain. For example, some of our CROs have delayed the commencement of preclinical studies due to shelter in place orders.

Beginning the week of March 16, 2020, substantially all of our workforce began working from home either all or substantially all of the time, except for a limited number of staff in our research and development laboratory. The effects of the stay-at-home orders and our work-from-home policies may negatively impact productivity, disrupt our business and delay our development programs and regulatory timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course.

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

The spread of COVID-19, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, the COVID-19 pandemic, may be difficult to assess or predict, it is currently resulting in significant disruption of global financial markets. This disruption, if sustained or recurrent, could make it more difficult for us to access capital or to comply with the covenants contained in the Loan Agreement, which could negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

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

RISKS RELATED TO OUR COMMON STOCK

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

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

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

- failure to meet or exceed financial projections we may provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- disruptions caused by man-made or natural disasters, public health pandemics or epidemics or other business interruptions, including, for example, the COVID-19 pandemic;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our collaboration partners or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

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

The requirements of being a publicly traded company may strain our resources and divert management's attention.

As a publicly traded company, we have incurred, and will continue to incur, significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and The Nasdaq Capital Market have imposed various requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act (the "Dodd-Frank Act") was enacted. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel have devoted and will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

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

From time to time, the Financial Accounting Standards Board ("FASB"), either alone or jointly with other organizations, promulgates new accounting principles that could have an adverse impact on our financial position, results of operations or reported cash flows.

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

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

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

these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

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

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, preferred stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time, any of which may result in material dilution to investors and/or our existing stockholders. New investors could also be issued securities with rights superior to those of our existing stockholders. As of December 31 2020, warrants to exercise an aggregate of 66.0 million shares of our common stock were outstanding at a weighted-average exercise price per share of $0.78. In addition, as of December 31, 2020, an aggregate of 19.3 million shares were issuable upon conversion of shares of our Class A-1, Class A-2 and Class A-3 preferred stock at the option of the holder, subject to beneficial ownership limitations.

Pursuant to our 2019 Equity Incentive Plan (the "2019 Plan"), our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. In addition, the number of shares available for future grant under the 2019 Plan will automatically increase on January 1st each year commencing on January 1, 2021 through January 1, 2029, by 5% of all shares of our capital stock outstanding as of December 31st of the preceding calendar year, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. Furthermore, we may grant or provide for the grant of rights to purchase shares of our common stock pursuant to our 2012 Employee Stock Purchase Plan ("ESPP"). The number of shares of our common stock reserved for issuance under the ESPP will automatically increase on January 1 of each calendar year by the lessor of 1% of the total number of shares of our common stock outstanding on December 31st of the preceding calendar year and 41,666 shares, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under the 2019 Plan and the ESPP each year.

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

Our common stock is currently listed on The Nasdaq Capital Market. In order to maintain the listing of our common stock on The Nasdaq Capital Market, we must satisfy minimum financial and other continued listing requirements and standards, including a minimum closing bid price requirement for our common stock of $1.00 per share and a minimum stockholders' equity requirement of $2.5 million.

We have failed to comply with Nasdaq's minimum bid price requirement and minimum stockholders' equity requirement on multiple other occasions during the last several years, although we have regained compliance in such previous occasions. 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 may be the subject of putative securities class action litigation in the future.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. 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. On May 27, 2020, the court entered an order preliminarily approving the settlement. On October 21, 2020, the court formally approved the settlement. On December 29, 2020, the court entered the final judgment and dismissed the action with prejudice. It is possible that additional lawsuits will be filed, or allegations made by stockholders, with respect to these same or other matters and also naming us and/or our officers and directors as defendants. While we carry liability insurance, there is no assurance that any losses we incur in connection with the current lawsuits or any future lawsuits will be covered or that coverage, if any, will be sufficient. In addition, the current lawsuits and similar future litigation could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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

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

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

As of December 31, 2020, we had net operating loss ("NOL") carryforwards for U.S. federal and California state tax purposes of $342.4 million and $289.2 million, respectively. A portion of the federal and California state NOL carryforwards will begin to expire, if not utilized, in 2030 and 2031, respectively. NOLs that expire unused will be unavailable to offset future income tax liabilities. Under the Tax Act, federal NOLs incurred in taxable years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal NOLs in tax years beginning after December 31, 2020 is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to the Tax Act or the CARES Act. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "Code"), and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income and taxes may be limited. We have determined that we triggered an "ownership change" limitation at the completion of our initial public offering in October 2012 and in July 2015. The Company has not performed a Section 382 ownership-change analysis through December 31, 2020, and it is possible there may have been additional ownership changes. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. As a result, if we earn net taxable income, our ability to use our pre-ownership change NOL carryforwards to offset U.S. federal taxable income will be subject to limitations, which could harm our future operating results by effectively increasing our future tax obligations. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For example, California imposed limits on the usability of California state net operating losses to offset taxable income in tax years beginning after 2019 and before 2023. As a result, if we earn net taxable income, we may be unable to use all or a material portion of our net operating loss carryforwards and other tax attributes, which could potentially result in increased future tax liability to us and adversely affect our future cash flows.

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

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

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

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

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

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

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

On February 11, 2021, we entered into a lease agreement (the "Campus Point Lease") with ARE-SD Region No. 58 LLC ("Campus Point Landlord"), for the lease of approximately 13,438 square feet of rentable area located at 4224 Campus Point Court, Suite 210, San Diego, California 92121 (the "Campus Point Premises"). The commencement date of the Campus Point Lease is expected to be on or before April 15, 2021. We expect to use the Campus Point Premises as our new principal executive offices and as a laboratory for research and development, manufacturing and other related uses. The term of the Campus Point Lease ("Campus Point Initial Term") is 60 months, ending May 1, 2026 (assuming an April 15, 2021 commencement date).

Our lease of approximately 8,728 square feet of space at located 10628 Science Center Drive, Suite 225, San Diego, California 92121 will be assigned to a third party upon commencement of the Campus Point Lease.

We believe that our existing facilities are adequate and that the Campus Point Premises will be adequate for our current and future 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 $0.2 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. On May 27, 2020, the court entered an order preliminarily approving the settlement. On October 21, 2020, the court held a hearing regarding approval of the settlement and on October 29, 2020 the court entered its order granting final approval of the settlement. On December 29, 2020, the court entered the final judgment and dismissed the action with prejudice. The consolidated actions were dismissed on December 29, 2020. In July 2020, in connection with the proposed settlement, we remitted approximately $0.2 million into escrow, which represents the amount payable by us under the settlement, net of $0.7 million of D&O insurance carrier proceeds. We relieved the $0.9 million loss contingency that was recorded as a current liability on our balance sheet at December 31, 2019, as well as the $0.7 million of insurance proceeds that was recorded as a current receivable on our balance sheet at December 31, 2019. The $0.2 million settlement amount payable by the Company was recorded to the statement of operations and comprehensive loss for the year ended December 31, 2019.

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 5, 2021, there were 9 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

Not required.

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

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

OVERVIEW

We are a clinical-stage biopharmaceutical company focused on discovering and developing first-in-class drugs targeting *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, 2020, we have relied primarily on the sale of our equity and convertible debt securities to fund company operations. We have received $361.8 million from the sale of our equity and convertible debt securities, $101.8 million from our collaborations, principally from upfront payments, research funding and preclinical and clinical milestones, and $19.8 million in net proceeds from our Term Loan. As of December 31, 2020, we had cash and cash equivalents of approximately $31.1 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 collaboration agreements.

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

Research and development expenses

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

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

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

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

Since our inception, we have incurred a total of approximately $373.4 million in research and development expenses through December 31, 2020.

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

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

General and administrative expenses

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

Other income (expense), net

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

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

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.

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, 2020 and 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019 (in thousands):

	Years ended December 31,	
	2020	2019
Revenue under collaborations	$ 10,006	$ 6,832
Research and development expenses	15,347	12,349
General and administrative expenses	8,814	11,317
Interest and other expenses, net	(1,575)	(1,757)

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, program material sales payments and payments for other research services. Revenue under collaborations was $10.0 million for the year ended December 31, 2020, compared to $6.8 million for the year ended December 31, 2019. The increase was attributable to the recognition of the Enrollment Milestone under the 2020 Sanofi Amendment and the recognition of program-related materials under the 2020 Sanofi Amendment as revenue during the year ended December 31, 2020.

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):

					Increase (decrease)	
	2020	% of total	2019	% of total	$	%
Research and development						
Personnel and internal expenses	$ 5,864	38 %	$ 6,669	54 %	$ (805)	(12)%
Third-party and outsourced expenses	8,342	54 %	4,799	39 %	3,543	74 %
Non-cash stock-based compensation	693	5 %	309	2 %	384	124 %
Depreciation	448	3 %	572	5 %	(124)	(22)%
Total research and development expenses	$ 15,347	100 %	$ 12,349	100 %	$ 2,998	24 %

Research and development expenses increased by $3.0 million for the year ended December 31, 2020 compared to the year ended December 31, 2019. The aggregate increase was driven by a $3.5 million increase in external development costs, primarily attributable to the fact that FDA lifted the partial clinical hold on the RGLS4326 Phase 1 MAD study in December 2019 and we recommenced that study in February 2020, with the final dosing completed in July 2020. Further contributing to the increase in external development costs were costs associated with activities leading up to, and including, patient dosing in our RGLS4326 Phase 1b study, with the first patient having been dosed in October 2020.

General and administrative expenses

General and administrative expenses were $8.8 million for the year ended December 31, 2020, compared to $11.3 million for the year ended December 31, 2019. These amounts reflect personnel-related and ongoing general business operating costs. The decrease during the year ended December 31, 2020, as compared to the year ended December 31, 2019, are primarily attributable to continued cost reduction efforts subsequent our corporate restructurings.

Interest and other expenses, net

Net interest and other expenses were $1.6 million for the year ended December 31, 2020 compared to $1.8 million for the year ended December 31, 2019. 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 of the remaining 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;
- 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;
- the extent to which our PPP Loan is forgiven; and
- payments under our Term Loan.

The following table shows a summary of our cash flows for the years ended December 31, 2020 and 2019 (in thousands):

	Years ended December 31,	
	2020	2019
Net cash (used in) provided by:		
Operating activities	$ (12,536)	$ (19,821)
Investing activities	(11)	74
Financing activities	9,513	39,933
Total	$ (3,034)	$ 20,186

Operating activities

Net cash used in operating activities decreased to $12.5 million for the year ended December 31, 2020, compared to $19.8 million for the year ended December 31, 2019. Net cash used in operating activities were primarily attributable to net losses of $15.7 million and $18.6 million for the years ended December 31, 2020 and 2019, respectively. Adjustments for non-cash charges, including stock-based compensation, decreased to $3.2 million for the year ended December 31, 2020, compared to $5.4 million for the year ended December 31, 2019. Changes in working capital resulted in net cash used in operating activities of less than $0.1 million for the year ended December 31, 2020, compared to net cash used in operating activities of $6.6 million for the year ended December 31, 2019.

Investing activities

Net cash used in investing activities for the year ended December 31, 2020 was attributable to the acquisition of intangible assets. Net cash provided by investing activities for the year ended December 31, 2019 was primarily related to the sale of property and equipment.

Financing activities

Net cash provided by financing activities was $9.5 million for the year ended December 31, 2020, compared to net cash provided by financing activities of $39.9 million for the year ended December 31, 2019. Net cash provided by financing activities for the year ended December 31, 2020 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 December 2020 of $18.2 million, partially offset by the remittance of $10.0 million of principal amortization payments under our Term Loan. 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.

Off Balance Sheet Arrangements

As of December 31, 2020, 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 short-term investments to fluctuate. Financial instruments that potentially subject us to significant concentrations of credit risk consist primarily of cash and cash equivalents. We invest our excess cash primarily in money market funds. The primary objectives of our investment activities are to ensure liquidity and to preserve principal while at the same time maximizing the income we receive from our investments without significantly increasing risk. We have established guidelines regarding approved investments and maturities of investments, which are designed to maintain safety and liquidity.

Because of the short-term maturities of our cash equivalents, we do not believe that an increase in market rates would have any significant impact on the realized value of our cash equivalents. If a 10% change in interest rates were to have occurred on December 31, 2020, 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, 2020, the outstanding principal amount of the Term Loan was $4.7 million. The Term Loan bears interest at a floating per annum rate equal to (i) 8.51% plus (ii) the greater of (a) the 30 day U.S. Dollar LIBOR rate reported in *The Wall Street Journal* on the last business day of the month that immediately precedes the month in which the interest will accrue and (b) 0.44%. Changes in the U.S. Dollar LIBOR rate may therefore affect our interest expense associated with the Term Loan. LIBOR is currently scheduled to be phased out by the end of 2021. Before LIBOR is phased out, we may need to renegotiate the Term Loan to replace LIBOR with SOFR. The consequences of these developments cannot be entirely predicted, but could result in higher interest rates on the principal amount of the Term Loan.

If a 10% change in interest rates were to have occurred on December 31, 2020, this change would not have had a material effect on our interest expense as of that date.

Item 8. Financial Statements and Supplementary Data

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Regulus Therapeutics Inc. (the Company) as of December 31, 2020 and 2019, 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, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, 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 Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

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

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

Critical Audit Matter

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

Clinical Trial and Preclinical Study Accruals

Description of the Matter	During 2020, the Company incurred $15.3 million for research and development expense and as of December 31, 2020, the Company accrued $1.1 million for clinical trial and preclinical study expenses. As described in Note 1 to the financial statements, the Company records accruals for estimated costs of clinical trial and preclinical studies that include services provided by clinical trial investigational sites and contract research organizations and other clinical trial-related activities. Clinical trial and preclinical study activities performed by third parties are accrued and expensed based upon estimates of the time period over which these services will be performed and the level of effort to be expended in each period. Auditing management's accounting for clinical trial and preclinical study accruals is especially challenging as evaluating the progress or stage of completion of the activities under the Company's research and development agreements is dependent on information from third-party service providers and internal clinical personnel, which includes both subjective and qualitative aspects.
How We Addressed the Matter in Our Audit	To test the Company's accrued expenses for clinical trial and pre-clinical study activities, among other procedures, we obtained supporting evidence of the research and development activities performed for significant clinical trials and preclinical studies. We inspected summaries of project status meetings with accounting personnel and clinical project managers to corroborate the status of significant research and development activities. To verify the appropriate measurement of clinical trial and preclinical study accruals, we compared the costs for a sample of transactions against the related invoices and contracts and confirmed amounts incurred to-date with third-party service providers. We also examined a sample of subsequent payments to evaluate the completeness of the clinical trial and preclinical study accruals.

/s/ Ernst & Young LLP

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

San Diego, California
March 9, 2021

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

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 31,087	$ 34,121
Contract and other receivables	503	1,141
Prepaid materials, net	3,314	3,924
Prepaid expenses and other current assets	1,826	1,221
Total current assets	36,730	40,407
Property and equipment, net	472	921
Intangibles, net	125	266
Other assets	277	487
Total assets	$ 37,604	$ 42,081
Liabilities and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 535	$ 1,321
Accrued liabilities	581	770
Accrued research and development expenses	1,097	147
Accrued compensation	1,743	1,676
Current portion of term loan, less debt issuance costs	4,652	14,631
Current portion of contract liabilities	—	6
Other current liabilities	2,970	3,047
Total current liabilities	11,578	21,598
Other long-term liabilities	—	468
Total liabilities	11,578	22,066
Stockholders' equity (deficit):		
Class A-1 convertible preferred stock, $0.001 par value; 256,700 and 415,898 shares authorized, issued and outstanding at December 31, 2020 and 2019, respectively	—	1
Class A-2 convertible preferred stock, $0.001 par value; 1,416,453 and 3,288,390 shares authorized, issued and outstanding at December 31, 2020 and 2019, respectively	1	3
Class A-3 convertible preferred stock, $0.001 par value; 258,707 and 0 shares authorized, issued and outstanding at December 31, 2020 and 2019, respectively	1	—
Common stock, $0.001 par value; 200,000,000 shares authorized, 67,432,712 and 21,018,663 shares issued and outstanding at December 31, 2020 and 2019, respectively	67	21
Additional paid-in capital	453,002	431,305
Accumulated deficit	(427,045)	(411,315)
Total stockholders' equity	26,026	20,015
Total liabilities and stockholders' equity	$ 37,604	$ 42,081

See accompanying notes to these financial statements.

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

	2020	2019
Revenues:		
Revenue under collaborations	$ 10,006	$ 6,832
Total revenues	10,006	6,832
Operating expenses:		
Research and development	15,347	12,349
General and administrative	8,814	11,317
Total operating expenses	24,161	23,666
Loss from operations	(14,155)	(16,834)
Other income (expense):		
Interest and other income	233	374
Interest and other expense	(1,808)	(2,131)
Loss before income taxes	(15,730)	(18,591)
Income tax expense	—	(1)
Net loss and comprehensive net loss	$ (15,730)	$ (18,592)
Net loss per share, basic and diluted	$ (0.45)	$ (1.08)
Weighted average shares used to compute basic and diluted net loss per share	34,977,378	17,260,176

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 deficit	Total stockholders' equity (deficit)
	Shares	Amount	Shares	Amount			
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
Issuance of common stock upon exercise of options	—	—	6,842	—	5	—	5
Issuance of common stock upon exercise of warrants	—	—	1,038,970	1	691	—	692
Issuance of common stock upon vesting of restricted stock units	—	—	75,384	—	—	—	—
Issuance of common stock, preferred stock and warrants from private placement, net of offering costs	272,970	—	24,341,607	25	18,141	—	18,166
Stock-based compensation expense	—	—	—	—	2,614	—	2,614
Issuance of common stock under Employee Stock Purchase Plan	—	—	4,998	—	2	—	2
Issuance of common stock through ATM	—	—	492,268	—	262	—	262
Conversions of convertible preferred stock	(2,045,398)	(2)	20,453,980	20	(18)	—	—
Net loss	—	—	—	—	—	(15,730)	(15,730)
Balance at December 31, 2020	1,931,860	$ 2	67,432,712	$ 67	$ 453,002	$ (427,045)	$ 26,026

See accompanying notes to these financial statements.

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

	Years ended December 31,	
	2020	2019
Operating activities		
Net loss	$ (15,730)	$ (18,592)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and amortization expense	467	931
Stock-based compensation	2,614	2,288
Gain on reduction of lease liability	—	1,839
Other	154	293
Change in operating assets and liabilities:		
Contracts and other receivables	638	(1,115)
Prepaid materials	610	270
Prepaid expenses and other assets	(395)	(242)
Accounts payable	(786)	(393)
Accrued liabilities	(188)	(281)
Accrued research and development expenses	949	(427)
Accrued compensation	66	75
Contract liabilities	(6)	(2,572)
Other liabilities	(929)	(1,895)
Net cash used in operating activities	(12,536)	(19,821)
Investing activities		
Purchases of property and equipment	—	(221)
Sales of property and equipment	—	318
Acquisition of intangibles	(11)	(23)
Net cash (used in) provided by investing activities	(11)	74
Financing activities		
Proceeds from issuance of securities through private placement, net of issuance costs	18,166	40,084
Proceeds from issuance of common stock, net	957	2,086
Proceeds from borrowing under Paycheck Protection Program	662	—
Proceeds from exercise of common stock options	5	3
Payments on financing leases	(277)	(263)
Principal payments on term loan	(10,000)	(1,977)
Net cash provided by financing activities	9,513	39,933
Net (decrease) increase in cash and cash equivalents	(3,034)	20,186
Cash and cash equivalents at beginning of period	34,121	13,935
Cash and cash equivalents at end of period	$ 31,087	$ 34,121
Supplemental disclosure of cash flow information		
Interest paid	$ (1,356)	$ (1,655)
Income taxes paid	$ (1)	$ (1)
Supplemental disclosure of non-cash investing and financing activities		
Unsettled sales of common stock through ATM	$ 392	$ —
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 *micro*RNAs 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 $483.4 million. As of December 31, 2020, we had approximately $31.1 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, 2020 and 2019, due to the considerations discussed above and the assessment that the material adverse change clause under the Term Loan is not within our control. During the period after December 31, 2020, we received a waiver from the Lender (as defined below) with respect to noncompliance with a covenant under the Loan Agreement (as defined below) and are in compliance with all Loan Agreement covenants 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 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. Though the impact of the COVID-19 pandemic to our business and operating results presents additional uncertainty, we continue to use the best information available to inform our critical accounting estimates.

Revenue Recognition

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

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

Collaborative Arrangements

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

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

License Fees

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

Milestone Payments

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

Royalties

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

Stock-Based Compensation

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

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

Clinical Trial and Preclinical Study Accruals

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

Prepaid Materials

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

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. 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.

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, 2020 and 2019.

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, 2020 or 2019.

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. There were no transactions resulting in other comprehensive income or loss during the periods presented; as such, net loss equals other comprehensive loss for all periods presented.

Leases

At the inception of a contractual arrangement, we determine whether the contract contains a lease by assessing whether there is an identified asset and whether the contract conveys the right to control the use of the identified asset in exchange for consideration over a period of time. For operating leases with an initial term greater than 12 months, we recognize operating lease 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 an initial 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. 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. 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.

Recent Accounting Pronouncements

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

In 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. The adoption of this guidance on January 1, 2020 did not have a material 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. The adoption of this guidance on January 1, 2020 did not have a material 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 adoption of this guidance on January 1, 2020 had no impact on our financial statements.

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

relationships entered into or evaluated, after December 31, 2022. We are assessing the impact this standard will have on our financial statements and disclosures.

2. Net Loss Per Share

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

Potentially dilutive securities not included in the calculation of diluted net loss per common share, because to do so would be anti-dilutive were (in common stock equivalent shares) 23,741,466 for the year ended December 31, 2020, consisting of convertible preferred stock, stock options and restricted stock units, and 6,569,337 for the year ended December 31, 2019, consisting of convertible preferred stock, stock options and restricted stock units.

3. Investments

Historically, we have invested our excess cash primarily in debt instruments of financial institutions, corporations, U.S. government-sponsored agencies and the U.S. treasury. We generally hold our investments until to maturity and do not sell our investments before we have recovered our amortized cost basis. As of December 31, 2020 and 2019, our cash balance was comprised entirely of cash and cash equivalents (money market funds) and there was no unrealized gain or loss in either period.

4. Fair Value Measurements

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

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

- Level 1 includes financial instruments for which quoted market prices for identical instruments are available in active markets.
- Level 2 includes financial instruments for which there are inputs other than quoted prices included within Level 1 that are observable for the instrument such as quoted prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets with insufficient volume or infrequent transactions (less active markets) or model-driven valuations in which significant inputs are observable or can be derived principally from, or corroborated by, observable market data.
- Level 3 includes financial instruments for which fair value is derived from valuation techniques in which one or more significant inputs are unobservable, including management’s own assumptions.

Financial Assets Measured at Fair Value

The following table presents our fair value hierarchy for assets measured at fair value on a recurring basis as of December 31, 2020 and 2019 (in thousands):

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

	Fair value as of December 31, 2019			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents (money market funds)	$ 8,909	$ 8,909	$ —	$ —
	$ 8,909	$ 8,909	$ —	$ —

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 $10.0 million for the year ended December 31, 2020 and $6.8 million for the year ended December 31, 2019.

Sanofi

In July 2012, we amended and restated our collaboration and license agreement with Sanofi to expand the potential therapeutic applications of the *micro*RNA alliance targets to be developed under such agreement. 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 *micro*RNA targets; and (2) a research license under our technology collaboration.

In June 2013, the original research term expired, upon which we and Sanofi entered into an option agreement pursuant to which Sanofi was granted an exclusive right to negotiate the co-development and commercialization of certain of our unencumbered *micro*RNA programs and we were granted the exclusive right to negotiate with Sanofi for co-development and commercialization of certain miR-21 anti-miRs in oncology and Alport syndrome. In 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 chooses to exercise its option on any of these programs, Sanofi would reimburse us for a significant portion of our preclinical and clinical development costs and would also pay us an option exercise fee for any such program, provided that $1.25 million of the $2.5 million upfront option fee paid to us by Sanofi in connection with the June 2013 option agreement will be creditable against such option exercise fee. We are eligible to receive royalties on *micro*RNA therapeutic products commercialized by Sanofi and will have the right to co-promote these products relating to our preclinical program targeting miR-221/222. As indicated below, we entered into an additional amendment with Sanofi in November 2018, under which Sanofi's opt-in rights to our miR-21 programs under the 2014 Sanofi Amendment were relinquished. Sanofi's opt-in rights with regard to our miR-221/222 preclinical program under the 2014 Sanofi Amendment remained unchanged.

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 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 recognized the $0.4 million allocated consideration into revenue ratably over the estimated period of performance of the miR-221/222 program.

We are eligible to receive milestone payments related to the development and commercialization of miR-221/222 for HCC of up to $38.8 million for proof-of-concept option exercise fees (net of $1.25 million creditable, as noted above), $25.0 million for clinical milestones and up to $130.0 million for regulatory and commercial milestones. In addition, we are entitled to receive royalties based on a percentage of net sales of any products from the miR-221/222 program which, in the case of sales in the United States, will be in the middle of the 10% to 20% range, and, in the case of sales outside of the United States, will range from the low end to the middle of the 10% to 20% range, depending upon the volume of sales. If we exercise our option to co-promote a miR-221/222 product, we will continue to be eligible to receive royalties on net sales of each product in the United States at the same rate, unless we elect to share a portion of Sanofi's profits from sales of such product in the United States in lieu of royalties.

In November 2018, we entered into an amendment to the 2014 Sanofi Amendment with Sanofi to modify the parties' rights and obligations with respect to our miR-21 programs, including our RG-012 program (the "2018 Sanofi Amendment"). Under the terms of the 2018 Sanofi Amendment, we have granted Sanofi a worldwide, royalty-free, fee-bearing, exclusive license, with the right to grant sublicenses, under our know-how and patents to develop and commercialize miR-21 compounds and products for all indications, including Alport Syndrome. Sanofi will control and will assume all responsibilities and obligations for developing and commercializing each of our miR-21 programs, including our obligations regarding the administration and expense of clinical trials and all other costs, including in-license royalties and other in-license payments, related to our miR-21 programs. Under the terms of the 2018 Sanofi Amendment, we have assigned to Sanofi certain agreements, product-specific patents and all materials directed to miR-21 or to any miR-21 compound or product and are required to provide reasonable technical assistance to Sanofi for a period of 24 months after the date of the 2018 Sanofi Amendment. Under the terms of the 2018 Sanofi Amendment, we were eligible to receive approximately $6.8 million in upfront payments for the license and for miR-21 program-related materials (collectively, the "Upfront Amendment Payments"). We were also eligible to receive up to $40.0 million in development milestone payments, including a $10.0 million payment for an interim enrollment milestone (the "Enrollment Milestone"). In addition, Sanofi has agreed to reimburse us for certain out-of-pocket transition activities and assume our upstream license royalty obligations. 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. In 2019, we completed the performance obligations under the 2018 Sanofi Amendment and recognized revenue for the $6.8 million in Upfront Amendment Payments. As of December 31, 2019, the $40.0 million in development milestone payments (variable consideration) was fully constrained and therefore, did not meet the criteria for revenue recognition.

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

As of December 31, 2020, the $25.0 million development milestone payment (variable consideration) is fully constrained and therefore, does 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,	
	2020	2019
Laboratory equipment	$ 4,967	$ 4,967
Computer equipment and software	281	281
Furniture and fixtures	—	—
Leasehold improvements	83	83
	5,331	5,331
Less accumulated depreciation and amortization	(4,859)	(4,410)
Property and equipment, net	$ 472	$ 921

Depreciation and amortization of property and equipment of $0.5 million and $0.9 million was recorded for the years ended December 31, 2020 and 2019, respectively.

7. Intangible Assets, net

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

	December 31,	
	2020	2019
Patents	$ 219	$ 465
Accumulated amortization - Patents	(94)	(199)
Intangibles, net	$ 125	$ 266

Intangible asset amortization of less than $0.1 million was recorded for the years ended December 31, 2020 and 2019. 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, 2020 is expected to be recognized is approximately 13.9 years.

8. Commitments and Contingencies

License Agreements

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

9. Debt

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 we received $20.0 million in proceeds, net of debt issuance costs on June 22, 2016 (the "Term Loan").

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

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 Enrollment Milestone 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 "May 2019 SPA") (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 May 2019 SPA, 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 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. 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 Enrollment Milestone, 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.

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

On August 25, 2020 we entered into a tenth amendment to the Term Loan with the Lender (the "Tenth Amendment"). Pursuant to the terms of the Tenth Amendment, we are eligible for up to an additional seven months of interest only payments in the event we paid down $10 million in loan principal before April 30, 2021 (the "Principal Paydown Event"). In the event the Principal Paydown Event did not occur by April 30, 2021, we would make principal and accrued interest payments, in arrears, commencing May 1, 2021, in accordance with the terms of the Eighth Amendment. If the Principal Paydown Event occured after April 30, 2021 but on or before July 31, 2021, we would recommence an extended interest only payment period through December 31, 2021. In the event we received the additional interest only period, principal and accrued interest payments would recommence on January 1, 2022.

We received $1.0 million, $4.0 million and $5.0 million in proceeds from Sanofi (see Note 7) on September 30, 2020, October 8, 2020 and November 30, 2020, respectively. Under the terms of the Tenth Amendment, we prepaid $1.0 million, $4.0 million and $5.0 million of outstanding principal to the Lender on September 30, 2020, October 8, 2020 and November 30, 2020, respectively, for a total of $10.0 million. We also paid the applicable 5.5% final payment fees related to the three prepayments to the Lender. As the Principal Paydown Event occurred by April 30, 2021, we received an additional seven months of interest only payment extension and are not obligated to make principal payments on the Term Loan until January 1, 2022.

We used the proceeds from the Term Loan solely for working capital and to fund our general business requirements. Our obligations under the Loan Agreement are secured by a first priority security interest in substantially all of our current and future assets, other than our intellectual property, for which Oxford currently has a positive lien, and certain assets under finance lease obligations. We have also agreed not to encumber our intellectual property assets, except as permitted by the Loan Agreement. The Loan Agreement includes customary events of default, including instances of a material adverse change in our operations, that may require prepayment of the outstanding Term Loan. During the period after December 31, 2020, we received a waiver from the Lender with respect to noncompliance with a covenant under the Loan Agreement and are in compliance with all Loan Agreement covenants as of the date of the filing of this Form 10-K.

As of December 31, 2020, $4.7 million was outstanding under the Term Loan. An additional $1.3 million is also payable at the conclusion of the Term Loan (presented in other current liabilities on our balance sheet at December 31, 2020). We had less than $0.1 million of debt issuance costs outstanding as of December 31, 2020, which are being accreted to interest expense over the life of the Term Loan using an effective interest rate of 8.98%. The exit fees are being accrued over the life of the Term Loan through interest expense.

As of December 31, 2020, future principal payments for the Term Loan due under the Loan Agreement are as follows (in thousands):

2021	—
2022	4,681
	$ 4,681

Paycheck Protection Program Loan

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

All or a portion of the PPP Loan may be forgiven by the SBA upon our application and upon documentation of expenditures in accordance with the SBA requirements. Under the CARES Act and PPP Flexibility Act, loan forgiveness is available for the sum of documented payroll costs, covered mortgage interest, covered rent payments and covered utilities

during the 24 week period beginning on the date of loan disbursement. For purposes of the PPP, payroll costs exclude compensation of an individual employee in excess of $100,000, annualized, prorated for the covered period. Not more than 40% of the forgiven amount may be for non-payroll costs. Forgiveness is reduced if full-time headcount declines during the covered period as compared to specified reference periods, or if salaries and wages for employees with salaries of $100,000 or less annually are reduced by more than 25%, unless certain safe harbors are satisfied. In the event the PPP Loan, or any portion thereof, is forgiven pursuant to the PPP, the amount forgiven is applied to outstanding principal and includes accrued interest.
We have used all proceeds from the PPP Loan to retain employees, maintain payroll and make lease and utility payments, and are seeking forgiveness in accordance with the program. The $0.7 million proceeds from the PPP Loan is presented in other current liabilities on our balance sheet at December 31, 2020.

10. Stockholders' Equity

Common Stock

As of December 31, 2020, there were 67,432,712 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, 2020, 868,432 shares of common stock were available for new equity award grants under the 2019 Plan and 6,847,361 shares of common stock are reserved for issuance pursuant to equity awards outstanding as of December 31, 2020. The number of shares authorized for issuance under the 2019 Plan may be increased by (a) the shares subject to outstanding stock awards granted under the Company's 2009 Equity Incentive Plan (the "2009 Plan") and the Company's 2012 Equity Incentive Plan (together the with 2009 Plan, the "Prior Plans") that on or after the effective date of the 2019 Plan (i) expire or terminate for any reason prior to exercise or settlement; (ii) are forfeited because of the failure to meet a contingency or condition required to vest such shares or otherwise return to the Company, or (iii) are reacquired, withheld (or not issued) to satisfy a tax withholding obligation in connection with an award or to satisfy the purchase price or exercise price of a stock award. No further grants will be made under the Prior Plans. In addition, on January 22, 2020, an additional 4,166,860 shares of common stock became available for issuance under the 2019 Plan pursuant to the Milestone Closing 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 Placements 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.

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

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

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

The following table summarizes preferred stock conversions and warrant exercises (and the related impact on common stock) under the 2019 SPA and 2020 SPA for the years ended December 31, 2020 and 2019 (in thousands):

	Class A-1 Convertible Preferred Stock	Class A-2 Convertible Preferred Stock	Class A-3 Convertible Preferred Stock	Warrants	Common Stock
Balance at December 31, 2018	—	—	—	—	—
Initial Closing	416	—	—	13,890	9,731
Milestone Closing	—	3,288	—	32,884	—
Conversions/Exercises	—	—	—	—	—
Balance at December 31, 2019	416	3,288	—	46,774	9,731
2020 Closing	—	—	273	20,303	24,342
Conversions/Exercises	(159)	(1,872)	(14)	(1,039)	21,493
Balance at December 31, 2020	257	1,416	259	66,038	55,566

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 492,268 shares were sold and settled for proceeds of $0.3 million (net of less than $0.1 million in commissions) under the ATM Offering during the year ended December 31, 2020. We sold a total of 309,485 shares for proceeds of $0.4 million (net of less than $0.1 million in commissions) under the ATM Offering during the year ended December 31, 2020 that had not been settled as of December 31, 2020. Those shares were settled as of January 5, 2021. 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. At December 31, 2020, approximately $7.1 million remained eligible to be drawn down under the ATM Offering. A total of 3,096,003 shares were sold under the ATM Offering subsequent to December 31, 2020 for proceeds of $4.4 million (net of approximately $0.1 million in commissions). The ATM Offering is no longer available for use.

Shares Reserved for Future Issuance

The following shares of common stock were reserved for future issuance as of December 31, 2020 (in thousands):

Class A-1 convertible preferred stock outstanding (as-converted)	2,567
Class A-2 convertible preferred stock outstanding (as-converted)	14,165
Class A-3 convertible preferred stock outstanding (as-converted)	2,587
2019 PIPE Initial Closing warrants	13,890
2019 PIPE Milestone Closing warrants	31,845
2020 PIPE warrants	20,303
Common stock options outstanding	6,813
RSUs outstanding	34
Common stock available for future grant under the 2019 Equity Incentive Plan	868
Employee Stock Purchase Plan	188
Total common shares reserved for future issuance	93,260

The following table summarizes our stock option activity under all equity incentive plans for the year ended December 31, 2020 (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, 2019	3,098	$ 1.17		
Granted	3,889	$ 1.19		
Exercised	(7)	$ 0.70		
Canceled/forfeited/expired	(167)	$ 4.63		
Options outstanding at December 31, 2020	6,813	$ 1.10	8.57	$ 2,662
Exercisable at December 31, 2020	1,953	$ 1.33	7.51	$ 971

The weighted average grant date fair value per share of employee stock options granted during the years ended December 31, 2020 and 2019 was $0.91 and $0.52, respectively.

The total intrinsic value of stock options exercised was less than $0.1 million for the years ended December 31, 2020 and 2019. Cash received from the exercise of stock options was less than $0.1 million for the years ended December 31, 2020 and 2019.

The total compensation cost related to stock options not yet recognized was $1.8 million as of December 31, 2020. The weighted-average period over which this expense is expected to be recognized is approximately 2.1 years.

The following table summarizes our RSU activity under all equity incentive plans for the year ended December 31, 2020 (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, 2019	129	$ 1.50		
Granted	—	$ —		
Vested	(76)	$ 1.50		
Canceled/forfeited/expired	(19)	$ 1.50		
RSUs outstanding at December 31, 2020	34	$ 1.50	0.25	$ 46

The total compensation cost related to non-vested RSUs not yet recognized was $0.1 million as of December 31, 2020. The weighted-average period over which this expense is expected to be recognized is approximately 0.3 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,	
	2020	2019
Stock options		
Risk-free interest rate	1.1 %	1.7 %
Volatility	95.4 %	94.6 %
Dividend yield	—	—
Expected term (years)	6.1	6.1
Performance stock options		
Risk-free interest rate	1.4 %	2.6 %
Volatility	95.4 %	93.8 %
Dividend yield	—	—
Expected term (years)	6.1	6.1
Employee stock purchase plan shares		
Risk-free interest rate	0.6 %	2.3 %
Volatility	98.0 %	110.5 %
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,	
	2020	2019
Research and development	$ 693	$ 309
General and administrative	1,921	1,979
Total	$ 2,614	$ 2,288

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, 2020, 96,946 shares of our common stock had been issued under the 2012 Purchase Plan, with 4,998 shares of common stock issued for the year ended December 31, 2020. Under the 2012 Purchase Plan, 187,689 shares of our common stock were reserved for future issuance and have been authorized for purchase as of December 31, 2020.

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, 2020 and 2019.

12. Income Taxes

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

	Year ended December 31,	
	2020	2019
Current:		
Federal	$ (13)	$ (13)
State	1	1
	(12)	(12)
Deferred:		
Federal	12	13
State	—	—
	12	13
Income tax expense	$ —	$ 1

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,	
	2020	2019
Expected income tax benefit at federal statutory tax rate	$ (3,309)	$ (3,904)
State income taxes, net of federal benefit	(927)	(1,390)
Tax credits	(1,216)	(374)
Change in valuation allowance	2,606	603
Return to provision adjustments	(14)	(358)
Stock compensation	1,644	3,934
Reserve for uncertain tax positions	1,179	1,444
Other	37	46
Income tax expense	$ —	$ 1

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

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss carryovers	$ 82,747	$ 79,675
Research and development and other tax credits	34,337	33,429
Deferred revenue	—	1
Intangibles and property and equipment basis difference	715	782
Stock compensation expense	283	1,389
Lease liability	88	164
Other	281	461
Total deferred tax assets	118,451	115,901
Total deferred tax liabilities	(282)	(325)
Net deferred tax asset	118,169	115,576
Valuation allowance	(118,169)	(115,564)
Net deferred tax asset	$ —	$ 12

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 $118.2 million.

As of December 31, 2020, we had NOL carryforwards for U.S. federal and California state tax purposes of $342.4 million and $289.2 million, respectively, portions of which begin to expire in 2030 and 2031, respectively. Our federal NOL carryforwards generated in tax years beginning after December 31, 2017, of $79.0 million will carry forward indefinitely. On March 27, 2020, the CARES Act was signed into law in response to the economic challenges facing US businesses. Under the CARES Act, the Internal Revenue Code was amended to allow for federal NOL carrybacks for five years to offset previous years income, or can be carried forward indefinitely to offset 100% of taxable income for the tax year 2020 and 80% of taxable income for tax years 2021 and thereafter.

As of December 31, 2020, we also had federal and California research and development tax credit carryforwards of $32.1 million and $9.4 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, 2020 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,	
	2020	2019
Beginning balance of unrecognized tax benefits	$ 16,573	$ 14,700
Decrease for prior year tax positions	(1)	(7)
Increase for current year tax positions	1,367	1,880
Total	$ 17,939	$ 16,573

Included in unrecognized tax benefits of $17.9 million at December 31, 2020 was $14.5 million of tax benefits that, if recognized, would reduce our annual effective tax rate, subject to valuation allowance. We do not expect that there will be a significant change in the unrecognized tax benefits over the next 12 months.

We are subject to taxation in the United States and state jurisdictions where applicable. Our tax years for 2010 and forward are subject to examination by the U.S. tax authorities and our tax years for 2011 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, 2020 and 2019, we have not recognized any interest or penalties related to income taxes.

13. Leases

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. 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 were 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 were $0.1 million in 2019 and $0.4 million in 2020 and is $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, 2020 and 2019 (in thousands):

	Year Ended December 31,	
	2020	2019
Assets		
Operating	$ 253	$ 464
Financing	288	466
Total ROU assets	$ 541	$ 930
Liabilities		
Current:		
Operating	$ 417	$ 361
Financing	56	277
Long-term:		
Operating	—	417
Financing	—	56
Total lease liabilities	$ 473	$ 1,111

The table below summarizes our lease costs from our statement of operations and cash payments from our statement of cash flows during the years ended December 31, 2020 and 2019 (in thousands):

	Year Ended December 31,	
	2020	2019
Lease cost:		
Operating lease cost	$ 278	$ 715
Finance lease cost:		
Amortization of right-of-use assets	178	182
Interest expense on lease liabilities	10	5
Total finance lease cost	$ 188	$ 187
Cash payment information:		
Operating cash used for operating leases	$ 429	$ 756
Operating cash used for finance leases	10	24
Financing cash used for finance leases	277	263
Total cash paid for amounts included in the measurement of lease liabilities	$ 716	$ 1,043

The table below summarizes other non-cash information under our operating and financing lease obligations as of December 31, 2020 and 2019 (in thousands, except years and rates):

	Year Ended December 31,	
	2020	2019
Supplemental non-cash information:		
Operating lease liabilities arising from obtaining right-of-use assets	$ —	$ 778
Weighted-average remaining lease term (years) - operating leases	1.0	2.0
Weighted-average remaining lease term (years) - finance leases	0.2	1.2
Weighted-average discount rate - operating leases	10.9 %	10.9 %
Weighted-average discount rate - finance leases	4.9 %	4.9 %

Our future lease payments under operating and finance leases at December 31, 2020 are as follows (in thousands):

	Operating Leases	Finance Leases
2021	$ 442	$ 56
Total lease payments	442	56
Less: amount representing interest	(25)	—
Present value of obligations under leases	417	56
Less: current portion	(417)	(56)
Long-term lease obligations	$ —	$ —

14. Selected Quarterly Financial Data (Unaudited)

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 2020 and 2019 are as follows (in thousands, except per share data):

	For the quarters ending			
	March 31	June 30	September 30	December 31
2020				
Total revenues	$ 6	$ —	$ 5,000	$ 5,000
Total operating expenses	(5,541)	(6,496)	(6,095)	(6,028)
Net loss	(5,937)	(6,947)	(1,524)	(1,322)
Net loss per share, basic and diluted (1)	$ (0.25)	$ (0.23)	$ (0.04)	$ (0.03)
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)

(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.

15. Subsequent Events

Corporate Headquarters Lease Agreement

On February 11, 2021, we entered into a lease agreement (the "Campus Point Lease") with ARE-SD Region No. 58 LLC ("Campus Point Landlord"), for the lease of approximately 13,438 square feet of rentable area located at 4224 Campus Point Court, Suite 210, San Diego, California, 92121 (the "Campus Point Premises"). The commencement date of the Campus Point Lease is targeted at nine weeks subsequent to the mutual execution and delivery of the Campus Point Lease by both the Company and the Campus Point Landlord, or April 15, 2021. We expect to use the Campus Point Premises as our new principal executive offices and as a laboratory for research and development, manufacturing and other related uses. The term of the Campus Point Lease (“Campus Point Initial Term”) is 60 months, ending April 30, 2026 (assuming an April 15, 2021 commencement date). The aggregate base rent due over the initial term of the Campus Point Lease is approximately $3.8 million. We will also be responsible for the payment of additional amounts to cover our share of the annual operating expenses of the building, the annual tax expenses of the building and the utilities costs for the building.

On February 11, 2021, concurrently with entry into the Campus Point Lease, we entered into an Assignment and Assumption of Lease (the “Assignment Agreement”) with Turning Point Therapeutics, Inc. (“Assignee”) and a Consent to Assignment (the "Consent") with Landlord. Pursuant to the Assignment Agreement, we will assign all rights, title, and interest under the New Lease to Assignee and deliver the New Premises to Assignee within five business days following the date that Campus Point Landlord delivers the Campus Point Premises to us. Pursuant to the Assignment Agreement, Assignee is required to pay us $60,000 in non-refundable assignment consideration. Additionally, the Consent stipulates that we will not be required to pay a fee pursuant to the New Lease in connection with the assignment.

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 rea65sonable 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, 2020, 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, 2020.

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, 2020, 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, 2020, 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

DIRECTORS

Our Board of Directors ("Board of Directors" or "Board") currently consists of ten directors. The brief biographies below include information, as of the date of this Annual Report, regarding the specific and particular experience, qualifications, attributes or skills of each director.

Name	Age	Position Held With the Company
Dr. Stelios Papadopoulos	72	Chairman of the Board of Directors
Ms. Kathryn J. Collier	53	Director
Dr. David Baltimore	83	Director
Mr. Joseph P. Hagan	52	Director, President and Chief Executive Officer
Dr. Alice S. Huang	81	Director
Mr. Jake R. Nunn	50	Director
Dr. William H. Rastetter	72	Director
Dr. Hugh Rosen	62	Director
Dr. Simos Simeonidis	51	Director
Ms. Pascale Witz, MBA, MSc	53	Director

Stelios Papadopoulos, Ph.D. Chairman of the Board, has served on our Board of Directors since our conversion to a corporation in January 2009 and as our Chairman since June 2013, and prior to that was a director of Regulus Therapeutics LLC since July 2008. Since 1994, Dr. Papadopoulos has served as a director and, since 1998, as Chairman of the Board for Exelixis, Inc., a publicly held biotechnology company, which he co-founded. Since July 2008, Dr. Papadopoulos has served as a member of the board of directors of Biogen Inc. (formerly Biogen Idec Inc.), a publicly held biopharmaceutical company, and has served as its chairman of the board of directors since June 2014. Since August 2020, Dr. Papadopoulos has served as chairman of the board of Eucrates Biomedical Acquisition Corp., a special purpose acquisition corporation. From 2003 to 2018, Dr. Papadopoulos served as a member of the board of directors of BG Medicine, Inc., a publicly-held life sciences company. From 2000 to 2006, Dr. Papadopoulos served as Vice Chairman with Cowen and Co., LLC, an investment banking firm. From 1987 to 2000, Dr. Papadopoulos served in several positions with PaineWebber, Incorporated, most recently as Chairman of PaineWebber Development Corp., a PaineWebber subsidiary focusing on biotechnology. Dr. Papadopoulos holds an M.S. in Physics, a Ph.D. in Biophysics and an MBA in Finance from New York University. Our Nominating and Corporate Governance Committee believes that Dr. Papadopoulos is qualified to serve on our Board of Directors due to his knowledge and expertise regarding the biotechnology and healthcare industries, his broad leadership experience on various boards and his experience with financial matters.

David Baltimore, Ph.D. has served on our Board of Directors since our conversion to a corporation in January 2009, and prior to that was a director of Regulus Therapeutics LLC since November 2007. Since 2006, Dr. Baltimore has served as President Emeritus and Robert Andrews Millikan Professor of Biology at the California Institute of Technology, and before that from 1997 to 2006, Dr. Baltimore served as President of the California Institute of Technology. From 1968 to 1972, Dr. Baltimore served as an associate professor at the Massachusetts Institute of Technology, and from 1972 to 1997 was a professor at the Massachusetts Institute of Technology. From 1990 to 1994, Dr. Baltimore served as professor at The Rockefeller University where he also served as the President from July 1990 to December 1991. Dr. Baltimore served as a director of Amgen Inc., a publicly held biotechnology company from 1997 to May 2018, and also served as a director of Immune Design Corp., a publicly held biotechnology company, from 1997 until its acquisition by Merck & Co., Inc. in February 2019. In 1975, Dr. Baltimore received the Nobel Prize in Medicine as a co-recipient. Dr. Baltimore holds a Ph.D. in Biology from The Rockefeller University and a B.A. with High Honors in Chemistry from Swarthmore College. Our Nominating and Corporate Governance Committee believes that Dr. Baltimore is qualified to serve on our Board of Directors due to the many years Dr. Baltimore has spent in scientific academia, which has provided him with a deep understanding of our industry and our activities.

Kathryn J. Collier has served on our Board of Directors since April 2018. Since July 2019, Ms. Collier has served as the vice president for audit services of Sempra Energy, a publicly-traded energy services holding company whose subsidiaries provide electricity, natural gas and value-added products and services. In this position, Ms. Collier oversees the internal audit

function for Sempra Energy, including the Financial Leadership Program and audit oversight of Sempra's operating companies. From March 2019 to July 2019, Ms. Collier served as the chief strategy and origination officer for Sempra LNG, a wholly-owned subsidiary of Sempra Energy. From August 2018 to March 2019, Ms. Collier served as chief financial officer and chief administrative officer for Sempra North America Infrastructure. Ms. Collier also previously served as vice president and treasurer for Sempra Energy from April 2012 to August 2018. Prior to joining Sempra Energy in 2012, Ms. Collier held several executive positions within global corporate and investment banking at Bank of America Merrill Lynch. Ms. Collier holds a bachelor's degree in accounting from Valparaiso University, Valparaiso, Indiana. Our Nominating and Corporate Governance Committee believes that Ms. Collier is qualified to serve on our Board of Directors due to her extensive financial and operational experience, her experience in investment banking and her corporate governance experience with various boards.

Joseph P. Hagan has served as our President and Chief Executive Officer and principal executive officer since May 2017. Mr. Hagan previously served as our Chief Operating Officer, principal financial officer and principal accounting officer from January 2016 to May 2017. From June 2011 through December 2015, Mr. Hagan served as the Executive Vice President, Chief Financial Officer and Chief Business Officer of Orexigen Therapeutics, Inc. From May 2009 to June 2011, Mr. Hagan served as Orexigen's Senior Vice President, Corporate Development, Strategy and Communications. From September 1998 to April 2008, Mr. Hagan served as Managing Director of Amgen Ventures. Prior to starting the Amgen Ventures Fund, Mr. Hagan served as Head of corporate development for Amgen Inc. Before joining Amgen, Mr. Hagan spent five years in the bioengineering labs at Genzyme and Advanced Tissue Sciences. Mr. Hagan has served on the board of directors of Zosano Pharma, a publicly-traded biotechnology company, since May 2015 and on the board of Aurinia Pharmaceuticals, Inc., since February 2018. He received an M.B.A. from Northeastern University and a B.S. in Physiology and Neuroscience from the University of California, San Diego. Our Nominating and Corporate Governance Committee believes that Mr. Hagan's expertise in business development, commercialization and financing of public companies qualify him to serve on our Board of Directors.

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

Jake R. Nunn has served on our Board of Directors since June 2019. Mr. Nunn is currently a venture advisor at New Enterprise Associates, Inc., a venture capital firm, where he was a partner from June 2006 until January 2019. Prior to joining NEA, he served as a partner and an analyst for the MPM BioEquities Fund, a life sciences fund at MPM Capital, L.P., a private equity firm. Previously, he was a healthcare research analyst and portfolio manager at Franklin Templeton Investments and an investment banker with Alex. Brown & Sons. Mr. Nunn has served on the board of directors of Trevena, Inc., a publicly-held biotechnology company focused on CNS since July 2013 and Addex Therapeutics Ltd., a publicly-held biopharmaceutical company focused on allosteric modulators for neurological disorders since June 2019 and Oventus Medical Ltd., a publicly-held medical device company since February 2020. Mr. Nunn served on the board of directors of Dermira, Inc., a publicly-held biopharmaceutical company focused on dermatology, from May 2011 until its acquisition by Eli Lilly and Company in February 2020. From 2009 to May 2015, Mr. Nunn served on the board of directors of Hyperion Therapeutics, Inc. and from 2008 to February 2016, Mr. Nunn served on the board of directors of TriVascular Technologies, Inc. Mr. Nunn received his A.B. in economics from Dartmouth College and his M.B.A. from the Stanford Graduate School of Business. He also holds the Chartered Financial Analyst designation and is a member of the CFA Society of San Francisco. Our Nominating and Corporate Governance Committee believes that Mr. Nunn is qualified to serve on our Board of Directors due to his extensive financial experience, his experience in investment banking and his corporate governance experience with various boards.

William H. Rastetter, Ph.D. has served on our Board of Directors since April 2013. From 2006 to February 2013, Dr. Rastetter served as a partner in the venture capital firm, Venrock. He served as Chief Executive Officer of IDEC Pharmaceuticals from December 1986 through November 2003, and as Chairman from May 1996 to November 2003. Upon the

merger of IDEC Pharmaceuticals and Biogen in November 2003, Dr. Rastetter served as Executive Chairman of Biogen Idec until the end of 2005. Dr. Rastetter served as chairman of the board of Illumina, Inc., a publicly held biotechnology company, from 2005 to January 2016 and served on its board of directors from 1998 to January 2016. He was a founder of Receptos, Inc. in 2009 and served as its chairman until the sale of the publicly held company to Celgene in 2015. Currently, he has served as the chairman of the board of directors of Fate Therapeutics, Inc., a publicly held biotechnology company, since November 2011; chairman of the board of directors of Neurocrine Biosciences, Inc., a publicly held biotechnology company, since May 2011 and on its board of directors since February 2010; on the board of directors of Grail, Inc., a privately-held company, since January 2016, and as its chairman from August 2017 to November 2018. Dr. Rastetter served on the board of directors of Cerulean Pharma Inc., a publicly held biotechnology company since January 2014, as its lead independent director from April 2014 to June 2016, and as its chairman from June 2016 until July 2017 when Cerulean and Daré Bioscience Inc. completed a reverse merger and he currently serves as chairman of the board of the surviving company, Daré Bioscience Inc., a publicly-traded company. In addition, he serves as an advisor to Illumina Ventures. He is the author of numerous scientific papers and patent applications in the fields of organic and bioorganic chemistry, protein and enzyme engineering, and biotechnology. Dr. Rastetter holds an S.B. in Chemistry from the Massachusetts Institute of Technology and received his M.A. and Ph.D. in Chemistry from Harvard University. Our Nominating and Corporate Governance Committee believes that Dr. Rastetter's knowledge and expertise regarding the biotechnology industry and his leadership experience on various biotechnology company boards of directors qualifies him to serve on our Board of Directors.

Hugh Rosen, M.D., Ph.D. has served on our Board of Directors since June 2016. Since April 2017, Dr. Rosen has served as the President and Chairman of the Board of Activx Biosciences, Inc., a wholly owned biopharmaceutical subsidiary of Kyorin Pharmaceutical Co., Ltd. From 2002 until March 2017, Dr. Rosen served as a Professor of Chemical Physiology at The Scripps Research Institute (TSRI) in La Jolla, California where he focused on pursuing his primary interests in lymphocyte trafficking and barrier regulation by signaling lipids, and contributing towards the development of translational infrastructure at TSRI. He also served as Chairman of the Committee for Advanced Human Therapeutics of TSRI. Prior to joining The Scripps Research Institute, Dr. Rosen served in various capacities with Merck Research Laboratories most recently serving as Executive Director in Immunology, Rheumatology and Infectious Diseases and Chair of the Worldwide Business Strategy Team for Antibacterials and Antifungals, reporting to the Management Committee. Dr. Rosen was a scientific founder of Receptos, Inc., now a wholly owned biopharmaceutical subsidiary of Celgene Corporation, and of RBNC Therapeutics. He received his M.D. from the University of Cape Town, South Africa and his Ph.D. in Physiological Sciences from Oxford. Our Nominating and Corporate Governance Committee believes that Dr. Rosen is qualified to serve on our Board of Directors due to the many years Dr. Rosen has spent in scientific academia as well as the biopharmaceutical industry, which has provided him with a deep understanding of our industry and our activities.

Simos Simeonidis, Ph.D. has served on our Board of Directors since June 2019. Since June 2017, Dr. Simeonidis has served as a Partner at Sarissa Capital. Prior to joining Sarissa Capital, he was a Managing Director and Senior Biotechnology Analyst at the Royal Bank of Canada (RBC) in New York from July 2014 to June 2017. Since October 2020, Dr. Simeonidis has also served on the board of Sarissa Capital Acquisition, a publicly-held special acquisition company focused on healthcare. Dr. Simeonidis spent more than a decade covering the biotechnology sector as an analyst at a number of investment banks, including Cowen and Company, First Albany Capital and Morgan Stanley. In addition to his investment management and financial expertise, Dr. Simeonidis combines both biopharmaceutical industry and biomedical research expertise, having worked at Novartis in Business Development and Strategic Planning, and prior to his corporate career, having served as a faculty member at Harvard Medical School. Dr. Simeonidis received his BS in Biology from Loyola University Chicago, and his MA, MPhil and PhD degrees in Cellular, Molecular and Biophysical Sciences from Columbia University's College of Physicians & Surgeons. He completed his Postdoctoral Fellowship at the laboratory of Professor Tucker Collins at Harvard Medical School and the Brigham and Women's Hospital, where he worked on the transcriptional regulation of gene expression. Dr. Simeonidis also holds an MBA in Healthcare Management at the Wharton School of the University of Pennsylvania. Our Nominating and Corporate Governance Committee believes that Dr. Simeonidis is qualified to serve on our Board of Directors due to his extensive experience in investment banking and as an analyst covering the life sciences industry, his prior employment in the biopharmaceutical industry, and his medical and scientific background.

Pascale Witz, MBA, MSc has served on our Board of Directors since June 2017. Ms. Witz is the founder and since November 2016, the president of PWH Advisors a consultancy firm advising management at life science companies and investment firms. From September 2015 through May 2016, Ms. Witz served as the Executive Vice President, Diabetes & Cardiovascular for Sanofi, S.A. Prior to that position, Ms. Witz served as the Executive Vice President, Global Divisions and Strategic Development, commencing in July 2013. During her tenure at Sanofi, she launched multiple medicines across three continents, and strengthened the pipeline through licensing and partnerships, including with Verily, a first-in-industry joint venture with a tech company. From 2009 to 2013, Ms. Witz served as President and CEO of GE's Pharmaceutical Diagnostics, a $2 billion integrated Pharmaceutical organization that encompassed Research and Development, Industrial Affairs through Commercial. Ms. Witz joined GE Healthcare in 1996, where she held various positions of increasing responsibilities; her 17-year career brought her to lead global businesses based out of the USA, France and the UK. She formerly worked for Becton Dickinson Pharmaceutical Systems from 1991 to 1996.Ms. Witz has served on the board of Fresenius Medical Care AG & Co.

KGaA, since May 2016 Horizon Pharma, since August 2017 and Perkin Elmer, since October 2017, and. Ms. Witz also served on the board of TESARO, Inc., from May 2018 until its acquisition by GlaxoSmithKline plc in January 2019 and from May 2016 to April 2018, served on the board of Savencia SA,. Ms. Witz received her Master of Business Administration from INSEAD, Fontainebleau, France and her Master of Science in Biochemistry from the Institut National des Sciences Appliquées (INSA) Lyon, France She was also a Ph.D. student in Molecular Biology at the Centre National de la Recherche Scientifique, Strasbourg, France. Our Nominating and Corporate Governance Committee believes that Ms. Witz is qualified to serve on our Board of Directors due to her knowledge, expertise and prior employment in the pharmaceutical industry and her experience on other company boards, which has provided her with a deep understanding of our industry and our activities.

EXECUTIVE OFFICERS

The following table sets forth our current executive officers, their ages, and the positions held by each such person with the Company:

Name	Age	Position Held With the Company
Joseph P. Hagan	52	President and Chief Executive Officer
Christopher Aker	60	Senior Vice President and General Counsel
Cris Calsada	51	Chief Financial Officer
Denis Drygin, Ph.D.	47	Chief Scientific Officer

Mr. Hagan's biographical information is set forth above under Proposal 1.

Christopher Aker has served as our Senior Vice President and General Counsel since January 2019, and before that served as our Senior Director, Legal Affairs since February 2011. Prior to joining us, Mr. Aker served as the Senior Director, Administration and Senior Corporate Counsel for Phenomix Corporation, a privately-held biopharmaceutical company, and was responsible for operational and legal oversight. Prior to Phenomix, Mr. Aker was Senior Corporate Counsel at SUGEN, Inc., a wholly-owned subsidiary of Pharmacia, until its acquisition by Pfizer. Prior to SUGEN, Mr. Aker was in private practice with various law firms. Mr. Aker received his Bachelor of Arts degree in International Relations from the University of California, Davis and his J.D. from Santa Clara University.

Cris Calsada joined Regulus in August 2019 and currently serves as our Chief Financial Officer. Prior to joining us, she served as Chief Financial Officer for Sanifit Therapeutics, S.A. since December 2017. Prior to her employment with Sanifit, Ms. Calsada was self-employed as a finance consultant to various life sciences companies. From 2004 until its acquisition in 2015, she served in positions of increasing responsibility with Ambrx, Inc., most recently serving as its Chief Operating Officer and Vice President of Finance. Prior to Ambrx, she worked for Sony Online Entertainment as its Executive Director of Finance and Controller. Earlier in her career, she practiced as a certified public accountant. Ms. Calsada received a B.S. in Business Administration with emphasis in Accounting from San Diego State University and an M.B.A. from the University of Southern California Marshall School of Business.

Denis Drygin, Ph.D. joined Regulus in August 2020 and currently serves as Chief Scientific Officer. Prior to joining Regulus, Dr. Drygin served as Vice President of Research & Development for Pimera Inc., a privately held biopharmaceutical company of which Dr. Drygin is a Founder. Before Pimera, Dr. Drygin was with Cylene Pharmaceuticals, most recently serving as Vice President of Biology. Dr. Drygin led discovery and/or development of multiple therapeutics including first selective inhibitor of CK2 kinase Silmitasertib (CX-4945), first selective inhibitor of RNA Polymerase I transcription (Pol I) CX-5461, as well as second generation Pol I inhibitor PMR-116. Dr. Drygin received a B.S. and M.S. in Chemistry from Moscow State University, an M.S. and Ph.D. in Molecular and Cellular Biology from University of Massachusetts at Amherst and Post-Doctoral training in Pharmacology and Toxicology from Ionis Pharmaceuticals.

CORPORATE GOVERNANCE

Code of Ethics

The Company has adopted a Code of Business Conduct and Ethics that applies to all directors, officers (including our principal executive officer, principal financial officer and principal accounting officer) and employees. The Code of Business Conduct and Ethics is available on the Company's website at www.regulusrx.com under the Corporate Governance section of our Investor Relations page. If the Company makes any substantive amendments to the Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer, principal accounting officer, controller or persons performing similar functions, or grants any waiver from a provision of the Code of Business Conduct and Ethics to any of these

specified individuals that is required to be disclosed pursuant to SEC rules and regulations, the Company will promptly disclose the nature of the amendment or waiver on its website.

Hedging Policy

The Company's insider trading and window period policy provides that no officer, director, other employee or consultant of the Company may engage in short sales, transactions in put or call options, hedging transactions or other inherently speculative transactions with respect to the Company's stock at any time. In addition, no officer, director, other employee or consultant of the Company may margin, or make any offer to margin, any of the Company's stock, including without limitation, borrowing against such stock, at any time.

BOARD LEADERSHIP STRUCTURE

Our Board of Directors is currently chaired by Stelios Papadopoulos, Ph.D. As a general policy, our Board of Directors believes that separation of the positions of Chairman and Chief Executive Officer reinforces the independence of the Board of Directors from management, creates an environment that encourages objective oversight of management's performance and enhances the effectiveness of the Board of Directors as a whole. As such, Mr. Hagan serves as our President and Chief Executive Officer while Dr. Papadopoulos serves as our Chairman of the Board of Directors but is not an officer. We expect and intend the positions of Chairman of the Board of Directors and Chief Executive Officer to continue to be held by separate individuals in the future.

ROLE OF THE BOARD IN RISK OVERSIGHT

One of the key functions of our Board of Directors is informed oversight of our risk management process. The Board of Directors does not have a standing risk management committee, but rather administers this oversight function directly through the Board of Directors as a whole, as well as through various standing committees of our Board of Directors that address risks inherent in their respective areas of oversight. In particular, our Board of Directors is responsible for monitoring and assessing strategic risk exposure, and our Audit Committee has the responsibility to consider and discuss our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies to govern the process by which risk assessment and management is undertaken. The Audit Committee also monitors compliance with legal and regulatory requirements. Our Nominating and Corporate Governance Committee monitors the effectiveness of our corporate governance practices, including whether they are successful in preventing illegal or improper liability-creating conduct. Our Compensation Committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking.

As a result of the COVID-19 pandemic, we have and may in the future experience disruptions that could severely impact our business, preclinical studies and clinical trials. Given the evolving nature of the pandemic, our senior management and our Board of Directors are communicating and meeting more frequently to monitor potential business impacts and further strategic planning.

MEETINGS OF THE BOARD OF DIRECTORS

The Board of Directors met thirteen times during the last fiscal year and four times in executive session. All directors who served in 2020 attended at least 75% of the aggregate number of meetings of the Board and of the committees on which they served, held during the portion of the last fiscal year for which they were directors or committee members, respectively.

INFORMATION REGARDING COMMITTEES OF THE BOARD OF DIRECTORS

The Board maintains an Audit Committee, a Compensation Committee and a Nominating and Corporate Governance Committee. The following table provides membership and meeting information for the year ended December 31, 2020 for each of the Board committees:

Name	Audit	Compensation	Nominating and Corporate Governance
Dr. David Baltimore			X *
Kathryn J. Collier	X *		
Jake Nunn	X		
Dr. Stelios Papadopoulos	X		X
Dr. William H. Rastetter		X *	
Dr. Hugh Rosen		X	
Dr. Simos Simeonidis			X
Pascale Witz		X	
Total meetings in 2020	5	3	2

* Committee Chairperson

Below is a description of each committee of the Board of Directors. Each of the committees has authority to engage legal counsel or other experts or consultants, as it deems appropriate to carry out its responsibilities. Our Board of Directors has determined that each member of each committee meets the applicable Nasdaq rules and regulations regarding "independence" and that each member is free of any relationship that would impair his or her individual exercise of independent judgment with regard to the Company.

Audit Committee

The Audit Committee of our Board of Directors was established by our Board of Directors in accordance with Section 3(a)(58)(A) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), to oversee the Company's corporate accounting and financial reporting processes and audits of its financial statements. For this purpose, our Audit Committee performs several functions. Our Audit Committee evaluates the performance of and assesses the qualifications of the independent auditors; determines and approves the engagement of the independent auditors; determines whether to retain or terminate the existing independent auditors or to appoint and engage new independent auditors; reviews and approves the retention of the independent auditors to perform any proposed permissible non-audit services; monitors the rotation of partners of the independent auditors on the Company's audit engagement team as required by law; reviews and approves or rejects transactions between the Company and any related persons; confers with management and the independent auditors regarding the effectiveness of internal controls over financial reporting; establishes procedures, as required under applicable law, for the receipt, retention and treatment of complaints received by the Company regarding accounting, internal accounting controls or auditing matters and the confidential and anonymous submission by employees of concerns regarding questionable accounting or auditing matters; and meets to review the Company's annual audited financial statements and quarterly financial statements with management and the independent auditor, including a review of the Company's disclosures under "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Our Audit Committee is currently composed of three directors: Ms. Collier, Mr. Nunn and Dr. Papadopoulos. The Audit Committee met five times during the last fiscal year. Our Board of Directors has adopted a written charter of the Audit Committee that is available to stockholders on the Company's website at www.regulusrx.com. Our Board of Directors reviews the Nasdaq listing standards definition of independence for Audit Committee members on an annual basis and has determined that all members of our Audit Committee are independent (as independence is currently defined in Rule 5605(c)(2)(A) of the Nasdaq listing standards).

Our Board of Directors has determined that Ms. Collier qualifies as an "audit committee financial expert," as defined in applicable SEC rules. Our Board of Directors has made a qualitative assessment of Ms. Collier's level of knowledge and experience based on a number of factors, including her formal education, her experience in the investment banking industry and as the holder of various positions with responsibility for finance of a subsidiary of a major publicly-traded energy services holding company.

Compensation Committee

The Compensation Committee is currently composed of three directors: Dr. Rastetter, Dr. Rosen and Ms. Witz. The Board of Directors reviews the Nasdaq listing standards definition of independence for Compensation Committee members on an annual basis and has determined that all members of the Company's Compensation Committee are independent (as independence is currently defined in Rule 5605(d)(2)(A of the Nasdaq listing standards). The Compensation Committee met eight times during the last fiscal year. The Compensation Committee has adopted a written charter that is available to stockholders on the Company's website at www.regulusrx.com.

The Compensation Committee acts on behalf of the Board to review, adopt and/or recommend for adoption and oversee the Company's compensation strategy, policies, plans and programs. The functions of the Compensation Committee include, among other things:

- reviewing, modifying and approving (or if it deems appropriate, making recommendations to the full Board of Directors regarding) our overall compensation strategy and policies;

- reviewing and recommending to our Board of Directors the compensation and other terms of employment of our executive officers;

- reviewing and recommending to our Board of Directors the performance goals and objectives relevant to the compensation of our executive officers and assessing their performance against these goals and objectives;

- reviewing and approving (or if it deems it appropriate, making recommendations to the full Board of Directors regarding) the equity incentive plans, compensation plans and similar programs advisable for us, as well as modifying, amending or terminating existing plans and programs;

- evaluating risks associated with our compensation policies and practices and assessing whether risks arising from our compensation policies and practices for our employees are reasonably likely to have a material adverse effect on us;

- reviewing and approving (or if it deems it appropriate, making recommendations to the full Board of Directors regarding) the type and amount of compensation to be paid or awarded to our non-employee board members;

- establishing policies for allocating between long-term and currently paid out compensation, between cash and non-cash compensation and the factors used in deciding between the various forms of compensation;

- establishing policies with respect to votes by our stockholders to approve executive compensation as required by Section 14A of the Exchange Act and determining our recommendations regarding the frequency of advisory votes on executive compensation;

- reviewing and assessing the independence of compensation consultants, legal counsel and other advisors as required by Section 10C of the Exchange Act;

- establishing elements of corporate performance for purposes of increasing or decreasing compensation;

- administering our equity incentive plans;

- establishing policies with respect to equity compensation arrangements;

- reviewing regional and industry-wide compensation practices and trends to assess the competitiveness of our executive compensation programs and evaluating the effectiveness of our compensation policy and strategy in achieving expected benefits to us;

- reviewing the adequacy of its charter on a periodic basis;

- reviewing with management and approving our disclosures under the caption "Compensation Discussion and Analysis" in our periodic reports or proxy statements to be filed with the SEC, as applicable; and

- preparing the compensation committee report as required by SEC rules.

Compensation Committee Processes and Procedures

Typically, the Compensation Committee meets at least twice annually and with greater frequency if necessary. The agenda for each meeting is usually developed by the Chair of the Compensation Committee, in consultation with the Chief Executive Officer. The Compensation Committee meets regularly in executive session. However, from time to time, various members of management and other employees as well as outside advisors or consultants may be invited by the Compensation Committee to make presentations, to provide financial or other background information or advice or to otherwise participate in

Compensation Committee meetings. The Chief Executive Officer may not participate in, or be present during, any deliberations or determinations of the Compensation Committee regarding his compensation. The charter of the Compensation Committee grants the Compensation Committee full access to all books, records, facilities and personnel of the Company, as well as authority to obtain, at the expense of the Company, advice and assistance from internal and external legal, accounting or other advisors and consultants and other external resources that the Compensation Committee considers necessary or appropriate in the performance of its duties. In particular, the Compensation Committee has the sole authority to retain compensation consultants to assist in its evaluation of executive and director compensation, including the authority to approve the consultant's reasonable fees and other retention terms.

During fiscal year 2020, the Compensation Committee engaged Aon/Radford as a compensation consultant. The Committee engaged Aon/Radford to provide a competitive assessment of the Company's executive compensation program compared to executive compensation paid to executives at selected publicly traded peer companies. Following a gap analysis of the peer companies, Aon/Radford made certain recommendations to the Compensation Committee to make modest increases in the level of equity grants to the Company's executive team and to increase annual cash compensation for certain Company executives and Board Committee members who were paid below the median compared to the peer companies. The Compensation Committee analyzed whether the work of Aon/Radford as a compensation consultant raised any conflict of interest, taking into consideration the following factors: (i) the provision of other services to the Company by the compensation consultant; (ii) the amount of fees from the Company paid to the compensation consultant as a percentage of the firm's total revenue; (iii) the policies and procedures of the compensation consultant that are designed to prevent conflicts of interest; (iv) any business or personal relationship of the compensation consultant or the individual compensation advisors employed by this firm with an executive officer of the Company; (v) any business or personal relationship of the individual compensation advisors with any member of the Compensation Committee; and (vi) any stock of the Company owned by the compensation consultant or the individual compensation advisors employed by this firm. The Compensation Committee concluded, based on its analysis of the above factors, that the work of Aon/Radford and the individual compensation advisors employed by this firm as a compensation consultant to the Company has not created any conflict of interest.

Under its charter, the Compensation Committee may form, and delegate authority to, subcommittees as appropriate. In 2012, the Compensation Committee formed a Non-Management Stock Option Committee, currently composed of Mr. Hagan, to which it delegated authority to grant, without any further action required by the Compensation Committee, stock awards to employees who are not officers of the Company. The purpose of this delegation of authority is to enhance the flexibility of option administration within the Company and to facilitate the timely grant of options to non-management employees, particularly new employees, within specified limits approved by the Compensation Committee. In particular, the subcommittee may grant options only within pre-approved guidelines and not to any employee who will have a vice president title or higher. Typically, as part of its oversight function, the Committee will review on a regular basis the list of grants made by the subcommittee. During fiscal year 2020, the subcommittee exercised its authority to grant options and stock awards to purchase an aggregate of 752,750 shares of the Company's common stock to non-officer employees.

Historically, the Compensation Committee has made most of the significant adjustments to annual compensation, determined bonus and equity awards and established new performance objectives at one or more meetings held during the last quarter of the year. However, the Compensation Committee also considers matters related to individual compensation, such as compensation for new executive hires, as well as high-level strategic issues, such as the efficacy of the Company's compensation strategy, potential modifications to that strategy and new trends, plans or approaches to compensation, at various meetings throughout the year. Generally, the Compensation Committee's process comprises two related elements: the determination of compensation levels and the establishment of performance objectives for the current year. For executives other than the Chief Executive Officer, the Compensation Committee solicits and considers evaluations and recommendations submitted to the Committee by the Chief Executive Officer. In the case of the Chief Executive Officer, the evaluation of his performance is conducted by the Compensation Committee, which determines any adjustments to his compensation as well as awards to be granted. For all executives and directors as part of its deliberations, the Compensation Committee may review and consider, as appropriate, materials such as financial reports and projections, operational data, tax and accounting information, tally sheets that set forth the total compensation that may become payable to executives in various hypothetical scenarios, executive and director stock ownership information, company stock performance data, analyses of historical executive compensation levels and current Company-wide compensation levels and recommendations of the Company's General Counsel, including analyses of executive and director compensation paid at other companies identified by the Company's General Counsel.

Nominating and Corporate Governance Committee

The Nominating and Corporate Governance Committee of the Board of Directors is responsible for identifying, reviewing and evaluating candidates to serve as directors of the Company (consistent with criteria approved by the Board), reviewing and evaluating incumbent directors, recommending to the Board for selection candidates for election to the Board of Directors,

making recommendations to the Board regarding the membership of the committees of the Board, assessing the performance of the Board, and monitoring the Company's adherence to its Code of Business Conduct and Ethics.

The Nominating and Corporate Governance Committee is composed of three directors: Dr. Baltimore, Dr. Papadopoulos and Dr. Simeonidis. All members of the Nominating and Corporate Governance Committee are independent (as independence is currently defined in Rule 5605(a)(2) of the Nasdaq listing standards). The Nominating and Corporate Governance Committee met twice during 2020. The Nominating and Corporate Governance Committee has adopted a written charter that is available to stockholders on the Company's website and www.regulusrx.com.

The Nominating and Corporate Governance Committee believes that candidates for director, both individually and collectively, can and do provide the integrity, experience, judgment, commitment (including having sufficient time to devote to the Company and level of participation), skills, diversity and expertise appropriate for the Company. In assessing the directors, both individually and collectively, the Nominating and Corporate Governance Committee may consider the current needs of the Board and the Company to maintain a balance of knowledge, experience and capability in various areas. However, the Nominating and Corporate Governance Committee retains the right to modify these qualifications from time to time. Candidates for director nominees are reviewed in the context of the current composition of the Board, the operating requirements of the Company and the long-term interests of stockholders. In conducting this assessment, the Nominating and Corporate Governance Committee typically considers diversity, age, skills and such other factors as it deems appropriate given the current needs of the Board and the Company, to maintain a balance of knowledge, experience and capability. In the case of incumbent directors whose terms of office are set to expire, the Nominating and Corporate Governance Committee reviews these directors' overall service to the Company during their terms, including the number of meetings attended, level of participation, quality of performance and any other relationships and transactions that might impair the directors' independence. In the case of new director candidates, the Nominating and Corporate Governance Committee also determines whether the nominee is independent for Nasdaq purposes, which determination is based upon applicable Nasdaq listing standards, applicable SEC rules and regulations and the advice of counsel, if necessary. The Nominating and Corporate Governance Committee then uses its network of contacts to compile a list of potential candidates, but may also engage, if it deems appropriate, a professional search firm. The Nominating and Corporate Governance Committee conducts any appropriate and necessary inquiries into the backgrounds and qualifications of possible candidates after considering the function and needs of the Board. The Nominating and Corporate Governance Committee meets to discuss and consider the candidates' qualifications and then selects a nominee for recommendation to the Board by majority vote.

The Nominating and Corporate Governance Committee will consider director candidates recommended by stockholders. The Nominating and Corporate Governance Committee does not intend to alter the manner in which it evaluates candidates, including the minimum criteria set forth above, based on whether or not the candidate was recommended by a stockholder. Stockholders who wish to recommend individuals for consideration by the Nominating and Corporate Governance Committee to become nominees for election to the Board may do so by delivering a written recommendation to the Nominating and Corporate Governance Committee at the Company's principal executive offices, Attn: Secretary, no later than the 90th day and no earlier than the 120th day prior to the one year anniversary of the preceding year's annual meeting. Submissions must include (1) the name and address of the Company stockholder on whose behalf the submission is made; (2) the number of Company shares that are owned beneficially by such stockholder as of the date of the submission; (3) the full name of the proposed candidate; (4) a description of the proposed candidate's business experience for at least the previous five years; (5) the complete biographical information for the proposed candidate; (6) a description of the proposed candidate's qualifications as a director; and (7) any other information required by the Company Bylaws. The Company may require any proposed nominee to furnish such other information as it may reasonably require to determine the eligibility of such proposed nominee to serve as an independent director of the Company or that could be material to a reasonable stockholder's understanding of the independence, or lack thereof, of such proposed nominee.

Stockholder Communications with the Board of Directors

The Company's Board has adopted a formal process by which stockholders may communicate with the Board or any of its directors. Stockholders who wish to communicate with the Board may do so by sending written communications addressed to the Secretary of Regulus Therapeutics Inc. at the Company's principal executive offices. Each communication must set forth: the name and address of the Company stockholder on whose behalf the communication is sent; and the number of Company shares that are owned beneficially by such stockholder as of the date of the communication. Each communication will be reviewed by the Company's Secretary to determine whether it is appropriate for presentation to the Board or relevant directors.

Communications determined by the Company's Secretary to be appropriate for presentation to the Board or any relevant directors are submitted to the Board or relevant directors on a periodic basis.

Item 11. Executive Compensation

EXECUTIVE COMPENSATION

The Company is a "smaller reporting company" under Item 10 of Regulation S-K promulgated under the Securities and Exchange Act of 1934, and the following compensation disclosure is intended to comply with the requirements applicable to smaller reporting companies. Although the rules allow the Company to provide less detail about its executive compensation program, the Compensation Committee is committed to providing the information necessary to help stockholders understand its executive compensation-related decisions. Accordingly, this section includes supplemental narratives that describe the 2020 executive compensation program for our Named Executive Officers.

Named Executive Officers. The following individuals are our "Named Executive Officers" or "NEOs" for the year ended December 31, 2020:

- Joseph P. Hagan, our President and Chief Executive Officer;
- Christopher R. Aker, our Senior Vice President and General Counsel; and
- Cris Calsada, our Chief Financial Officer.

Summary Compensation Table

The following table shows, for the fiscal years ended December 31, 2020 and December 31, 2019, compensation awarded to, paid to, or earned by, the Named Executive Officers.

Name and Principal Position	Year	Salary ($)	Stock Options ($)[1]	Restricted Stock Units (RSUs) ($)[1]	Non-Equity Incentive Plan Compensation ($)[2]	All Other Compensation ($)[3]	Total ($)
Joseph P. Hagan	2020	551,500	1,507,054	—	264,720	9,860	2,333,134
President & Chief Executive Officer	2019	535,600	540,342	69,079	860,652	8,610	2,014,283
Christopher R. Aker	2020	315,000	351,646	—	132,300	10,172	809,118
SVP & General Counsel	2019	290,000	188,913	23,696	275,500	9,798	787,907
Cris Calsada	2020	315,000	251,176	—	132,300	9,350	707,826
Chief Financial Officer	2019	104,526	151,749	—	45,965	636	302,876

(1) In accordance with SEC rules, this column reflects the aggregate grant date fair value of the stock awards granted during the years indicated, computed in accordance with Financial Accounting Standard Board ASC Topic 718 for stock-based compensation transactions, or ASC 718. Assumptions used in the calculation of these amounts are included in Note 10 to the Financial Statements in our Annual Report on Form 10-K for the year ended December 31, 2020. These amounts do not reflect the actual economic value that will be realized by the Named Executive Officer upon the vesting of the stock awards, the exercise of the stock options, or the sale of the common stock underlying such stock awards. The grant date fair value of the stock awards granted during 2020 that vest based on performance conditions is reported based on the probable outcome of such performance conditions, as determined in accordance with ASC 718, which is the same as the grant date fair value of such awards at the grant date, assuming that the highest level of performance conditions will be achieved.

(2) Amounts shown include annual performance bonuses paid to Mr. Hagan, Mr. Aker and Ms. Calsada, earned for the years indicated. For more information, see below under "Annual Performance-Based Bonus Opportunity." The 2019 amounts shown for Mr. Hagan and Mr. Aker also include a Board of Directors approved discretionary bonus and retention award paid in recognition of their contributions following our July 2018 corporate restructuring and reduction in workforce and our entry into a private placement financing transaction in May 2019.

(3) Amounts shown include term life insurance and long-term disability insurance paid by us on behalf of the Named Executive Officers, matching payments made to the NEO's Health Savings Account (if the NEO participated in our high deductible health plan)

and matching contributions we paid under the terms of our 401(k) plan. All of these benefits are provided to the Named Executive Officers on the same terms as provided to all of our regular full-time employees in the United States. For more information regarding these benefits, see below under “Other Compensation.”

Narrative Disclosure to Summary Compensation Table

The three principal components of our executive compensation program for our Named Executive Officers in 2020 were base salary, annual performance-based bonus opportunity and equity compensation. We do not have any formal policies for allocating compensation among salary, performance bonus awards and equity grants, short-term and long-term compensation or among cash and non-cash compensation. Instead, the Compensation Committee uses its judgment to establish a total compensation program for each named executive officer that is a mix of current, short-term and long-term incentive compensation, and cash and non-cash compensation, that it believes appropriate to achieve the goals of our executive compensation program and our corporate objectives. In line with our pay for performance philosophy, we structured a significant portion of our Named Executive Officers' 2020 compensation to be variable, at risk and tied directly to our measurable performance in the form of performance-based bonuses and equity incentives.

The Compensation Committee uses the services of an independent compensation consultant who is retained by, and reports directly to, the Compensation Committee to provide the Compensation Committee with an additional external perspective with respect to its evaluation of relevant market and industry practices. Since 2013, the Compensation Committee has used Radford, an AON Hewitt Company, as a third-party compensation consultant to assist the Compensation Committee in establishing overall compensation levels. Radford conducted analyses and provided advice on, among other things, the appropriate peer group, executive compensation for our executive officers and compensation trends in the life sciences industry.

The peer group of companies used by the Compensation Committee in making 2020 compensation decisions was comprised of the following companies:

Alpine Immune Sciences	aTyr Pharma	Caladrius Biosciences	Calithera Biosciences	Capricor Therapeutics
Catalyst Biosciences	Chimerix	Cidara Therapeutics	Conatus Pharmaceuticals	ContraFect
Corvus Pharmaceuticals	Flex Pharma	Infinity Pharmaceuticals	Lineage Cell Therapeutics	Miragen Therapeutics
Otonomy	Protagonist Therapeutics	Sienna Biopharmaceuticals	Sunesis Pharmaceuticals	Synthetic Biologics
Tocagen	TRACON Pharmaceuticals			

The peer group was recommended by Radford and chosen in late-2019 based on the following parameters: biopharmaceutical companies that were pre-commercial and with programs in early clinical development, had market values generally under $200 million and with a preference for companies with headcounts under 100. At the time we choose our peer group companies, our market value was approximately $15 million and our headcount was 24 employees.

Base Salary

In December 2019, the Compensation Committee reviewed the base salaries for our then-current Named Executive Officers, the market data from Radford, our 3% Company-wide corporate merit increase target for base salaries, the scope of each executive's responsibilities for 2019, each executive's prior experience and internal pay equity in order to determine 2020 base salaries of our NEOs.

The Named Executive Officers' 2020 annual base salaries (effective January 1, 2020) and increases from 2019 annual base salaries approved by the Compensation Committee were as follows:

Name	2020 Base Salary ($)	Increase from 2019 Base Salary (%)
Joseph P. Hagan	551,500	3.0%
Christopher R. Aker	315,000	8.6%
Cris Calsada	315,000	1.6%

Annual Performance-Based Bonus Opportunity

The annual performance-based bonus each Named Executive Officer is eligible to receive is based on (1) the individual's target bonus, as a percentage of base salary, (2) a Company-based performance factor ("CPF"), and (3) an individual performance factor ("IPF"). The actual performance-based bonus paid, if any, is calculated by taking into consideration the executive officer's annual base salary, target bonus percentage, percentage attainment of the CPF and percentage attainment of the IPF. Except for the Chief Executive Officer whose entire annual bonus depends upon the CPF, 20% of each other NEO's annual bonus is also dependent upon such individual's IPF. At the end of the year, our Compensation Committee approves the extent to which we achieved the CPF based on achievement of the corporate goals. The extent to which each individual Named Executive Officer achieves his or her IPF is determined based on our Chief Executive Officer's review and recommendation to our Compensation Committee, except our Chief Executive Officer and our other Named Executive Officers do not make recommendations with respect to their own achievement, and our Compensation Committee makes the final decisions with respect to each IPF. Additionally, our Compensation Committee has the discretion to determine the weighting of each of the goals that comprise the CPF and IPF. Our Compensation Committee may award a bonus in an amount above or below the amount resulting from the calculation described above, based on other factors that our Compensation Committee determines, in its sole discretion, are material to our corporate performance and provide appropriate incentives to our executives, for example based on events or circumstances that arise after the original CPF and IPF goals are set. Our Compensation Committee did not exercise any such discretion in 2020.

Each Named Executive Officer's target bonus for 2020, represented as a percentage of base salary, or a target bonus percentage, was 50% of base salary, with the exception of Mr. Hagan's target bonus percentage, which was 60% of base salary.
The Compensation Committee determined the target bonuses of each of our NEOs other than our Chief Executive Officer should be consistent to promote internal equity and reinforce teamwork across our leadership team.

The CPF and IPF goals are determined by our Compensation Committee and communicated to our Named Executive Officers each year, prior to or shortly following the beginning of the year to which they relate. The CPF is composed of several goals that relate to our annual corporate goals and various business accomplishments which vary from time to time depending on our overall strategic objectives. The IPF is composed of factors that relate to each Named Executive Officer's ability to drive his or her own performance and the performance of his or her direct employee reports towards reaching our corporate goals. The proportional emphasis placed on each goal within the CPF and IPF may vary from time to time depending on our overall strategic objectives and our Compensation Committee's subjective determination of which goals have more impact on our performance.

For 2020, the CPF goals related primarily to advancing our most promising program, RGLS4326 for the treatment of autosomal dominant polycystic kidney disease ("ADPKD"), while also make some progress on our preclinical pipeline. The specific CPF goals were as follows:

- Complete the RGLS4326 Multiple Ascending Dose (the "MAD") study in healthy volunteers with top-line data by mid-year 2020;
- Start the RGLS4326 Mechanism of Action (the "MOA") study by early fourth quarter of 2020;
- Gain alignment or input from FDA on a framework for addressing the requirements for the partial clinical hold;
- Nominate a development candidate for at least one research program by year end 2020;
- Advance a discovery research program to lead identification; and
- Extend our cash runway by providing sufficient cash to complete the Mechanism of Action study.

In December 2020, after careful review, our Board of Directors, upon the recommendation of our Compensation Committee, concluded that we had achieved 80% of our CPF goals, based on the following:

- We initiated the MAD study on time and completed the study despite the challenges of the COVID pandemic;
- We redesigned the MOA study to an adaptive open-label design, saving money, providing optionality based on clinical outcomes and generating additional data for our future interactions with the U.S. Food & Drug Administration concerning this program. While we did not seek to gain alignment from FDA on our remaining clinical hold requirements we did engage key experts to build a robust model based on the new data generated from the additional preclinical work to better address the remaining hold requirements;
- We commenced the MOA study enrolling the first patient in October 2020 and were on track to have the first cohort of the study fully enrolled by January 2021 thereby enabling data at the end of the first quarter of 2021;

- We advanced toward development two candidates from other preclinical programs, although we did not nominate a candidate;
- We commenced new research around possible targets in new therapeutic areas and produced some early promising data; and
- We closed a private financing netting approximately $18.2 million to fund on our ongoing development programs.

The IPF goals varied by individual and included individual performance contributions towards maintaining a leading position in *micro*RNA research, accelerating efforts in *micro*RNA therapeutic development, supporting our growth with additional capital, fostering a culture of value creation, attracting and retaining key talent and building good processes and policies. Our Chief Executive Officer did not have IPF goals as his bonus is entirely dependent on our CPF goals, because our Chief Executive Officer has a direct impact on, and responsibility for, our corporate performance.

Based on our Chief Executive Officer's recommendations with respect to each other Named Executive Officer, and our Compensation Committee's deliberations with respect to each Named Executive Officer's individual performance against the IPF, our Compensation Committee and Board of Directors approved a performance-based bonus for each of our Named Executive Officers as set forth in the table below based on a 80% CPF and IPF as indicated, weighted 80% and 20%, respectively, except for our Chief Executive Officer, whose bonus was weighted 100% on CPF goals:

Name	Target Bonus ($)	IPF Achievement (%)	Cash Bonus Paid ($)
Joseph P. Hagan	$ 330,900	—	$ 264,720
Christopher Aker[(1)]	$ 157,500	100%	$ 132,300
Cris Calsada[(2)]	$ 157,500	100%	$ 132,300

(1) Mr. Aker's performance-based bonus was approved based on 80% CPF and 100% IPF in recognition of his roles in procuring additional capital, assisting in the initiation of the RGLS4326 MOA study including contracting with the clinical sites, his operational leadership concerning our response to the COVID pandemic and his role in recruiting additional scientific talent.

(2) Ms. Calsada's performance-based bonus was approved based on the 80% CPF and 100% IPF in recognition of her leadership in procuring additional capital, her active management of our research and administrative budgets, and her oversight of financial reporting.

Equity-Based Incentive Awards

Equity incentives are a key component of our executive compensation program that the Compensation Committee believes motivate executive officers to achieve our business objectives by tying incentives to the appreciation of our common stock and, in the case of performance-vesting awards, measurable performance goals. In the past, we have primarily granted equity awards in the form of stock options that vest based on achievement of specific Company performance goals and/or continued service and, more recently, RSU stock awards that vest based on continued service.

Stock Awards. In 2020, each of our Named Executive Officers received time-vesting stock options and performance-based stock options in the amounts listed below.

Name	Time-Vesting Stock Options (# of shares)[(1)]	Performance-Vesting Stock Options (# of shares)[(2)]
Joseph P. Hagan	900,000	600,000
Christopher R. Aker	210,000	140,000
Cris Calsada	150,000	100,000

(1) Consists of a stock option granted on January 22, 2020 with a vesting commencement date of January 1, 2020 with an exercise price of $1.31per share vesting in equal monthly installments over a 48 month period, subject to the recipient's continued service to the Company through each such vesting date.

(2) Consists of two equal performance-vesting stock options granted on January 22, 2020 with an exercise price of $1.31 per share. The options will vest only upon achievement of two specified development goals related to our RGLS4326 program. Upon achievement of each goal, 50% of the options subject to the grant immediately vested with the remaining options vesting in equal monthly installments over the following 24 months, subject to the recipient's continued service to the Company through each such vesting date.

The performance-vesting stock options vest and can be earned only if performance goals key to our future success are achieved (in addition to continued service), thereby further incentivizing our Named Executive Officers to achieve these goals to drive increases in our long-term value for stockholders.

Other Compensation

Our Named Executive Officers are eligible to participate in all of our employee benefit plans, including our medical, dental, vision, group life and disability insurance plans, in each case on the same basis as other employees. We also pay the premiums for term life insurance and long-term disability for all of our employees, including our Named Executive Officers. None of our Named Executive Officers participate in or have account balances in qualified or non-qualified defined benefit plans sponsored by us. We generally do not provide perquisites or personal benefits to our Named Executive Officers, although we may from time to time provide signing bonuses or other reasonable benefits as our Compensation Committee determines appropriate.

All of our full-time employees in the United States, including our Named Executive Officers, are eligible to participate in our 401(k) plan, which is a retirement savings defined contribution plan established in accordance with Section 401(a) of the Code. Pursuant to our 401(k) plan, employees may elect to defer their eligible compensation into the plan on a pre-tax basis, up to the statutorily prescribed annual limit of $19,500 in 2020 (additional salary deferrals not to exceed $6,500 are available to those employees 50 years of age or older) and to have the amount of this reduction contributed to our 401(k) plan. In 2020, we provided a $0.50 match for every dollar our employees elect to defer up to 6% of their eligible compensation. In general, eligible compensation for purposes of the 401(k) plan includes an employee's wages, salaries, fees for professional services and other amounts received for personal services actually rendered in the course of employment with us to the extent the amounts are includible in gross income, and subject to certain adjustments and exclusions required under the Code. The 401(k) plan currently does not offer the ability to invest in our securities.

Agreements with Named Executive Officers

Employment Agreements. We entered into employment agreements with each of our Named Executive Officers. The agreements provide for at will employment and for certain base salary, target bonus and severance payments to our Named Executive Officers.

Employment Agreement with Mr. Hagan. In December 2015, we entered into an employment agreement with Mr. Hagan, with an effective date of January 1, 2016. Pursuant to his employment agreement, Mr. Hagan is entitled to receive an annual base salary of $415,000 and is eligible to receive an annual performance bonus, with a target bonus amount of 40% of his annual base salary. Mr. Hagan's base salary and target bonus are subject to periodic review and adjustment from time to time in the discretion of our Board of Directors or the Compensation Committee and have been subsequently increased. In May 2017, Mr. Hagan was appointed as our President and Chief Executive Officer. At that time, his base salary was increased to $500,000 and his target bonus was increased to 50%. Additionally, Mr. Hagan's employment agreement provides for the grant of stock option awards, which were made in January 2016. Pursuant to Mr. Hagan's employment agreement, all outstanding stock options subject to vesting based on Company performance that are held by Mr. Hagan immediately before a change in control shall become fully vested and exercisable as of immediately before, and contingent upon, the change in control, provided that Mr. Hagan remains employed by us as of such date. In 2020, Mr. Hagan's base salary was increased to $551,500 and his target bonus (which was increased in 2019) remained at 60% of his annual base salary.

If we terminate Mr. Hagan's employment without cause (other than due to his death or complete disability) or if Mr. Hagan resigns for good reason at any time other than during the period beginning one month before and ending 12 months following a change in control, Mr. Hagan will receive, subject to receiving an effective release and waiver of claims from him, (1) a lump sum severance payment equal to 12 months of his then-current base salary (disregarding any decrease that forms the basis for a resignation for good reason), (2) a lump sum cash amount equal to 229.56% multiplied by the total cost of the projected premiums for group medical, dental and vision insurance for a period of 12 months and (3) vesting acceleration of all outstanding options and other equity incentive awards subject to time-based vesting held by Mr. Hagan as of such termination or resignation.

If we terminate Mr. Hagan's employment without cause (other than due to his death or complete disability) or if Mr. Hagan resigns for good reason, in each case during the period beginning one month before and ending 12 months following a change in control, in addition to the severance payment described above, we will also be obligated to pay Mr. Hagan, subject to receiving an effective release and waiver of claims from him, a lump sum payment equal to the target amount of Mr. Hagan's annual performance bonus for the year of termination or resignation.

Employment Agreement with Mr. Aker. In July 2018, we entered into an amended and restated employment agreement with Mr. Aker. Pursuant to his amended and restated employment agreement, Mr. Aker is entitled to receive an annual base

salary of $246,376 and is eligible to receive an annual performance bonus, with a target bonus amount of 50% of his annual base salary. Mr. Aker's base salary and target bonus are subject to periodic review and adjustment from time to time in the discretion of our Board of Directors or the Compensation Committee and his base salary has been subsequently increased. Pursuant to Mr. Aker's amended and restated employment agreement, all outstanding stock options subject to vesting based on Company performance that are held by Mr. Aker immediately before a change in control shall become fully vested and exercisable as of immediately before, and contingent upon, the change in control, provided that Mr. Aker remains employed by us as of such date. In 2020, Mr. Aker's base salary was increased to $315,000 and his target bonus remained at 50% of his annual base salary.

If we terminate Mr. Aker's employment without cause (other than due to his death or complete disability) or if Mr. Aker resigns for good reason at any time other than during the period beginning one month before and ending 12 months following a change in control, Mr. Aker will receive, subject to receiving an effective release and waiver of claims from him, (1) a lump sum severance payment equal to 12 months of his then-current base salary (disregarding any decrease that forms the basis for a resignation for good reason), (2) a lump sum cash amount equal to 229.56% multiplied by the total cost of the projected premiums for group medical, dental and vision insurance for a period of 12 months and (3) vesting acceleration of all outstanding options and other equity incentive awards subject to time-based vesting held by Mr. Aker as of such termination or resignation.

If we terminate Mr. Aker's employment without cause (other than due to his death or complete disability) or if Mr. Aker resigns for good reason, in each case during the period beginning one month before and ending 12 months following a change in control, in addition to the severance payment described above, we will also be obligated to pay Mr. Aker, subject to receiving an effective release and waiver of claims from him, a lump sum payment equal to the target amount of Mr. Aker's annual performance bonus for the year of termination or resignation.

Employment Agreement with Ms. Calsada. In August 2019, we entered into an employment agreement with Ms. Calsada with an effective date of August 30, 2019 upon her commencement of employment as our Chief Financial Officer. Pursuant to her employment agreement, Ms. Calsada is entitled to receive an annual base salary of $310,000 and is eligible to receive an annual performance bonus, with a target bonus amount of 50% of her annual base salary. Ms. Calsada's base salary and target bonus are subject to periodic review and adjustment from time to time in the discretion of our Board of Directors or the Compensation Committee and her base salary has been subsequently increased. At the time she commenced her employment with us, Ms. Calsada also received an initial stock option grant of 100,000 shares. Pursuant to Ms. Calsada's employment agreement, all outstanding stock options subject to vesting based on Company performance that are held by Ms. Calsada immediately before a change in control shall become fully vested and exercisable as of immediately before, and contingent upon, the change in control, provided that Ms. Calsada remains employed by us as of such date. In 2020, Ms. Calsada's base salary was increased to $315,000 and her target bonus remained at 50% of her annual base salary.

If we terminate Ms. Calsada's employment without cause (other than due to her death or complete disability) or if Ms. Calsada resigns for good reason at any time other than during the period beginning one month before and ending 12 months following a change in control, Ms. Calsada will receive, subject to receiving an effective release and waiver of claims from her, (1) a lump sum severance payment equal to 12 months of her then-current base salary (disregarding any decrease that forms the basis for a resignation for good reason), (2) a lump sum cash amount equal to 229.56% multiplied by the total cost of the projected premiums for group medical, dental and vision insurance for a period of 12 months and (3) vesting acceleration of all outstanding options and other equity incentive awards subject to time-based vesting held by Ms. Calsada as of such termination or resignation.

If we terminate Ms. Calsada's employment without cause (other than due to her death or complete disability) or if Ms. Calsada resigns for good reason, in each case during the period beginning one month before and ending 12 months following a change in control, in addition to the severance payment described above, we will also be obligated to pay Ms. Calsada, subject to receiving an effective release and waiver of claims from her, a lump sum payment equal to the target amount of Ms. Calsada's annual performance bonus for the year of termination or resignation.

Change in Control and Severance Benefits

Under the terms of the employment agreements with each of our Named Executive Officers described above, either we or the executive may terminate the executive's employment at any time. Each of our Named Executive Officers is eligible, under the terms of his or her respective employment agreement, to receive, in exchange for a release of claims, severance benefits upon the termination of employment either by us without cause or by the executive for good reason, with additional severance benefits provided in the event the termination is in connection with a change in control. In addition, the terms of the equity awards granted to our Named Executive Officers are subject to the terms of our equity plans and award agreements thereunder, which includes accelerated vesting provisions upon certain material change in control transactions. We do not provide any excise tax gross-ups on change-in-control benefits.

Outstanding Equity Awards at Fiscal Year-End

The following table shows certain information regarding outstanding equity awards as of December 31, 2020 for the Named Executive Officers:

		Option Awards[1]					Stock Awards[1]	
Name	Grant Date	Number of Securities Underlying Unexercised Stock Options (#) Exerciseable	Number of Securities Underlying Unexercised Stock Options (#) Unexerciseable	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested ($) (2)
Joseph P. Hagan	11/12/2018 (3)						164,837	31,790
	2/5/2019 (4)	31,145	33,855		0.95	2/4/2029		
	2/5/2019 (5)	8,958	1,042		0.95	2/4/2029		
	10/10/2019 (4)	170,083	416,948		0.64	10/09/2029		
	1/22/2020 (4)	206,250	675,000		1.31	1/21/2030		
	1/22/2020 (7)			300,000	1.31	1/21/2030		
	1/22/2020 (7)			300,000	1.31	1/21/2030		
Christopher R. Aker	11/12/2018 (3)						33,698	6,499
	2/5/2019 (4)	11,979	13,021		0.95	2/4/2029		
	2/5/2019 (5)	6,718	782		0.95	2/4/2029		
	10/10/2019 (4)	97,708	237,292		0.64	10/09/2029		
	1/22/2020 (4)	48,125	161,875		1.31	1/21/2030		
	1/22/2020 (7)			70,000	1.31	1/21/2030		
	1/22/2020 (7)			70,000	1.31	1/21/2030		
Cris Calsada	8/30/2019 (6)	33,333	66,667		0.62	8/29/2029		
	10/10/2019 (6	61,250	148,750		0.64	10/09/2029		
	1/22/2020 (4)	34,375	115,625		1.31	1/21/2030		
	1/22/2020 (7)			50,000	1.31	1/21/2030		
	1/22/2020 (7)			50,000	1.31	1/21/2030		

(1) Stock awards granted prior to October 2019 were granted under the 2012 Equity Incentive Plan. Stock awards granted thereafter were granted under the 2019 Equity Incentive Plan. The terms of the 2012 Equity Incentive Plan and 2019 Equity Incentive Plan are described below under “Equity Compensation Plans and Other Benefit Plans.”

(2) Represents the number of unvested RSUs multiplied by the closing stock price as of December 31, 2020.

(3) Consists of performance-vesting RSUs granted to each Named Executive Officer in the tender offer completed in November 2018, in which eligible options were exchanged for RSUs on a value-for-value basis. The new RSUs that our employees received in the exchange offer can be earned only if performance goals key to our future success are achieved (in addition to continued service). On May 14, 2019, the Board of Directors concluded the Company had met the criteria to commence vesting of the RSUs consisting of a Board-approved transaction which the Board, in its sole discretion, determines is reasonably expected to provide adequate cash runway for achievement of the Company’s strategic objectives. Because of the achievement of the performance

objective, 50% of the RSUs subject to the grant immediately vested with the remaining RSUs vesting in quarterly installments over the following 24 months, subject to the recipient's continued service to the Company through each such vesting date. The number of shares underlying outstanding stock options held by each Named Executive Officers as of immediately before the tender offer exchange in November 2018 were as follows: Mr. Hagan: 278,714 shares; Mr. Aker: 62,297.

(4) Consists of stock options vesting in equal monthly installments over a 48 month period, subject to the recipient's continued service to the Company through each such vesting date.

(5) Consists of performance-vesting stock option with an exercise price of $0.95 per share, which only vest upon achievement of a previously-specified performance objective. On May 14, 2019, the Board of Directors concluded the Company had met the criteria to commence vesting of the performance-vesting stock option consisting of a Board-approved transaction which the Board, in its sole discretion, determines is reasonably expected to provide adequate cash runway for achievement of the Company's strategic objectives. Because of the achievement of the performance objective, 50% of the shares subject to the grant immediately vested with the remaining shares vesting in equal monthly installments over the following 24 months, subject to the recipient's continued service to the Company through each such vesting date.

(6) Consists of a stock option that vests as follows: 25% of the shares subject to the grant vest on the first anniversary of the grant with the remainder vesting in equal monthly installments over a 36 month period, subject to the recipient's continued service to the Company through each such vesting date.

(7) Consists of performance-vesting stock option with an exercise price of $1.31 per share which only vest upon achievement of a previously-specified performance objective. Upon achievement of the performance objective, 50% of the shares subject to the grant immediately vested with the remaining shares vesting in equal monthly installments over the following 24 months, subject to the recipient's continued service to the Company through each such vesting date.

Equity Compensation Plans

From October 2012 until August 2019, all equity awards (other than inducement awards) were granted pursuant to our 2012 Equity Incentive Plan (the "2012 Plan"). Beginning in August 2019, all equity awards (other than inducement awards) will be granted pursuant to our 2019 Equity Incentive Plan (the "2019 Plan"). In addition, we may grant inducement awards to new employees under our 2015 Inducement Plan ("2015 Inducement Plan"). The terms of these plans are described below.

2019 Equity Incentive Plan

The 2019 Plan, which became effective in August 2019, provides for the grant of incentive stock options, or ISOs, within the meaning of Section 422 of the Code, nonstatutory stock options, or NSOs, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance-based stock awards, and other forms of equity compensation, or collectively, stock awards. Additionally, the 2019 Plan provides for the grant of performance cash awards. ISOs may be granted only to employees, subject to certain limitations. All other awards may be granted to employees, including officers, and to non-employee directors and consultants.

Our Board of Directors, or a duly authorized committee thereof, has the authority to administer the 2019 Plan. Our Board of Directors has delegated its authority to administer the 2019 Plan to our Compensation Committee under the terms of our Compensation Committee's charter. Our Board of Directors may also delegate certain authority to one or more of our officers. Our Board of Directors or its authorized committee is referred to herein as the plan administrator.

Stock options are generally granted with an exercise price equal to the fair market value of our common stock on the date of grant, vest at the rate specified by the plan administrator (often over a four-year period) and may have a term up to a maximum of 10 years. The exercise price for an ISO or NSO generally cannot be less than 100% of the fair market value of our common stock on the date of grant. Unless the terms of an optionee's stock option agreement provides otherwise, if an optionee's service relationship with us, or any of our affiliates, ceases for any reason other than disability, death or cause, the optionee may generally exercise any vested options for a period of three months following the cessation of service. The option term may be extended in the event that exercise of the option following such a termination of service is prohibited by applicable securities laws or our insider trading policy. If an optionee's service relationship with us, or any of our affiliates, ceases due to disability or death, or an optionee dies within a certain period following cessation of service, the optionee or a beneficiary may generally exercise any vested options for a period of 12 months in the event of disability and 18 months in the event of death. In the event of a termination for cause, options generally terminate immediately upon the termination of the individual. In no event may an option be exercised beyond the expiration of its term.

Restricted stock units generally stop vesting upon the holder's termination of service with us and any unvested restricted stock units are forfeited, unless otherwise provided in an agreement with the holder.

Corporate transactions. In the event of certain specified significant corporate transactions (as defined in the 2019 Plan), the plan administrator has the discretion to take any of the following actions with respect to stock awards:

• arrange for the assumption, continuation or substitution of a stock award by a surviving or acquiring entity or parent company;

• arrange for the assignment of any reacquisition or repurchase rights held by us to the surviving or acquiring entity or parent company;

• accelerate the vesting of the stock award and provide for its termination prior to the effective time of the corporate transaction;

• arrange for the lapse of any reacquisition or repurchase right held by us;

• cancel or arrange for the cancellation of the stock award in exchange for such cash consideration, if any, as our Board of Directors may deem appropriate; or

• make a payment equal to the excess of (a) the value of the property the participant would have received upon exercise of the stock award over (b) the exercise price otherwise payable in connection with the stock award.

Change in control. The plan administrator may provide, in an individual award agreement or in any other written agreement between a participant and us, that the stock award will be subject to additional acceleration of vesting and exercisability in the event of a change in control (as defined in the 2019 Plan). For example, a stock award may provide for accelerated vesting upon the participant's termination without cause or resignation for good reason in connection with a change in control. In the absence of such a provision, no such acceleration of the stock award will occur.

Repricings. The plan administrator may not: (i) reduce the exercise price of any outstanding options, or (ii) cancel any outstanding options that have an exercise price greater than the current fair market value of the Company's common stock in exchange for cash or other stock awards under the 2019 Plan, unless the stockholders of the Company have approved such an action within twelve months prior to such an event.

Amendment and termination. The Board has the authority to amend, suspend, or terminate the 2019 Plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. No ISOs may be granted after the tenth anniversary of the date our Board of Directors adopted the 2019 Plan.

2012 Equity Incentive Plan

The 2012 Plan, which became effective in connection with our initial public offering in October 2012, and was in effect until the approval by our stockholders of our 2019 Plan in August 2019. The 2012 Plan provided for the grant of ISOs, NSOs, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance-based stock awards, and other forms of equity compensation, or collectively, stock awards. Additionally, the 2012 Plan provided for the grant of performance cash awards. ISOs were to be granted only to employees, subject to certain limitations. All other awards could be granted to employees, including officers, and to non-employee directors and consultants.

Our Board of Directors, or a duly authorized committee thereof, administered the 2012 Plan. Our Board of Directors had delegated its authority to administer the 2012 Plan to our Compensation Committee under the terms of our Compensation Committee's charter. Our Board of Directors also delegated certain authority to one or more of our officers. Our Board of Directors or its authorized committee is referred to herein as the plan administrator.

Stock options are generally granted with an exercise price equal to the fair market value of our common stock on the date of grant, vest at the rate specified by the plan administrator (often over a four-year period) and may have a term up to a maximum of 10 years. The exercise price for an ISO or NSO generally cannot be less than 100% of the fair market value of our common stock on the date of grant. Unless the terms of an optionee's stock option agreement provides otherwise, if an optionee's service relationship with us, or any of our affiliates, ceases for any reason other than disability, death or cause, the optionee may generally exercise any vested options for a period of three months following the cessation of service. The option term may be extended in the event that exercise of the option following such a termination of service is prohibited by applicable securities laws or our insider trading policy. If an optionee's service relationship with us, or any of our affiliates, ceases due to disability or death, or an optionee dies within a certain period following cessation of service, the optionee or a beneficiary may generally exercise any vested options for a period of 12 months in the event of disability and 18 months in the event of death. In the event of a termination for cause, options generally terminate immediately upon the termination of the individual. In no event may an option be exercised beyond the expiration of its term. Restricted stock units generally stop vesting upon the holder's termination of service with us and any unvested restricted stock units are forfeited, unless otherwise provided in an agreement with the holder.

Corporate transactions. In the event of certain specified significant corporate transactions (as defined in the 2012 Plan), the plan administrator has the discretion to take any of the following actions with respect to stock awards:

• arrange for the assumption, continuation or substitution of a stock award by a surviving or acquiring entity or parent company;

• arrange for the assignment of any reacquisition or repurchase rights held by us to the surviving or acquiring entity or parent company;

• accelerate the vesting of the stock award and provide for its termination prior to the effective time of the corporate transaction;

• arrange for the lapse of any reacquisition or repurchase right held by us;

• cancel or arrange for the cancellation of the stock award in exchange for such cash consideration, if any, as our Board of Directors may deem appropriate; or

• make a payment equal to the excess of (a) the value of the property the participant would have received upon exercise of the stock award over (b) the exercise price otherwise payable in connection with the stock award.

Change in control. The plan administrator may provide, in an individual award agreement or in any other written agreement between a participant and us, that the stock award will be subject to additional acceleration of vesting and exercisability in the event of a change in control (as defined in the 2012 Plan). For example, a stock award may provide for accelerated vesting upon the participant's termination without cause or resignation for good reason in connection with a change in control. In the absence of such a provision, no such acceleration of the stock award will occur.

2012 Employee Stock Purchase Plan

Additional long-term equity incentives are provided through the 2012 Employee Stock Purchase Plan (the "ESPP"), which became effective in connection with our initial public offering in October 2012. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the Code. Our Board of Directors has delegated its authority to administer the ESPP to our Compensation Committee. Under the ESPP, generally all of our regular employees (including our Named Executive Officers during their employment with us) may participate and may contribute, normally through payroll deductions, up to 15% of their earnings for the purchase of our common stock. The ESPP is implemented through a series of offerings of purchase rights to eligible employees. Under the ESPP, we may specify offerings with a duration of not more than six months, and may specify shorter purchase periods within each offering. Each offering will have one or more purchase dates on which our common stock will be purchased for employees participating in the offering. Unless otherwise determined by our Compensation Committee, shares are purchased for accounts of employees participating in the ESPP at a price per share equal to the lower of (a) 85% of the fair market value of our common stock on the first date of an offering or (b) 85% of the fair market value of our common stock on the date of purchase.

Equity Compensation Plan Information

The following table provides information as of December 31, 2020, with respect to shares of our common stock that may be issued under our existing equity compensation plans:

	(a)	(b)	(c)
Plan Category	**Number of securities to be issued upon exercise of outstanding options, awards, warrants and rights**	**Weighted-average exercise price of outstanding options, awards, warrants and rights**	**Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))**
Equity compensation plans approved by stockholders:			
2009 Equity Incentive Plan	912 [1]	$31.34	—
2012 Equity Incentive Plan	203,464 [2]	$5.59	—
2019 Equity Incentive Plan	6,608,684 [1]	$0.96	868,432
2012 Employee Stock Purchase Plan	—	—	187,689
Equity compensation plans not approved by stockholders:			
None			

(1) All shares issuable upon exercise of options.

(2) Consists of 203,464 shares issuable upon exercise of options and 34,301 restricted stock units.

DIRECTOR COMPENSATION

The following table shows certain information with respect to the compensation of all non-employee directors of the Company for the fiscal year ended December 31, 2020:

Name	Fees Earned or Paid in Cash($)[1]	Option Awards ($)[2]	Total ($)
David Baltimore, Ph.D.[4]	48,000	15,544 [3]	63,544
Kathryn J. Collier[4]	60,000	15,544 [3]	75,544
Jake Nunn[4]	50,000	15,544 [3]	65,544
Stelios Papadopoulos, Ph.D.[4]	84,000	15,544 [3]	99,544
William H. Rastetter, Ph.D.[4]	52,000	15,544 [3]	67,544
Hugh Rosen, M.D., Ph.D.[4]	46,000	15,544 [3]	61,544
Simos Simeonidis, Ph.D.[4]	0	15,544 [3]	15,544
Pascale Witz[4]	46,000	15,544 [3]	61,544

(1) Amounts listed represent cash payments made for Board and Committee service which were earned in 2020. Dr. Simeonidis is required by his employer, Sarissa Capital, to assign his cash payments to Sarissa Capital.

(2) Amounts listed represent the aggregate grant date fair value amount computed as of the grant date of each option awarded during 2020 in accordance with ASC 718. Assumptions used in the calculation of these amounts are included in Note 10 to the Financial Statements in our Annual Report on Form 10-K for the year ended December 31, 2020.

(3) Represents the annual option grant to purchase 23,350 shares of our common stock granted to each of our non-employee directors serving on June 16, 2020 under our non-employee director compensation policy, as further described below.

(4) As of December 31, 2020, each director held outstanding options to purchase 58,125 shares.

Directors who are also employees do not receive cash or equity compensation for service on our Board of Directors in addition to the compensation payable for their service as our employees. We have a non-employee director compensation policy, or our director compensation policy, that became effective following our initial public offering. Under our director compensation policy, our Compensation Committee determines individual non-employee members of our Board of Directors who will be eligible to receive compensation and who we refer to as our Eligible Directors. All of our non-employee directors were Eligible Directors for 2020 compensation under our director compensation policy. Pursuant to our director compensation policy in effect in 2020, we provide cash compensation in the form of an annual retainer of $40,000 to each of our Eligible Directors and $70,000 to our Chairman of the Board. We also pay an additional annual retainer of $20,000 to the chairman of our Audit Committee, $10,000 to other independent Eligible Directors who serve on our Audit Committee, $12,000 to the chairman of our Compensation Committee, $6,000 to other independent Eligible Directors who serve on our Compensation Committee, $8,000 to the chairman of our Nominating and Corporate Governance Committee and $4,000 to other independent Eligible Directors who serve on our Nominating and Corporate Governance Committee. We have reimbursed and will continue to reimburse our non-employee directors for travel, lodging and other reasonable expenses incurred in attending meetings of our Board of Directors and committees of our Board of Directors.

Pursuant to our director compensation policy, each Eligible Director who is first elected to our Board of Directors is granted an option to purchase shares of the Company's common stock on the date of his or her initial election to our Board of Directors. The number of options is usually determined in December of the prior year. In addition, the Board of Directors also determines the number of stock options to be awarded to each director re-elected at our next annual stockholder meeting.

In December 2019, the Board of Directors, upon the recommendation of the Compensation Committee, approved (i) an initial option grant of shares to any new Eligible Directors appointed to the Board in 2020 and (ii) an annual option grant to each Eligible Director re-elected at our annual meeting of stockholders in 2020 of 23,250 shares.

Each initial option granted to such Eligible Directors described above will vest and become exercisable with respect to one-third of the shares subject to the option on the first anniversary of the date of grant and the balance of the shares will vest and become exercisable in a series of 24 equal monthly installments thereafter, such that the option is fully vested on the third

anniversary of the date of grant, subject to the Eligible Director continuing to provide services to us through such dates. Each annual option granted to such Eligible Directors described above will vest and become exercisable in 12 equal monthly installments such that the option will be fully vested on the first anniversary of the date of grant, or as of the date of the next annual meeting of the Company's stockholders, whichever occurs first and subject to the Eligible Director continuing to provide services to us through such dates. The term of each option granted to an Eligible Director is 10 years. All awards granted under our director compensation policy will vest in full upon the closing of a change in control of the Company.

In January 2021, Alice Huang, Ph.D., was appointed to our Board of Directors, and the Compensation Committee determined that Dr. Huang is an Eligible Director under our director compensation policy. Accordingly, in January 2021, following determination of the appropriate number of options by our Board of Directors in December 2020, Dr. Huang was granted an initial option grant to purchase 80,000 shares of our common stock at an exercise price of $1.55 per share. These options will vest and become exercisable as provided under our director compensation policy.

The options granted to our non-employee directors are granted under our 2019 Plan, the terms of which are described in more detail above under "Equity Compensation Plans and Other Benefit Plans-2019 Equity Incentive Plan."

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

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth certain information regarding the ownership of the Company's common stock as of February 28, 2021 by: (i) each of our directors; (ii) each of our Named Executive Officers as defined above under the heading "Executive Compensation"; (iii) each person known by us to beneficially own more than 5% of our common stock and (iv) all of our current executive officers and directors as a group.

Beneficial ownership is determined in accordance with the rules of the SEC and includes voting and investment power with respect to the securities. This table is based upon information supplied by officers, directors and principal stockholders and Schedules 13D and 13G filed with the SEC. Except as indicated by footnote, and subject to applicable community property laws, we believe the persons named in the table have sole voting and investment power with respect to all shares of common stock shown as beneficially owned by them.

Percentage of beneficial ownership is based on 72,504,772 shares of common stock outstanding as of February 28, 2021. The number of shares of common stock used to calculate the percentage ownership of each listed person includes the shares of common stock underlying options held by such persons that are exercisable, or restricted stock units which will vest, within 60 days following February 28, 2021. Unless otherwise indicated, the address for the persons and entities listed in the table below is c/o Regulus Therapeutics Inc., 10628 Science Center Drive, Suite 225, San Diego, CA 92121.

Beneficial Owner	Beneficial Ownership	
	Number of Shares	Percent of Total
Greater than 5% Stockholders		
Entities affiliated with RS Investments[1]	14,548,183	18.52%
One Bush Street, Suite 400 San Francisco, CA 94104		
Entities affiliated with Sarissa Capital Management LP[2]	12,166,942	14.69%
c/o Sarissa Capital Management LP 660 Steamboat Road Greenwich, CT 06830		
Entities affiliated with New Enterprise Associates, Inc.[3]	6,709,193	9.99%
1954 Greenspring Dr., Suite 600 Timonium Maryland 21093		
Entities affiliated with BVF Partners, L.P.[4]	6,760,484	9.99%
1 Sansome Street, 30th Floor San Francisco, California 94104		
Point72 Associates LLC[5]	5,627,013	7.51%
72 Cummings Point Road Stamford, Connecticut 06902		
Altium Growth Fund, LP[6]	4,557,581	5.91%
551 Fifth Avenue, FL 19 New York, New York 10176		
Entities affiliated with Asymmetry Capital[7]	4,220,258	5.68%
One Sansome Street, Suite 1810 San Francisco, CA 94104		
Named Executive Officers and Directors		
Christopher Aker[8]	265,112	*
David Baltimore, Ph.D.[9]	91,479	*
Cris Calsada[10]	174,583	*
Kathryn J. Collier[11]	93,294	*
Joseph P. Hagan[12]	1,188,211	1.64%
Jake R. Nunn[13]	65,875	*
Stelios Papadopoulos, Ph.D.[14]	4,717,418	6.51%
William H. Rastetter, Ph.D.[15]	775,285	1.07%
Hugh Rosen, M.D., Ph.D.[16]	83,592	*
Simos Simeonidis, Ph.D.[17]	65,875	*
Pascale Witz, MBA, MSc[18]	278,246	*
All current executive officers and directors as a group (12 persons)[19]	7,806,470	10.77%

* Less than one percent.

(1) Consists of an aggregate of 8,519,242 shares of common stock and 6,028,941 shares of common stock issuable upon the exercise of warrants to purchase common stock held collectively by USAA Science & Technology Fund and Victory RS Science and Technology Fund, a Series of Victory Portfolios (the "RS Funds"). RS Investments as the Investment Advisor to the RS Funds may be deemed to have the shared power to vote or direct the vote of (and the shared power to dispose or direct the disposition of) the shares of our common stock held by the RS Funds. Shares of common stock beneficially owned by the Victory Funds are owned individually and not jointly. By delegation from each Victory Fund and each Victory Fund's respective Board of Trustees, Victory Capital has the power to dispose of the securities acting through Chris Clark, a member of its investment franchise, RS Investments Growth, and to vote the securities in accordance with its proxy voting policy through its proxy committee, which is composed of seven individuals.

(2) Consists of an aggregate of 1,851,851 shares of common stock, 6,083,471 shares of common stock issuable upon the exercise of warrants to purchase common stock and 4,231,620 shares of common stock issuable upon the conversion of

Class A-2 convertible preferred stock held collectively by Sarissa Capital Offshore Master Fund LP, or Sarissa Offshore, Sarissa Capital Catapult Fund LLC, or Sarissa Catapult, and Sarissa Capital Hawkeye Fund LP, or Sarissa Hawkeye, or, collectively, the Sarissa Funds. Sarissa Capital Management LP, or Sarissa Capital, as the Investment Advisor to the Sarissa Funds may be deemed to have the shared power to vote or direct the vote of (and the shared power to dispose or direct the disposition of) the shares of our common stock held by the Sarissa Funds. By virtue of his positions as the Chief Investment Officer of Sarissa Capital and as the managing member of Sarissa Capital's general partner and as controlling the ultimate general partner of each of the Sarissa Funds, Alexander J. Denner, Ph.D. may be deemed to have the shared power to vote or direct the vote of (and the shared power to dispose or direct the disposition of) the shares of our common stock by the Sarissa Funds. Each Sarissa Reporting Person disclaims beneficial ownership of all applicable shares except to the extent of their actual pecuniary interest therein.

(3) Consists of 6,451,057 shares of common stock and 258,136 shares of common stock issuable upon the exercise of warrants to purchase common stock, collectively, the GEO Shares, held by Growth Equity Opportunities Fund V, LLC, or GEO. New Enterprise Associates 16, L.P., or NEA 16, is the sole member of GEO, NEA Partners 16, L.P., or NEA Partners 16, is the sole general partner of NEA 16 and NEA 16 GP, LLC, or NEA 16 LLC, is the sole general partner of NEA Partners 16. Peter J. Barris, Forest Baskett, Ali Behbahani, Carmen Chang, Anthony A. Florence, Jr., Mohamad H. Makhzoumi, Joshua Makower, David M. Mott, Scott D. Sandell, Peter W. Sonsini and Paul Walker, or, collectively, the Managers, are the managers of NEA 16 LLC. The persons named herein are referred to individually herein as a NEA Reporting Person and collectively as the NEA Reporting Persons. GEO is the record owner of the GEO Shares. As the sole member of GEO, NEA 16 may be deemed to own beneficially the GEO Shares. As the general partner of NEA 16, NEA Partners 16 may be deemed to own beneficially the GEO Shares. As the sole general partner of NEA Partners 16, NEA 16 LLC may be deemed to own beneficially the GEO Shares. Each of the Managers of NEA 16 LLC may be deemed to own beneficially the GEO Shares. The number of shares beneficially owned by the NEA Reporting Persons in the aggregate is limited by beneficial ownership limitations applicable to the warrants and shares of Class A-1, Class A-2 and Class A-3 convertible preferred stock held by GEO, which limit the number of shares the NEA Reporting Persons can beneficially own to a maximum of 9.99% of our outstanding common stock. As a result of such limitations, the number of shares beneficially owned does not include up to an aggregate of 17,693,822 shares of common stock issuable upon the exercise of warrants and 2,567,000 shares of common stock issuable upon the conversion of our Class A-1 convertible preferred stock, 9,009,000 shares of common stock issuable upon the conversion of Class A-2 convertible preferred stock and 2,587,070 shares of common stock issuable upon the conversion of Class A-3 convertible preferred stock held by GEO. Each NEA Reporting Person disclaims beneficial ownership of all applicable shares except to the extent of their actual pecuniary interest therein.

(4) Consists of an aggregate of 5,988,932 shares of common stock and 771,552 shares of common stock issuable upon the exercise of warrants to purchase common stock held collectively by (i) Biotechnology Value Fund, LP, or BVF, (ii) Biotechnology Value Fund II, LP, or BVF II, (iii) Biotechnology Value Trading Fund OS, L.P., or BVFOS, and (v) MSI BVF SPV, L.L.C., or MSI, and, collectively, the BVF Investment Entities. BVF Partners L.P., or BVF Partners, is the general partner of BVF, BVF II and BVFOS and the investment advisor of MSI and may be deemed to beneficially own the shares held by the BVF Investment Entities. BVF, Inc., as the general partner of BVF Partners, may be deemed to beneficially own the shares beneficially owned by BVF Partners. Mark Lampert, as a director and officer of BVF Inc., may be deemed to beneficially own the shares beneficially owned by BVF, Inc. The number of shares beneficially owned by BVF Partners in the aggregate is limited by beneficial ownership limitations applicable to the exercise of warrants held by the BVF Investment Entities, which limit the number of shares BVF Partners can beneficially own after the exercise of warrants and conversion of shares of convertible preferred stock to a maximum of 9.99% of our outstanding common stock. As a result of such limitations, the number of shares beneficially owned does not include up to an aggregate of 10,659,455 shares of common stock issuable upon the exercise of warrants held by the BVF Investment Entities.

(5) Consists of an aggregate of 3,215,436 shares of common stock and 2,411,577 shares of common stock issuable upon the exercise of warrants to purchase common stock held by Point72 Associates, LLC, or Point72 Associates. Point72 Asset Management, L.P. maintains investment and voting power with respect to the securities held by certain investment funds it manages, including Point72 Associates. Point72 Capital Advisors, Inc. is the general partner of Point72 Asset Management, L.P. Mr. Steven A. Cohen controls each of Point72 Associates and Point72 Asset Management, L.P. and Point72 Capital Advisors, Inc and may be deemed to beneficially own the shares held of record by Point72 Associates. By reason of the provisions of Rule 13d-3 of the Exchange Act, each of Point72 Asset Management, L.P., Point72 Capital Advisors, Inc., and Mr. Cohen may be deemed to beneficially own the securities held of record by Point72 Associates reflected herein. Each of Point72 Asset Management, L.P., Point72 Capital Advisors, Inc., and Mr. Cohen disclaims beneficial ownership of any such securities.

(6) Consists of 4,557,581 shares of common stock issuable upon the exercise of warrants to purchase common stock held by Altium Growth Fund, LP, or Altium Growth. Altium Capital Management, LP is the investment adviser of, and may be deemed to beneficially own securities owned by, Altium Growth. Altium Growth GP, LLC is the general partner of, and may be deemed to beneficially own securities owned by, Altium Growth. Each of Altium Capital Management, LP and Altium Growth GP, LLC, or, together, Altium, shares voting and disposal power over the shares.

(7) Consists of an aggregate of 2,411,576 shares of common stock and 1,808,682 shares of common stock issuable upon the exercise of warrants to purchase common stock held collectively by Atom Master Fund LP, Asymmetry Global Healthcare Fund, L.P. Portland House Partners, Preclude Opportunity Fun and Asymmetry Global Healthcare (Master) Fund, Ltd., the Asymmetry Funds. Asymmetry Capital Management, LP, or Asymmetry Management, as the Sub-Advisor to Atom, Portland and Prelude, may be deemed to have the shared power to dispose or direct the disposition of the shares of our common stock held by Atom, Portland and Prelude and the shared power to vote or direct the vote of the shares held by Prelude. Craig Fischer, as General Counsel and Chief Compliance Officer of Atom, has power to vote or direct the vote of (and the shared power to dispose or direct the disposition of) the shares of our common stock held by Atom. Tim Collins, as President of Portland, has power to vote or direct the vote of (and the shared power to dispose or direct the disposition of) the shares of our common stock held by Portland. Chris Zellner, as COO of Asymmetry Management, Asymmetry Global and Asymmetry Master, has shared power to dispose or direct the disposition of the shares held by the Asymmetry Funds and shared power to vote or direct the vote of the shares held by Asymmetry Global, Prelude and Asymmetry Master.

(8) Consists of 41,207 shares of common stock held by Mr. Aker and 221,498 shares that Mr. Aker has the right to acquire from us within 60 days of February 28, 2021 pursuant to the exercise of stock options and 2,407 shares that Mr. Aker will acquire upon the vesting of RSUs.

(9) Consists of 25,604 shares of common stock held by Dr. Baltimore and 65,875 shares that Dr. Baltimore has the right to acquire from us within 60 days of February 28, 2021 pursuant to the exercise of stock options.

(10) Consists of 174,583 shares that Ms. Calsada has the right to acquire from us within 60 days of February 28, 2021 pursuant to the exercise of stock options.

(11) Consists of 27,419 shares of common stock held by Ms. Collier and 65,875 shares that Ms. Collier has the right to acquire from us within 60 days of February 28, 2021 pursuant to the exercise of stock options.

(12) Consists of (i) 233,454 shares of common stock held by Joseph P. Hagan and 728,329 shares that Mr. Hagan has the right to acquire from us within 60 days of February 28, 2021 pursuant to the exercise of stock options and 11,174 shares that Mr. Hagan will acquire upon the vesting of RSUs, and (ii) 138,804 shares of common stock issuable upon the exercise of warrants and 75,850 shares of common stock upon the conversion of Class A-2 preferred stock to purchase common stock held by PENSCO Trust Company LLC Custodian FBO Joseph Hagan IRA, or PENSCO. Mr. Hagan is the economic beneficiary and may be deemed to be the beneficial owner of the shares held by PENSCO.

(13) Consists of 65,875 shares of common stock that Mr. Nunn has the right to acquire from us within 60 days of February 28, 2021 pursuant to the exercise of stock options.

(14) Consists of 2,839,707 shares of common stock and 1,811,836 shares of common stock issuable upon the exercise of warrants to purchase common stock and 65,875 shares that Dr. Papadopoulos has the right to acquire from us within 60 days of February 28, 2021 pursuant to the exercise of stock options.

(15) Consists of 390,581 shares of common stock and 318,829 shares of common stock issuable upon the exercise of warrants to purchase common stock, and 65,875 shares that Dr. Rastetter has the right to acquire from us within 60 days of February 28, 2021 pursuant to the exercise of stock options held by The Rastetter Family Trust, or the Rastetter Trust. Dr. Rastetter is trustee of the Rastetter Trust and may be deemed to be the beneficial owner of the shares held by the Rastetter trust.

(16) Consists of 17,717 shares of common stock held by Dr. Rosen and 65,875 shares that Dr. Rosen has the right to acquire from us within 60 days of February 28, 2021 pursuant to the exercise of stock options.

(17) Consists of 65,875 shares of common stock that Dr. Simeonidis has the right to acquire from us within 60 days of February 28, 2021 pursuant to the exercise of stock options.

(18) Consists of 47,341 shares of common stock, 97,330 shares of common stock issuable upon the exercise of warrants to purchase common stock, 67,700 shares of common stock upon the conversion of Class A-2 preferred stock held by Pascale Witz and 65,875 shares of common stock that Ms. Witz has the right to acquire from us within 60 days of February 28, 2021 pursuant to the exercise of stock options.

(19) Includes all shares described in notes (8) through (18) above. Also, represents 7,500 shares of common stock that one other executive officer has the right to acquire from us within 60 days of February 28, 2021 pursuant to the exercise of stock options.

Item 13. Certain Relationships and Related Transactions and Director Independence

TRANSACTIONS WITH RELATED PERSONS

We have adopted a written related-person transactions policy that sets forth our policies and procedures regarding the identification, review, consideration, approval and oversight of "related-person transactions." A "related-person transaction" is a past, present or future transaction, arrangement or relationship (or any series of similar transactions, arrangements or relationships) in which we and any "related person" are participants involving an amount that exceeds the lesser of $120,000 or 1% of the average of our total assets at year-end of the last two completed fiscal years.

Transactions involving compensation for services provided to us by an employee, consultant or director are not considered related-person transactions under this policy. A "related person," as determined since the beginning of our last fiscal year, is any executive officer, director or a holder of more than five percent of our common stock, including any of their immediate family members and any entity owned or controlled by such persons.

The policy imposes an affirmative duty upon each director and executive officer to identify any transaction involving them, their affiliates or immediate family members that may be considered a related party transaction before such person engages in the transaction. Under the policy, where a transaction has been identified as a related-person transaction, management must present information regarding the proposed related-person transaction to our audit committee (or, where review by our audit committee would be inappropriate, to another independent body of our board of directors) for review. The presentation must include a description of, among other things, the material facts, the direct and indirect interests of the related persons, the benefits of the transaction to us and whether any alternative transactions are available. In considering related-person transactions, our audit committee or other independent body of our board of directors takes into account the relevant available facts and circumstances including, but not limited to:

- the risks, costs and benefits to us of the transaction;
- the impact on a director's independence in the event the related person is a director, immediate family member of a director or an entity with which a director is affiliated;
- the terms of the transaction;
- the availability of other sources for comparable services or products; and
- the terms available to or from, as the case may be, unrelated third parties or to or from our employees generally.

In the event a director has an interest in the proposed transaction, the director must recuse himself or herself from the deliberations and approval. Our policy requires that, in reviewing a related party transaction, our audit committee must consider, in light of known circumstances, and determine in the good faith exercise of its discretion whether the transaction is in, or is not inconsistent with, the best interests of us and our stockholders.

We describe below transactions and series of similar transactions, since January 1, 2019 with respect to which we were a party, will be a party, or otherwise benefited, in which:

- the amounts involved exceeded or will exceed the lesser of $120,000 or 1% of the average of our total assets at year end of the last two completed fiscal years; and
- a director, executive officer, holder of more than 5% of our common stock or any member of their immediate family had or will have a direct or indirect material interest.

We also describe below certain other transactions with our directors, executive officers and stockholders. We believe that the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that would be paid or received, as applicable, in arm's-length transactions.

Private Placement Financing Transaction

On May 3, 2019, we entered into a Securities Purchase Agreement (the "Purchase Agreement") with certain institutional and other accredited investors (the "Purchasers"), pursuant to which we agreed to sell and issue shares of common stock, shares of our newly designated non-voting convertible preferred stock, and warrants to purchase common stock, in up to two closings (collectively, the "Private Placement").

In May 2019, we completed the initial closing of the Private Placement (the "Initial Closing") 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 study of RGLS4326 in the first quarter of 2020, we completed a second and final closing under the Purchase Agreement (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.

The participants in the Private Placement included the following executive officers, directors and holders of more than five percent of our common stock or entities affiliated with them. The following table sets forth the aggregate number of shares of common stock, Class A-1 convertible preferred stock and warrants to purchase common stock issued to these related parties in the Initial Closing and Class A-2 convertible preferred stock and warrants issued to these related parties in the Milestone Closing of the Private Placement. The aggregate shares and warrants set forth below reflect the number issued at the time of the Initial Closing and the Milestone Closing and do not reflect any subsequent conversions:

Name of Related Person	Common Stock Issued in the Initial Closing	Warrants Issued in the Initial Closing	Class A-1 Convertible Preferred Stock Issued in the Initial Closing	Class A-2 Convertible Preferred Stock Issued in the Milestone Closing	Warrants Issued in the Milestone Closing	Aggregate Purchase Price of Common Stock, Warrants and Preferred Stock Purchased in the Private Placement
Entities affiliated with New Enterprise Associates, Inc.	1,136,704	3,703,704	256,700	900,900	9,009,000	$ 11,589,087.72
Entities affiliated with BVF Partners, L.P.	1,000,592	2,592,572	159,198	630,628	6,306,280	$ 8,112,356.33
Entities affiliated with Sarissa Capital Management LP [1]	1,851,851	1,851,851	—	423,162	4,231,620	$ 5,578,701.75
Altium Growth Fund, LP	1,327,801	1,327,801	—	322,978	3,229,780	$ 4,154,759.79
Entities affiliated with EcoR1 Capital, LLC	1,111,110	1,111,110	—	253,897	2,538,970	$ 3,347,220.08
Samsara BioCapital, L.P.	1,111,111	1,111,111	—	253,897	2,538,970	$ 3,347,221.29
Stelios Papadopoulos, Ph.D. *Chairman of the Board*	370,370	370,370	—	84,632	846,320	$ 1,115,739.63
Joseph P. Hagan[2] *President, Chief Executive Officer and Directo*	33,194	33,194	—	7,585	75,850	$ 99,996.93
William H. Rastetter[2] *Director*	92,889	92,889	—	22,594	225,940	$ 290,653.39
Pascale Witz *Director*	29,630	29,630	—	6,770	67,700	$ 89,259.17

(1) Dr. Simeonidis, a director of the Company, is a partner at Sarissa Capital Management.

(2) Securities purchased or to be purchased through an affiliated investment entity.

On December 1, 2020, we entered into a Securities Purchase Agreement (the "Purchase Agreement") with certain institutional and other accredited investors (the "Purchasers"), pursuant to which we agreed to sell and issue shares of common stock, shares of our newly designated non-voting convertible preferred stock, and warrants to purchase common stock, in up to two closings (collectively, the "Private Placement").

In December 2020, we completed the initial closing of the Private Placement (the "2020 Closing") pursuant to which we sold and issued (i) 24,341,607 shares of common stock and accompanying warrants to purchase up to an aggregate of 18,256,204 shares of common stock at a combined purchase price of $0.7464 per share (the combined purchase price for officers and directors of the Company was $0.7551), and (ii) 272,970 shares of non-voting Class A-3 convertible preferred stock, in lieu of shares of common stock, at a price of $6.22 per share, and accompanying warrants to purchase an aggregate of 2,047,276 shares of common stock at a price of $0.125 for each share of common stock underlying such warrants. Each share of non-voting Class A-3 convertible preferred stock is convertible into 10 shares of common stock, subject to certain beneficial ownership conversion limitations. The warrants are exercisable for a period of five years following the date of issuance and have an exercise price of $0.7464 per share, subject to proportional adjustments in the event of stock splits or combinations or similar events.

The participants in the Private Placement included the following executive officers, directors and holders of more than five percent of our common stock or entities affiliated with them. The following table sets forth the aggregate number of shares of common stock, Class A-3 convertible preferred stock and warrants to purchase common stock issued to these related parties

in the 2020 Closing. The aggregate shares and warrants set forth below reflect the number issued at the time of the 2020 Closing and do not reflect any subsequent conversions:

Name of Related Person	Common Stock Issued in the 2020 Closing	Warrants Issued in the 2020 Closing	Class A-3 Convertible Preferred Stock Issued in the Initial Closing	Aggregate Purchase Price of Common Stock, Warrants and Preferred Stock Purchased in the Private Placement
Entities affiliated with New Enterprise Associates, Inc.	4,398,602	5,239,254	258,707	$ 4,999,994.73
Entities affiliated with BVF Partners, L.P.	3,233,577	2,532,155	14,263	$ 2,416,520.13
Stelios Papadopoulos, Ph.D. *Chairman of the Board*	793,528	595,146	—	$ 574,395.24
Joseph P. Hagan[(1)] *President, Chief Executive Officer and Director*	39,680	29,760	—	$ 28,722.37

(1) Securities purchased or to be purchased through an affiliated investment entity.

Alliance and Collaboration Agreements

Sanofi

In February 2014, we amended and restated our 2012 amended and restated license and collaboration agreement with Sanofi, a greater than 5% stockholder of the Company, extending our strategic alliance with Sanofi. Aventisub LLC (formerly Aventis Holdings Inc.) concurrently made a $10.0 million investment in our common stock at a purchase price of $7.67 per share, representing the average of the daily volume weighted average price per share of our common stock during the 30 trading days ending on the date immediately preceding the date of the investment. 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 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. In November 2018, we received $2.5 million of the approximately $6.8 million in Upfront Amendment Payments under the 2018 Sanofi Amendment. In March 2019, we received $1.8 million in payment of materials purchased by Sanofi from us related to the RG-012 program. We have received approximately $16.8 million in upfront payments, payment for program-related materials and interim enrollment milestones. We are also eligible to receive a $30.0 million development milestone payment.

In September 2014, we entered into an agreement with Sanofi-Aventis Deutschland GmbH ("Sanofi Deutschland"), a contract manufacturing subsidiary of Sanofi, for the manufacture of certain drug substance requirements and other services to support our preclinical and clinical activities associated with the RG-012 program. Pursuant to this agreement, we may engage Sanofi Deutschland from time-to-time to manufacture RG-012 drug product on our behalf. To date, we have engaged Sanofi Deutschland to manufacture multiple cGMP batches of RG-012 and to perform stability testing and related activities at a cost of $1,831,992. These activities were ongoing during 2018 and in 2019 we paid Sanofi $45,000 for activities completed in 2018. Pursuant to the assignment of the RG-012 program to Sanofi, we do not expect to incur any further material charges related to Sanofi Deutschland's activities.

Indemnification Agreements

We have entered into separate indemnification agreements with our directors and executive officers, in addition to the indemnification provided for in our bylaws. These agreements, among other things, require us to indemnify our directors and

executive officers for certain expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or executive officer in any action or proceeding arising out of his or her services as one of our directors or executive officers or any other company or enterprise to which the person provides services at our request. We believe that these indemnification agreements, together with the provisions in our bylaws, are necessary to attract and retain qualified persons as directors and officers.

INDEPENDENCE OF THE BOARD OF DIRECTORS

As required under the Nasdaq Stock Market ("Nasdaq") listing standards, a majority of the members of a listed company's Board of Directors must qualify as "independent," as affirmatively determined by the Board of Directors. The Board consults with the Company's counsel to ensure that the Board's determinations are consistent with relevant securities and other laws and regulations regarding the definition of "independent," including those set forth in pertinent listing standards of Nasdaq, as in effect from time to time.

Consistent with these considerations, after review of all relevant identified transactions or relationships between each director, or any of his family members, and the Company, its senior management and its independent auditors, the Board has affirmatively determined that the following nine directors are independent directors within the meaning of the applicable Nasdaq listing standards: Dr. Baltimore, Ms. Collier, Dr. Huang, Mr. Nunn, Dr. Papadopoulos, Dr. Rastetter, Dr. Rosen, Dr. Simeonidis and Ms. Witz. In making this determination, the Board found that none of these directors or nominees for director had a material or other disqualifying relationship with the Company.

Item 14. Principal Accounting Fees and Services

AUDIT AND ALL OTHER FEES

The following table represents aggregate fees incurred by the Company for the fiscal years ended December 31, 2020 and December 31, 2019, by Ernst & Young LLP ("Ernst & Young"), the Company's principal accountant. All fees described below were pre-approved by the Audit Committee.

	Fiscal Year Ended	
	2020	2019
	(in thousands)	
Audit Fees[1]	$ 305	$ 359
Audit-related Fees	—	—
Tax Fees	—	—
All Other Fees	104	—
Total Fees	$ 409	$ 359

(1) Audit fees consist of fees incurred for professional services by Ernst & Young for audit and quarterly review of our financial statements and review of our registration statements on Form S-3 and Form S-8, and related services that are normally provided in connection with statutory and regulatory filings or engagements.

In connection with the audit of each of the 2020 and 2019 financial statements, the Company entered into engagement agreements with Ernst & Young, which sets forth the terms by which Ernst & Young will perform audit services for the Company. Such agreements are subject to alternative dispute resolution procedures.

PRE-APPROVAL POLICIES AND PROCEDURES

The Audit Committee must pre-approve the audit and non-audit services rendered by the Company's independent registered public accounting firm.

PART IV

Item 15. Exhibits, Financial Statement Schedules

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

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.

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on August 3, 2016.
3.2	Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on October 2, 2018).
3.3	Certificate of Designation of Preferences, Rights and Limitations of Class A-1 Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on May 9, 2019).
3.4	Certificate of Designation of Preferences, Rights and Limitations of Class A-2 Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on December 26, 2019).
3.5	Certificate of Designation of Preferences, Rights and Limitations of Class A-3 Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Registrants' Current Report on Form 8-K (File No. 001-35670) filed with the SEC on December 4, 2020).
3.6	Certificate of Amendment to the Certificate of Designation of Preferences, Rights and Limitations of Class A-1 Convertible Preferred Stock (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on December 4, 2020).
3. 7	Certificate of Amendment to the Certificate of Designation of Preferences, Rights and Limitations of Class A-2 Convertible Preferred Stock (incorporated by reference to Exhibit 3.3 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on December 4, 2020).
3.8	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on June 8, 2016).
4.1	Reference is made to Exhibits 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7 and 3.8.
4.2	Form of Common Stock Certificate of the Registrant (incorporated by reference to Exhibit 4.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on November 9, 2018).
4.3	Description of Common Stock (incorporated by reference to Exhibit 4.3 to the Registrant's Annual Report on From 10-K (File No. 001-35670), filed with the SEC on) March 12, 2020).
4.4	Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on May 9, 2019).

4.5	Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on December 4, 2020).
10.1*	Form of Indemnity Agreement between the Registrant and its directors and officers (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012).
10.2*	Regulus Therapeutics Inc. 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).
10.3*	2012 Equity Incentive Plan and Form of Stock Option Agreement and Form of Stock Option Grant Notice thereunder (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012).
10.4*	Non-Employee Director Compensation Policy, as amended (incorporated by reference to Exhibit 10.6 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on November 12, 2019).
10.5*	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).
10.6*	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).
10.7*	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).
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).
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*	Joseph P. Hagan, Yearly Discretionary Base Salary Increase, effective January 1, 2019.
10.14*	Joseph P. Hagan, Yearly Discretionary Base Salary Increase, effective January 1, 2020.
10.15*	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).
10.16*	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).

10.17*	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).
10.18*	Employment Agreement between the Registrant and Denis Drygin, dated August 3, 2020.
10.19†	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).
10.20†	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).
10.21†	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).
10.22†	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).
10.23	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).
10.24†	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 No. 333-183384), originally filed with the SEC on August 17, 2012).
10.25†	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).
10.26†	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).
10.27††	Second Amendment to Second Amended and Restated Collaboration and License Agreement, dated August 25, 2020, by and among the Registrant and Sanofi (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 5, 2020).
10.28	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).
10.29	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).
10.30††	Second Amendment to Loan and Security Agreement, dated March 6, 2018, by and between the Registrant and Oxford Finance LLC
10.31†	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).

10.32	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).
10.33	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).
10.34	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).
10.35	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).
10.36	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).
10.37	Ninth Amendment to Loan and Security Agreement, dated May 1, 2020, by and among the Registrant and Oxford Finance, LLC (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on May 14, 2020).
10.38	Tenth Amendment to Loan and Security Agreement, dated August 25, 2020, by and among the Registrant and Oxford Finance, LLC (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on November 5, 2020).
10.39	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).
10.40	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).
10.41	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).
10.42	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).
10.43	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).
10.44	Lease Agreement, dated February 11, 2021, by and between the Registrant and ARE-SD Region No. 44 LLC.
10.45	Assignment and Assumption of Lease, dated February 11, 2021, by and between the Registrant and Turning Point Therapeutics, Inc.
10.46	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).
10.47	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).
10.48	Securities Purchase Agreement, dated December 1, 2020, 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 December 4, 2020).

23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney. Reference is made to the signature page hereto.
31.1	Certification of the Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
31.2	Certification of the Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
32.1**	Certification of the Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	Inline XBRL Instance Document.
101.SCH	Inline XBRL Taxonomy Extension Schema Document.
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibit 101. INS)

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

†† Certain portions of this exhibit (indicated by "[***]") have been omitted as the Registrant has determined (i) the omitted information is not material and (ii) the omitted information would likely cause harm to the Registrant if publicly disclosed.

* 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.

Regulus Therapeutics Inc.

Date: March 9, 2021

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.

Signature	Title	Date
/s/ Joseph P. Hagan Joseph P. Hagan	President & Chief Executive Officer and Director (Principal Executive Officer)	March 9, 2021
/s/ Cris Calsada Cris Calsada	Chief Financial Officer (Principal Financial Officer)	March 9, 2021
/s/ Daniel J. Penksa Daniel J. Penksa	Controller (Principal Accounting Officer)	March 9, 2021
/s/ Stelios Papadopoulos Stelios Papadopoulos, Ph.D.	Chairman of the Board of Directors	March 9, 2021
/s/ David Baltimore David Baltimore, Ph.D.	Director	March 9, 2021
/s/ Kathryn Collier Kathryn Collier	Director	March 9, 2021
/s/ Alice Huang Alice Huang, Ph.D.	Director	March 9, 2021
/s/ Jake R. Nunn Jake R. Nunn	Director	March 9, 2021
/s/ William H. Rastetter William H. Rastetter, Ph.D.	Director	March 9, 2021
/s/ Hugh Rosen Hugh Rosen, M.D., Ph.D.	Director	March 9, 2021
/s/ Simos Simeonidis Simos Simeonidis, Ph.D.	Director	March 9, 2021
/s/ Pascale Witz Pascale Witz	Director	March 9, 2021