UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2019

OR

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

Commission File Number 001-38890

Cortexyme, Inc.

(Exact name of registrant as specified in its Charter)

Delaware	**90-1024039**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
269 East Grand Ave.	
South San Francisco, California	**94080**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (415) 910-5717

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	CRTX	Nasdaq Global Select Market

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, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

The aggregate market value of the common stock held by non-affiliates of the registrant as of June 28, 2019 (the last business day of the registrant's most recently completed second fiscal quarter) was approximately $669.0 million, based on the closing price of the registrant's common stock, as reported by the NASDAQ Global Select Market on June 28, 2019 of $42.51 per share.

The number of shares of the registrant's common stock outstanding as of March 13, 2020 was 29,402,240.

DOCUMENTS INCORPORATED BY REFERENCE

Part III incorporates by reference certain information from the registrant's definitive proxy statement (the "Proxy Statement") relating to its 2020 Annual Meeting of Stockholders. The Proxy Statement will be filed with the United States Securities and Exchange Commission within 120 days after the end of the fiscal year to which this report relates.

Table of Contents

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements. All statements other than statements of historical facts contained in this report, including statements regarding our future results of operations and financial position, business strategy, product candidates, planned preclinical studies and clinical trials, research and development costs, regulatory approvals, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. In some cases, forward-looking statements may be identified by words such as "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "could," "would," "expect," "objective," "plan," "potential," "seek," "grow," "target," "if," and similar expressions intended to identify forward-looking statements.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy short-term and long-term business operations and objectives and financial needs. These forward-looking statements are subject to known and unknown risks, uncertainties and assumptions, including risks described in the section titled “Risk Factors” set forth in Part I, Item 1A of this Annual Report on Form 10-K and in our other filings with the Securities and Exchange Commission (the "SEC"). It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the future events and trends discussed in this Annual Report on Form 10-K may not occur, and actual results may differ materially and adversely from those anticipated or implied in the forward-looking statements. Forward-looking statements contained in this Annual Report on Form 10-K include, but are not limited to, statements about:

- our financial performance;
- the sufficiency of our existing cash and cash equivalents to fund our future operating expenses and capital expenditure requirements;
- our ability to obtain funding for our operations, including funding necessary to develop and commercialize our drug candidates;
- the ability of our clinical trials to demonstrate safety and efficacy of our drug candidates, and other positive results;
- the success, cost and timing of our development activities, preclinical studies and clinical trials
- the timing and focus of our future clinical trials, and the reporting of data from those trials;
- our plans relating to commercializing our drug candidates, if approved;
- our plans and ability to establish sales, marketing and distribution infrastructure to commercialize any drug candidates for which we obtain approval;
- our ability to attract and retain key scientific and clinical personnel;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our reliance on third parties to conduct clinical trials of our drug candidates, and for the manufacture of our drug candidates for preclinical studies and clinical trials;
- our ability to expand our drug candidates into additional indications and patient populations;
- the success of competing therapies that are or may become available;
- the beneficial characteristics, safety and efficacy of our drug candidate;
- regulatory developments in the United States and other jurisdictions;
- our ability to obtain and maintain regulatory approval of our drug candidates, and any related restrictions, limitations and/or warnings in the label of any approved drug candidate;
- our plans relating to the further development and manufacturing of our drug candidates, including additional indications for which we may pursue;
- our plans and ability to obtain or protect intellectual property rights, including extensions of existing patent terms where available;

- the scope of protection we are able to establish and maintain for intellectual property rights covering our drug candidates and technology and;
- potential claims relating to our intellectual property.

We caution you that the foregoing list may not contain all of the forward-looking statements made in this Annual Report on Form 10-K.

You should not rely upon forward-looking statements as predictions of future events. The events and circumstances reflected in the forward-looking statements may not be achieved or occur. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we do not intend to update any of these forward-looking statements after the date of this Annual Report on Form 10-K or to conform these statements to actual results or revised expectations.

You should read this Annual Report on Form 10-K with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

This Annual Report on Form 10-K contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. We obtained the industry, market and similar data set forth in this report from our own internal estimates and research and from academic and industry research, publications, surveys and studies conducted by third parties, including governmental agencies. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. While we believe that the data we use from third parties are reliable, we have not separately verified these data. Further, while we believe our internal research is reliable, such research has not been verified by any third party. You are cautioned not to give undue weight to any such information, projections and estimates.

PART I

Item 1. Business.

We are a clinical stage biopharmaceutical company pioneering a novel disease-modifying therapeutic approach to treat what we believe to be a key underlying cause of Alzheimer's and other degenerative diseases. Our approach is based on the seminal discovery of the presence of *Porphyromonas gingivalis*, or *P. gingivalis*, and its secreted toxic virulence factor proteases, called gingipains, in the brains of greater than 90% of more than 100 Alzheimer's patients observed across multiple studies to date. Additionally, we have observed that *P. gingivalis* infection causes Alzheimer's pathology in animal models, and these effects have been successfully treated with a gingipain inhibitor in preclinical studies. Our proprietary lead drug candidate, COR388, is an orally administered, brain-penetrating small molecule gingipain inhibitor. COR388 was well-tolerated with no concerning safety signals in our Phase 1a and Phase 1b clinical trials conducted to date, which enrolled a total of 67 subjects, including nine patients with mild to moderate Alzheimer's disease. We initiated a global Phase 2/3 clinical trial of COR388, called the GAIN trial, in mild to moderate Alzheimer's patients in April 2019 in the United States and in September 2019 in Europe and expect top-line results by the end of 2021.

COR388 is the first and only selective inhibitor of gingipain activity being investigated in clinical trials for the treatment of Alzheimer's disease. COR388 is designed to target an upstream driver of multiple Alzheimer's pathological pathways, including amyloid beta production, inflammation and neurodegeneration, in contrast to mechanisms of action targeting downstream effects, such as amyloid plaques and tau tangles, which have been largely unsuccessful in clinical trials to date. Accordingly, we believe COR388 could represent a disease-modifying therapy for the chronic treatment of Alzheimer's disease.

Our Phase 1a and Phase 1b clinical trials enrolled a total of 67 subjects, including nine patients with mild to moderate Alzheimer's disease. In these placebo-controlled trials, COR388 was well-tolerated with no concerning safety signals. In the Alzheimer's patients treated with COR388 for 28 days, we found changes in a number of pharmacodynamic biomarkers associated with Alzheimer's disease, including RANTES, an inflammatory marker, and Apolipoprotein protein E, or ApoE, a target for gingipains. For example, fragments of ApoE in the CSF were reduced compared to placebo, and blood levels of RANTES were significantly reduced. In addition, data from the Alzheimer's patients treated with COR388 in our Phase 1b clinical trial showed improvements across several exploratory cognitive tests. These improvements in cognitive tests should be interpreted with caution because they were not all statistically significant. We identified bacterial DNA from *P. gingivalis* in the cerebral spinal fluid, or CSF, of all nine Alzheimer's patients, and this finding is supported by additional data from larger studies conducted by our team both independently and in collaboration with academic institutions. Moreover, we observed that COR388 successfully penetrated the blood-brain barrier. In addition, in our preclinical studies, we observed that COR388 reduced bacterial load in the brain, reduced amyloid beta levels, protected neurons and reduced markers of neuroinflammation. We plan to enroll approximately 570 mild to moderate Alzheimer's patients in our Phase 2/3 GAIN trial, or GingipAIN Inhibitor for the Treatment of Alzheimer's Disease Trial, to evaluate safety and efficacy after one year of treatment as measured on key endpoints that have previously supported regulatory approval of drugs for Alzheimer's disease, including the Alzheimer's disease Assessment Scale-Cognitive Subscale 11, or ADAS-Cog11. We expect to report top-line data from this trial by the end of 2021. In addition, we intend to conduct an interim analysis after approximately 100 patients in each of the GAIN trial's three arms complete six months of treatment by the end of 2020.

Alzheimer's disease represents one of the most significant unmet medical needs of our time and there are no marketed treatments that address the underlying cause of the disease. The disease afflicts an estimated 5.7 million people in the United States and more than 30 million people worldwide and is expected to grow to 14.0 million people in the United States by 2050. The direct costs of caring for individuals with Alzheimer's disease and other dementias in the United States were estimated to total $277 billion in 2018 and are projected to increase to $1.1 trillion by 2050, according to the Alzheimer's Association. Historical challenges in developing effective therapeutics for this disease include a poor understanding of disease causation and animal models that do not translate to efficacy in humans. We believe our novel approach can overcome these challenges by targeting an upstream cause of neuroinflammation and neurodegeneration. Our drug candidate has demonstrated proof of concept in a new physiological animal model that we believe is representative of human Alzheimer's disease pathology.

Understanding the Foundation of Our Therapeutic Approach

P. gingivalis is an intracellular bacterial pathogen, and its gingipains are essential for *P. gingivalis* survival and pathogenicity. Our new understanding of the *P. gingivalis* brain infection and associated gingipain production, which we have observed to cause Alzheimer's pathology in animal models, provides a new opportunity for successful upstream treatment of all aspects of Alzheimer's disease pathology. Significant evidence in the last decade has shown that neurodegenerative diseases, including Alzheimer's disease, are linked to a dysfunctional immune system. Furthermore, the pathology of Alzheimer's disease has been shown in studies to be consistent with that of infection, including, for example, the pathological presence of amyloid beta, which recently has been characterized as an antimicrobial peptide produced in response to infection.

In preclinical mouse models, we and others have demonstrated that *P. gingivalis* is capable of accessing the brain and that its presence causes amyloid beta production, inflammation and neurodegeneration, which are characteristic pathology observed in the brain of Alzheimer's patients. *P. gingivalis* and gingipains have been observed in the brains of greater than 90% of more than 100 Alzheimer's patients across multiple studies conducted by our team both independently and in collaboration with academic institutions.

Our Lead Drug Candidate-COR388

We have discovered and developed a proprietary library of protease inhibitors from which we have selected our lead drug candidate, COR388, an orally administered, brain-penetrating small molecule being developed for chronic treatment of Alzheimer's disease.

We believe that the development of this compound represents a new paradigm for potential disease modification in Alzheimer's disease, based on our published and unpublished data, as well as a large body of third-party research. We maintain rights to COR388 and hold issued U.S. patents providing composition of matter coverage through 2035 and pending U.S. and foreign patent applications, which, if issued, could extend coverage.

Summary of Our Clinical and Preclinical Data

We have completed two Phase 1 clinical trials for COR388 which enrolled 67 subjects, including nine patients with mild to moderate Alzheimer's disease. We believe the following clinical and preclinical data generated to date by COR388 support its development as a potential disease-modifying treatment for Alzheimer's disease:

- We tested COR388 in two placebo-controlled Phase 1 clinical trials: (i) a Phase 1a single ascending dose, or SAD, study in 34 healthy volunteers and (ii) a Phase 1b multiple ascending dose, or MAD, study in 24 older healthy volunteers and nine Alzheimer's patients. We observed COR388 to be well-tolerated with no concerning safety signals.
- Our Phase 1 clinical trials also demonstrated that COR388 affected a number of pharmacodynamic biomarkers associated with Alzheimer's disease, including blood levels of RANTES and fragments of ApoE in the CSF. Additionally, although not powered for statistical significance, in our Phase 1b clinical trial, data from the small group of Alzheimer's patients treated with COR388 showed improvements across several exploratory cognitive tests including:
    - a statistically significant improvement in three measures on the Winterlight speech-based cognitive assessment, or WLA, relative to baseline;
    - a numerical improvement in Mean Mini-Mental State Exam, or MMSE, scores relative to both baseline and placebo, which was not statistically significant; and
    - an improvement in several measures of cognitive function in the Cambridge Neuropsychological Test Automated Battery, or CANTAB, relative to both baseline and placebo, which was not statistically significant.
- Using a proprietary polymerase chain reaction, or PCR, method, we identified fragmented bacterial DNA unique to *P. gingivalis* bacteria in the CSF of all nine mild to moderate Alzheimer's patients in our Phase 1b clinical trial, as well as all 50 Alzheimer's patients in a separate human observational study. We believe that finding fragments of this specific bacterial DNA in the CSF is consistent with a bacterial brain infection with *P. gingivalis*.
- We and other research organizations have separately demonstrated that oral infection of wild type mice by *P. gingivalis* results in brain infiltration, neuroinflammation, amyloid beta production and plaque formation. This model and pathological reproduction closely resembles non-familial, or sporadic, Alzheimer's disease, which represents over 95% of Alzheimer's disease cases in humans. As a result, we believe our new physiological animal model is representative of Alzheimer's disease in human patients, unlike other animal models to date, which have historically not translated to successful disease modifying treatment in humans.
- In our preclinical studies using wild type mice infected with *P. gingivalis*, we have observed that gingipain inhibitors, including COR388, prevented further neurodegeneration, reduced amyloid beta levels and reduced markers of neuroinflammation.
- In our preclinical chronic toxicology studies, ranging from six to nine months in length, we observed a large potential therapeutic window with no adverse findings or dose-limiting toxicities after chronic administration.

Our Phase 2/3 GAIN Clinical Trial of COR388 in Mild to Moderate Alzheimer's Patients

We initiated a global Phase 2/3 randomized, double-blind, placebo-controlled study in April 2019, which we refer to as the GingipAIN Inhibitor for the Treatment of Alzheimer's Disease, or GAIN, trial. This study is designed to assess the efficacy, safety and tolerability of two dose levels of COR388 (40 mg and 80 mg) in subjects with mild to moderate Alzheimer's disease compared to placebos. The study is intended to enroll approximately 570 male and female subjects between the ages of 55 and 80. Enrolled subjects must have a diagnosis of mild to moderate Alzheimer's disease dementia, with MMSE scores between 12 and 24 points, a range that is documented to provide an average decline in the placebo group sufficient to show efficacy of a disease slowing treatment over a one-year treatment period. Randomization will be stratified by baseline MMSE and ApoE4 genotype to assure balanced distribution of mild and moderate Alzheimer's disease and a balanced distribution of ApoE4 carriers, across treatment arms. Patients will be able to remain on stable doses of background medications, including symptomatic Alzheimer's disease treatments, during the trial. The study will consist of a treatment period of up to 48 weeks and a safety follow-up period of 6 weeks. Periodic safety reviews will be conducted during the study. All supporting studies to update the COR388 IND, including the GAIN trial protocol, chronic toxicology studies and metabolite studies, have been submitted to the FDA and have completed the 30-day review period indicating acceptance of the IND update and clearance to proceed with the Phase 2/3 GAIN trial. Following discussion with the FDA in February 2020, we also intend to conduct an interim analysis for overwhelming efficacy in our GAIN trial. We plan to conduct the interim analysis by the end of 2020 after approximately 100 patients in each of the GAIN trial's three arms complete six months of treatment.

The co-primary endpoints will be the mean change in ADAS-Cog11 and change in Clinical Dementia Rating-Sum of Boxes, CDR-SB from baseline to the end of treatment period at 48 weeks versus placebo. A secondary endpoint in all subjects will include change in Alzheimer's Disease Cooperative Study Group-Activities of Daily Living, or ADCS-ADL. Exploratory endpoints will include change from baseline to the end of treatment period in the following measures: (i) MMSE score; (ii) Neuropsychiatric Inventory, or NPI; (iii) blood, saliva and CSF biomarkers; (iv) WLA measures; and (v) MRI brain measurements. Additionally, periodontal disease, including pocket depth and bleeding on probing, will be tracked in a subset of patients. For the interim analysis, the co-primary endpoints will be change from baseline in ADAS-Cog11 and CDR-SB versus placebo.

Placebo and treated patients who complete our Phase 2/3 GAIN trial in the United States may be eligible to participate in an open label extension in which patients will receive 80 mg COR388 twice daily. The purpose of this extension study is to evaluate the long-term safety and tolerability of COR388 as well as encourage patient enrollment and retention.

Our Strategy

Our objective is to transform the treatment of Alzheimer's and other degenerative diseases by creating a broad portfolio of innovative therapeutics that target significant unmet medical needs. Our novel therapeutic approach is focused on targets that show evidence of disease causation with impacts on multiple downstream pathways, rather than targeting downstream effects or rare genetic risk factors that are unlikely to have a large impact on the course of disease progression. To achieve this objective, we are pursuing the following strategies:

- Rapidly advance COR388 through clinical development in patients with Alzheimer's disease. Based on the strength of the data we observed in our two completed Phase 1 clinical trials, we initiated a Phase 2/3 randomized, double-blind, placebo-controlled trial in April 2019 that is designed to assess the efficacy, safety and tolerability of COR388 in mild to moderate Alzheimer's patients.
- Develop COR388 for other diseases. P. gingivalis infection and associated protein-cleaving, or proteolytic, gingipain activity have been implicated in multiple disease pathologies in preclinical and epidemiological studies. We plan to conduct clinical trials of COR388 in other indications where both human observational data and preclinical experiments support its therapeutic potential.
- Expand our portfolio by developing additional compounds. A key element of our portfolio strategy is to advance additional molecules from our proprietary library. We have initiated several other protease inhibitor programs. Additionally, we are developing a positron emission tomography, or PET, imaging agent for detection of gingipains in the human brain and advancing candidate compounds through lead optimization.
- Optimize value of COR388 and future drug candidates in major markets. We own rights to COR388 and our library of compounds. We plan to develop and pursue approval of COR388 and other future drug candidates in major markets. Where appropriate, we may use strategic collaborations and partnerships to accelerate the development and maximize the commercial potential of our programs.

Pipeline Compounds

We have a library of small molecule protease inhibitors, including additional gingipain inhibitors with structures that are distinct from COR388. *P. gingivalis* expresses two types of gingipains, lysine and arginine gingipain, both of which appear to be essential for toxicity and bacterial survival. The most advanced of the lysine gingipain (Kgp) inhibitors, aside from COR388, have been shown to be potent at less than 100 picomolar concentrations, highly selective for Kgp versus human anti-targets and to possess good oral bioavailability, favorable pharmacokinetic profiles and sufficient brain levels in multiple preclinical species. In a 28-day toxicology study in mice, these compounds were dosed with exposures significantly above predicted levels needed for efficacy with no changes in clinical pathology laboratory parameters, no clinical observations and no brain histopathology findings.

Our library of inhibitors also includes a series of arginine gingipain (Rgp) inhibitor lead compounds. Key compounds in this series are potent and highly selective for Rgp vs human anti-targets, with efficacy demonstrated in a mouse model of *P. gingivalis* brain infection. We are advancing multiple lead compounds. Our compound collection was also used to develop activity-based probe reagents that bind the active sites of Kgp and Rgp, enabling the detection of their activity as well as potential target engagement and inhibition by therapeutic compounds. These probe reagents are utilized in biomarker studies helping to establish target potency and inhibition in studies.

We are additionally screening our library of cysteine protease inhibitors for efficacy in other indications, including for the treatment of coronaviruses via inhibition of a cysteine protease required for replication, called 3CLpro.

We are additionally leveraging our library of inhibitors to develop a positron emission tomography, or PET, imaging agent for detection of gingipains in the human brain. We are seeking to identify candidates and planning to advance a PET agent through lead optimization.

Additional Markets of Interest

Periodontal Disease

P. gingivalis has been identified as a key pathogen in the development of periodontal disease. Periodontal disease is a common age-related disease affecting nearly 50% of the population over 50 years of age, or 65 million people, in the United States. The disease presents with symptoms including chronic inflammation, degeneration of gum tissue and tooth loss. Periodontal disease is associated with increased risk of cardiovascular disease, diabetes and certain cancers. The disease is often chronic and recurring due to persistent bacterial infection and antibiotic resistance. Current standard of care for the treatment of periodontal disease commonly involves scaling and root planning to remove bacterial plaque and tartar, in addition to local delivery of antibiotics in some cases. COR388 reduced periodontal disease and associated bone loss in multiple animal models of periodontal disease. Target engagement and efficacy data for COR388 in aged dogs was published in January 2020 in the journal *Pharmacology Research and Perspectives*. In our Phase 2/3 GAIN trial periodontal pocket depth is being assessed as an exploratory endpoint.

Other Systemic Disease Indications

P. gingivalis infection has been associated with disease pathology in a number of large market opportunities including atherosclerosis, diabetes, cancer and arthritis. We continue to conduct preclinical research in physiological animal models representing these disease states to assess the potential for other novel gingipain inhibitors in our portfolio to be disease modifying.

Manufacturing

We do not currently own or operate facilities for manufacturing, storing, distributing or testing our drug candidates. We rely on third-party contract manufacturing organizations, or CMOs, to manufacture and supply our preclinical and clinical materials to be used during the development of our drug candidates.

We currently have sufficient COR388 on hand in the United States to complete our Phase 2/3 GAIN trial in Alzheimer’s disease as currently planned and ongoing preclinical studies. Additional cGMP drug substance campaigns with our contract manufacturer and suppliers in various countries in Asia and Europe are in process to ensure full supply for our open label extension, ongoing product development campaigns, and additional clinical studies of COR388.

COR388 is a low molecular weight compound isolated as a stable crystalline solid. We believe the synthesis of COR388 is reliable and reproducible from readily available starting materials, and the synthetic routes are amenable to large-scale production and do not require unusual equipment or handling in the manufacturing process. We are in the process of further optimizing the synthetic route for commercial manufacturing as well as developing related methodologies for the production of analog compounds in our pipeline. We expect to continue to identify and develop drug candidates that are amenable to cost-effective production at CMOs.

Our COR388 drug product is currently neat powder in a capsule which has demonstrated stability for 6 months enabling a shelf life of 18 months at room temperature. Drug substance has demonstrated stability for 24 months enabling a retest date of 36 months when stored refrigerated. Stability studies are ongoing and we are currently optimizing a formulated drug product to be marketed. Currently our drug substance is stored refrigerated, out of an abundance of caution while stability studies are ongoing, while the storage condition for our drug product is room temperature.

We have established relationships with several key CMOs to enable both the non-clinical and clinical supply lines for COR388 active pharmaceutical ingredient, or drug substance, as well as drug product under cGMP protocols. To date the cGMP drug substance manufacturing process has been completed with a single vendor from readily available commercial starting materials and reagents. We currently have arrangements in place for redundant supply of bulk drug substance with a second GMP manufacturer. The drug product capsule filling and formulation can be readily accomplished at multiple vendors.

Commercialization Plan

We do not currently have any approved drugs and we do not expect to have any approved drugs in the near term. Therefore, we have no sales, marketing or commercial product distribution capabilities and have no experience as a company in marketing drugs.

When and if any of our drug candidates are approaching commercialization, we intend to develop a commercialization infrastructure for those drug candidates in the United States and potentially in certain other key markets. We may also rely on partnerships to provide commercialization infrastructure, including sales and marketing and commercial distribution.

Competition

We face competition from a number of different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, governmental agencies and public and private research institutions. We believe that the key competitive factors affecting the success of COR388 and any other drug candidates will include efficacy, safety profile, method of administration, cost, level of promotional activity and intellectual property protection. We know of no competitors developing clinical stage therapeutics targeting *P. gingivalis* or gingipains for the chronic treatment of Alzheimer's disease.

Our drug candidates, if successfully developed and approved, will compete with current therapies approved for the treatment of Alzheimer's disease, which to date have been primarily targeted at treating the symptoms of such diseases rather than halting or slowing the progression of the disease. However, in addition to such currently approved therapies, we believe that our drug candidates, if approved, may also compete with other potential therapies intended to halt or slow the progression of neurodegenerative disease that are being developed by a number of companies and institutions, including but not limited to potentially disease modifying therapeutics that are being developed by several large and specialty pharmaceutical and biotechnology companies, including AbbVie Inc., Biogen Inc., Eli Lilly and Company, Eisai Co., Ltd., Merck & Company, Inc., Novartis AG and Roche Holding AG (including Genentech, its wholly owned subsidiary), as well as companies pursuing a dysfunctional immune system approach to Alzheimer's disease or other types of therapies.

Intellectual Property

We maintain rights to COR388 and hold issued U.S. patents providing composition of matter and method of use coverage through 2035. We also hold pending U.S. and foreign patent applications, which, if issued, could extend coverage for COR388. Our foreign patent applications are currently pending in Argentina, Australia, Brazil, Canada, Chile, China, Colombia, the European Patent Office, Hong Kong, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, Peru, the Philippines, Russia, Singapore, Taiwan, and South Africa.

Other patent families in our patent portfolio disclose and claim other small-molecule inhibitors of lysine gingipain and arginine gingipain, gingipain activity probes for biological imaging, and assay methods for the detection of microbial pathogens in cerebrospinal fluid and other bodily fluids. As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our drug candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, our pending patent applications, and any patent applications that we may in the future file or license from third parties may not result in the issuance of patents. We cannot guarantee that our owned pending patent applications, or any patent applications that we may in the future file or license from third parties, will result in the issuance of patents. We also cannot predict the scope of claims that may be allowed or enforced in our patents. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we may not obtain or maintain adequate patent protection for any of our programs and drug candidates. Any issued patents that we may receive in the future may be challenged, invalidated or circumvented. For example, we cannot be certain of the priority rights of inventions covered by pending third-party patent applications. If third parties prepare and file patent applications in the United States or other jurisdictions that also claim technology or therapeutics to which we have rights, we may have to participate in interference proceedings, post-grant review, reissue, or reexamination in the USPTO and equivalent foreign courts to determine priority rights of invention, which could result in substantial costs to us even if the eventual outcome, which is highly unpredictable, is favorable to us. In addition, because of the extensive time required for clinical development and regulatory review of a drug candidate we may develop, it is possible that, before any of our drug candidates can be commercialized, any related

patent may expire or remain in force for only a short period following commercialization, thereby limiting any protection such patent would afford the respective product and any competitive advantage such patent may provide. For more information regarding the risks related to our intellectual property, see "Risk Factors—Risks Related to Our Intellectual Property."

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 earliest date of filing a non-provisional patent application in the United States. In the United States, the patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration 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. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to an approved drug may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it 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. In the future, if and when our drug candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those drug candidates. We plan to seek patent term extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions. For more information regarding the risks related to our intellectual property, see "Risk Factors—Risks Related to Our Intellectual Property."

In addition to patent protection, we also rely on trademark registration, trade secrets, know how, other proprietary information and continuing technological innovation to develop and maintain our competitive position. We seek to protect and maintain the confidentiality of proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets and we cannot guarantee, however, that these agreements will afford us adequate protection of our intellectual property and proprietary information rights. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. Our agreements with employees also provide that all inventions conceived by the employee in the course of employment with us or from the employee's use of our confidential information are our exclusive property. However, such confidentiality agreements and invention assignment agreements can be breached, and we may not have adequate remedies for any such breach. Additionally, some of our trade secrets and know-how for which we decide to not pursue additional patent protection may, over time, be disseminated within the industry through independent development and public presentations describing the methodology. For more information regarding the risks related to our intellectual property, see "Risk Factors—Risks Related to Our Intellectual Property."

The patent positions of biotechnology companies like ours are generally uncertain and involve complex legal, scientific and factual questions. Our commercial success will also depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our drugs or processes, obtain licenses or cease certain activities. Our breach of any license agreements or our failure to obtain a license to proprietary rights required to develop or commercialize our future drug candidates may have a material adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference or derivation proceedings in the USPTO to determine priority of invention. For more information, see "Risk Factors—Risks Related to Our Intellectual Property."

Regulatory Matters

Government authorities in the United States at the federal, state and local level, and in other countries and jurisdictions, including the European Union, 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, sampling and export and import of pharmaceutical products. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. Drug Development

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires 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 post-market may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to

approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an Investigational New Drug application, or IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each proposed indication;
- preparation and submission to the FDA of a New Drug Application, or NDA, requesting marketing for one or more proposed indications;
- review by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as *in vitro* and animal studies to assess the potential safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

The IND and IRB Processes

The authorization for an IND must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation

may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain FDA regulatory requirements in order to use the study as support for an IND or application for marketing approval. Specifically, the FDA has promulgated regulations governing the acceptance of foreign clinical studies not conducted under an IND, establishing that such studies will be accepted as support for an IND or application for marketing approval if the study was conducted in accordance with GCP including review and approval by an independent ethics committee, or IEC, and informed consent from subjects, and the FDA is able to validate the data from the study through an on-site inspection if the FDA deems such inspection necessary. The GCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies. If a marketing application is based solely on foreign clinical data, the FDA requires that the foreign data be applicable to the U.S. population and U.S. medical practice; the studies must have been performed by clinical investigators of recognized competence; and the FDA must be able to validate the data through an on-site inspection or other appropriate means, if the FDA deems such an inspection to be necessary.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Human Clinical Studies in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in the following sequential phases, which may overlap or be combined:

- *Phase 1:* The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
- *Phase 2:* The drug is administered to 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 and optimal dosage.
- *Phase 3:* The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.
- *Phase 4:* Post-approval studies, which are conducted following initial approval, are typically conducted to gain additional experience and data from treatment of patients in the intended therapeutic indication.

The clinical drug development phases described above are general guidelines. The phases are not clearly delineated from each other in every regard, and it is common practice to separate (e.g., Phase 1a and 1b trials) or combine (e.g., a Phase 2/3 trial) phases, which is accepted by the FDA and other global regulatory agencies. As one example of overlapping definitions, both Phase 2 and Phase 3 involve patient populations with assessments of both efficacy and safety. The GAIN trial combines a Phase 2 dose-finding design to identify the optimal dosage, with a Phase 3 magnitude of enrollment adequate to statistically evaluate the efficacy and safety. For indications like Alzheimer's disease with cognitive endpoints requiring a large number of subjects for sufficient

powering to demonstrate convincing efficacy, it may be beneficial to advance rapidly to Phase 3 when the investigational drug is relatively well tolerated and is not producing concerning safety signals. In other indications or for other therapeutics, a smaller Phase 2 (or even a Phase 2a followed by a Phase 2b) may be useful and appropriate prior to progression to a larger Phase 3 study.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, 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. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often 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.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, and the sponsor of an approved NDA is also subject to annual program fees.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and informs the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the filing date, and most applications for "priority review" products are meant to be reviewed within six months of the filing date. The review process and the Prescription Drug User Fee Act goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing (such as active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application 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 one or more clinical sites to assure compliance with GCP.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. A REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. A REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides 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.

Fast Track, Breakthrough Therapy and Priority Review Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation and priority review designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete, subject to agreement between the sponsor and the FDA on a schedule for the submission of the various sections of the NDA and the sponsor's payment of applicable user fees. However, the FDA's PDUFA goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Furthermore, fast track designation, priority review, and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process. We may explore some of these opportunities for our drug candidates as appropriate.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warning or other safety information about the product;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

The 21st Century Cures Act

On December 13, 2016, then-President Obama signed 21st Century Cures Act, or the Cures Act, into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increased funding for the FDA to spend on innovation projects. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

Regulation Outside the United States

European Union Drug Development

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The EU clinical trials legislation currently is undergoing a transition process mainly aimed at harmonizing and streamlining clinical-trial authorization, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. In April 2014, the EU passed the Clinical Trials Regulation (Regulation 536/2014), which will replace the current Clinical Trials Directive. To ensure that the rules for clinical trials are identical throughout the European Union, the EU Clinical Trials Regulation was passed as a regulation that is directly applicable in all EU Member States. All clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive until the Clinical Trials Regulation becomes applicable. According to the current plans of the EMA, the Clinical Trials Regulation is expected to become applicable during 2020. In the meantime, Clinical Trials Directive 2001/20/EC continues to govern all clinical trials performed in the EU.

European Union Drug Review and Approval

In the European Economic Area, or EEA, which is comprised of the 27 Member States of the European Union (including Norway and excluding Croatia), Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations.

- The Community MA is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicines such as gene-therapy, somatic cell-therapy or tissue-engineered medicines and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided, and reimbursement is adequate to cover a significant portion of the cost of our products. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Even if our drug candidates are approved, sales of our products will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such products. The process for determining whether a payor will provide coverage for a product is separate from the process for setting the price or reimbursement rate that the payor will pay for the product if coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, drug candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover our drug candidates could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a 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 and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Within the United States, if we obtain appropriate approval in the future to market any of our drug product candidates, those products could potentially be covered by various government health benefit programs as well as purchased by government agencies. The participation in such programs or the sale of products to such agencies is subject to regulation. For example:

- Medicaid is a joint federal and state program that is administered by the states for low income and disabled beneficiaries. Under the Medicaid Drug Rebate Program, participating manufacturers are required to pay a rebate for each unit of product reimbursed by the state Medicaid programs. The amount of the rebate for each product is set by law and may be subject to an additional discount if certain pricing increases more than inflation.
- Medicare is a federal program that is administered by the federal government that covers individuals age 65 and over as well as those with certain disabilities. Drugs may be covered under Medicare Part D. Medicare Part D provides coverage to enrolled Medicare patients for self-administered drugs (i.e., drugs that do not need to be injected or otherwise administered by a physician). Medicare Part D is administered by private prescription drug plans approved by the U.S. government and each drug plan establishes its own Medicare Part D formulary for prescription drug coverage and pricing, which the drug plan may modify from time-to-time. The prescription drug plans negotiate pricing with manufacturers and may condition formulary placement on the availability of manufacturer discounts. Since 2011, manufacturers with marketed brand name drugs have been required to provide a 50% discount the negotiated price for on brand name prescription drugs utilized by Medicare Part D

beneficiaries when those beneficiaries reach the coverage gap in their drug benefits, and, beginning in 2019, that discount increased to 70%.

- Drug products are subject to discounted pricing when purchased by federal agencies via the Federal Supply Schedule (FSS). FSS participation is required for a drug product to be covered and reimbursed by certain federal agencies and for coverage under Medicaid, Medicare Part B and the Public Health Service (PHS) pharmaceutical pricing program. FSS pricing is negotiated periodically with the Department of Veterans Affairs. FSS pricing is intended not to exceed the price that a manufacturer charges its most-favored non-federal customer for its product. In addition, prices for drugs purchased by the Veterans Administration, Department of Defense (including drugs purchased by military personnel and dependents through the TRICARE retail pharmacy program), Coast Guard, and PHS are subject to a cap on pricing (known as the "federal ceiling price") and may be subject to an additional discount if pricing increases more than the rate of inflation.
- To maintain coverage of drugs under the Medicaid Drug Rebate Program, manufacturers are required to extend discounts to certain purchasers under the PHS pharmaceutical pricing program. Purchasers eligible for discounts include hospitals that serve a disproportionate share of financially needy patients, community health clinics and other entities that receive health services grants from the PHS.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company’s revenue generated from the sale of any approved products. 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 a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future. Recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, reform government program reimbursement methodologies. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation 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. At the federal level, the Trump administration's budget proposals for fiscal years 2019 and 2020 contain further drug price control measures that could be enacted during the budget process or in other future legislation. Further, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services has already started soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical 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, designed to encourage importation from other countries and bulk purchasing. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent the generation of revenue, attainment of profitability, or commercialization of products. In addition, it is possible that there will be further legislation or regulation that could harm the business, financial condition and results of operations.

Outside the United States, ensuring adequate coverage and payment for our drug candidates will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of our drug candidates or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies (so called health technology assessment, or HTA) in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on healthcare costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade (arbitrage between low-priced and high-priced member states), can further reduce prices. 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, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians, certain other healthcare providers and teaching hospitals and patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government.
- HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by HITECH, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the U.S. Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians, certain other healthcare providers, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and pricing information. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States

In March 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for drug products under government healthcare programs. Among the provisions of the ACA of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures, or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 70% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, then-President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Since its enactment, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the ACA. Some of the provisions of the ACA have yet to be implemented, and there have been legal and political challenges to certain aspects of the ACA. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the ACA. Moreover, the Tax Cuts and Jobs Act of 2017, or the Tax Act, was enacted on December 22, 2017, and includes a provision repealing, 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." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. While the Trump Administration and CMS have both stated that the ruling will have no immediate effect, it is unclear how this decision, subsequent appeals, if any, and other efforts to repeal and replace the ACA will impact the ACA and our business. Moreover, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress may consider other legislation to repeal or replace additional elements of the ACA. We continue to evaluate the effect that the ACA, the repeal of the individual mandate, and any additional repeal and replacement efforts may have on our business but expect that the ACA, as currently enacted or as it may be amended in the future, and other healthcare reform measures that may be adopted in the future could have a material adverse effect on our industry generally and on our ability to maintain or increase sales of our existing products that we successfully commercialize or to successfully commercialize our drug candidates, if approved. In addition to the ACA, there will continue to be proposals by legislators at both the federal and state levels, regulators and third-party payors to keep healthcare costs down while expanding individual healthcare benefits.

Employees and Consultants

As of December 31, 2019, we had 23 employees, including 17 in research and development and 6 in general and administrative functions. We also utilize 13 consultants in various roles related to our clinical study and research and development areas. We believe our employee relations are good.

Corporate Information

We were incorporated in Delaware on June 20, 2012. Our principal executive offices are located at 269 East Grand Avenue, South San Francisco, CA 94080. Our telephone number at that location is (415) 910-5717. Our corporate website address is www.cortexyme.com. Information contained on, or that may be accessed through, our website is not incorporated by reference into this Annual Report on Form 10-K and should not be considered a part of this Annual Report on Form 10-K.

Cortexyme is a registered trademark of Cortexyme, Inc. All other brand names or trademarks appearing in this Annual Report on Form 10-K are the property of their respective holders. Solely for convenience, the trademarks and trade names in this Annual Report on Form 10-K are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Available Information

We make available, free of charge through our website, our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, and amendments to those reports, filed or furnished pursuant to Sections 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after they have been electronically filed with, or furnished to, the SEC.

The SEC maintains an internet site (http://www.sec.gov) that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC.

Item 1A. Risk Factors.

Our operations and financial results are subject to various risks and uncertainties, including those described below that could adversely affect our business, financial condition, results of operations, cash flows and the trading price of our common stock. You should carefully consider the following risks, together with all of the other information in this Annual Report on Form 10-K, including our financial statements and the related notes included elsewhere in this Annual Report on Form 10-K.

Risks Relating Our Financial Position

We are a clinical stage biopharmaceutical company with a limited operating history.

We are a clinical stage biopharmaceutical company with a limited operating history focused on developing therapeutics for degenerative diseases, including Alzheimer's disease. We were incorporated in June 2012 and commenced material operations in June 2014. We have a very limited operating history, which may make it difficult to evaluate the success of our business to date and assess our future viability. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. We have recently initiated clinical trials for our lead drug candidate, COR388, and have not initiated clinical trials for any of our other drug candidates. To date, we have not initiated or completed a pivotal clinical trial, obtained marketing approval for any drug candidate, manufactured a commercial scale drug candidate, arranged for a third party to do so on our behalf, or conducted sales and marketing activities necessary for successful drug candidate commercialization. Our short operating history as a company makes any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields, and we have not yet demonstrated an ability to overcome such risks and difficulties successfully. If we do not address these risks and difficulties successfully, our business will suffer.

We have no drug candidates approved for commercial sale, we have never generated any revenue from sales, and we may never be profitable.

We have no drug candidates approved for sale, have never generated any revenue from sales, have never been profitable and do not expect to be profitable in the foreseeable future. We have incurred net losses in each year since our inception. For the years ended December 31, 2019 and 2018, our net losses were $37.0 million and $12.5 million, respectively. We had an accumulated deficit of $69.8 million as of December 31, 2019.

To date, we have devoted most of our financial resources to our corporate overhead and research and development of COR388, including our preclinical development activities and clinical trials of COR388. We expect that it will be several years, if ever, before we have a drug candidate ready for commercialization. We expect to continue to incur losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for our drug candidates, prepare for and begin the commercialization of any approved drug candidates, and add infrastructure and personnel to support our drug development efforts and operations as a public company. We anticipate that any such losses could be significant for the next several years. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. Further, these net losses have fluctuated significantly in the past and are expected to continue to significantly fluctuate from quarter-to-quarter or year-to-year. To become and remain profitable, we must develop and eventually commercialize a drug with significant revenue.

We may never succeed in developing a commercial drug and, even if we succeed in commercializing one or more drug candidates, we may never generate revenues that are significant or large enough to achieve profitability. In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown challenges. Because of these numerous risks and uncertainties, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to generate revenues or achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis and we will continue to incur substantial research and development and other expenditures to develop and market additional drug candidates.

We will require substantial additional funding to finance our operations, complete the development and commercialization of COR388 and evaluate future drug candidates. If we are unable to raise this funding when needed, we may be forced to delay, reduce or eliminate our drug development programs or other operations.

Since our inception, we have used substantial amounts of cash to fund our operations, and we expect our expenses to increase substantially in the foreseeable future in connection with our ongoing activities, particularly as we continue the research and development of, initiate clinical trials of, and seek marketing approval for, COR388. Developing COR388 and conducting clinical trials for the treatment of Alzheimer's disease and any other indications that we may pursue in the future will require substantial amounts of capital. In addition, if we obtain marketing approval for COR388 or any future drug candidates, we expect to incur significant commercialization expenses related to sales, marketing, manufacturing and distribution.

Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. As of December 31, 2019, we had $116.6 million in cash, cash equivalents and investments. In February 2020, we also received net proceeds of approximately $117.6 million from the issuance and sale of common stock in a private placement to certain accredited investors. We believe that our existing capital resources will be sufficient to fund our projected operations through at least 2021. However, changing circumstances may cause us to increase our spending significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control. We may need to raise additional funds sooner than we anticipate if we choose to expand more rapidly than we presently anticipate.

The amount and timing of our future funding requirements will depend on many factors, some of which are outside of our control, including but not limited to:

- the progress, costs, trial design, results of and timing of our Phase 2/3 GAIN trial and other clinical trials of COR388, including for potential additional indications that we may pursue beyond Alzheimer's disease;
- the willingness of the U.S. Food and Drug Administration, or FDA, and European Medicines Agency, or EMA, to accept our GAIN trial, as well as data from our completed and planned clinical and preclinical studies and other work, as the basis for review and approval of COR388 for Alzheimer's disease;
- the outcome, costs and timing of seeking and obtaining FDA, EMA and any other regulatory approvals;
- the number and characteristics of drug candidates that we pursue;
- our ability to manufacture sufficient quantities of our drug candidates;
- our need to expand our research and development activities;
- the costs associated with securing and establishing commercialization and manufacturing capabilities;
- the costs of acquiring, licensing or investing in businesses, drug candidates and technologies;
- our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;
- our need and ability to retain management and hire scientific and clinical personnel;
- the effect of competing drugs and drug candidates and other market developments;
- our need to implement additional internal systems and infrastructure, including financial and reporting systems; and
- the economic and other terms, timing of and success of any collaboration, licensing or other arrangements into which we may enter in the future.

Additional funding may not be available to us on acceptable terms or at all. Any such funding may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may affect our business. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail one or more of our research or development programs. We also could be required to seek funds through arrangements with collaborative partners or otherwise that may require us to relinquish rights to some of our technologies or drug candidates or otherwise agree to terms unfavorable to us.

Risks Related to Our Business and the Development of Our Drug Candidates

We are substantially dependent on the success of COR388, which will require significant additional clinical testing before we can seek regulatory approval and potentially launch commercial sales, and which may not be successful in clinical trials, receive regulatory approval or be successfully commercialized, even if approved.

To date, we have invested substantially all of our efforts and financial resources in the research and development of COR388, which is currently our only drug candidate. Before seeking marketing approval from regulatory authorities for the sale of COR388, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the drug in humans. We are not permitted to market or promote any of our drug candidates before we receive regulatory approval from the FDA, or comparable foreign regulatory authorities, and we may never receive such regulatory approval. We cannot be certain that COR388 will be successful in clinical trials. Further, COR388 may not receive regulatory approval even if it is successful in clinical trials. If we do not receive regulatory approvals for COR388, we may not be able to continue our operations. Our prospects, including our ability to finance our operations and generate revenue, will depend entirely on the successful development, regulatory approval and commercialization of COR388. The clinical and commercial success of COR388 will depend on a number of factors, including the following:

- the results from our Phase 2/3 GAIN trial, as well as other clinical trials of COR388;
- the frequency and severity of adverse effects of COR388;
- the ability of third-party manufacturers to manufacture supplies of COR388 and to develop, validate and maintain a commercial-scale manufacturing process that is compliant with current good manufacturing practices, or cGMP;

- our ability to demonstrate COR388's safety and efficacy to the satisfaction of the FDA and foreign regulatory authorities;
- whether we are required by the FDA to conduct additional clinical trials prior to the approval to market COR388 and whether the FDA may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the receipt of necessary marketing approvals from the FDA and foreign regulatory authorities;
- whether the FDA may require implementation of a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval or post-approval;
- our ability to successfully commercialize COR388, if approved for marketing and sale by the FDA or foreign regulatory authorities, whether alone or in collaboration with others;
- our success in educating physicians and patients about the benefits, administration and use of COR388;
- acceptance of COR388 as safe and effective by patients and the medical community;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of alternative and competing treatments;
- achieving and maintaining compliance with all regulatory requirements applicable to COR388;
- the effectiveness of our own or any future collaborators' marketing, pricing, coverage and reimbursement, sales and distribution strategies and operations;
- our ability to maintain our existing patents and obtain newly issued patents that cover COR388 and to enforce such patents and other intellectual property rights in and to COR388;
- our ability to avoid third-party intellectual property claims; and
- a continued acceptable safety profile of COR388 following approval.

Many of these factors are beyond our control. Accordingly, we cannot assure you that we will ever be able to generate revenue through the sale of COR388. If we are not successful in commercializing COR388, or are significantly delayed in doing so, our business will be materially harmed.

Our approach to the potential treatment of the underlying cause of Alzheimer's and other neurodegenerative diseases is based on a novel therapeutic approach, which exposes us to unforeseen risks.

We have discovered and are developing a proprietary library of protease inhibitors from which we have selected our lead drug candidate, COR388, which is under development to treat Alzheimer's disease and other degenerative diseases. Our approach is based on the discovery of *P. gingivalis* and its secreted virulence factor proteases, gingipains, and represents a new approach to disease modification in Alzheimer's disease. There is no current academic or general consensus on the causation of Alzheimer's disease or method of action or current drugs that purport to treat Alzheimer's disease. Based on the results of our preclinical and clinical studies to date, we believe COR388 is neuroprotective and with potential to prevent further neurodegeneration, reduce amyloid beta levels and reduce inflammation, when administered orally. However, these ideas and this approach are novel, and we currently have only limited data based on physiological mouse models of Alzheimer's disease and our Phase 1 a/b clinical trials which enrolled 67 subjects, including nine patients with mild to moderate Alzheimer's disease. Our physiological animal model may not result in disease modifying treatment in humans. We are not aware of any other brain-penetrating gingipain protease inhibitors being tested in humans. We may ultimately discover that COR388, or any of our other protease inhibitors, do not possess certain properties required for therapeutic effectiveness. We have no long-term evidence regarding the efficacy, safety and tolerability of COR388 or other compounds in our proprietary library of protease inhibitors in humans. We may spend substantial funds attempting to develop these drug candidates and never succeed in doing so.

Clinical drug development is a lengthy, expensive and uncertain process. The results of preclinical studies and early clinical trials are not always predictive of future results. Any drug candidate that we advance into clinical trials may not achieve favorable results in later clinical trials, if any, or receive marketing approval.

The research and development of drugs is extremely risky. Only a small percentage of drug candidates that enter the development process ever receive marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any drug candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain.

The results of preclinical studies and completed clinical trials are not necessarily predictive of future results, and our current drug candidate may not be further developed or have favorable results in later studies or trials. Clinical trial failure may result from a multitude of factors including, but not limited to, flaws in study design, dose selection, placebo effect, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits. As such, failure in clinical trials can occur at any stage of testing. A number of companies in the pharmaceutical industry have suffered setbacks in the advancement of their drug candidates into later-stage clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding results in earlier preclinical studies or clinical trials. The Phase 1a and Phase 1b clinical trials for our lead drug candidate, COR388, included only nine Alzheimer's patients and 58 healthy volunteers. Further, the results of our earlier stage clinical trials and our preclinical animal studies may not be predictive of the results of outcomes in later-stage clinical studies. For example, data from six Alzheimer's patients treated with COR388 in our Phase 1b clinical trial showed improvements across several exploratory cognitive tests. However, these improvements should be interpreted with caution because they were not all statistically significant. When evaluated in a larger patient population, COR388 may not show similar improvements toward cognitive effects or may demonstrate different chemical and pharmacological properties in patients in unforeseen or harmful ways. Based upon negative or inconclusive results, we may decide, or regulatory authorities may require us, to conduct additional clinical trials or preclinical studies. In addition, data obtained from preclinical trials and clinical trials are susceptible to varying interpretations, and regulatory authorities may not interpret our data as favorably as we do, which may further delay, limit or prevent development efforts, clinical trials or marketing approval. Furthermore, as more competing drug candidates within a particular class of drugs proceed through clinical development to regulatory review and approval, the amount and type of clinical data that may be required by regulatory authorities may increase or change.

If we are unable to complete preclinical studies or clinical trials of current or future drug candidates, due to safety concerns, or if the results of these trials are not sufficient to convince regulatory authorities of their safety or efficacy, we will not be able to obtain marketing approval for commercialization on a timely basis or at all. Even if we are able to obtain marketing approval for our current and any future drug candidates, those approvals may be for indications or dose levels that deviate from our desired approach or may contain other limitations that would adversely affect our ability to generate revenue from sales of those drug candidates. Moreover, if we are not able to differentiate our drug candidate against other approved drug candidates within the same class of drugs, or if any of the other circumstances described above occur, our business would be harmed and our ability to generate revenue from that class of drugs would be severely impaired.

Adverse side effects or properties or other safety risks associated with COR388 or any future drug candidates could delay or preclude approval, cause us to suspend or discontinue clinical trials, abandon further development, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

As is the case with pharmaceuticals generally, it is possible that there may be side effects and adverse events associated with the use of COR388 or any future drug candidates. COR388 was well-tolerated with no concerning safety signals in our Phase 1a and Phase 1b clinical trials. While some subjects experienced minor changes in electrocardiograms, or ECGs, in particular transient increases in the QRS duration and PR interval, these changes were not clinically significant, which means they did not result in the need to consider changes to the treatment of the patient. Similar measurements were seen at higher doses in animal studies. There were no discernable trends in the QTcF interval in human or animal studies. Relative to placebo, there were no patterns in laboratory abnormalities or changes in ECGs, vital signs or the results of physical examinations observed during these trials that would be deemed practically relevant to the treatment of the patient with COR388.

In addition, results of our Phase 2/3 GAIN trial, and future clinical trials, could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics as the clinical trials progress to longer exposures and a larger number of patients. Undesirable side effects caused by, or unexpected or unacceptable characteristics associated with, COR388 or any future drug candidates could result in the delay, suspension or termination of clinical trials by us, the FDA or other regulatory authorities for a number of reasons. We may also elect to limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which may limit the commercial expectations for such drug candidate if approved. If we elect or are required to further delay, suspend or terminate any clinical trial of any drug candidates that we develop, the commercial prospects of such drug candidates will be harmed and our ability to generate drug revenues from any such drug candidates will be delayed or eliminated.

It is possible that, as we test COR388 in our Phase 2/3 GAIN trial or other trials, or as the use of COR388 becomes more widespread if it receives regulatory approval, we may identify additional adverse events that were not identified or not considered significant in our earlier trials. If such side effects become later known in development or upon approval, if any, such findings may harm our business, financial condition, results of operations and prospects significantly. If we or others later identify undesirable side effects, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw, suspend or limit approval of COR388 or any future drug candidates;
- we may be required to recall a drug or change the way such drug is administered to patients;
- regulatory authorities may require additional warnings or statements in the labeling, such as a boxed warning or a contraindication or issue safety alerts, press releases or other communications containing warnings or other safety information about the drug candidate, for example, field alerts to physicians and pharmacies;

- regulatory authorities may require a medication guide outlining the risks of such side effects for distribution to patients, or that we implement a risk evaluation and mitigation strategy, or REMS, to ensure that the benefits of the drug outweigh its risks; we may be required to change the way a drug is distributed or administered, conduct additional clinical trials or change the labeling of a drug, or be required to conduct additional post-marketing studies or surveillance;
- we could be sued and held liable for harm caused to patients;
- sales of the drug may decrease significantly or COR388 or any future drug could become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of COR388 or any future drug candidates, if approved, and could significantly harm our business, financial condition, results of operations and prospects.

Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials.

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a drug candidate. Preclinical tests and Phase 1 and Phase 2 clinical trials are primarily designed to test safety, to study pharmacokinetics and pharmacodynamics and to understand the side effects of drug candidates at various doses and schedules. Success in preclinical or animal studies and early clinical trials does not ensure that later large-scale efficacy trials will be successful, nor does it predict final results. Our drug candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our drug candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

Partial clinical hold imposed by the FDA will prevent us from administering COR388 at much higher doses than currently utilized.

Preclinical data for COR388 showed toxicity at very high exposure levels in mice and, as a result, the FDA placed COR388 on partial clinical hold to enforce an exposure cap on COR388 dosages in humans at approximately 2.4 times the currently planned top dose in our Phase 2/3 GAIN trial. Although the FDA has permitted the continuation of clinical trials at the planned doses of COR388, if we determine that we need to increase the dosage of COR388 in humans, the partial hold may have a negative impact on our ability to carry out such clinical studies, which could delay or prevent the commercialization of COR388 and may harm our business and financial condition.

We may not be successful in our efforts to continue to create a pipeline of drug candidates or to develop commercially successful drugs. If we fail to successfully identify and develop additional drug candidates, our commercial opportunity may be limited.

One of our strategies is to identify and pursue clinical development of additional drug candidates. We currently have four programs in the early phase of development, all of which are in the research, discovery and preclinical stages of development. Identifying, developing, obtaining regulatory approval and commercializing additional drug candidates will require substantial additional funding and is prone to the risks of failure inherent in drug development. We cannot provide you any assurance that we will be able to successfully identify or acquire additional drug candidates, advance any of these additional drug candidates through the development process, successfully commercialize any such additional drug candidates, if approved, or assemble sufficient resources to identify, acquire, develop or, if approved, commercialize additional drug candidates. If we are unable to successfully identify, acquire, develop and commercialize additional drug candidates, our commercial opportunity may be limited.

We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our drug candidates.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our drug candidates, including:

- regulatory authorities, institutional review boards or ethics committees, or IRBs or ECs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site or we may fail to reach a consensus with regulatory authorities on trial design;
- regulatory authorities in jurisdictions in which we seek to conduct clinical trials may differ from each other on our trial design, and it may be difficult or impossible to satisfy all such authorities with one approach;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different contract research organizations, or CROs, and trial sites;
- clinical trials of our drug candidates may produce negative or inconclusive results, and we may decide, or regulatory authorities may require us, to conduct additional clinical trials or abandon drug development programs;
- the number of patients required for clinical trials of our drug candidates may be larger than we anticipate;
- enrollment in our clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- changes to clinical trial protocols;
- our third-party contractors, including clinical investigators, contract manufacturers and vendors may fail to comply with applicable regulatory requirements, lose their licenses or permits, or otherwise fail, or lose the ability to, meet their contractual obligations to us in a timely manner, or at all;
- we might have to suspend or terminate clinical trials of our drug candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- regulatory authorities or IRBs may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our drug candidates may be greater than we anticipate, and we may lack adequate funding to continue one or more clinical trials;
- the supply or quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate;
- our drug candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulatory authorities or institutional review boards to suspend or terminate the trials; and
- occurrence of serious adverse events in trials of the same class of agents conducted by other companies.

Clinical trials are expensive and time consuming, additional or unsuccessful clinical trials could cause our clinical development activities to be delayed or otherwise adversely affected.

If we are required to conduct additional clinical trials or other testing of our drug candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our drug candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

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

Drug development costs will also increase if we experience delays in testing or in obtaining marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be amended 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 drug candidates, could allow our competitors to bring drug candidates to market before we do, and could impair our ability to successfully commercialize our drug candidates, if approved, any of which may harm our business and results of operations. In addition, many of the factors that cause, or lead to a delay in the commencement or completion of, clinical trials may also ultimately lead to termination or suspension of a clinical trial. Any of these occurrences may harm our business, financial condition and prospects significantly. Any termination of any clinical trial of our drug candidates will harm our commercial prospects and our ability to generate revenues.

Risks Relating to Regulatory Review and Approval of Our Drug Candidates and Other Legal Compliance Matters

We cannot be certain that COR388 or any of our future drug candidates will receive regulatory approval, and without regulatory approval we will not be able to market our drug candidates.

We currently have no drug candidates approved for sale and we cannot guarantee that we will ever have marketable drug candidates. We are initially developing COR388 for the treatment of patients with Alzheimer's disease and are also consulting with investigators to consider other possible indications. Our ability to generate revenue related to sales, if ever, will depend on the successful development and regulatory approval of COR388 for the treatment of Alzheimer's disease and other indications.

The development of a drug candidate and issues relating to its approval and marketing are subject to extensive regulation by the FDA in the United States, the EMA in Europe and regulatory authorities in other countries, with regulations differing from country to country. We are not permitted to market our drug candidates in the United States or Europe until we receive approval of a new drug application, or NDA, from the FDA or a marketing authorization application, or MAA, from the EMA, respectively. We have not submitted any marketing applications for any of our drug candidates.

NDAs and MAAs must include extensive preclinical and clinical data and supporting information to establish the drug candidate's safety and effectiveness for each desired indication. NDAs and MAAs must also include significant information regarding the chemistry, manufacturing and controls for the drug. Obtaining approval of a NDA or a MAA is a lengthy, expensive and uncertain process, and we may not be successful in obtaining approval. The FDA and the EMA review processes can take years to complete and approval is never guaranteed. If we submit a NDA to the FDA, the FDA must decide whether to accept or reject the submission for filing. We cannot be certain that any submissions will be accepted for filing and review by the FDA. Regulators of other jurisdictions, such as the EMA, have their own procedures for approval of drug candidates. Even if a drug is approved, the FDA or the EMA, as the case may be, may limit the indications for which the drug may be marketed, require extensive warnings on the drug labeling or require expensive and time-consuming clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the United States and Europe also have requirements for approval of drug candidates with which we must comply prior to marketing in those countries. Obtaining regulatory approval for marketing of a drug candidate in one country does not ensure that we will be able to obtain regulatory approval in any other country. In addition, delays in approvals or rejections of marketing applications in the United States, Europe or other countries may be based upon many factors, including regulatory requests for additional analyses, reports, data, preclinical studies and clinical trials, regulatory questions regarding different interpretations of data and results, changes in regulatory policy during the period of drug development and the emergence of new information regarding our drug candidates or other drug candidates. Also, regulatory approval for any of our drug candidates may be withdrawn.

We initiated our Phase 2/3 GAIN trial in patients with Alzheimer's disease in April 2019. Before we submit a NDA to the FDA or a MAA to the EMA for COR388 for the treatment of patients with Alzheimer's disease, we must successfully complete at least our Phase 2/3 GAIN trial and potentially additional late-stage clinical trials. The FDA generally requires two pivotal clinical trials to support approval. In addition, we must scale up manufacturing and complete other standard preclinical and clinical studies. We cannot predict whether our future trials will be successful or whether regulators will agree with our conclusions regarding the preclinical studies and clinical trials we have conducted to date and will conduct in the future.

We have concentrated our research and development efforts on the treatment of degenerative diseases, a field that has seen very limited success in drug development. Further, our drug candidates are based on new approaches and novel technology, which makes it difficult to predict the time and cost of drug candidate development and the regulatory approval process.

We have focused our research and development efforts on addressing degenerative diseases. Collectively, efforts by pharmaceutical companies in the field of degenerative diseases have seen very limited successes in drug development. There are few effective therapeutic options available for patients with Alzheimer's disease and other degenerative diseases. Our future success is highly dependent on the successful development of our technology and our drug candidates for treating degenerative diseases. Developing and, if approved, commercializing our drug candidates for treatment of degenerative diseases subjects us to a number of challenges, including ensuring that we have selected the optimal dose of the therapeutic to block gingipains in the brain, executing an appropriate trial to test for efficacy and obtaining regulatory approval from the FDA and other regulatory authorities.

Our approach to the treatment of degenerative diseases aims to understand the cause of disease pathogensis, select the right patient population, discover and develop potent and selective small molecules that act directly in the brain or other organs on these targets, and leverage both preclinical and human pharmacodynamic data for dose selection. This strategy may not prove to be successful. We cannot be sure that our approach will yield satisfactory therapeutic drug candidates that are safe and effective, scalable, or profitable. Moreover, public perception of drug safety issues, including adoption of new therapeutics or novel approaches to treatment, may adversely influence the willingness of subjects to participate in clinical trials, or if approved, of physicians to prescribe novel treatments.

Clinical failure can occur at any stage of clinical development and we have never conducted a Phase 3 trial or submitted an NDA or MAA before.

We have initiated our Phase 2/3 GAIN trial for Alzheimer's disease. The conduct of our Phase 2/3 GAIN trials and the submission of a successful NDA is a complicated process. As an organization, we have never conducted a registrational clinical trial and have limited experience in preparing, submitting and prosecuting regulatory filings, and have not submitted a NDA. Failure to commence or complete, or delays in, our planned clinical trials would prevent us from or delay us in seeking approval for, and if approved, commercializing our drug candidates, and failure to successfully complete any of these activities in a timely manner for any of our drug candidates could have a material adverse impact on our business and financial performance. The commencement, enrollment and completion of clinical trials can be delayed or suspended for a variety of reasons, including:

- inability to obtain sufficient funds required for a clinical trial;
- inability to reach agreements on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical holds, other regulatory objections to commencing or continuing a clinical trial or the inability to obtain regulatory approval to commence a clinical trial in countries that require such approvals;
- discussions with the FDA or non-U.S. regulators regarding the scope or design of our clinical trials;
- inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same indications targeted by our drug candidates;
- inability to obtain approval from IRBs to conduct a clinical trial at their respective sites;
- severe or unexpected drug-related adverse effects experienced by patients;
- inability to timely manufacture sufficient quantities of the drug candidate required for a clinical trial;
- difficulty recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including meeting the enrollment criteria for our study and competition from other clinical trial programs for the same indications as our drug candidates;
- inability to retain enrolled patients after a clinical trial is underway; and
- enrollment may be delayed or interrupted or patients may drop out of clinical trials such as our Phase 2/3 Gain trial due to or the fear of natural disasters, such as earthquakes, tsunamis, power shortages or outages, floods, or monsoons, public health crises, such as pandemics and epidemics, political crisis, such as terrorism, war, political instability or other conflict, cyberattacks, or other events outside of our control occurring at or around our clinical trials sites in the United States or Europe. For example, the coronavirus outbreak may delay or impede enrollment in our clinical trials due to prioritization of hospital resources toward the outbreak, and some patients may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services, which would delay our ability to release clinical results and could impact our product candidate testing, development and timelines.

In addition, the design of a clinical trial can determine whether its results will support approval of a drug and flaws in the design of a clinical trial may not become apparent until the clinical trial is well-advanced. Changes in regulatory requirements and guidance may also occur and we may need to amend clinical trial protocols to reflect these changes with appropriate regulatory authorities. Amendments may require us to resubmit clinical trial protocols to IRBs for re-examination, which may impact the costs, timing or successful completion of a clinical trial.

In addition, if we are required to conduct additional clinical trials or other preclinical studies of our drug candidates beyond those contemplated, our ability to obtain regulatory approval of these drug candidates and generate revenue from their sales would be similarly harmed.

If clinical trials of our drug candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA or similar regulatory authorities outside the United States 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 drug candidates.

Before obtaining regulatory approvals for the commercial sale of any of our drug candidates, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our drug candidates are both safe and effective for use in each target indication. Each drug candidate must demonstrate an adequate risk versus benefit profile in its intended patient population and for its intended use.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies of our drug candidates may not be predictive of the results of early-stage or later-stage clinical trials, and results of early clinical trials of our drug candidates may not be predictive of the results of later-stage clinical trials. The results of clinical trials in one set of patients or disease indications may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same drug candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. Drug candidates in later stages of clinical trials may fail to show the desired safety and efficacy profile despite having progressed through preclinical studies and initial clinical trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. This is particularly true in degenerative diseases, where failure rates historically have been higher than in many other disease areas. Most drug candidates that begin clinical trials are never approved by regulatory authorities for commercialization.

In addition, even if such clinical trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our drug candidates for approval. Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or other regulatory authorities. The FDA or other regulatory authorities may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected the integrity of the study. The FDA or other regulatory authorities may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or other regulatory authorities, as the case may be, and may ultimately lead to the denial of marketing approval of any of our drug candidates. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our drug candidates. Even if regulatory approval is secured for any of our drug candidates, the terms of such approval may limit the scope and use of our drug candidate, which may also limit its commercial potential.

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

We currently rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct some aspects of our research and preclinical testing and our clinical trials. Any of these third parties may terminate their engagements with us or be unable to fulfill their contractual obligations. If we need to enter into alternative arrangements, it would delay our drug development activities.

Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with current good clinical practice regulations, or GCP, for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible, reproducible and accurate and that the rights, integrity, and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any drug candidates we may develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines.

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

We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer, more advanced or more effective than ours.

The development and commercialization of new drugs is highly competitive. Moreover, the degenerative disease field is characterized by strong competition and a strong emphasis on intellectual property. We may face competition with respect to any drug candidates that we seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of large pharmaceutical and biotechnology companies that are currently pursuing the development of drug candidates for the treatment of the degenerative disease indications for which we have research programs, including Alzheimer's disease. Companies that we are aware are developing therapeutics in the degenerative disease field include large companies with significant financial resources, such as AbbVie Inc., Biogen Inc., Eli Lilly and Company, Eisai Co., Ltd., Merck & Company, Inc., Novartis AG, and Roche Holding AG Group (including Genentech, its wholly owned subsidiary), as well as companies pursuing a dysfunctional immune system approach to Alzheimer's disease or other types of therapies.

Many of our current or potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved drug candidates than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drug candidates that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any drug candidates that we may develop. Furthermore, currently approved drug candidates could be discovered to have application for treatment of degenerative disease indications, which could give such drug candidates significant regulatory and market timing advantages over any of our drug candidates. Our competitors also may obtain FDA, EMA or other regulatory approval for their drug candidates more rapidly than we may obtain approval for ours from the FDA for indications our drug candidates are targeting, which could result in our competitors establishing a strong market position before we are able to enter the market.

Additionally, drug candidates or technologies developed by our competitors may render our potential drug candidates uneconomical or obsolete, and we may not be successful in marketing any drug candidates we may develop against competitors. If our competitors market drug candidates that are more effective, safer or less expensive than our drug candidates, if approved, or that reach the market sooner than our drug candidates, if approved, we may not achieve commercial success. In addition, the pharmaceutical industry is characterized by rapid technological change. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or drug candidates developed by our competitors may render our technologies or drug candidates obsolete, less competitive or not economical.

If we or any of our third-party manufacturers encounter difficulties in production of our current or any future drug candidate, or fail to meet rigorously enforced regulatory standards, our ability to provide supply of our drug candidates for clinical trials or for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.

The processes involved in manufacturing our drug candidates are highly regulated and subject to multiple risks. As drug candidates are developed through preclinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our drug candidates to perform differently and affect the results of planned clinical trials or other future clinical trials.

In order to conduct clinical trials of our drug candidates, or supply commercial drug candidates, if approved, we will need to manufacture them in small and large quantities. We currently rely on third parties to manufacture COR388 for clinical trial purposes, and our manufacturing partners will have to modify and scale-up the manufacturing process when we transition to commercialization of our drug candidates. Our manufacturing partners may be unable to successfully modify or scale-up the manufacturing capacity for any of our drug candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If our manufacturing partners are unable to successfully scale-up the manufacture of our drug candidates in sufficient quality and quantity, the development, testing and clinical trials of that drug candidate may be delayed or become infeasible, and regulatory approval or commercial launch of any resulting drug may be delayed or not obtained, which could

significantly harm our business. The same risks would apply to our internal manufacturing facilities, should we in the future decide to build internal manufacturing capacity. In addition, building internal manufacturing capacity would carry significant risks in terms of being able to plan, design and execute on a complex project to build manufacturing facilities in a timely and cost-efficient manner.

In addition, the manufacturing process for any drug candidates that we may develop is subject to FDA, EMA and foreign regulatory requirements, and continuous oversight, and we will need to contract with manufacturers who can meet all applicable FDA, EMA and foreign regulatory authority requirements, including complying with current good manufacturing practices, or cGMPs, on an ongoing basis. If we or our third-party manufacturers are unable to reliably produce drug candidates in accordance with the requirements of the FDA, EMA or other regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such drug candidates. Even if we obtain regulatory approval for any of our drug candidates, there is no assurance that either we or our third party contract manufacturers will be able to manufacture the approved drug in accordance with the requirements of the FDA, EMA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the drug, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our drug candidate, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations and growth prospects.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any drug candidates we may develop, we may not be successful in commercializing those drug candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing, or distribution of pharmaceutical drug candidates. To achieve commercial success for any approved drug candidate for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing, and commercial support infrastructure to sell, or participate in sales activities with collaborators for, some of our drug candidates if and when they are approved.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, factors that may inhibit our efforts to commercialize any approved drug candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales, marketing, coverage or reimbursement, customer service, medical affairs, and other support personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future approved drug candidates;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors;
- the inability to price our drug candidates at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our drug candidates to segments of the patient population;
- the lack of complementary drug candidates to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive drug candidate lines; and
- unforeseen costs and expenses associated with creating an independent commercialization organization.

If the commercial launch of a drug candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel.

If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our sales revenue or the profitability of sales revenue may be lower than if we were to market and sell any drug candidates we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our drug candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our drug candidates effectively. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our drug candidates if approved.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our drug candidates.

We face an inherent risk of product liability as a result of the clinical testing of our drug candidates and will face an even greater risk when and if we commercialize any drug candidates. For example, we may be sued if our drug candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Product liability claims may be brought against us by participants enrolled in our clinical trials, patients, health care providers or others using, administering or selling our drug candidates. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit testing and commercialization of our drug candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased or interrupted demand for our drug candidates;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- drug recalls, withdrawals or labeling, marketing or promotional restrictions;
- termination of clinical trial sites or entire trial programs;
- injury to our reputation and significant negative media attention;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any drug candidate; and
- a decline in our share price.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of drug candidates we develop, alone or with potential collaborators. Our insurance policies may have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

We may be exposed to a variety of international risks that could materially adversely affect our business.

We may enter into agreements with third parties for the development and commercialization of drug candidates in international markets. International business relationships will subject us to additional risks that may materially adversely affect our ability to attain or sustain profitable operations, including:

- differing regulatory requirements for drug approvals internationally;
- potentially reduced protection for intellectual property rights;
- potential third-party patent rights in countries outside of the United States;
- the potential for so-called "parallel importing," which is what occurs when a local seller, faced with relatively high local prices, opts to import goods from another jurisdiction with relatively low prices, rather than buying them locally;
- unexpected changes in tariffs, trade barriers and regulatory requirements;

- economic weakness, including inflation, or political instability, particularly in non-U.S. economies and markets, including several countries in Europe;
- compliance with tax, employment, immigration and labor laws for employees traveling abroad;
- taxes in other countries;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, 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 geo-political actions, including war and terrorism, or natural disasters, including earthquakes, volcanoes, typhoons, floods, hurricanes and fires.

Natural disasters, public health crises, political crises, and other catastrophic events or other events outside of our control may be detrimental to our capabilities or the capabilities of third parties on which we depend.

Our headquarters are located in California near major geologic faults that have experienced earthquakes in the past. An earthquake or other natural disaster or power shortages or outages could disrupt operations, impair critical systems or result in loss of clinical samples. Any of these disruptions or other events outside of our control could have a material adverse impact on our business, harming our operating results. In addition, if any of our suppliers or third-party service providers, such as our manufacturing partners or CROs, are affected by natural disasters, such as earthquakes, tsunamis, power shortages or outages, floods or monsoons, public health crises, such as pandemics and epidemics, political crises, such as terrorism, war, political instability or other conflict, cyberattacks, or other events outside of our control, our business and operating results could suffer. Disasters, public health crises and political crises occurring at third-party facilities also could negatively impact our clinical development and regulatory approval timelines, our reputation and the perception of our company. For example, if the COVID-19 outbreak continues to spread, we or our third-party service providers may need to limit operations or implement limitations, including work-from-home policies. Furthermore, new quarantines for COVID-19 or other viruses could impact personnel at contract manufacturing facilities in China, Europe or elsewhere to deliver key materials or the availability or cost of starting materials. Any disruption of our ability to manufacture COR388 or the ability of our contract manufacturing vendors in China, Europe or elsewhere to deliver key materials on a timely basis could have a material adverse effect on the initiation of new trials, the duration of open label extension studies and overall product development.

We will need to expand our operations and increase the size of our company, and we may experience difficulties in managing growth.

As we increase the number of ongoing drug development programs and advance our drug candidates through preclinical studies and clinical trials, we will need to increase our drug development, scientific and administrative headcount to manage these programs. In addition, to meet our obligations as a public company, we will need to increase our general and administrative capabilities. Our management, personnel and systems currently in place may not be adequate to support this future growth. Our need to effectively manage our operations, growth and various projects requires that we:

- successfully attract and recruit new employees or consultants with the expertise and experience we will require;
- manage our clinical programs effectively, which we anticipate being conducted at numerous clinical sites;
- develop a marketing and sales infrastructure; and
- continue to improve our operational, financial and management controls, reporting systems and procedures.

If we are unable to successfully manage this growth and increased complexity of operations, our business may be adversely affected.

We may not be able to manage our business effectively if we are unable to attract and retain key personnel and consultants.

We may not be able to attract or retain qualified management, finance, scientific and clinical personnel and consultants due to the intense competition for qualified personnel and consultants among biotechnology, pharmaceutical and other businesses. If we are not able to attract and retain necessary personnel and consultants to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of Casey C. Lynch, our co-founder, and President and Chief Executive Officer. If we lose our Chief Executive Officer, our ability to implement our business strategy successfully could be seriously harmed. Any of our executive officers or key employees or consultants may terminate their employment at any time.

Replacing executive officers, key employees and consultants may be difficult and may take an extended period because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize drug candidates successfully. Competition to hire and retain employees and consultants from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel and consultants. Our failure to retain key personnel or consultants could materially harm our business.

We have scientific and clinical advisors and consultants who assist us in formulating our research, development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. Non-compete agreements are not permissible or are limited by law in certain jurisdictions and, even where they are permitted, these individuals typically will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. In addition, our advisors may have arrangements with other companies to assist those companies in developing drug candidates or technologies that may compete with ours.

Failure to build our finance infrastructure and improve our accounting systems and controls could impair our ability to comply with the financial reporting and internal controls requirements for publicly traded companies.

As a public company, we operate in an increasingly demanding regulatory environment, which requires us to comply with the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, the regulations of Nasdaq Global Select Market, the rules and regulations of the Securities and Exchange Commission, expanded disclosure requirements, accelerated reporting requirements and more complex accounting rules. Company responsibilities required by the Sarbanes-Oxley Act include establishing corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud. Commencing in 2020, we must perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Form filing for 2020, as required by Section 404 of the Sarbanes-Oxley Act. Prior to our initial public offering in May 2019, we had never been required to test our internal controls within a specified period and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner.

We anticipate that the process of building our accounting and financial functions and infrastructure will require significant additional professional fees, internal costs and management efforts. We expect that we will need to implement a new internal system to combine and streamline the management of our financial, accounting, human resources and other functions. However, such a system would likely require us to complete many processes and procedures for the effective use of the system or to run our business using the system, which may result in substantial costs. Any disruptions or difficulties in implementing or using such a system could adversely affect our controls and harm our business. Moreover, such disruption or difficulties could result in unanticipated costs and diversion of management attention. In addition, we may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. For example, we previously reported a material weakness in internal control over financial reporting related to the fact that we had not deployed adequate qualified resources in our corporate accounting department which resulted in material audit adjustments that were needed to modify the financial statements to comply with accounting principles generally accepted in the United States. Certain transactions were not adequately analyzed for accounting ramifications and accounting records contained errors and inaccuracies. During 2019, we completed the remediation measures related to the material weakness. Completion of remediation does not provide assurance that our remediation or other controls will continue to operate properly.

Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system’s objectives will be met.

Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed, investors could lose confidence in our reported financial information and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities.

Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading, which could significantly harm our business.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties 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 health care 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 health care 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 serious harm to our reputation. 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, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Our insurance policies are expensive and only protect us from some business risks, which will leave us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, products liability and directors' and officers' insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our financial position and results of operations.

Failure to comply with health and data protection laws and regulations could lead to government enforcement actions, which could include civil or criminal penalties, private litigation, and/or adverse publicity and could negatively affect our operating results and business.

We and any of our potential collaborators may be subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws, that govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of collaborators. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH. Depending on the facts and circumstances, we could be subject to civil, criminal, and administrative penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

Several foreign jurisdictions, including the European Union, or the EU, its member states, the United Kingdom and Australia, among others, have adopted legislation and regulations that increase or change the requirements governing the collection, use, disclosure and transfer of the personal information of individuals in these jurisdictions. These laws and regulations are complex and change frequently, at times due to changes in political climate, and existing laws and regulations are subject to different and conflicting interpretations, which adds to the complexity of processing personal data from these jurisdictions. These laws have the potential to increase costs of compliance, risks of noncompliance and penalties for noncompliance.

The General Data Protection Regulation, or GDPR, replaced the EU Data Protection Directive on May 25, 2018. The GDPR introduced new data protection requirements in the EU, as well as potential fines for noncompliant companies of up to the greater of €20 million or 4% of annual global revenue. The regulation imposes numerous new requirements for the collection, use and disclosure of personal information, including more stringent requirements relating to consent and the information that must be shared with data subjects about how their personal information is used, the obligation to notify regulatory authorities and affected individuals of personal data breaches, extensive new internal privacy governance obligations, and obligations to honor expanded rights of individuals in relation to their personal information (for example, the right to access, correct and delete their data). In addition, the GDPR generally maintains the EU Data Protection Directive's restrictions on cross-border data transfer. The GDPR will increase our responsibility and liability in relation to personal data that we process, and we may be required to put in place additional potential mechanisms to ensure compliance with the new EU data protection rules.

Further, the United Kingdom's vote in favor of exiting the EU (often referred to as "Brexit") has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear whether the United Kingdom will enact data protection legislation equivalent to the GDPR and how data transfers to and from the United Kingdom will be regulated.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal and administrative penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

Changes in healthcare law and implementing regulations, as well as changes in healthcare policy, may impact our business in ways that we cannot currently predict, and may have a significant adverse effect on our business and results of operations.

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of drug candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any drug candidates for which we obtain marketing approval. Among policy makers and payors in the United States and elsewhere, including in the European Union, or EU, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/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.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the Affordable Care Act, substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The Affordable Care Act, among other things: (i) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and expanded rebate liability from fee-for-service Medicaid utilization to include the utilization of Medicaid managed care organizations as well; (ii) established a branded prescription drug fee that pharmaceutical manufacturers of branded prescription drugs must pay to the federal government; (iii) expanded the list of covered entities eligible to participate in the 340B drug pricing program by adding new entities to the program; (iv) established a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; (v) extended manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations; (vi) 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 individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability; (vii) established 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 (viii) established a Center for Medicare Innovation at the Centers for Medicare and Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the Affordable Care Act. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the Affordable Care Act or otherwise circumvent some of the requirements for health insurance mandated by the Affordable Care Act. Additionally, CMS promulgated regulations in 2018 that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the Affordable Care Act for plans sold through such marketplaces. Concurrently, Congress has considered legislation that would repeal, or repeal and replace, all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. The Tax Cuts and Jobs Act of 2017, or the Tax Act, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act 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." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the Affordable Care Act are invalid as well. While the Trump Administration and the Centers for Medicare & Medicaid Services, or CMS, have both stated that the ruling will have no immediate effect, it is unclear how this decision, subsequent appeals, if any, and other efforts to repeal and replace the Affordable Care Act will

impact the Affordable Care Act and our business. Moreover, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress may consider additional legislation to repeal, or repeal and replace, other elements of the Affordable Care Act. We continue to evaluate the Affordable Care Act and its possible repeal and replacement, as it remains uncertain the extent to which any such changes may impact our business or financial condition.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year pursuant to the Budget Control Act of 2011 and subsequent laws, which began in 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027 unless additional Congressional action is taken. New laws may result in additional reductions in Medicare and other healthcare funding, which may adversely affect customer demand and affordability for our drug candidates and, accordingly, the results of our financial operations. Additional changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, which will first affect physician payment in 2019. At this time, it is unclear how the introduction of the Medicare quality payment program will impact overall physician reimbursement.

Also, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed drug candidates, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological drug pricing, including price or patient reimbursement constraints, discounts, restrictions on certain drug access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, since 2016, Vermont requires certain manufacturers identified by the state to justify their price increases. Similar prescription drug price transparency laws have been enacted in Oregon and California, and more are pending in several other states.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients with life-threatening diseases or conditions to access certain investigational new drug candidates that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drugs available to eligible patients as a result of the Right to Try Act.

We expect that these and other 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 drug candidate. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drug candidates, once marketing approval is obtained.

Our ability to successfully commercialize any drugs that we develop depends in part on the extent to which coverage and adequate reimbursement are available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, each individually decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Government authorities currently impose mandatory discounts for certain patient groups, such as Medicare, Medicaid and Veterans Affairs, or VA, hospitals, and may seek to increase such discounts at any time. Future regulation may negatively impact the price of our product candidates, if approved. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage or reimbursement will be available for any drug candidate that we commercialize and, if coverage or reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any drug candidate for which we obtain marketing approval. In order to get coverage and reimbursement, physicians may need to show that patients have superior treatment outcomes with our products compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any drug candidate for which we obtain marketing approval. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors, and coverage decisions and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the medicine is approved by the FDA, EMA or other comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, but make their determinations independently and may impose additional restrictions. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize drug candidates, and our overall financial condition.

In the EU, coverage and reimbursement status of any drug candidates for which we obtain regulatory approval are provided for by the national laws of EU Member States. The requirements may differ across the EU Member States. Also, at national level, actions have been taken to enact transparency laws regarding payments between pharmaceutical companies and health care professionals.

If we engage in acquisitions, we will incur a variety of costs and we may never realize the anticipated benefits of such acquisitions.

Although we currently have no plans to do so, we may attempt to acquire businesses, technologies or drug candidates that we believe are a strategic fit with our business. If we do undertake any acquisitions, the process of integrating an acquired business, technology or drug candidates into our business may result in unforeseen operating difficulties and expenditures, including diversion of resources and management's attention from our core business. In addition, we may fail to retain key executives and employees of the companies we acquire, which may reduce the value of the acquisition or give rise to additional integration costs. Future acquisitions could result in additional issuances of equity securities that would dilute the ownership of existing stockholders. Future acquisitions could also result in the incurrence of debt, contingent liabilities or the amortization of expenses related to other intangible assets, any of which could adversely affect our operating results. In addition, we may fail to realize the anticipated benefits of any acquisition.

We are currently conducting and in the future may conduct clinical trials for our drug candidates outside the United States, and the FDA, EMA and applicable foreign regulatory authorities may not accept data from such trials.

We currently are conducting parts of the GAIN trial outside the United States and in the future choose to conduct one or more of our clinical trials outside the United States, including in Europe. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA, EMA or applicable foreign regulatory authorities may be subject to certain conditions. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to cGCP regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA or any applicable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA, EMA or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our drug candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

Interim, top-line and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or top-line data from our clinical studies, which are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top-line data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our clinical studies.

In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular drug candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, drug candidate or our business. If the top-line data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our drug candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

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

The ability of the FDA to review and approve new drugs can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the 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 other government agencies 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 prolong 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, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA 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.

Even if we obtain regulatory approval for a drug candidate, it will remain subject to extensive ongoing regulatory review and requirements.

If any of our drug candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive requirements imposed by the FDA, EMA and comparable foreign regulatory authorities, including ensuring that quality control and manufacturing procedures conform to cGMPs regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA or MAA. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our drug candidates will be subject to limitations on the approved indicated uses for which the drug candidate may be marketed and promoted or to the conditions of approval (including the potential for a requirement to implement a Risk Evaluation and Mitigation Strategy), or contain requirements for potentially costly post-marketing testing. We will be required to report certain adverse reactions and production problems, if any, to the FDA, EMA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in drug development or commercialization, or increased costs to assure compliance. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of drug candidates to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. We will have to comply with requirements concerning advertising and promotion for our drug candidates. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the drug candidate's approved label. As such, we may not promote our drug candidates for indications or uses for which they do not have approval. The holder of an approved NDA or MAA must submit new or supplemental applications and obtain approval for certain changes to the approved drug candidate labeling, or manufacturing process. We could also be asked to conduct post-marketing clinical trials to verify the safety and efficacy of our drug candidates in general or in specific patient subsets. If original marketing approval was obtained via the accelerated approval pathway, we could be required to conduct a successful post-marketing clinical trial to confirm clinical benefit for our drug candidates. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval.

If a regulatory agency discovers previously unknown problems with a drug, such as adverse events of unanticipated severity or frequency, or problems with the facility where the drug candidate is manufactured, or disagrees with the promotion, marketing or labeling of a drug candidate, such regulatory agency may impose restrictions on that drug candidate or us, including requiring withdrawal of the drug candidate from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue warning or untitled letters that would result in adverse publicity;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approvals;
- suspend any of our ongoing clinical trials;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;
- require us to enter into a consent decree or permanent injunction, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- withdraw regulatory approval;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities;
- seize or detain drug candidates; or
- require a drug candidate recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our drug candidates. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

The policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these executive actions will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose restrictions on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

Non-compliance by us or any future collaborator with regulatory requirements, including safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population can also result in significant financial penalties.

If we fail to comply with healthcare laws, we could face substantial penalties and our business, operations and financial condition could be adversely affected.

Our operations are subject to various federal and state fraud and abuse laws. The laws that may impact our operations include:

- federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, 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 False Claims Act;

- federal civil and criminal false claims laws and civil monetary penalty laws, including the False Claims Act, which impose criminal and civil penalties, including through civil "qui tam" or "whistleblower" actions, against individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other third-party payors that are false or fraudulent or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization;
- the federal Physician Payment Sunshine Act, created under the Affordable Care Act, and its implementing regulations, which require manufacturers of drugs, devices and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the U.S. Department of Health and Human Services under the Open Payments Program, information related to payments or other transfers of value made to physicians, certain other healthcare professionals and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payer, 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 that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; 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.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities, including compensating physicians with stock or stock options, could, despite our efforts to comply, be subject to challenge under one or more of such laws. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our drug candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

If we or any contract manufacturers and suppliers we engage 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 and any contract manufacturers and suppliers we engage are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and radioactive materials. Our operations also produce hazardous waste. 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. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research, drug development and manufacturing efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. 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, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific hazardous waste insurance coverage, and our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our business activities may be subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery and anti-corruption laws.

Our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we may operate, including the U.K. Bribery Act. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently the Securities and Exchange Commission, or SEC, and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents, contractors, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of our facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our drug candidates in one or more countries and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize potential future drug candidates.

While we currently have no intention to enter into a collaboration agreement for COR388, in the future we may consider collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of drug candidates depending on the merits of retaining or divesting some or all commercialization rights. We will face, to the extent that we decide to enter into collaboration agreements, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time-consuming to negotiate, document, implement and maintain. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements should we so chose to enter into such arrangements. The terms of any collaborations or other arrangements that we may establish may not be favorable to us.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include that:

- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of our drug candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to the acquisition of competitive drug candidates, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a drug candidate, repeat or conduct new clinical trials or require a new formulation of a drug candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, drug candidates that compete directly or indirectly with our drug candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more drug candidates may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that causes the delay or termination of the research, development or commercialization of our current or future drug candidates or that results in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated, and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable current or future drug candidates;
- collaborators may own or co-own intellectual property covering our drug candidates that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and
- a collaborator’s sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

Risks Relating to Our Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for our drug candidates, or if the scope of the intellectual property protection is not sufficiently broad, our competitors could develop and commercialize drug candidates similar or identical to ours, and our ability to successfully commercialize our drug candidates may be adversely affected.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection of our current and future drug candidates and the methods used to manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our drug candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

The patent positions of biotechnology and pharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States or in many jurisdictions outside of the United States. Changes in either the patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be enforced in the patents that may be issued from the applications we currently or may in the future own or license from third parties. Further, if any patents we obtain or license are deemed invalid and unenforceable, our ability to commercialize or license our technology could be adversely affected.

Others may have filed, and in the future are likely to file, patent applications covering drug candidates that are similar, identical or competitive to ours or important to our business. We cannot be certain that any patent application owned by a third party will not have priority over patent applications filed or in-licensed by us, or that we or our licensors will not be involved in interference, opposition or invalidity proceedings before U.S. or non-U.S. patent offices.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use our drug candidates and proprietary technologies and erode or negate any competitive advantage we may have, which could have a material adverse effect on our financial condition and results of operations. For example:

- others may be able to make compounds that are similar to our drug candidates but that are not covered by the claims of our patents;
- we might not have been the first to make the inventions covered by our pending patent applications;
- we might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- any patents that we obtain may not provide us with any competitive advantages;
- we may not develop additional proprietary technologies that are patentable; or
- the patents of others may have an adverse effect on our business.

We have applied, and we intend to continue applying, for patents covering aspects of our drug candidates, proprietary technologies and their uses that we deem appropriate. However, we may not be able to apply for patents on certain aspects of our current or future drug candidates, proprietary technologies and their uses in a timely fashion, at a reasonable cost, in all jurisdictions, or at all, and any potential patent coverage we obtain may not be sufficient to prevent substantial competition. As of December 31, 2019, we were the owner of record of three issued U.S. patents, one non-U.S. patent, and 59 pending U.S. and non-U.S. patent applications (collectively, “the Cortexyme patent portfolio”).

Two issued U.S. patents in the Cortexyme patent portfolio relate to COR388, with claims directed to COR388 and related pharmaceutical compounds, pharmaceutical compositions containing these compounds, and methods of using these compounds in the treatment of various indications. Pending U.S. and non-U.S. patent applications in the Cortexyme patent portfolio relate to COR388 and related pharmaceutical compounds, pharmaceutical compositions containing these compounds, methods of using these compounds in the treatment of various indications, and methods of making these compounds.

In addition, one issued U.S. patent in the Cortexyme patent portfolio relates to pharmaceutical compounds that do not encompass COR388, with claims directed to pharmaceutical compounds, pharmaceutical compositions containing these compounds, and methods of using these compounds in the treatment of various indications. Pending U.S. and non-U.S. patent applications relate to additional compounds in these areas; as well as to diagnostic methods and assay methods.

Without patent protection on the composition of matter of our drug candidates, our ability to assert our patents to stop others from using or selling our drug candidates in a non-pharmaceutically acceptable formulation may be limited. Due to the patent laws of a country, or the decisions of a patent examiner in a country, or our own filing strategies, we may not obtain patent coverage for all of our drug candidates or methods involving the use of these candidates in a particular patent application. We plan to pursue divisional patent applications or continuation patent applications in the United States and other countries, where applicable, to obtain claim coverage for inventions which were disclosed but not claimed in a particular parent patent application.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our actual or potential future collaborators will be successful in protecting our drug candidates, proprietary technologies and their uses by obtaining and/or defending patents. These risks and uncertainties include the following:

- the U.S. Patent and Trademark Office, or USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;

- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use and sell our potential drug candidates;
- other parties may have designed around our claims or developed technologies that may be related or competitive to our platform, may have filed or may file patent applications and may have received or may receive patents that overlap or conflict with our patent applications, either by claiming the same compounds, compositions or methods or by claiming subject matter that could dominate our patent position;
- any successful opposition to any patents owned by or licensed to us could deprive us of rights necessary to prevent others from practicing our technologies or to successfully commercialize any drug candidates that we may develop;
- because patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our drug candidates, proprietary technologies and their uses;
- an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of applications we may in-license which have an effective filing date before March 16, 2013;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing drug candidates.

The patent prosecution process is also expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. We may also rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or feasible. However, trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

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. Further, our issued patents could be found invalid or unenforceable if challenged in court, and we may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights.

Competitors may infringe our intellectual property rights. To prevent infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. If we choose to go to court to stop another party from using the inventions claimed in any patents we obtain, that individual or company has the right to ask the court to rule that such patents are invalid or should not be enforced against that third party. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. Similar mechanisms for challenging the validity and enforceability of a patent exist in non-U.S. patent offices and may result in the revocation, cancellation, or amendment of any non-U.S. patents we hold in the future. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more drug candidates. Such a loss of patent protection would have a material adverse impact on our business.

These lawsuits are expensive and would consume time and resources and divert the attention of managerial and scientific personnel even if we were successful in stopping the infringement of such patents. In addition, there is a risk that the court will decide that such patents are not valid and that we do not have the right to stop the other party from using the claimed inventions. There is also the risk that, even if the validity of such patents is upheld, the court will refuse to stop the other party on the ground that such other party’s activities do not infringe our rights to such patents. In addition, the U.S. Supreme Court has recently modified some tests used by the USPTO in granting patents over the past 20 years, which may decrease the likelihood that we will be able to obtain patents and increase the likelihood of challenge of any patents we obtain or license.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. 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 or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our drug candidates to market.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

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.

Our ability to enforce our patent rights depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their drug candidates. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's drug candidate. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents covering our drug candidates are invalidated or found unenforceable, or if a court found that valid, enforceable patents held by third parties covered one or more of our drug candidates, our competitive position could be harmed or we could be required to incur significant expenses to enforce or defend our rights. If we initiate lawsuits to protect or enforce our patents, or litigate against third party claims, such proceedings would be expensive and would divert the attention of our management and technical personnel.

We may infringe the intellectual property rights of others, which may prevent or delay our drug development efforts and stop us from commercializing or increase the costs of commercializing our drug candidates.

Our success will depend in part on our ability to operate without infringing the intellectual property rights of third parties. We cannot guarantee that our drug candidates, or manufacture or use of our drug candidates, will not infringe third-party patents.

Furthermore, a third party may claim that we or our manufacturing or commercialization collaborators are using inventions covered by the third party's patent rights and may go to court to stop us from engaging in our normal operations and activities, including making or selling our drug candidates. These lawsuits are costly and could affect our results of operations and divert the attention of managerial and scientific personnel. There is a risk that a court would decide that we or our commercialization collaborators are infringing the third party's patents and would order us or our collaborators to stop the activities covered by the patents. In that event, we or our commercialization collaborators may not have a viable way around the patent and may need to halt commercialization of the relevant drug candidate. In addition, there is a risk that a court will order us or our collaborators to pay the other party damages for having violated the other party's patents. If we collaborate with third parties in the development of technology in the future, our collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability. Further, our collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability. In the future, we may agree to indemnify our collaborators against certain intellectual property infringement claims brought by third parties. The pharmaceutical and biotechnology industries have produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of drug candidates or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform.

Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing COR388 or our other drug candidates until the asserted patent expires or is finally held invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- require us to pay damages to the party whose intellectual property rights we may be found to be infringing, which may include treble damages if we are found to have been willfully infringing such intellectual property;
- require us to pay the attorney's fees and costs of litigation to the party whose intellectual property rights we may be found to be infringing; and/or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all.

If we are sued for patent infringement, we would need to demonstrate that our drug candidates or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Proving invalidity is difficult.

For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and divert management's time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, which may not be available, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid, we may incur substantial monetary damages, encounter significant delays in bringing our drug candidates to market and be precluded from manufacturing or selling our drug candidates.

We do not routinely conduct independent reviews of pending patent applications of and patents issued to third parties. We cannot be certain that others have not filed patent applications for technology covered by our pending applications, or that we were the first to invent the technology, because:

- some patent applications in the United States may be maintained in secrecy until the patents are issued;
- patent applications in the United States and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived;
- pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our drug candidates or the use of our drug candidates;
- identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims;
- patent applications in the United States are typically not published until 18 months after the priority date; and
- publications in the scientific literature often lag behind actual discoveries.

Furthermore, the scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history and can involve other factors such as expert opinion. Our interpretation of the relevance or the scope of claims in a patent or a pending application may be incorrect, which may negatively impact our ability to market our drug candidates. Further, we may incorrectly determine that our technologies, or drug candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending patent application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our drug candidates.

Our competitors may have filed, and may in the future file, patent applications covering technology similar to ours, and others may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our drug candidates and future approved products or impair our competitive position. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing drug candidates. There may be third-party patents or patent applications with claims to compositions, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our drug candidates. Any such patent application may have priority over our patent applications, which could further require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to ours, we may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful if, unbeknownst to us, the other party had independently arrived at the same or similar inventions prior to our own inventions, resulting in a loss of our U.S. patent position with respect to such inventions. Other countries have similar laws that permit secrecy of patent applications, and may be entitled to priority over our applications in such jurisdictions.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm to pay these fees due to the USPTO and non-U.S. patent agencies. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. If we license intellectual property we may have to rely upon our licensors to comply with these requirements and effect payment of these fees with respect to any patents and patent applications that we license. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers. If we are not able to adequately prevent disclosure of trade secrets and other proprietary information, the value of our technology and drug candidate could be significantly diminished.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, or we, have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. We may also be subject to claims that former employees, or other third parties have an ownership interest in our patents or other intellectual property. In addition, we may face claims by third parties that our agreements with employees, contractors or consultants obligating them to assign intellectual property to us are ineffective or in conflict with prior or competing contractual obligations of assignment, which could result in ownership disputes regarding intellectual property we have developed or will develop and interfere with our ability to capture the commercial value of such intellectual property. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors, and invention assignment agreements with employees, consultants and advisors, to protect our trade secrets and other proprietary information. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using commonly accepted physical and

technological security measures. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and these agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

In addition, such security measures may not provide adequate protection for our proprietary information, for example, in the case of misappropriation of a trade secret by an employee, consultant, customer or third party with authorized access. Our security measures may not prevent an employee, consultant or customer from misappropriating our trade secrets and providing them to a competitor, and any recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our drug candidates that we consider proprietary. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time-consuming, and the outcome is unpredictable. Even though we use commonly accepted security measures, the criteria for protection of trade secrets can vary among different jurisdictions.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. Trade secrets could over time be disseminated within the industry through independent development, the publication of journal articles and the movement of personnel skilled in the art from company to company or academic to industry scientificpositions.

Though our agreements with third parties typically restrict the ability of our advisors, employees, licensors, suppliers, third-party contractors and consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Because from time to time we expect to rely on third parties in the development, manufacture, and distribution of our drug candidates and provision of our services, we must, at times, share trade secrets with them. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed.

In the future, we may need to obtain licenses of third-party technology that may not be available to us or are available only on commercially unreasonable terms, and which may cause us to operate our business in a more costly or otherwise adverse manner that was not anticipated.

From time to time we may be required to license technology from third parties to further develop or commercialize our drug candidates. Should we be required to obtain licenses to any third-party technology, including any such patents required to manufacture, use or sell our drug candidates, such licenses may not be available to us on commercially reasonable terms, or at all. The inability to obtain any third-party license required to develop or commercialize any of our drug candidates could cause us to abandon any related efforts, which could seriously harm our business and operations.

Where we obtain licenses from or collaborate with third parties, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties, or such activities, if controlled by us, may require the input of such third parties. We may also require the cooperation of our licensors and collaborators to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business, in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. Moreover, if we do obtain necessary licenses, we will likely have obligations under those licenses, including making royalty and milestone payments, and any failure to satisfy those obligations could give our licensor the right to terminate the license.

Termination of a necessary license, or expiration of licensed patents or patent applications, could have a material adverse impact on our business. Our business would suffer if any such licenses terminate, if the licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Furthermore, if any exclusive licenses terminate, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, drug candidates identical to ours. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations, we would be required to pay on sales of future drug candidates, if any, the amounts may be significant. The amount of our future royalty obligations will likely depend on the technology and intellectual property we use in drug candidates that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize drug candidates, we may be unable to achieve or maintain profitability.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make drug candidates that are similar to ours but that are not covered by the claims of the patents that we own;
- we or future collaborators might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive drug candidates for sale in our major commercial markets;
- we cannot ensure that any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect our drug candidates;
- we cannot ensure that any patents issued to us or our licensors will provide a basis for an exclusive market for our commercially viable drug candidates or will provide us with any competitive advantages;
- we cannot ensure that our commercial activities or drug candidates will not infringe upon the patents of others;
- we cannot ensure that we will be able to successfully commercialize our drug candidates on a substantial scale, if approved, before the relevant patents that we own or license expire;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they would significantly harm our business, results of operations and prospects.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.

Because of the expense and uncertainty of litigation, we may conclude that even if a third party is infringing our issued patent, any patents that may be issued as a result of our pending or future patent applications or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our stockholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

We may not be able to protect our intellectual property rights throughout the world.

Patents are of national or regional effect, and filing, prosecuting and defending patents on all of our drug candidates throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. As such, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing drug candidates made using our inventions in and into the United States or other jurisdictions. Further, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing drug candidates in violation of our proprietary rights generally. In addition, certain developing countries, including China and India, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit, and in those countries, we and our licensors and licensees may have limited remedies if patents are infringed or if we or our licensors or licensees are compelled to grant a license to a third party, which could diminish the value of those patents. This could limit our potential revenue opportunities. Further, competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own drug candidates and, further, may export otherwise infringing drug candidates to territories where we have patent protection but where enforcement is not as strong as that in the United States. These drug candidates may compete with our drug candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Changes in patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our drug candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Our patent rights may be affected by developments or uncertainty in U.S. or non-U.S. patent statutes, patent case laws in USPTO rules and regulations or in the rules and regulations of non-U.S. patent offices.

Obtaining and enforcing patents in the pharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act (the Leahy-Smith Act), signed into law on September 16, 2011, could increase those uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review, inter partes review, and derivation proceedings. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. In addition, Congress may pass patent reform legislation that is unfavorable to us.

The U.S. Supreme Court has ruled on several patent cases in recent years, narrowing the scope of patent protection available in certain circumstances and weakening the rights of patent owners in certain situations. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We may become subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may be subject to claims that former employees or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our drug candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Patent terms may be inadequate to protect our competitive position on our drug candidates for an adequate amount of time, and if we do not obtain patent term extension for our drug candidates, our business may be materially harmed.

Patent rights are of limited duration. In the United States, the natural expiration of a patent is generally 20 years after its first effective non-provisional filing date. In addition, although upon issuance a U.S. patent's life can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such drug candidates are commercialized. Even if patents covering our drug candidates are obtained, once the patent life has expired for a drug candidate, we may be open to competition from generic products. A patent term extension of up to five years based on regulatory delay may be available in the United States under the

Hatch-Waxman Act. However, only a single patent can be extended for each marketing approval, and any patent can be extended only once, for a single drug candidate. Moreover, the scope of protection during the period of the patent term extension does not extend to the full scope of the claim, but instead only to the scope of the drug candidate as approved. Further, a patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of drug candidate approval and only those claims covering such approved drug candidate, a method for using it or a method for manufacturing it may be extended. Laws governing analogous patent term extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our drug candidate will be shortened and our competitors may obtain approval of competing drug candidates following our patent expiration, and our revenue could be reduced.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our current or future trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

Moreover, any name we have proposed to use with our drug candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed drug candidate names, including an evaluation of potential for confusion with other drug candidate names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary drug candidate names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

If COR388, our lead drug candidate, obtains regulatory approval, additional competitors could enter the market with generic versions, which may result in a material decline in sales of affected drugs.

Under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application, or ANDA, seeking approval of a generic copy of an approved, small molecule innovator drug. Under the Hatch-Waxman Act, a manufacturer may also submit a new drug application, or NDA, under section 505(b)(2) that references the FDA's prior approval of the small molecule innovator drug. A 505(b)(2) NDA drug may be for a new or improved version of the original innovator drug. The Hatch-Waxman Act also provides for certain periods of regulatory exclusivity, which preclude FDA approval (or in some circumstances, FDA filing and reviewing) of an ANDA or 505(b)(2) NDA. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, drug formulation or an approved use of the drug, which would be listed with the drug in the FDA publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," known as the "Orange Book." If there are patents listed in the Orange Book, a generic or 505(b)(2) applicant that seeks to market its drug before expiration of the patents must include in the ANDA a "Paragraph IV certification," challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must be given to the innovator, too, and if within 45 days of receiving notice the innovator sues to protect its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, if any of our small molecule drug candidates receive FDA approval, competitors could file ANDAs for generic versions of our drugs or 505(b)(2) NDAs that reference our drugs, respectively. If there are patents listed for COR388 in the Orange Book, those ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict how any generic competitor would address patents we may list in the Orange Book, if any, whether we would sue on any such patents, or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for drug candidates and technologies we develop or license. Moreover, if any of our owned or in-licensed patents that are listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected drug could immediately face generic competition and its sales would likely decline rapidly and materially. Should sales decline, we may have to write off a portion or all of the intangible assets associated with the affected drug and our results of operations and cash flows could be materially and adversely affected.

Risks Relating to Owning Our Common Stock

The market price of our common stock is likely to be volatile and could fluctuate or decline, resulting in a substantial loss of your investment.

The market price of our common stock has been and may continue to be volatile and could be subject to wide fluctuations in response to many risk factors listed in this section, and others beyond our control, including:

- results of clinical trials and, in particular, our Phase 2/3 GAIN trial;
- results of clinical trials of other drug candidates being evaluated for Alzheimer's disease or other neurodegenerative diseases;
- regulatory actions with respect to our drug candidates or our competitors' drug candidates;
- actual or anticipated fluctuations in our financial condition and operating results, including fluctuations in our quarterly and annual results;
- announcements of technological innovations by us or our competitors;

- overall conditions in our industry and the markets in which we operate;
- addition or loss of significant customers, or other developments with respect to significant customers;
- changes in laws or regulations applicable to our drug candidates;
- actual or anticipated changes in our growth rate relative to our competitors;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- additions or departures of key personnel;
- competition from existing drug candidates or new drug candidates that may emerge;
- issuance of new or updated research or reports by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- disputes or other developments related to proprietary rights, including patents, litigation matters, and our ability to obtain intellectual property protection for our technologies;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us or our stockholders;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- market conditions for pharmaceutical stocks in general;
- the expiration of contractual lock-up agreements with our executive officers, directors and stockholders; and
- general economic and market conditions.

Furthermore, the stock markets have experienced price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies. These fluctuations often have been unrelated or disproportionate to the operating performance of those companies. These broad market and industry fluctuations, as well as general economic, political and market conditions such as recessions, interest rate changes or international currency fluctuations, may negatively impact the market price of our common stock. In the past, stockholders have instituted securities class action litigation following periods of market volatility. If we were to become involved in securities litigation, it could subject us to substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

Future sales of our common stock in the public market could cause our share price to fall.

Sales of a substantial number of shares of our common stock in the public market, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities.

Certain holders of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in Securities Act registration statements that we may file for ourselves or other stockholders. Once we register these shares, they can be freely sold in the public market. Moreover, we have also registered under the Securities Act shares of common stock that we may issue under our equity compensation plans.

In addition, in the future, we may issue additional shares of common stock or other equity or debt securities convertible into common stock in connection with a financing, acquisition, litigation settlement, employee arrangements or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and could cause our stock price to decline.

We have never paid dividends on our common stock and we do not intend to pay dividends for the foreseeable future. Consequently, any gains from an investment in our common stock will likely depend on whether the price of our common stock increases.

We have never declared or paid any dividends on our common stock and do not intend to pay any dividends in the foreseeable future. We anticipate that we will retain all of our future earnings for use in the operation of our business and for general corporate purposes. Any determination to pay dividends in the future will be at the discretion of our board of directors. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any future gains on their investments.

Insiders have substantial control over us and will be able to influence corporate matters.

Our directors and executive officers and our affiliates beneficially own, in the aggregate, approximately 26.9% of our outstanding capital stock. As a result, these stockholders will be able to exercise significant influence over all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions, such as a merger or other sale of our company or its assets. This concentration of ownership could limit stockholders' ability to influence corporate matters and may have the effect of delaying or preventing a third party from acquiring control over us.

Our charter documents and Delaware law could prevent a takeover that stockholders consider favorable and could also reduce the market price of our stock.

Our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could delay or prevent a change in control of our company. These provisions could also make it more difficult for stockholders to elect directors and take other corporate actions. These provisions include:

- providing for a classified board of directors with staggered, three-year terms;
- authorizing our board of directors to issue preferred stock with voting or other rights or preferences that could discourage a takeover attempt or delay changes in control;
- prohibiting cumulative voting in the election of directors;
- providing that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- prohibiting the adoption, amendment or repeal of our amended and restated bylaws or the repeal of the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors without the required approval of at least 66.67% of the shares entitled to vote at an election of directors;
- prohibiting stockholder action by written consent;
- limiting the persons who may call special meetings of stockholders; and
- requiring advance notification of stockholder nominations and proposals.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. In addition, the provisions of Section 203 of the Delaware General Corporate Law, or the DGCL, govern us. These provisions may prohibit large stockholders, in particular those owning 15% or more of our outstanding voting stock, from merging or combining with us for a certain period of time without the consent of our board of directors.

These and other provisions in our amended and restated certificate of incorporation and our amended and restated bylaws and under Delaware law could discourage potential takeover attempts, reduce the price investors might be willing to pay in the future for shares of our common stock and result in the market price of our common stock being lower than it would be without these provisions.

Our amended and restated certificate of incorporation will provide that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' abilities to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provide that, unless we consent to the selection of an alternative forum, to the fullest extent permitted by law, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of a fiduciary duty owed by, or other wrongdoing by, any of our directors, officers, employees or agents or our stockholders;
- any action asserting a claim against us arising under the DGCL, our amended and restated certificate of incorporation, or our amended and restated bylaws; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine;

provided that, the exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated certificate of incorporation also provide that the federal district courts of the United States of America will be the exclusive forum for the resolution of any complaint asserting a cause of action against us or any of our directors, officers, employees or agents and arising under the Securities Act.

We believe these provisions may benefit us by providing increased consistency in the application of Delaware law and federal securities laws by chancellors and judges, as applicable, particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. However, these provisions may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in such action. For example, in December 2018, the Delaware Court of Chancery invalidated provisions in the certificates of incorporation of Delaware companies that purport to designate federal district courts as the exclusive forum in which a stockholder could bring a claim under the Securities Act. Consequently, we do not intend to enforce the federal forum selection provision in our amended and restated certificate of incorporation unless and until such time there is a final determination by the Delaware Supreme Court regarding the validity of provisions such as the federal forum selection provision. To the extent the Delaware Supreme Court makes a final determination that provisions such as the federal forum selection provision are not valid as a matter of Delaware law, we intend to amend our amended and restated certificate of incorporation to remove the federal forum selection provision.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the DGCL, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- we will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful;
- we may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law;
- we are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification;
- we will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification;
- the rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons; and
- we may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

We are an "emerging growth company," and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act, and we have and intend to continue to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- not being required to hold non-binding advisory votes on executive compensation or new executive compensation arrangements in connection with a merger, acquisition, consolidation, proposed sale or disposition of all or substantially all of our assets.

Further, the JOBS Act permits an "emerging growth company" such as us to take advantage of an extended transition time to comply with new or revised accounting standards as applicable to public companies. We have irrevocably opted out of the extended transition period for complying with new or revised accounting standards applicable to public companies.

We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) December 31, 2024, (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th and (4) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Our internal computer systems, or those used by our third-party research institution collaborators, CROs or other contractors or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems and those of our future CROs and other contractors and consultants may be vulnerable to damage from computer viruses and unauthorized access. Although to our knowledge we have not experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on our third-party research institution collaborators for research and development of our drug candidates and other third parties for the manufacture of our drug candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our drug candidates could be delayed.

Our ability to utilize our federal net operating loss and tax credit carryforwards may be limited under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code.

The limitations apply if a corporation undergoes an "ownership change," which is generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period. If we have experienced an ownership change at any time since our incorporation, we may already be subject to limitations on our ability to utilize our existing net operating losses, or NOLs, and other tax attributes to offset taxable income or tax liability. In addition, future changes in our stock ownership, which may be outside of our control, may trigger an ownership change. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. As a result, even if we earn net taxable income in the future, our ability to use our pre-change NOL carryforwards and other tax attributes to offset such taxable income or tax liability may be subject to limitations, which could potentially result in increased future income tax liability to us.

Recent U.S. tax legislation and future changes to applicable U.S. tax laws and regulations may have a material adverse effect on our business, financial condition and results of operations.

Changes in laws and policy relating to taxes may have an adverse effect on our business, financial condition and results of operations. For example, the U.S. government recently enacted significant tax reform legislation, and certain provisions of the new law may adversely affect us. Changes include, but are not limited to, a federal corporate income tax rate decrease to 21% for tax years beginning after December 31, 2017, a reduction to the maximum deduction allowed for net operating losses generated in tax years after December 31, 2017 and the elimination of carrybacks of net operating losses. The legislation is unclear in many respects and could be subject to potential amendments and technical corrections and is subject to interpretations and implementing regulations by the Treasury and Internal Revenue Service, any of which could mitigate or increase certain adverse effects of the legislation. In addition, it is unclear how these U.S. federal income tax changes will affect state and local taxation. Generally, future changes in applicable U.S. tax laws and regulations, or their interpretation and application could have an adverse effect on our business, financial condition and results of operations.

Item 1B. Unresolved Staff Comments.

None

Item 2. Properties.

Our corporate headquarters are currently located in South San Francisco, California, where we sublease 3,464 square feet of office, research and development, and laboratory space pursuant to a lease agreement that expires in July 2021. We believe that these facilities will be adequate for our near-term needs. If required, we believe that suitable additional or alternative space would be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings.

From time to time, we may become involved in legal proceedings arising in the ordinary course of business. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources, negative publicity and reputational harm and other factors.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Holders of Common Stock

As of March 15, 2020, there were 37 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees.

Dividend Policy

We have never declared or paid any cash dividends on our common stock or any other securities. We anticipate that we will retain all available funds and any future earnings, if any, for use in the operation of our business and do not anticipate paying cash dividends in the foreseeable future. In addition, future debt instruments may materially restrict our ability to pay dividends on our common stock. Payment of future cash dividends, if any, will be at the discretion of the board of directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs, the requirements of current or then-existing debt instruments and other factors the board of directors deems relevant.

Sales of Unregistered Securities

From January 1, 2019 through May 9, 2019 (the date of the filing of our registration statement on Form S-8), we issued and sold to our employees, consultants and other service providers an aggregate of unregistered 158,236 shares of common stock upon the exercise of stock options under our 2014 Plan. The securities issued in these transactions were exempt from the registration requirements of the Securities Act in reliance upon Rule 701 promulgated under the Securities Act or Section 4(a)(2) of the Securities Act.

Use of Proceeds

On May 8, 2019, our registration statement on Form S-1 (File No. 333-230853) was declared effective by the SEC for our IPO. At the closing of our IPO on May 13, 2019 we sold 5,073,800 shares of common stock which included the exercise in full by the underwriters of their option to purchase additional shares, at a public offering price of $17.00 per share and received gross proceeds of $86.3 million, which resulted in net proceeds to us of approximately $77.8 million, after deducting underwriting discounts and commissions of approximately $6.0 million and offering related transaction costs of approximately $2.5 million. None of the expenses associated with the IPO were paid to directors, officers, persons owning ten percent or more of any class of equity securities or to their affiliates. Merrill Lynch, Pierce, Fenner & Smith Incorporated and Credit Suisse Securities (USA) LLC. acted as joint book-running managers for the offering.

There has been no material change in the planned use of proceeds from our IPO from that described in the final prospectus filed by us with the SEC on May 9, 2019.

Issuer Purchases of Equity Securities

None.

Item 6 Selected Financial Data

Not required as a smaller reporting company.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes thereto included elsewhere in this Annual Report of Form 10-K. This discussion contains forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations, and intentions, that are based on the beliefs of our management. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the "Risk Factors" section of this Annual Report on Form 10-K

Overview

We are a clinical stage biopharmaceutical company pioneering a novel disease-modifying therapeutic approach to treat what we believe to be a key underlying cause of Alzheimer's and other degenerative diseases. Our approach is based on the seminal discovery of the presence of *Porphyromonas gingivalis*, or *P. gingivalis*, and its secreted toxic virulence factor proteases, called gingipains, in the brains of greater than 90% of more than 100 Alzheimer's patients observed across multiple studies to date. Additionally, we have observed that *P. gingivalis* infection causes Alzheimer's pathology in animal models, and these effects have been successfully treated with a gingipain inhibitor in preclinical studies. Our proprietary lead drug candidate, COR388, is an orally administered, brain-penetrating small molecule gingipain inhibitor. COR388 was well-tolerated with no concerning safety signals in our Phase 1a and Phase 1b clinical trials conducted to date, which enrolled a total of 67 subjects, including nine patients with mild to moderate Alzheimer's disease. We initiated a global Phase 2/3 clinical trial of COR388, called the GAIN trial, in mild to moderate Alzheimer's patients in April 2019 in the United States and in September 2019 in Europe and expect top-line results by the end of 2021.

Financial Overview

Since commencing material operations in 2014, we have devoted substantially all of our efforts and financial resources to building our research and development capabilities, establishing our corporate infrastructure and most recently, executing our Phase 1a, Phase 1b and Phase 2/3 clinical trials of COR388.

To date, we have not generated any revenue and we have never been profitable. We have incurred net losses since the commencement of our operations. As of December 31, 2019, we had an accumulated deficit of $69.8 million. We incurred a net loss of $37.0 million in the year ended December 31, 2019. We do not expect to generate product revenue unless and until we obtain marketing approval for and commercialize a drug candidate, and we cannot assure you that we will ever generate significant revenue or profits.

To date, we have financed our operations primarily through the issuance and sale of convertible promissory notes and redeemable convertible preferred stock and common stock. From inception through December 31, 2019, we received net proceeds of approximately $177.3 million from the issuance of redeemable convertible preferred stock, convertible promissory notes and common stock. In February 2020, we also received net proceeds of approximately $117.6 million from the issuance and sale of common stock in a private placement to certain accredited investors

As of December 31, 2019 and 2018, we had cash, cash equivalents and short-term investments of $99.9 million and $71.7 million, respectively. The balances exclude long-term investments of $16.8 million and $0 as of those same periods.

Our cash equivalents, short-term and long-term investments are held in money market funds, certificate of deposits, repurchase agreements, investments in corporate debt securities and government agency obligations.

We believe that our existing cash, cash equivalents and short-term investments will be sufficient to fund our planned operations through 2021, including through the completion and the announcement of the top-line results of our Phase 2/3 GAIN trial. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect.

We expect to incur substantial expenditures in the foreseeable future as we expand our pipeline and advance our drug candidates through clinical development, the regulatory approval process and, if approved, commercial launch activities. Specifically, in the near term we expect to incur substantial expenses relating to our ongoing and planned clinical trials, the development and validation of our manufacturing processes, and other development activities.

We will need substantial additional funding to support our continuing operations and pursue our development strategy. Until such time as we can generate significant revenue from sales of an approved drug, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources. Adequate funding may not be available to us on acceptable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and commercialization of our drug candidates or delay our efforts to expand our product pipeline.

Components of Operating Results

Operating Expenses

Research and Development Expenses

Our research and development expenses consist of expenses incurred in connection with the research and development of our research programs. These expenses include payroll and personnel expenses, including stock-based compensation, for our research and product development employees, laboratory supplies, product licenses, consulting costs, contract research, preclinical and clinical expenses, allocated rent, facilities costs and depreciation. We expense both internal and external research and development costs as they are incurred. Non-refundable advance payments and deposits for services that will be used or rendered for future research and development activities are recorded as prepaid expenses and recognized as an expense as the related services are performed.

To date, substantially all of our research and development expenses have supported the advancement of COR388 and our other drug candidates are in early-stage preclinical development. As a result, we do not allocate our costs to individual drug candidates. We expect that at least for the foreseeable future, a substantial majority of our research and development expense will support the clinical and regulatory development of COR388.

We expect our research and development expenses to increase substantially during the next few years as we seek to complete existing and initiate additional clinical trials, pursue regulatory approval of COR388 and advance other drug candidates into preclinical and clinical development. Over the next few years, we expect our preclinical, clinical and contract manufacturing expenses to increase significantly relative to what we have incurred to date. Predicting the timing or the final cost to complete our clinical program or validation of our manufacturing and supply processes is difficult and delays may occur because of many factors.

General and Administrative Expenses

General and administrative expenses consist principally of personnel-related costs, including payroll and stock-based compensation, for personnel in executive, finance, human resources, business and corporate development, and other administrative functions, professional fees for legal, consulting, insurance and accounting services, allocated rent and other facilities costs, depreciation, and other general operating expenses not otherwise classified as research and development expenses.

We anticipate that our general and administrative expenses will increase as the size of our business operations grows to support additional research and development activities.

Interest Income

Interest and other income, net consists primarily of interest earned on our short-term and long-term investments portfolio,

Change in fair value of derivative liability

The change in the fair value of the derivative liability is the change in valuation of the bifurcated redemption premium related to the convertible promissory notes which fully settled upon completion of Series B financing.

Critical Accounting Policies, Significant Judgments and Use of Estimates

Our financial statements have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenue and expenses incurred during the reporting periods. Our estimates are based on our 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 readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management’s judgments and estimates.

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

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development expenses consist primarily of personnel costs for our research and product development employees. Also included are non-personnel costs such as professional fees payable to third parties for preclinical and clinical studies and research services, laboratory supplies and equipment maintenance, product licenses, and other consulting costs.

We estimate preclinical and clinical study and research expenses based on the services performed, pursuant to arrangements with contract research organizations, or CROs that conduct and manage preclinical and clinical studies and research services on our behalf. We estimate these expenses based on regular reviews with internal management personnel and external service providers as to the progress or stage of completion of services and the contracted fees to be paid for such services. Based upon the combined inputs of internal and external resources, if the actual timing of the performance of services or the level of effort varies from the original estimates, we will adjust the accrual accordingly. Payments associated with licensing agreements to acquire exclusive licenses to develop, use, manufacture and commercialize products that have not reached technological feasibility and do not have alternate commercial use are expensed as incurred. Payments made to third parties under these arrangements in advance of the performance of the related services by the third parties are recorded as prepaid expenses until the services are rendered.

Stock-Based Compensation Expense

Stock-based compensation expense represents the cost of the grant date fair value of employee and non-employee awards over the requisite service period of the awards (usually the vesting period) on a straight-line basis. For stock awards for which vesting is subject to performance-based milestones, the expense is recorded over the remaining service period after the point when the achievement of the milestone becomes probable. We estimate the fair value of all stock option grants using the Black-Scholes option pricing model and recognize forfeitures as they occur.

The fair value of a stock-based award is recognized over the period during which an optionee is required to provide services in exchange for the option award, known as the requisite service period (usually the vesting period) on a straight-line basis. Stock-based compensation expense is recognized based on the fair value determined on the date of grant and is reduced for forfeitures as they occur.

Estimating the fair value of equity-settled awards as of the grant date using valuation models, such as the Black-Scholes option pricing model, is affected by assumptions regarding a number of complex variables. Changes in the assumptions can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require significant analysis and judgment to develop.

We estimate the fair value of stock-based compensation utilizing the Black-Scholes option-pricing model, which is impacted by the following variables:

Expected Term—We have opted to use the “simplified method” for estimating the expected term of options, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option (generally 10 years).

Expected Volatility—Due to our limited operating history and a lack of company specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility data was computed using the daily closing prices for the selected companies’ shares during the equivalent period of the calculated expected term of the stock-based awards.

Risk-Free Interest Rate—The risk-free rate assumption is based on the U.S. Treasury instruments with maturities similar to the expected term of our stock options.

Expected Dividend—We have not issued any dividends in our history and do not expect to issue dividends over the life of the options and therefore have estimated the dividend yield to be zero.

Common Stock Valuations

The estimated fair value of the common stock underlying our stock options was determined at each grant date by our board of directors, with input from management. All options to purchase shares of our common stock are intended to be exercisable at a price per share not less than the per-share fair value of our common stock underlying those options on the date of grant.

Prior to our IPO in May 2019, on each grant date, our board of directors made a reasonable determination of the fair value of our common stock based on the information known to us on the date of grant, upon a review of any recent events and their potential impact on the estimated fair value per share of the common stock, and timely valuations from an independent third-party valuation in accordance with guidance provided by the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation* (the Practice Aid). The methodology to determine the fair value of our common stock included estimating the fair value of the enterprise using a market approach, which estimates the fair value of the company by including an estimation of the value of the business based on guideline public companies under a number of different scenarios. In determining the fair value of our common stock on each grant date, our board of directors considered numerous objective and subjective factors, including the results of independent third party valuations, external market conditions affecting the pharmaceutical and biotechnology industry and trends within the industry; our stage of development; the rights, preferences and privileges of our redeemable convertible preferred stock relative to those of our common stock; the prices at which we sold shares of our redeemable convertible preferred stock; our financial condition and operating results, including our levels of available capital resources; the progress of our research and development efforts, our stage of development and business strategy; equity market conditions affecting comparable public companies; general U.S. market conditions and the lack of marketability of our common stock.

Following our IPO in May 2019, our board of directors determined the fair value of our common stock based on the closing price of our common stock on the date of grant.

Income Taxes

We account for income taxes under the asset and liability method. Current income tax expense or benefit represents the amount of income taxes expected to be payable or refundable for the current year. Deferred income tax assets and liabilities are determined based on differences between the financial statement reporting and tax bases of assets and liabilities and net operating loss and credit carryforwards and are measured using the enacted tax rates and laws that will be in effect when such items are expected to reverse. Deferred income tax assets are reduced, as necessary, by a valuation allowance when management determines it is more likely than not that some or all of the tax benefits will not be realized.

We account for uncertain tax positions in accordance with ASC 740-10, *Accounting for Uncertainty in Income Taxes*. We assess all material positions taken in any income tax return, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than fifty percent likely of being realized upon ultimate settlement. As of each balance sheet date, unresolved uncertain tax positions must be reassessed, and we will determine whether (i) the factors underlying the sustainability assertion have changed and (ii) the amount of the recognized tax benefit is still appropriate. The recognition and measurement of tax benefits requires significant judgment. Judgments concerning the recognition and measurement of a tax benefit might change as new information becomes available.

As of December 31, 2019, our total deferred tax assets were $16.5 million. A valuation allowance is established against the deferred tax assets to reduce their carrying value to an amount that is more likely than not to be realized. The deferred tax assets and liabilities are classified as noncurrent along with the related valuation allowance. Due to a lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance. The deferred tax assets were primarily comprised of federal and state tax net operating losses, or NOLs. Utilization of NOLs may be limited by the "ownership change" rules, as defined in Section 382 of the Code. Similar rules may apply under state tax laws. Our ability to use our remaining NOLs may be further limited if we experience an ownership change in connection with this offering, future offerings or as a result of future changes in our stock ownership.

Results of Operations

Comparison of the Years Ended December 31, 2019 and 2018

The following table summarizes our results of operations for the periods indicated (dollars in thousands):

	Year Ended December 31,		Change	
	2019	2018	$	%
Operating expenses:				
Research and development	$ 30,214	$ 10,085	$ 20,129	199.6 %
General and administrative	8,954	2,034	6,920	340.2 %
Loss from operations	(39,168)	(12,119)	(27,049)	223.2 %
Interest income	2,188	806	1,382	171.5 %
Interest expense	—	(957)	957	(100.0) %
Changes in fair value of derivative liability	—	(206)	206	(100.0) %
Net loss	$ (36,980)	$ (12,476)	$ (24,504)	196.4 %

Research and Development Expenses

The following table summarizes our research and development expenses:

	Year ended December 31,	
	2019	2018
	(in thousands)	
Direct research and development expenses:		
COR388	$ 23,422	$ 6,066
Other direct research costs	1,785	736
Indirect research and development expenses:		
Personnel related (including stock-based compensation)	4,005	2,403
Facilities and other research and development expenses	1,002	880
Total research and development expenses	$ 30,214	$ 10,085

Research and development expenses increased $20.1 million or 199.6% for the year ended December 31, 2019, primarily due to an increase of $17.4 million in expenses for our lead product candidate, COR388, which entered into our Phase 2/3 GAIN clinical trials. Personnel-related expenses, including stock-based compensation, increased by $1.6 million due to an increase in headcount as we launched and scaled the GAIN clinical trial during 2019. In addition, we had an increase of $1.1 million in research and development expenses related to other preclinical programs currently in development. We expect the clinical trial expenses to continue to increase as the study progresses to full enrollment in 2020.

General and Administrative Expenses

General and administrative expenses increased $6.9 million, or 340.2 %, primarily due to an increase of $2.6 million in personnel costs, including stock-based compensation, as a result of an increase in our employee headcount and an increase of $4.3 million in insurance, legal, accounting, investor relations and other compliance cost associated with becoming a public company. We anticipate these costs will increase as the full year effect of being a public company is realized in 2020.

Interest Income

Interest income increased $1.4 million or 171.5% due to increased average cash balances and on our investment portfolio as a result of the receipt of proceeds from our IPO in May 2019.

Interest Expense

Interest expense decreased $1.0 million due to the retirement of all interest-bearing obligations in 2018.

Change in fair value of derivative liability

The change in fair value of derivative liability decreased $0.2 million due to the extinguishment of the liability upon the conversion of the convertible promissory note to redeemable convertible preferred stock in May 2018.

Liquidity and Capital Resources

We have incurred cumulative net losses and negative cash flows from operations since our inception and anticipate we will continue to incur net losses for the foreseeable future. As of December 31, 2019, we had an accumulated deficit of $69.8 million. As of December 31, 2019, we had cash, cash equivalents and investments of $116.6 million.

Based on our existing business plan, we believe that our existing cash, cash equivalents and investments will be sufficient to fund our anticipated level of operations through at least the next 12 months.

We will continue to require additional capital to develop our drug candidates and fund operations for the foreseeable future. We may seek to raise capital through private or public equity or debt financings, collaborative or other arrangements with other companies, or through other sources of financing. Adequate additional funding may not be available to us on acceptable terms or at all. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategies. We anticipate that we will need to raise substantial additional capital, the requirements of which will depend on many factors, including:

- the progress, costs, trial design, results of and timing of our Phase 2/3 GAIN trial and other clinical trials of COR388, including for potential additional indications that we may pursue beyond Alzheimer's disease;
- the willingness of the FDA or EMA to accept our Phase 2/3 GAIN trial, as well as data from our completed and planned clinical and preclinical studies and other work, as the basis for review and approval of COR388 for Alzheimer's disease;
- the outcome, costs and timing of seeking and obtaining FDA, EMA and any other regulatory approvals;
- the number and characteristics of drug candidates that we pursue;
- our ability to manufacture sufficient quantities of our drug candidates;
- our need to expand our research and development activities;
- the costs associated with securing and establishing commercialization and manufacturing capabilities;
- the costs of acquiring, licensing or investing in businesses, drug candidates and technologies;
- our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;
- our need and ability to retain management and hire scientific and clinical personnel;
- the effect of competing drugs and drug candidates and other market developments;
- our need to implement additional internal systems and infrastructure, including financial and reporting systems; and
- the economic and other terms, timing of and success of any collaboration, licensing or other arrangements into which we may enter in the future.

If we raise additional funds by issuing equity securities, our stockholders will experience dilution. Any future debt financing into which we enter may impose upon us additional covenants that restrict our operations, including limitations on our ability to incur liens or additional debt, pay dividends, repurchase our common stock, make certain investments and engage in certain merger, consolidation or asset sale transactions. Any debt financing or additional equity that we raise may contain terms that are not favorable to us or our stockholders. If we are unable to raise additional funds when needed, we may be required to delay, reduce, or terminate some or all of our development programs and clinical trials. We may also be required to sell or license to others rights to our drug candidates in certain territories or indications that we would prefer to develop and commercialize ourselves.

Summary Statement of Cash Flows

The following table sets forth the primary sources and uses of cash and cash equivalents for each of the periods presented below (in thousands):

	Year Ended December 31,	
	2019	2018
Net cash (used in) provided by:		
Operating activities	$ (33,277)	$ (11,695)
Investing activities	(17,747)	(46,754)
Financing activities	77,366	75,928
Net increase in cash and cash equivalents	$ 26,342	$ 17,479

Cash Used in Operating Activities

Net cash used in operating activities was $33.3 million for the year ended December 31, 2019 and $11.7 million for the year ended December 31, 2018.

Cash used in operating activities in the year ended December 31, 2019 was primarily due to our net loss for the period of $37.0 million, which included non-cash expenses of $2.6 million and changes to operating assets and liabilities of $1.9 million offset by non-cash interest income of $0.8 million.

Cash used in operating activities in the year ended December 31, 2018 was primarily due to our net loss for the period of $12.5 million, and was also affected by changes to accrued interest, debt discount on conversion features, operating assets and liabilities, other current assets and long-term assets that totaled $1.5 million. Cash used in operating activities was also affected by changes in operating assets and liabilities, a decrease in prepaids of $0.7 million and increase in accrued liabilities of $0.3 million, and non-cash charges relating to depreciation and amortization and stock-based compensation expense of $0.1 million.

Cash Used in Investing Activities

Cash used in investing activities was $17.7 million in the year ended December 31, 2019, primarily related to the purchase of investments of $135.4 million and maturities of debt investments of $117.7 million.

Cash used in investing activities was $46.8 million in the year ended December 31, 2018, primarily related to the purchase of investments of $55.2 million, and maturities of short-term investments of $8.7 million.

Cash Provided by Financing Activities

Cash provided by financing activities was $77.4 million in the year ended December 31, 2019, which consisted of net proceeds of $77.8 million from our IPO, $0.1 million from the exercise of stock options, less payment on our finance leases of $0.5 million.

Cash provided by financing activities was $75.9 million in the year ended December 31, 2018, which consisted primarily of net proceeds of $75.7 million from the issuance and sale of shares of our Series B redeemable convertible preferred stock.

Contractual Obligations and Commitments

We enter into contracts in the normal course of business with third party contract organizations for clinical trials, non-clinical studies and testing, manufacturing, and other services and products for operating purposes. The amount and timing of the payments under these contracts varies based upon the timing of the services performed. We have not included in this disclosure any such contingent payment obligations as the amount, timing and likelihood of such payments are not known.

Off-Balance Sheet Arrangements

Since our inception, we have not engaged in any off-balance sheet arrangements, as defined in the rules and regulations of the Securities and Exchange Commission.

Indemnification

As permitted under Delaware law and in accordance with our bylaws, we indemnify our officers and directors for certain events or occurrences while the officer or director is or was serving in such capacity. We are also party to indemnification agreements with our officers and directors. We believe the fair value of the indemnification rights and agreements is minimal. Accordingly, we have not recorded any liabilities for these indemnification rights and agreements as of December 31, 2019 and December 31, 2018.

JOBS Act Accounting Election

The Jumpstart Our Business Startups Act of 2012 (the JOBS Act), permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We have chosen to irrevocably opt out of the extended transition period for complying with certain new or revised accounting standards pursuant to Section 107(b) of the JOBS Act.

We will remain an emerging growth company until the earlier of (1) December 31, 2024, (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700.0 million of the prior June 30th and (4) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

Recent Accounting Pronouncements

In August 2018, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement. The new guidance changes disclosure requirements related to fair value measurements as part of the disclosure framework project. The disclosure framework project aims to improve the effectiveness of disclosures in the notes to the financial statements by focusing on requirements that clearly communicate the most important information to users of the financial statements. This guidance is effective for fiscal years beginning after December 15, 2019, with early adoption permitted. The Company does not believe this pronouncement will have a material impact on its financial statements or disclosures.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"). ASU 2016-13 requires companies to measure credit losses utilizing a methodology that reflects expected credit losses and requires a consideration of a broader range of reasonable and supportable information to inform credit loss estimates. ASU 2016-13 is effective for public business entities that are SEC filers, excluding smaller reporting companies for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. All other entities, including smaller reporting companies the effective date is for fiscal years beginning after December 15, 2022. Accordingly, as a smaller reporting company, we will adopt the standard effective January 1, 2023. We are currently evaluating the impact that the adoption of this standard will have on our financial statements.

In August 2018, the FASB issued ASU No. 2018-15, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract* ("ASU 2018-15"), which clarifies the accounting for implementation costs in cloud computing arrangements. ASU 2018-15 is effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. We will adopt the standard prospectively on January 1, 2020. We do not expect the adoption of ASU 2018-15 to result in a material change to our financial statements.

Recently Adopted Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*. This ASU requires that substantially all leases be recognized by lessees on their balance sheet as a right-of-use asset and corresponding lease liability, including leases currently accounted for as operating leases. The ASU is effective for interim and annual periods beginning after December 15, 2018. Additionally, the FASB issued ASU No. 2018-11, *Leases (Topic 842): Targeted Improvements*, which offers an additional transition method whereby entities may apply the new leases standard at the adoption date and recognize a cumulative-effect adjustment to the opening balance of retained earnings rather than application of the new leases standard at the beginning of the earliest period presented in the financial statements. The Company elected this transition method and adopted ASC 842 on January 1, 2019 and as a result, recorded a right-of-use asset of $0.9 million, a short-term lease liability of $0.3 million, and a long-term lease liability of $0.6 million and no cumulative effect adjustment was made to the retained earnings as of the adoption date. The Company also elected the package of practical expedients under the transition guidance that will retain the historical lease classification and initial direct costs for any leases that exist prior to adoption of the new guidance and the practical expedient to not separate lease and nonlease components. See Note 6 to our audited financial statements for further information.

In July 2017, the FASB issued ASU No. 2017-11, *Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480), Derivatives and Hedging (Topic 815) I. Accounting for Certain Financial Instruments with Down Round Features II.* Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception ("ASU 2017-11"). Part I applies to entities that issue financial instruments such as warrants, convertible debt or redeemable convertible preferred stock that contain down-round features. Part II replaces the indefinite deferral for certain mandatorily redeemable noncontrolling interests and mandatorily redeemable financial instruments of nonpublic entities contained within ASC Topic 480 with a scope exception and does not impact the accounting for these mandatorily redeemable instruments. For public entities, ASU 2017-11 is required to be adopted for annual periods beginning after December 15, 2018, including interim periods within those fiscal years. The adoption of ASU 2017-11 did not have any impact on the Company's financial statements since we did not have any instruments subject to the scope of ASU 2017-11.

On December 18, 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), which removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. Most amendments within the standard are required to be applied on a prospective basis, while certain amendments must be applied on a retrospective or modified retrospective basis. The pronouncement is effective for fiscal years, and for interim periods within those fiscal years, beginning after December 15, 2020, with early adoption permitted. We early adopted ASU 2019-12 effective January 1, 2019. The adoption did not have a material impact on the financial statements.

All other newly issued accounting pronouncements not yet effective have been deemed either immaterial or not applicable.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Not required as a smaller reporting company.

Item 8. Financial Statements and Supplementary Data.

Cortexyme, Inc.
Index to Financial Statements

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Stockholders and Board of Directors
Cortexyme, Inc.
South San Francisco, California

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Cortexyme, Inc. (the "Company") as of December 31, 2019 and 2018, the related statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for the years then ended, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2019 and 2018, and the results of its operations and its cash flows the years then ended**,** in conformity with accounting principles generally accepted in the United States of America.

Change in Accounting Principle

As discussed in Note 2 to the financial statements, the Company has changed its method of accounting for leases in 2019 due to the adoption of the Accounting Standards Codification Topic 842, "Leases."

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.

/s/ BDO USA, LLP

March 16, 2020

We have served as the Company's auditor since 2018.
San Jose, California

CORTEXYME, INC.
BALANCE SHEETS
(in thousands except share and per share data)

	December 31, 2019	December 31, 2018
ASSETS		
Current assets:		
Cash and cash equivalents	$ 51,214	$ 24,872
Short term investments	48,650	46,844
Prepaid expenses and other current assets	6,192	868
Total current assets	106,056	72,584
Property and equipment, net	709	283
Operating lease right-of-use assets, net	625	—
Long term investments	16,763	—
Other assets	217	10
Total assets	$ 124,370	$ 72,877
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts Payable	$ 3,075	$ 495
Accrued expenses and other current liabilities	5,817	962
Total current liabilities	8,892	1,457
Total liabilities	8,892	1,457
Commitments and contingencies (See Note 7)		
Series A redeemable convertible preferred stock, par value $0.001, no shares authorized, issued and outstanding as of December 31, 2019 and 9,008,931 shares authorized, 9,008,919 shares issued and outstanding as of December 31, 2018; liquidation preference of $0 and $17,178 at December 31, 2019 and 2018, respectively	—	17,178
Series B redeemable convertible preferred stock, par value $0.001, no shares authorized, issued and outstanding as of December 31, 2019 and 9,430,145 shares authorized, 9,152,108 shares issued and outstanding as of December 31, 2018; liquidation preference of $0 and $87,972 at December 31, 2019 and 2018, respectively	—	86,868
Stockholders' equity (deficit):		
Preferred Stock, $0.001 par value, 10,000,000 authorized, no shares issued and outstanding December 31, 2019 and no shares authorized, issued and outstanding at December 31, 2018	—	—
Common stock, $0.001 par value, 100,000,000 and 24,794,114 shares authorized, 26,869,413 and 3,412,366 issued and outstanding as of December 31, 2019 and 2018, respectively	27	3
Additional paid in capital	185,196	245
Accumulated other comprehensive income (loss)	60	(49)
Accumulated deficit	(69,805)	(32,825)
Total stockholders' equity (deficit)	115,478	(32,626)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 124,370	$ 72,877

See accompanying notes to the financial statements

CORTEXYME, INC.
STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands except for share and per share amounts)

	Years Ended December 31,	
	2019	**2018**
Operating expenses:		
Research and development	$ 30,214	$ 10,085
General and administrative	8,954	2,034
Total operating expenses	39,168	12,119
Loss from operations	(39,168)	(12,119)
Interest income, net	2,188	806
Interest expense	—	(957)
Change in fair value of derivative liability	—	(206)
Net loss	(36,980)	(12,476)
Other comprehensive income (loss):		
Unrealized gain (loss) on available for sales securities	109	(49)
Total comprehensive loss	(36,871)	(12,525)
Net loss per share - basic and diluted	(1.94)	(3.71)
Weighted average shares of common stock outstanding - basic and diluted	19,031,940	3,362,192

See accompanying notes to the financial statements

CORTEXYME, INC.
STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands except share amounts)

For the years ended December 31, 2019 and 2018

	Series A Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Common Stock		Additional Paid in Capital	Other Comprehensive Income / (Loss)	Accumulated Deficit	Shareholders' Equity / (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance January 1, 2018	9,008,919	$ 17,178	—	$ —	3,361,016	$ 3	$ 66	$ —	$ (20,349)	$ (20,280)
Issuance of Series B redeemable convertible preferred stock, net of issuance costs of $157	—	—	7,890,466	75,688	—	—	—	—	—	—
Issuance of Series B redeemable convertible preferred stock in connection with the conversion of convertible promissory notes and accrued interest	—	—	1,147,205	11,027	—	—	—	—	—	—
Issuance of Series B redeemable convertible preferred stock in connection with the facility lease agreement	—	—	114,437	—	—	—	—	—	—	—
Vesting of Series B redeemable convertible preferred stock in lieu of rent	—	—	—	153	—	—	—	—	—	—
Exercise of stock options	—	—	—	—	51,350	—	24	—	—	24
Stock based compensation	—	—	—	—	—	—	155	—	—	155
Other comprehensive loss	—	—	—	—	—	—	—	(49)	—	(49)
Net loss	—	—	—	—	—	—	—	—	(12,476)	(12,476)
Balance December 31, 2018	9,008,919	$ 17,178	9,152,108	$ 86,868	3,412,366	$ 3	$ 245	$ (49)	$ (32,825)	$ (32,626)
Conversion of redeemable convertible preferred stock to common stock	(9,008,919)	(17,178)	(9,152,108)	(87,816)	18,161,027	18	104,976	—	—	104,994
Vesting of Series B redeemable convertible preferred stock in lieu of rent	—	—	—	948	—	—	—	—	—	—
Initial public offering of common stock, net of issuance costs of $8,427	—	—	—	—	5,073,800	5	77,822	—	—	77,827
Exercise of stock options	—	—	—	—	194,279	1	96	—	—	97
Stock based compensation	—	—	—	—	—	—	2,056	—	—	2,056
Exercise of stock warrant	—	—	—	—	27,941	—	1	—	—	1
Other comprehensive income	—	—	—	—	—	—	—	109	—	109
Net loss	—	—	—	—	—	—	—	—	(36,980)	(36,980)
Balance December 31, 2019	—	$ —	—	$ —	26,869,413	$ 27	$ 185,196	$ 60	$ (69,805)	$ 115,478

See accompanying notes to the financial statements

CORTEXYME, INC.
STATEMENTS OF CASH FLOWS
(in thousands)

	For the Year Ended December 31,	
	2019	2018
Cash flows from operating activities		
Net Loss	$ (36,980)	$ (12,476)
Adjustments to reconcile net loss to net cash used in operating activities:		
Non-cash interest expense related to convertible promissory notes	—	263
Non-cash rent expense	367	153
Stock based compensation	2,056	155
Depreciation and amortization	188	51
Accretion of discount on convertible promissory notes payable	—	694
Amortization of discount on available for sale investments	(812)	(351)
Change in fair value of derivative liability	—	206
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(5,324)	(690)
Other assets	(207)	50
Accounts payable	2,580	(23)
Accrued expenses and other current liabilities	4,855	273
Net cash used in operating activities	(33,277)	(11,695)
Cash flow from investing activities:		
Purchase of investments	(135,415)	(55,242)
Proceeds from maturities of investments	117,723	8,700
Purchase of property and equipment	(55)	(212)
Net cash used in investing activities	(17,747)	(46,754)
Cash flows from financing activities:		
Payments of finance leases	(559)	—
Proceeds from issuance of convertible promissory note payable	—	250
Proceeds from issuance of commons stock upon exercise of stock options	97	24
Proceeds from Series B redeemable convertible preferred stock, net of issuance costs	—	75,688
Proceeds from stock warrant exercise	1	—
Deferred initial public offering costs	—	(34)
Proceeds from initial public offering, net of stock offering costs	77,827	—
Net cash provided by financing activities	77,366	75,928
Net increase in cash and cash equivalents	26,342	17,479
Cash and cash equivalents at beginning of period	24,872	7,393
Cash and cash equivalents cash at end of period	$ 51,214	$ 24,872
Supplemental disclosures of non-cash information:		
Right-of-use assets obtained in exchange for new operating lease liabilities	$ 878	$ —
Conversion of Series A redeemable convertible preferred stock to common stock on initial public offering	$ 17,178	$ —
Conversion of Series B redeemable convertible preferred stock to common stock on initial public offering	$ 87,816	$ —
Acceleration of vesting of Series B redeemable convertible preferred stock on initial public offering	$ 856	$ —
Issuance of Series B redeemable convertible preferred stock in connection with conversion of convertible promissory notes and accrued interest	$ —	$ 11,027
Issuance of Series B redeemable convertible stock for facility lease	$ —	$ 1,100

See accompanying notes to the financial statements

Note 1. Organization

Description of Business

Cortexyme, Inc. (the "Company") was incorporated in the State of Delaware in June 2012 and is headquartered in South San Francisco, California. The Company is a clinical stage biopharmaceutical company focused on developing therapeutics based on data supporting a new theory of the cause of Alzheimer's disease and other degenerative disorders. Cortexyme is targeting a specific, infectious pathogen tied to neurodegeneration and chronic inflammation in humans and animal models.

Reverse Stock Split

On April 25, 2019, the Company's Board of Directors approved a one-for-0.367647 reverse split of the Company's issued and outstanding common stock, redeemable convertible preferred stock, and stock options. The par value of the common stock was not adjusted as a result of the reverse stock split. All share and per share amounts in the accompanying financial statements and notes to the financial statements have been retroactively adjusted for all periods presented to reflect the reverse stock split.

Initial Public Offering

On May 8, 2019, the Company's registration statement on Form S-1 (File No. 333-230853) for its initial public offering of common stock ("IPO") was declared effective by the Securities and Exchange Commission ("SEC"). On May 13, 2019, the Company closed its IPO with the sale of 5,073,800 shares of common stock, which included 661,800 shares of common stock issued upon the exercise in full of the underwriters' option to purchase additional shares, at a public offering price of $17.00 per share, resulting in net proceeds of $77.8 million, after deducting underwriting discounts and commissions and estimated offering expenses paid by the Company.

In addition, in connection with the closing of the IPO, all of the Company's outstanding shares of redeemable convertible preferred stock were automatically converted into 18,161,027 shares of common stock, and there are no shares of redeemable convertible preferred stock outstanding as of December 31, 2019.

Liquidity and Capital Resources

The Company has incurred losses and negative cash flows from operations since inception and expects to continue to generate operating losses for the foreseeable future. As of December 31, 2019, the Company had an accumulated deficit of $69.8 million. Since inception through December 31, 2019, the Company has funded operations primarily with the net proceeds from the issuance of convertible promissory notes, from the issuance of redeemable convertible preferred stock and from the net proceeds from the IPO. As of December 31, 2019, the Company had cash, cash equivalents, and short-term investments of $99.9 million, which it believes will be sufficient to fund its planned operations for a period of at least 12 months from the date of the issuance of the accompanying financial statements.

Management expects to incur additional losses in the future to fund its operations and conduct product research and development and may need to raise additional capital to fully implement its business plan. The Company may raise additional capital through the issuance of equity securities, debt financings or other sources in order to further implement its business plan. However, if such financing is not available when needed and at adequate levels, the Company will need to reevaluate its operating plan and may be required to delay the development of its product candidate.

Note 2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements and the notes thereto have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") pursuant to the instructions of the SEC on Form 10-K through the rules and interpretive releases of the SEC under federal securities law.

Use of Estimates

The preparation of the Company's financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, and expenses, as well as related disclosure of contingent assets and liabilities. The most significant estimates used in the Company's financial statements relate to the determination of the fair value of common stock prior to the initial public offering, stock-based awards and other issuances, valuation of derivative instruments, accruals for research and development costs, useful lives of long-lived assets, stock-based compensation and related assumptions, the incremental borrowing rate for leases and income tax uncertainties, including a valuation allowance for deferred tax assets; and contingencies. The Company bases its estimates on historical experience and on various other market specific and other relevant assumptions that it believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results could differ materially from the Company's estimates.

Risk and Uncertainties

The Company's future results of operations involve a number of risks and uncertainties. Factors that could affect the Company's future operating results and cause actual results to vary materially from expectations include, but are not limited to, uncertainty of results of clinical trials and reaching milestones, uncertainty of regulatory approval of the Company's potential drug candidates, uncertainty of market acceptance of the Company's drug candidates, competition from substitute products and larger companies, securing and protecting proprietary technology, strategic relationships and dependence on key individuals and sole source suppliers. The Company's drug candidate will require approvals from the U.S. Food and Drug Administration (FDA) and comparable foreign regulatory agencies prior to commercial sales in their respective jurisdictions. There can be no assurance that any drug candidate will receive the necessary approvals. If the Company was denied approval, approval was delayed or the Company was unable to maintain approval for any drug candidate, it could have a materially adverse impact on the Company.

Segments

The Company operates and manages its business as one reportable and operating segment, which is the business of developing and commercializing therapeutics. The Company's chief executive officer, who is the chief operating decision makers, reviews financial information on an aggregate basis for purposes of allocating and evaluating financial performance. All long-lived assets are maintained in the United States of America.

Cash, Cash Equivalents and Investments

The Company considers all highly liquid investments with maturities of three months or less when purchased to be cash equivalents. Cash equivalents include marketable securities. Management determines the appropriate classification of its investments in debt securities at the time of purchase and at the end of each reporting period. Investments with original maturities beyond three months at the date of purchase and which mature at, or less than twelve months from the balance sheet date are classified as short-term investments. Investments with a maturity beyond twelve months from the balance sheet date are classified as long-term investments. Collectively, cash equivalents, short-term investments and long-term investments are considered available-for-sale and are recorded at fair value. Unrealized gains and losses are recorded as a component of other comprehensive loss in the statement of operations and included as a separate component of redeemable convertible preferred stock and stockholders' equity (deficit). Realized gains and losses are included in interest and other income, net in the statements of operations and comprehensive loss.

Premiums (discounts) are amortized (accreted) over the life of the related investment as an adjustment to yield using the straight-line interest method. Dividend and interest income are recognized when earned. These amounts are recorded in "Interest income, net" in the Statement of Operations.

Property and Equipment, Net

Property and equipment are stated at cost and reduced by accumulated depreciation. Depreciation expense is recognized using the straight-line method over the estimated useful lives of the assets, generally five years. Maintenance and repairs are charged to expense as incurred, and improvements are capitalized. When assets are retired or otherwise disposed of, the cost and accumulated depreciation are removed from the balance sheet and any resulting gain or loss is reflected in operations in the period realized.

Concentration of Credit Risk

Cash equivalents short-term and long-term investments are financial instruments that potentially subject the Company to concentrations of credit risk. The Company invests in money market funds, repurchase agreements, treasury bills and notes, government bonds, commercial paper and corporate notes. The Company limits its credit risk associated with cash equivalents, short-term and long-term investments by placing them with banks and institutions it believes are highly credit worthy and in highly rated investments.

Impairment of Long-Lived Assets

The Company reviews long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. An impairment charge would be recorded when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. Impairment, if any, is assessed using discounted cash flows or other appropriate measures of fair value. The Company did not recognize any impairment charges for the years ended December 31, 2019 and 2018.

Deferred Offering Costs

Deferred offering costs, consisting of direct legal, accounting, filing and other fees directly related to the Company's initial public offering of its common stock (IPO), are capitalized. The deferred offering costs was reclassified to additional paid-in capital upon the closing of the IPO. The Company deferred $34,000 as of December 31, 2018, which is included in prepaid expense and other assets in the accompanying balance sheets.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development expenses consist primarily of personnel costs for the Company's research and product development employees. Also included are non-personnel costs such as professional fees payable to third parties for preclinical and clinical studies and research services, laboratory supplies and equipment maintenance, product licenses, and other consulting costs. The Company estimates preclinical and clinical study and research expenses based on the services performed, pursuant to contracts with contract research organizations ("CROs") that conduct and manage preclinical and clinical studies and research services on its behalf. Expenses related to clinical studies are based on estimates of the services received and efforts expended pursuant to contracts with many research institutions, clinical research organizations and other service providers that conduct and manage clinical studies on our behalf. The financial terms of these agreements are subject to negotiation and vary from contract to contract and may result in uneven payment flows. Generally, these agreements set forth the scope of work to be performed at a fixed fee or unit price. Payments under the contracts are mainly driven by time and materials incurred by these service providers. Payments made to third parties under these arrangements in advance of the performance of the related services by the third parties are recorded as prepaid expenses until the services are rendered. Expenses related to clinical studies are generally recorded based on the timing of when services that have been performed on the Company's behalf by the service providers and in accordance with the contracts. The determination of timing involves reviewing open contracts and purchase orders, communicating with applicable personnel to identify the timing of when services that have been performed on the Company's behalf and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of actual cost. The majority of service providers' invoice at least monthly in arrears for services performed. The Company periodically confirms the accuracy of estimates with the service providers and makes adjustments if necessary. Examples of estimated clinical expenses include:

- fees paid to Contract Research Organizations, or CROs, in connection with clinical studies;
- fees paid to investigative sites in connection with clinical studies;
- fees paid to contract manufacturers in connection with the production of clinical study materials; and
- fees paid to vendors in connection with preclinical development activities.

If the actual timing of the performance of services or the level of effort varies from the original estimates, the Company will adjust the prepaid or accrual accordingly. Payments associated with licensing agreements to acquire exclusive licenses to develop, use, manufacture and commercialize products that have not reached technological feasibility and do not have alternate commercial use are expensed as incurred.

Patent Costs

The Company has no historical data to support a probable future economic benefit for the arising patent applications, filing and prosecution costs. Therefore, patent costs are expensed as incurred.

Stock-Based Compensation

The Company accounts for stock-based compensation arrangements with employees in accordance with Accounting Standards Codification ("ASC") 718, Compensation—Stock Compensation. Stock-based awards granted include stock options with time-based vesting. ASC 718 requires the recognition of compensation expense, using a fair value-based method, for costs related to all stock-based payments. The Company's determination of the fair value of stock options with time-based vesting on the date of grant utilizes the Black-Scholes option-pricing model, and is impacted by its common stock price as well as other variables including: but not limited to, expected term that options will remain outstanding, expected common stock price volatility over the term of the option awards, risk-free interest rates and expected dividends. The fair value of a stock-based award is recognized over the period during which an optionee is required to provide services in exchange for the option award, known as the requisite service period (usually the vesting period) on a straight-line basis. Stock-based compensation expense is recognized based on the fair value determined on the date of grant and is reduced for forfeitures as they occur.

Redeemable Convertible Preferred Stock

The Company recorded all shares of convertible preferred stock at their respective fair values less issuance costs on the dates of issuance. The convertible preferred stock was recorded outside of stockholders' equity (deficit) because, in the event of certain deemed liquidation events considered not solely within the Company's control, such as a merger, acquisition and sale of all or substantially all of all the Company's assets, the convertible preferred stock will become redeemable at the option of the holders. Additionally, on or after May 23, 2025, 60% of the holders may have demanded redemption of the stock. In the event of a change of control of the Company, proceeds received from the sale of such shares would have been distributed in accordance with the liquidation preferences set forth in the Company's Amended and Restated Certificate of Incorporation unless the holders of convertible preferred stock had converted their shares of convertible preferred stock into shares of common stock. The Company determined not to adjust the carrying values of the convertible preferred stock to the liquidation preferences of such shares because of the uncertainty of whether or when such an event would occur. In connection with the closing of the IPO, all of the Company's outstanding shares of redeemable convertible preferred stock were automatically converted into 18,161,027 shares of common stock, and there are no shares of redeemable convertible preferred stock outstanding as of December 31, 2019.

Fair Value of Warrants

Warrants were recorded either as equity instruments or derivative liabilities at their estimated fair value at the date of issuance. In the case of warrants recorded as liabilities, subsequent changes in estimated fair value were recorded in the Company's statement of operations in each subsequent period. The warrants were measured at estimated fair value using the Black Scholes valuation model, which was based, in part, upon inputs for which there was little or no observable market data, requiring the Company to develop its own assumptions. Inherent in this model were assumptions related to expected stock price volatility, expected life, risk-free interest rate and dividend yield. The Company estimated the volatility of its common stock at the date of issuance, and at each subsequent reporting period, based on historical volatility that matched the expected remaining life of the warrants. The risk-free interest rate was based on the U.S. Treasury zero-coupon yield curve on the measurement date for a maturity similar to the expected remaining life of the warrants. The expected life of the warrants was assumed to be equivalent to their remaining contractual term. The dividend rate was based on the Company's historical rate, which was at zero. The assumptions used in calculating the estimated fair value of the warrants represented the Company's best estimates. However, these estimates involved inherent uncertainties and the application of management judgment. As a result, if factors changed and different assumptions were used, the warrant liability and the change in estimated fair value could be materially different. As of December 31, 2018, warrants to purchase 27,941 shares of common stock were outstanding and are recorded as equity instruments. In connection with the closing of the IPO, all the Company's outstanding warrants were exercised. No warrants are outstanding as of December 31, 2019

Derivative Liability

ASC 815-15, Derivatives and Hedging: Embedded Derivatives, generally provides three criteria that, if met, require companies to bifurcate conversion options from their host instruments and account for them as free standing derivative financial instruments. These three criteria include circumstances in which (a) the economic characteristics and risks of the embedded derivative instrument are not clearly and closely related to the economic characteristics and risks of the host contract, (b) the hybrid instrument that embodies both the embedded derivative instrument and the host contract is not re-measured at fair value under otherwise applicable generally accepted accounting principles with changes in fair value reported in earnings as they occur and (c) a separate instrument with the same terms as the embedded derivative instrument would be considered a derivative instrument subject to the requirement of ASC 815.

The Company issued certain convertible promissory notes in 2018 to current and new investors which contained an embedded derivative instrument, a share redemption feature that settles upon the next qualified preferred stock financing. This embedded put option was not considered clearly and closely related to the debt host and resulted in an embedded derivative that must be bifurcated and accounted for separately from the debt host. Accordingly, the Company recorded the bifurcated redemption feature as a derivative liability.

Derivative financial liabilities were initially recorded at fair value, with gains and losses arising for changes in fair value recognized in the statement of operations at each period end while such instruments were outstanding. In May 2018, the convertible promissory notes including the redemption premium were converted into Series B redeemable convertible preferred stock. See Note 10 for further discussion of the convertible promissory notes and the bifurcated derivative liability.

Income Taxes

The Company accounts for income taxes under the asset and liability method. Current income tax expense or benefit represents the amount of income taxes expected to be payable or refundable for the current year. Deferred income tax assets and liabilities are determined based on differences between the financial statement reporting and tax bases of assets and liabilities and net operating loss and credit carryforwards and are measured using the enacted tax rates and laws that will be in effect when such items are expected to reverse. Deferred income tax assets are reduced, as necessary, by a valuation allowance when management determines it is more likely than not that some or all of the tax benefits will not be realized.

The Company accounts for uncertain tax positions in accordance with ASC 740-10, *Accounting for Uncertainty in Income Taxes*. The Company assesses all material positions taken in any income tax return, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than fifty percent likely of being realized upon ultimate settlement. As of each balance sheet date, unresolved uncertain tax positions must be reassessed, and the Company will determine whether (i) the factors underlying the sustainability assertion have changed and (ii) the amount of the recognized tax benefit is still appropriate. The recognition and measurement of tax benefits requires significant judgment. Judgments concerning the recognition and measurement of a tax benefit might change as new information becomes available.

The Company includes any penalties and interest expense related to income taxes as a component of other expense and interest expense, net, as necessary.

Comprehensive Income (Loss)

The Company is required to report all components of comprehensive income (loss), including net loss, in the financial statements in the period in which they are recognized. Comprehensive income (loss) is defined as a change in equity of a business enterprise during a period, resulting from transactions and other events and circumstances from non-owner sources. The Company had unrealized gain from its available-for-sale securities during the year ended December 31, 2019 and an unrealized loss from its available-for sale securities during the year ended December 31, 2018, which are considered other comprehensive income (loss).

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of common shares outstanding during the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss by the weighted-average number of common shares and common share equivalents of potentially dilutive securities outstanding for the period. For purposes of the diluted net loss per share calculation, redeemable convertible preferred stock, warrants and common stock options are considered to be potentially dilutive securities. Because the Company reported a net loss for the years ended December 31, 2019 and 2018, and the inclusion of the potentially dilutive securities would be antidilutive, diluted net loss per share is the same as basic net loss per share for both periods.

Recent Accounting Pronouncements

In August 2018, the FASB issued ASU 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement. The new guidance changes disclosure requirements related to fair value measurements as part of the disclosure framework project. The disclosure framework project aims to improve the effectiveness of disclosures in the notes to the financial statements by focusing on requirements that clearly communicate the most important information to users of the financial statements. This guidance is effective for fiscal years beginning after December 15, 2019, with early adoption permitted. The Company does not believe this pronouncement will have a material impact on its financial statements or disclosures.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"). ASU 2016-13 requires companies to measure credit losses utilizing a methodology that reflects expected credit losses and requires a consideration of a broader range of reasonable and supportable information to inform credit loss estimates. For Smaller Reporting Companies as defined by the SEC, ASU 2016-13 is effective for fiscal years beginning after December 15, 2022, including interim periods within those fiscal years. The Company is evaluating the impact of the guidance on its financial statements.

In August 2018, the FASB issued ASU No. 2018-15, *Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40)": Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract* ("ASU 2018-15"), which clarifies the accounting for implementation costs in cloud computing arrangements. ASU 2018-15 is effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. The Company will adopt the standard prospectively on January 1, 2020. The Company does not expect the adoption of ASU 2018-15 to result in a material change to its financial statements.

Recently Adopted Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*. This ASU requires that substantially all leases be recognized by lessees on their balance sheet as a right-of-use asset and corresponding lease liability, including leases currently accounted for as operating leases. The ASU is effective for interim and annual periods beginning after December 15, 2018. Additionally, the FASB issued ASU No. 2018-11, *Leases (Topic 842)*: Targeted Improvements, which offers an additional transition method whereby entities may apply the new leases standard at the adoption date and recognize a cumulative-effect adjustment to the opening balance of retained earnings rather than application of the new leases standard at the beginning of the earliest period presented in the financial statements. The Company elected this transition method and adopted ASC 842 on January 1, 2019 and as a result, recorded a right-of-use asset of $0.9 million, a short-term lease liability of $0.3 million, and a long-term lease liability of $0.6 million and no cumulative effect adjustment was made to the retained earnings as of the adoption date. The Company has elected not to recognize a right-of-use asset and lease liability for short-term leases. A short-term lease is a lease with an expected lease term of 12 months or less and which does not include an option to purchase the underlying asset that the lessee is reasonably certain to exercise. The Company also elected the package of practical expedients under the transition guidance that will retain the historical lease classification and initial direct costs for any leases that exist prior to adoption of the new guidance and the practical expedient to not separate lease and nonlease components. See Note 6 for further disclosure.

In July 2017, the FASB issued ASU No. 2017-11, *Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480), Derivatives and Hedging (Topic 815) I. Accounting for Certain Financial Instruments with Down Round Features II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception* ("ASU 2017-11"). Part I applies to entities that issue financial instruments such as warrants, convertible debt or redeemable convertible preferred stock that contain down-round features. Part II replaces the indefinite deferral for certain mandatorily redeemable noncontrolling interests and mandatorily redeemable financial instruments of nonpublic entities contained within ASC Topic 480 with a scope exception and does not impact the accounting for these mandatorily redeemable instruments. For public entities, ASU 2017-11 is required to be adopted for annual periods beginning after December 15, 2018, including interim periods within those fiscal years. The adoption of ASU 2017-11 did not have any impact on the Company's financial statements since the Company did not have any instruments subject to the scope of ASU 2017-11.

On December 18, 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), which removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. Most amendments within the standard are required to be applied on a prospective basis, while certain amendments must be applied on a retrospective or modified retrospective basis. The pronouncement is effective for fiscal years, and for interim periods within those fiscal years, beginning after December 15, 2020, with early adoption permitted. The Company early adopted the new accounting standard effective January 1, 2019. The adoption did not have a material impact on the Company's financial statements.

All other newly issued accounting pronouncements not yet effective have been deemed either immaterial or not applicable.

Note 3. Fair Value Measurements

The fair value of our financial instruments reflects the amounts that we estimate we would receive in connection with the sale of an asset or pay in connection with the transfer of a liability in an orderly transaction between market participants at the measurement date (exit price). We disclose and recognize the fair value of our assets and liabilities using a hierarchy that prioritizes the inputs to valuation techniques used to measure fair value. The hierarchy gives the highest priority to valuations based upon unadjusted quoted prices in active markets for identical assets or liabilities (Level 1 measurements) and the lowest priority to valuations based upon unobservable inputs that are significant to the valuation (Level 3 measurements). The guidance establishes three levels of the fair value hierarchy as follows:

Level 1 - Inputs that reflect unadjusted quoted prices in active markets for identical assets or liabilities that we have the ability to access at the measurement date;

Level 2 - Inputs other than quoted prices that are observable for the assets or liability either directly or indirectly, including inputs in markets that are not considered to be active;

Level 3 - Inputs that are unobservable. Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

The carrying amounts of the Company's financial instruments, which include cash, accounts payable and accrued liabilities and other current liabilities approximate their fair values due to their short maturities.

Our assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability. During the years presented, the Company has not changed the manner in which it values assets and liabilities that are measured at fair value using Level 3 inputs. The Company recognizes transfers between levels of the fair value hierarchy as of the end of the reporting period. There were no transfers within the hierarchy during the years ended December 31, 2019 and 2018.

Financial assets and liabilities subject to fair value measurements on a recurring basis and the level of inputs used in such measurements by major security type as of December 31, 2019 and December 31, 2018 are presented in the following tables (in thousands):

	Fair Value Measurements at December 31, 2019			
	Total	Level 1	Level 2	Level 3
Money market funds	$ 30,054	$ 30,054	$ —	$ —
Certificates of Deposit	20,046	—	20,046	—
Repurchase Agreements	15,000	—	15,000	—
Corporate notes	38,783	—	38,783	—
Government notes	7,574	—	7,574	—
Commercial Paper	1,096	—	1,096	—
Total	$ 112,553	$ 30,054	$ 82,499	$ —

	Fair Value Measurements at December 31, 2018			
	Total	Level 1	Level 2	Level 3
Money market funds	$ 11,815	$ 11,815	$ —	$ —
Commercial Paper	14,360	—	14,360	—
Corporate notes	16,111	—	16,111	—
Government notes	8,979	—	8,979	—
Asset backed securities	9,192	—	9,192	—
Total	$ 60,457	$ 11,815	$ 48,642	$ —

The change in the derivative liability is as follows (in thousands):

	December 31,	
	2019	2018
Fair Value at beginning of period	$ —	$ 1,886
Bifurcated derivative liability	—	113
Change in fair value	—	206
Conversion of promissory notes to Series B redeemable convertible preferred stock	—	(2,205)
Fair value at end of period	$ —	$ —

See Note 10 for further discussion of the derivative liability.

Note 4: Cash, cash equivalents and investments

The following tables categorize the fair values of cash, cash equivalents, and short-term investments measured at fair value on a recurring basis on our balance sheet (in thousands):

	December 31,	
	2019	2018
Cash and cash equivalents:		
Cash	$ 4,074	$ 11,259
Money market funds	30,054	11,815
Commercial paper	—	1,798
Certificate of deposits	985	—
Repurchase agreements	15,000	—
Corporate notes	1,101	—
Total cash and cash equivalents	$ 51,214	$ 24,872
Short-term investments:		
Commercial paper	1,096	12,562
Corporate notes	24,552	16,111
Government notes	7,574	8,979
Certificate of deposits	15,428	9,192
Total short-term investments	$ 48,650	$ 46,844
Long-term investments:		
Corporate notes	13,130	—
Certificate of deposits	3,633	
Total long-term investments	$ 16,763	$ —

The investments are classified as available-for-sale securities. At December 31, 2019 and 2018 the balance in the Company's accumulated other comprehensive income (loss) was comprised solely of activity related to the Company's available-for-sale securities. There were no realized gains or losses recognized on the sale or maturity of available-for-sale securities for the year ended December 31, 2019 or 2018 and as a result, the Company did not reclassify any amounts out of accumulated other comprehensive income for the year. The Company has a limited number of available-for-sale securities in insignificant loss positions as of December 31, 2019 and 2018, which the Company does not intend to sell and has concluded it will not be required to sell before recovery of the amortized cost for the investment at maturity.

The following table summarizes the available-for-sale securities (in thousands):

	Fair Value Measurements at December 31, 2019			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Money market funds	$ 30,054	$ —	$ —	$ 30,054
Certificates of Deposit	19,992	54	—	20,046
Repurchase Agreements	15,000	—	—	15,000
Corporate notes	38,788	—	(5)	38,783
Government notes	7,563	11		7,574
Commercial Paper	1,096	—	—	1,096
Total cash equivalents and investments	$ 112,493	$ 65	$ (5)	$ 112,553
Classified as:				
Cash equivalents (maturities within 90 days)				$ 47,140
Short-term investments (maturities within one year)				48,650
Long-term investments (maturities beyond 1 year)				16,763
Total cash equivalents and investments				$ 112,553

	Fair Value Measurements at December 31, 2018			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Money market funds	$ 11,815	$ —	$ —	$ 11,815
Commercial paper	14,362	—	(2)	14,360
Corporate notes	16,129	—	(18)	16,111
U.S. government notes	8,980	—	(1)	8,979
Asset backed securities	9,220	—	(28)	9,192
Total cash equivalents and investments	$ 60,506	$ —	$ (49)	$ 60,457
Classified as:				
Cash equivalents (maturities within 90 days)				$ 13,613
Short-term investments (maturities within one year)				46,844
Total cash equivalents and investments				$ 60,457

Note 5: Balance Sheet Components

Prepaid expenses and other current assets

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31,	
	2019	2018
Prepaid expenses	$ 987	$ 47
Prepaid research and development expenses	4,517	753
Other current assets	688	68
	$ 6,192	$ 868

Property and equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2019	2018
Computer Equipment	$ 28	$ —
Lab Equipment	405	378
Finance lease right of use assets	559	—
Less: accumulated amortization and depreciation	(283)	(95)
Property and equipment, net	$ 709	$ 283

Depreciation expense for property and equipment was $188,000 and $51,000 for the years ended December 31, 2019 and 2018, respectively.

Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31,	
	2019	2018
Personnel expense	$ 1,261	$ 483
Research and development expenses	4,410	380
Professional fees	96	75
Other	50	24
Total accrued liabilities	$ 5,817	$ 962

Note 6. Leases

As described in “Note 2 Summary of Significant Accounting Policies,” the Company adopted Topic 842 as of January 1, 2019. Prior period amounts have not been adjusted and continue to be reported in accordance with historic accounting under Topic 840.

Real Estate Operating Leases

In June 2018, the Company entered into a three-year lease agreement with no renewal options with a related party, one of the investors in the Series B redeemable convertible preferred stock. The lease began on July 16, 2018 and provides 3,185 square feet of office and laboratory space in South San Francisco, California. The Company issued 114,437 shares of its Series B redeemable convertible preferred stock with a fair value of $1.1 million in exchange for the leased facility. No other payments are due under the lease. The common area maintenance and other operating costs are included in the base rent. 100% of the issued shares were initially subject to a repurchase option. Pursuant to the terms of the lease, each month beginning on the one-month anniversary of the commencement date of the lease, 1/36th of the total shares are released from the repurchase option until all shares are released over the lease period of three years. The scheduled release of shares ceased immediately upon the IPO which was a terminating event.

The Company completed its IPO on May 13, 2019 and as a result, pursuant to the terms of the lease agreement, all previously unvested shares were fully vested and as part of the IPO process, all outstanding shares of the Company’s redeemable convertible preferred stock including the Series B redeemable convertible preferred stock issued in connection with the lease agreement were converted into shares of the Company’s common stock on a 1-for-1 basis and the operating lease liability was extinguished as the entire lease became prepaid.

In May 2019 the Company entered into an amendment to the lease agreement to rent additional space in the same facility under the same terms as its existing facility lease except the terms of payment. Under the terms of the amendment, the Company paid a one-time fee of approximately $63,000 for the additional space and the lease agreement will terminate in July 2021. No other payments are due under the lease agreement and no renewal option is available. As the entire lease is prepaid, there is no associated lease liability.

The Company recognizes lease expense on a straight-line basis over the term of its operating lease. As of December 31, 2019, future rent expense of approximately $625,000 will be recognized over the remaining term of 19 months on a straight-line basis over the respective lease period.

Clinical Equipment Financing Lease

During the second quarter of 2019, the Company began using certain vendor supplied equipment in connection with its on-going clinical trial. The Company analyzed the agreements and determined that they contained embedded leases. Under the agreements, the Company has prepaid for the use of the equipment through the initial lease term of approximately three years. As a result, the Company has no lease liability associated with these right of use assets. The Company records the finance lease right of use assets in "Property and equipment, net" line on the Balance Sheet. The Company recognizes the amortization expense in research and development expenses in the statement of operations and recognizes expense on a straight-line basis starting when the equipment is placed into service until the end of the contract term. Equipment placed into service is amortized into expense over periods ranging from 28 to 34 months. Amortization expense of the financing lease right of use asset for the year ended December 31, 2019 was $107,000.

Operating and finance lease right of use asset amounts consist of the following as of December 31, 2019 (in thousands):

Operating lease right of use asset, net	$	625
Finance lease right of use asset		559
Finance lease accumulated amortization		(107)
Total finance lease right of use asset, net	$	452

The Company determined its operating and finance lease liabilities for operating lease using a discount rate of 4.00% based on the rate that the Company would have to pay to borrow on a collateralized basis for a similar lease an amount equal to the lease payments in a similar economic environment. As of December 31, 2019, the weighted-average remaining lease term for the operating leases was 1.6 years. The weighted-average remaining lease term for the finance leases was 2.09 years.

Lease costs for the years ended December 31, 2019 was approximately:

Lease costs:		
Finance lease amortization of right of use assets	$	107
Operating lease costs		374
Short-term lease costs		11
Total lease costs	$	492

For the year ended December 31, 2018, rent expense under operating leases computed under the previous accounting method, ASC 840, Leases, was approximately $387,000.

Note 7. Commitments and Contingencies

Legal Matters

The Company's industry is characterized by frequent claims and litigation, including claims regarding intellectual property. As a result, the Company may be subject to various legal proceedings from time to time. The results of any future litigation cannot be predicted with certainty, and regardless of the outcome, litigation can have an adverse impact on the Company because of defense and settlement costs, diversion of management resources and other factors. Management is not aware of any pending or threatened litigation.

Indemnification

As permitted under Delaware law and in accordance with the Company's bylaws, the Company is required to indemnify its officers and directors for certain events or occurrences while the officer or director is or was serving in such capacity. The Company is also party to indemnification agreements with its directors. The Company believes the fair value of the indemnification rights and agreements is minimal. Accordingly, the Company has not recorded any liabilities for these indemnification rights and agreements as of December 31, 2019.

Contingencies

From time to time, we may have certain contingent liabilities that arise in the ordinary course of our business activities. We accrue a liability for such matters when it is probable that future expenditures will be made, and such expenditures can be reasonably estimated.

Note 8. Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)

Redeemable Convertible Preferred Stock

As of December 31, 2018, the outstanding redeemable convertible preferred stock was as follows (in thousands except for share and per share amounts):

	Shares Authorized	Shares Issued and Outstanding	Issuance Price per share	Liquidation Preference	Carrying Value
Series A	9,008,931	9,008,919	$ 1.9067	$ 17,178	$ 17,178
Series B	9,430,145	9,152,108	$ 9.6122	$ 87,972	$ 86,868

On May 13, 2019 in connection with the closing of the IPO, these shares were automatically converted into 18,161,027 shares of common stock, and there are no shares of redeemable convertible preferred stock outstanding as of December 31, 2019.

Common Stock

As of December 31, 2019, the Company had reserved common stock for issuance as follows:

	December 31, 2019
Options issued and outstanding under the 2019 Stock Plan	2,393,934
Shares available for issuance under 2019 Stock Plan	2,439,779
Shares available for issuance under the Employee Stock Ownership Plan	268,295
Total	5,102,008

The Company is authorized to issue 100,000,000 shares of common stock with a par value of $0.001 per share. Each share of common stock is entitled to one vote. The holders of common stock are also entitled to receive dividends whenever funds are legally available and when and if declared by the board of directors, subject to the prior rights of holders of any preferred stock that may be outstanding at the time. The Company has never declared any dividends on common stock. As of December 31, 2019, and 2018, the Company had 26,869,413 and 3,412,366 shares of common stock issued and outstanding respectively.

Common Stock Warrant

In June 2014, in connection with a research grant and license agreement, the Company issued a warrant to purchase 27,941 shares of common stock at $0.03 per share. The grant date estimated fair value of such warrants was insignificant. The warrant was immediately exercisable and expires in June 2024. The warrant was fully exercised in May 2019.

Note 9. Stock Option Plan

On December 4, 2014, the Company's stockholders approved the 2014 Stock Plan ("2014 Plan"), and most recently amended the 2014 Plan on April 25, 2019. The 2014 Plan was amended, restated and re-named the 2019 Equity Incentive Plan (the "2019 Plan"), which became effective as of May 7, 2019, the day prior to the effectiveness of the registration statement filed in connection with the IPO. The remaining shares available for issuance under the 2014 Plan were added to the shares reserved for issuance under the 2019 Plan.

The 2019 Plan provides for the grant of stock options (including incentive stock options and non-qualified stock options), stock appreciation rights, restricted stock, RSUs, performance units, and performance shares to the Company's employees, directors, and consultants. The maximum aggregate number of shares that may be issued under the 2019 Plan is 5,131,549 shares of the Company's common stock. In addition, the number of shares available for issuance under the 2019 Plan will be annually increased on the first day of each of its fiscal years beginning with fiscal 2020, by an amount equal to the least of (i) 2,146,354 shares of common stock; (ii) 4% of the outstanding shares of its common stock as of the last day of its immediately preceding fiscal year; and (iii) such other amount as the Company's Board of Directors may determine.

The 2019 Plan may be amended, suspended or terminated by the Company's Board of Directors at any time, provided such action does not impair the existing rights of any participant, subject to stockholder approval of any amendment to the 2019 Plan as required by applicable law or listing requirements. Unless sooner terminated by the Company's Board of Directors, the 2019 Plan will automatically terminate on April 23, 2029.

As of December 31, 2019, the Company had 2,439,779 shares available for future issuance under the 2019 Plan.

In 2019 and 2018, the Company recognized $2,056,000 and $155,000 respectively, of stock-based compensation expense related to options granted to employees and non-employees. The compensation expense is allocated on a departmental basis, based on the classification of the option holder. No income tax benefits have been recognized in the statement of operations for stock-based compensation arrangements.

Future stock-based compensation for unvested employee and non-employee options granted and outstanding as of December 31, 2019 is $6.4 million to be recognized over a remaining weighted average requisite service period of 1.42 years.

Stock option activity under the 2019 Plan is as follows:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (Years)	Aggregate Intrinsic Value
Balance at December 31, 2017	**769,409**	$ 0.39	8.89	1,107,581
Options granted	1,316,342	2.08	—	—
Options exercised	(51,350)	0.46	—	—
Options cancelled	(148,897)	0.41	—	—
Balance at December 31, 2018	**1,885,504**	1.57	9.07	1,252,496
Options granted	932,639	15.87	—	—
Options exercised	(194,279)	0.51	—	—
Options forfeited / expired	(229,930)	21.09	—	—
Balance at December 31, 2019	**2,393,934**	$ 5.35	8.62	$ 121,592,682
Options vested and expected to vest to December 31, 2019	2,393,934	$ 5.35	8.62	$ 121,592,682
Options exercisable at December 31, 2019	751,334	$ 2.59	7.96	$ 40,235,852

Aggregate intrinsic value represents the difference between the Company's estimated fair value of its common stock as of their respective balance sheet dates and the exercise price of outstanding options. The total intrinsic value of options exercised was $886,989 and $91,000 for the year ended December 31, 2019 and 2018, respectively. During the year ended December 31, 2019, the weighted-average grant-date fair value of the options vested was $2.35 per share. The weighted-average grant date fair value of options granted during the years ended December 31, 2019 and 2018 was $11.11 and $1.26 per share, respectively.

The following table summarizes employee and non-employee stock-based compensation expense for the years ended December 31, 2019 and 2018 and the allocation within the statements of operations and comprehensive loss (in thousands):

	2019	2018
General and administrative expense	$ 1,378	$ 78
Research and development expense	678	77
Total stock-based compensation	2,056	155

The Company estimates the fair value of stock-based compensation utilizing the Black-Scholes option pricing model, which is dependent upon several variables, such as expected term, volatility, risk-free interest rate, and expected dividends. Each of these inputs is subjective and generally requires significant judgment to determine. Stock-based compensation is measured at the grant date based on the fair value of the award and is recognized as expense, over the requisite service period, which is generally the vesting period of the respective award. The Company recognizes compensation on a straight-line basis over the requisite vesting period for each award. Forfeitures are recognized as they occur. The following weighted average assumptions were used to calculate the fair value of stock-based compensation as of December 31, 2019 and 2018:

	2019	2018
Expected volatility	80.19%	69.6%
Expected dividend yield	—%	—%
Expected term (in years)	6.25	6.25
Risk-free interest rate	1.90%	2.91%

Expected Term — The Company has opted to use the "simplified method" for estimating the expected term of options, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option (generally 10 years).

Expected Volatility — Due to the Company's limited operating history and a lack of company specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards.

Risk-Free Interest Rate — The risk-free rate assumption is based on the U.S. Treasury instruments with maturities similar to the expected term of the Company's stock options.

Expected Dividend — The Company has not issued any dividends in its history and does not expect to issue dividends over the life of the options and therefore has estimated the dividend yield to be zero.

Fair value of Common Stock — The fair value of the shares of common stock underlying the stock-based awards has historically been determined by the board of directors, with input from management. Prior to the Company's IPO, there has been no public market for the Company's common stock, the board of directors determined the fair value of the common stock on the grant-date of the stock-based award by considering a number of objective and subjective factors, including enterprise valuations of the Company's common stock performed by an unrelated third-party specialist, valuations of comparable companies, sales of the Company's redeemable convertible preferred stock to unrelated third parties, operating and financial performance, the lack of liquidity of the Company's capital stock, and general and industry-specific economic outlook. Subsequent to the IPO date, the board of directors uses the closing price of stock on the date of grant to determine the fair value. The board of directors intends all options granted to be exercisable at a price per share not less than the estimated per share fair value of common stock underlying those options on the date of grant.

As of December 31, 2019 and 2018, there was a total of $6.0 million and $1.57 million, respectively, of unrecognized employee and non-employee compensation costs related to non-vested stock option awards. The fair value of shares vested during the respective years was $1,193,000 and $102,000, respectively.

Employee Stock Purchase Plan

On April 24, 2019, the Company's Board of Directors adopted its 2019 Employee Stock Purchase Plan ("2019 ESPP"), which was subsequently approved by the Company's stockholders and became effective on May 7, 2019, the day immediately prior to the effectiveness of the registration statement filed in connection with the IPO. The 2019 ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the Internal Revenue Code (the "Code") for U.S. employees. In addition, the 2019 ESPP authorizes grants of purchase rights that do not comply with Section 423 of the Code under a separate non-423 component for non-U.S. employees and certain non-U.S. service providers. The Company has reserved 268,295 shares of common stock for issuance under the 2019 ESPP. In addition, the number of shares reserved for issuance under the 2019 ESPP will be increased automatically on the first day of each fiscal year for a period of up to ten years, starting with the 2020 fiscal year, by a number equal to the lesser of: (i) 536,589 shares; (ii) 1% of the shares of common stock outstanding on the last day of the prior fiscal year; or (iii) such lesser number of shares determined by the Company's Board of Directors. The 2019 ESPP is expected to be implemented through a series of offerings under which participants are granted purchase rights to purchase shares of the Company's common stock on specified dates during such offerings. The Company has not yet approved an offering under the 2019 ESPP.

Note 10. Convertible Promissory Notes

In February 2017 the Company received $7.6 million from the issuance of convertible promissory notes to the Company's current investors. In June 2017 the Company received an additional $150,000 from an issuance under the same note facility to a new investor. In January 2018 the Company received $250,000 from a new investor under the same note facility for a total of $8.0 million in principal value under the note facility. The notes accrue simple interest on the outstanding principal amount at the rate of 8% per annum and were set to mature on February 1, 2019.

The convertible promissory notes have conversion and repayment options as follows: (a) in the event that the Company has an equity financing event of at least $10 million to new investors on or before the maturity date, then the outstanding principal amount of this convertible promissory note and any unpaid accrued interest will automatically convert in whole into equity securities sold in the qualified financing at a conversion price equal to 80% of the cash price paid per share for equity securities by the investors in the qualified financing, or (b) the Company consummates a merger of the Company where it does not maintain majority voting power or conducts a sale, lease, transfer, exclusive license or other disposition of all or substantially all of its assets while the convertible promissory notes remain outstanding, the Company shall repay the holders in cash in an amount equal to 200% of the outstanding principal and accrued interest amount of the convertible promissory notes.

The Company evaluated its convertible notes and determined that the redemption premium feature qualified as a derivative liability to be separately accounted for in accordance with ASC 815. The convertible promissory notes contained put options as follows:

1. On or before the maturity date, the principal and accrued interest of the notes will automatically convert into equity securities issued and sold in the initial closing of the Company's next qualified equity financing with gross proceeds of at least $10,000,000, exclusive of the conversion of the notes. The number of shares to be issued to the note holders will be equal to dividing the outstanding principal and any unpaid accrued interest by 80% of the price paid per share of the next equity security sold to investors. The discount in share price to note holders is not considered clearly and closely related to the debt host and results in an embedded derivative that must be bifurcated and accounted for separately from the debt host.

2. In the event of a merger or sale, lease, transfer, exclusive license or other disposition of all or substantially all of its assets prior to repayment, the outstanding principal and unpaid accrued interest will be repaid in cash, plus a repayment premium equal to 100% of the outstanding principal and accrued interest at the time of the merger or sale of assets. The premium to note holders is not considered clearly and closely related to the debt host and results in an embedded derivative that must be bifurcated and accounted for separately from the debt host.

Accordingly, upon the issuance of the February 2017 convertible promissory notes, the estimated fair value of the embedded derivative liability was determined using a bond plus option valuation model and assuming a probability of 80% that a qualified financing would occur and a zero probability that a merger or sale would occur. The Company recorded the estimated fair value of these put options (embedded derivatives) as a liability of $1.55 million with an offsetting amount recorded as debt discount, which offsets the carrying amount of the debt. The debt discount is amortized over the debt's expected term. The derivative liability is revalued at the end of each reporting period and any change in fair value is recognized in other income.

Upon the issuance of the June 2017 convertible promissory notes, the estimated fair value of the embedded derivatives were determined using a bond plus option valuation model and assuming a probability of 80% that a qualified financing would occur and a zero probability that a sale or merger would occur. The Company recorded the estimated fair value of these put options (embedded derivatives) as a liability of $30,000 with an offsetting amount recorded as debt discount, which offsets the carrying amount of the debt.

Upon issuance of the January 2018 convertible promissory notes, the estimated fair value of the embedded derivatives was determined using a bond plus option valuation model and assuming a probability of 90% that a qualified financing would occur and a zero probability that a merger or sale would occur. The Company recorded the estimated fair value of these put options (embedded derivatives) as a liability of $56,250 with an offsetting amount recorded as debt discount, which offsets the carrying amount of the debt.

The derivative liability is revalued at the end of each reporting period and any change in fair value is recognized in "Change in fair value of redemption premium liability" in the Statement of Operations.

In May 2018, the notes converted into 1,147,205 shares of the Company's Series B redeemable convertible preferred stock in conjunction with the Company's Series B redeemable convertible preferred stock financing (the "Series B Financing"), which was considered a Qualified Financing under the terms of the notes. In conjunction with the closing, the holders of the notes also converted their accrued and unpaid interest of $0.8 million and the Company recorded a change in the fair value of the derivative liability of $206,000.

Note 11. Related Party Transactions

In June 2014, the Company entered into a research grant and license agreement (the Agreement) with a stockholder of the Company. The Agreement requires the Company to pay royalties to the stockholder in the amount of 3% of gross revenues not to exceed $1.05 million. This agreement was amended in April 2019 and the royalty payment provision was removed.

As described in Note 6, the Company entered into a three-year lease agreement with a Series B redeemable preferred stock investor. The lease began on July 16, 2018 and provides 3,185 square feet of office space in South San Francisco, California. The Company issued 114,437 restricted shares of its Series B redeemable convertible preferred stock in exchange for the use of the leased facility. In May 2019, the Company entered into an amendment to the lease agreement to rent additional space in the same building for a one-time payment of approximately $63,000 on the same terms as the July 2018 agreement except rent.

Under the terms of the convertible promissory notes described in Note 10, certain board members provided $5.05 million in principal value in the note offering which accrued interest at 8% per annum. These board members received a total of $534,000 interest which converted per the terms of the promissory note into 69,465 shares of Series B redeemable convertible preferred stock on May 23, 2018.

As described in Note 1, the Company completed its IPO in May 2019. As a result of the IPO, in addition to the 229,453 shares of Series B redeemable convertible preferred stock held by the investor, an additional 82,649 shares of the Company's Series B redeemable convertible preferred stock under issued pursuant the lease agreement fully vested and were converted into common stock of the Company on a one-to-one basis.

Note 12. Income taxes

From inception through 2019, the Company has only generated pretax losses in the United States and has not generated any pretax income or loss outside of the United States. The Company did not record a provision (benefit) for income taxes for the years ended December 31, 2019 and 2018.

The provision for income taxes differs from the amount expected by applying the federal statutory rate to the loss before taxes as follows:

	Year ended December 31,	
	2019	2018
Federal statutory income tax rate	21.00 %	21.00 %
State income taxes	(1.12) %	6.24 %
Income tax credits	3.67 %	—
Non-deductible expenses and others	(0.38) %	(1.02) %
Non-deductible expenses related to the convertible promissory notes	— %	(1.96) %
Change in valuation allowance	(23.17) %	(24.26) %
	— %	— %

As of December 31, 2019 and 2018, the components of the Company's deferred tax assets are as follows (in thousands):

	Year ended December 31,	
	2019	2018
Deferred tax asset:		
Federal and State net operating loss carryforwards	$ 14,219	$ 8,010
Stock based compensation	238	—
Other accruals and deferred expense	185	—
Tax credits	1,867	—
Total deferred tax asset	16,509	8,010
Deferred tax liabilities:		
Property and equipment	(20)	(70)
Less valuation allowance	(16,489)	(7,940)
Net deferred tax assets	$ —	$ —

Deferred income taxes reflect the net tax effects of (a) temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes, and (b) operating losses and tax credit carryforwards.

The Company's accounting for deferred taxes involves the evaluation of a number of factors concerning the realizability of its net deferred tax assets. The Company primarily considered such factors as its history of operating losses, the nature of the Company's deferred tax assets, and the timing, likelihood and amount, if any, of future taxable income during the periods in which those temporary differences and carryforwards become deductible. At present, the Company does not believe that it is more likely than not that the deferred tax assets will be realized; accordingly, a full valuation allowance has been established and no deferred tax asset is shown in the accompanying balance sheets. The valuation allowance increased by approximately $8.5 million and $3.1 million respectively for the years ended December 31, 2019 and 2018.

At December 31, 2019, the Company has federal net operating loss carryforwards of approximately $62.3 million of which $46.4 million will not expire and $15.9 million begin expiring in 2034. The Company also has state net operating loss carryforwards of approximately $16.3 million which begin to expire in 2034. Additionally, the Company has federal and state tax credits of approximately $3.0 million which begin to expire in 2036.

Use of the net operating loss and credit carryforwards may be subject to a substantial annual limitation due to the ownership change provisions of U.S. tax law and similar state provisions. The annual limitation may result in the expiration of net operating losses and credits before use.

Uncertain Tax Positions

The Company follows the provisions of the FASB ASC 740-10, Accounting for Uncertainty in Income Taxes. ASC 740-10 prescribes a comprehensive model for the recognition, measurement, presentation and disclosure in financial statements of uncertain tax positions that have been taken or expected to be taken on a tax return. No liability related to uncertain tax positions is recorded in the financial statements.

The Company is subject to taxation in the United States. Because of the net operating loss and research credit carryforwards, all of the Company's tax years, from 2013 to 2019, remain open to U.S. federal and California state tax examinations. There were no interest or penalties accrued at December 31, 2019 and December 31, 2018.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	Year ended December 31,	
	2019	2018
Beginning balance	$ 356	$ 171
Additions for tax positions taken in a prior year	168	—
Additions for tax positions taken in a current year	535	185
Ending balance	$ 1,059	$ 356

Note 13. Net Loss per Share

The following table sets forth the computation of basic and diluted net loss per share (in thousands except for share and per share amounts):

	December 31,	
	2019	2018
Numerator:		
Net loss	$ (36,980)	$ (12,476)
Denominator		
Weighted average common shares outstanding	19,031,940	3,362,192
Net loss per share, basic and diluted	$ (1.94)	$ (3.71)

The following outstanding potentially dilutive securities were excluded from the computation of diluted net loss per share for the periods presented because including them would have been antidilutive:

	December 31,	
	2019	2018
Series A convertible preferred stock	—	9,008,919
Series B convertible preferred stock	—	9,152,108
Options issued and outstanding	2,393,934	1,885,504
Warrants	—	27,941
	2,393,934	20,074,472

Note 14. Employee Benefit Plan

The Company sponsors a 401(k) defined contribution plan for its employees. This plan provides for pre-tax and post-tax contributions for all employees. Employee contributions are voluntary. Employees may contribute up to 100% of their annual compensation to this plan, as limited by an annual maximum amount as determined by the Internal Revenue Service. The Company may match employee contributions, and may make profit sharing contributions, in amounts to be determined at the Company's sole discretion. The Company made no contributions to the plan for the years ended December 31, 2019 and 2018.

Note 15. Subsequent Events

Private Investment in Public Equity ("PIPE")

On February 10, 2020, the Company sold and issued 2,500,000 shares of common stock in a private placement to a group of institutional investors and an entity affiliated with a member of the Company's board of directors for aggregate gross proceeds of $125.0 million. Costs related to the offering were $7.4 million. In connection with the private placement, the Company is obligated to prepare and file with the SEC within 60 days of the closing date, a registration statement to register for resale the shares of common stock sold in the private placement.

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

None

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our disclosure controls and procedures are designed to ensure that information required to be disclosed by us in reports that we file or submit under the Securities Exchange Act of 1934, as amended or the Exchange Act, is recorded, communicated to our management to allow timely decisions regarding required disclosure, summarized and reported within the time periods specified in the SEC's rules and forms.

Under the supervision and with the participation of our management, including the Chief Executive Officer and Chief Financial Officer, we have evaluated the effectiveness of our disclosure controls and procedures as required under Rules 13a-15(e) and 15d-15(e) under the Exchange Act as of December 31, 2019. Based on that evaluation, the Chief Executive Officer and Chief Financial Officer have concluded that these disclosure controls and procedures are effective as of December 31, 2019.

Management's Report on Internal Control over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm on our internal control over financial reporting due to a transition period established by rules of the SEC for newly public companies. Additionally, for as long as we remain an emerging growth company, we intend to take advantage of the exemption permitting us not to comply with the requirement that our independent registered public accounting firm provide an attestation on the effectiveness of our internal control over financial reporting.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting during the quarter ended December 31, 2019 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.

Executive Officers and Directors

The names and ages of our executive officers and directors as of March 15, 2020, are as follows:

Name	Age	Position(s)
Executive Officers:		
Casey C. Lynch	46	President, Chief Executive Officer and Chairman of the Board
Christopher Lowe	52	Chief Financial Officer and Treasurer
Kristen Gafric	44	Senior Vice President, Legal and Administration, and Secretary
Michael Detke, M.D.	53	Chief Medical Officer
Stephen S. Dominy, M.D.	64	Chief Scientific Officer and Director
Leslie Holsinger, Ph.D.	54	Executive Vice President of Preclinical Development
Non-Employee Directors:		
David A. Lamond(2)(3)	45	Director
Margaret McLoughlin, Ph.D(2)(3).	57	Director
Una Ryan, OBE, Ph.D(1)(3).	78	Director
Christopher J. Senner(1)	52	Director
Kevin Young, CBE(1)(2)(3)	62	Director

(1) Member of the audit committee
(2) Member of the compensation committee
(3) Member of the nominating and corporate governance committee

Executive Officers

Casey C. Lynch has served as our President and Chief Executive Officer and a member of our board of directors since July 2014, and as Chairman of our board of directors since November 2018. Prior to co-founding Cortexyme, Ms. Lynch co-founded various companies and organizations in the biotechnology industry including Aspira Biosystems, Inc. and NeuroInsights, LLC. She served as Aspira's co-founder, President and Chief Executive Officer from 1999 to 2004 and she co-founded NeuroInsights, LLC and served as its Managing Director from 2004 to 2015. Ms. Lynch also co-founded Neurotechnology Industry Organization and served as a board member from March 2005 to September 2018. Ms. Lynch holds a B.S. in Neuroscience from the University of California, Los Angeles, an M.S. in Neuroscience from the University of California, San Francisco and obtained a certificate in Management Development for Entrepreneurs Program from the University of California, Los Angeles. We believe that Ms. Lynch is qualified to serve as a director because of her operational and historical expertise gained from serving as our President and Chief Executive Officer, and her extensive professional and educational experience in the biotechnology industry.

Christopher Lowe has served as our Chief Financial Officer since January 2019 and as our Treasurer since April 2019. From June 2018 until January 2019, Mr. Lowe served as a consultant to us and our interim Chief Financial Officer through his capacity as a partner at FLG Partners. Mr. Lowe has also served as the Managing Partner of the Innventus Fund at Innventure since January 2017 and he has served as a partner at FLG Partners since January 2014 and its Managing Partner since January 2018. Prior to joining Cortexyme, Mr. Lowe served as the Interim Chief Executive Officer and Chief Financial Officer of Hansen Medical from February 2014 to July 2016, and he served as the Chief Business Officer and Chief Financial Officer of Anthera Pharmaceuticals from September 2007 to June 2013. Mr. Lowe served as a director for Inspyr Therapeutics from September 2016 to December 2018. He also served as a director of EpiBiome from May 2016 to June 2018, and he served as a director and Chairman of the Audit Committee for Asante Solutions from December 2014 to October 2015. Mr. Lowe holds a B.S. in Business Administration from California Polytechnic State University and an M.B.A. from St. Mary's University.

Kristen Gafric has served as our Secretary since July 2014, as our Vice President of Operations since September 2017, and as our Senior Vice President, Legal and Administration since April 2019. Prior to co-founding Cortexyme, Ms. Gafric served as the Senior Manager of Commercial Contracts Management at Triton Container International from June 2014 to September 2016. Ms. Gafric was also the Senior Contracts Manager at San Francisco Health Plan from June 2013 to June 2014 and Manager of Contracts and Grants at the University of California San Francisco from October 2011 to June 2013. Ms. Gafric holds a B.A. in Psychology and Philosophy from Emory University and a J.D. from Cleveland State University.

Michael Detke, M.D., has served as our Chief Medical Officer since December 2018. Dr. Detke has over 25 years of research experience and extensive clinical and drug development expertise. Prior to joining Cortexyme, Dr. Detke served as the Chief Medical Officer at Embera NeuroTherapeutics, Inc. from September 2016 to December 2018, and he served as President of Detke Biopharma Consulting LLC from April 2013 to December 2018, including as Chief Medical Officer for CoMentis Pharmaceuticals. He served as Chief Medical Officer and Director of the MedAvante Research Institute of MedAvante, Inc. Dr. Detke joined MedAvante from Eli Lilly, Inc. where he served as Executive Director and head of early phase development of CNS therapeutics. At Lilly, he led clinical development of one of the industry's deepest and strongest pipelines of CNS products. He served as Senior Medical Director responsible for Phase III development for Cymbalta and Phase IV for Prozac. Dr. Detke has served as an Adjunct volunteer Clinical Professor of Psychiatry at Indiana University School of Medicine since July 2000. Dr. Detke holds a B.A. and M.S. in Psychology from Yale University and an M.A., M.D. and Ph.D. in Psychology and Behavioral Pharmacology from the University of Pennsylvania. He also received post-doctoral training in Psychiatry from Harvard Medical School.

Stephen S. Dominy, M.D., has served as a member of our board of directors since December 2015 and as our Chief Scientific Officer since April 2016. Prior to co-founding Cortexyme, Dr. Dominy served as a Division Director at San Francisco General Hospital and as Associate Professor of Psychiatry at the University of California, San Francisco School of Medicine from 2006 to 2016. Dr. Dominy holds a B.S. in Pharmacy from The Ohio State University College of Pharmacy and an M.D. from the Wright State University Boonshoft School of Medicine. We believe that Dr. Dominy is qualified to serve as a director because of his educational background, as well as his extensive research and technical experience that provides an important perspective on operations and development.

Leslie Holsinger, Ph.D., has served as our Executive Vice President of Preclinical Development since January 2018. She also served as our Vice President of Preclinical Development from April 2016 to December 2017. Prior to joining Cortexyme, Dr. Holsinger served as Director of Biology and Vice President of Biology at Virobay Inc. from 2006 to 2016. Prior to her work at Virobay, Dr. Holsinger held positions of increasing responsibility at Celera and Sugen Inc. Dr. Holsinger holds an A.B. in Biochemistry from Occidental College and a Ph.D. in Biochemistry, Molecular and Cellular Biology from Northwestern University. She also received post-doctoral training at Stanford University School of Medicine.

Non-employee Directors

David A. Lamond has served on our board of directors since December 2015. Mr. Lamond has served as the president of En Pointe LLC, an investment firm, since 2016. He served as the President, Chief Executive Officer and Chief Investment Officer of Lamond Capital Partners LLC from 2011 to 2016. He also serves on the board of directors of Applied Molecular Transport, a biotechnology company. Lucira Health Inc, a molecular diagnostics company, Inquis Medical, a medical device company and Genelpis SAS, a biotech company. He previously served on the board of Arrinex, a medical device company until its acquisition by Stryker Corporation in February 2019. In addition, he serves on the board of directors of two non-profit organizations, Tipping Point Community and Ubuntu Pathways. Mr. Lamond holds a B.A. in History from Duke University and a J.D. from Duke Law School. We believe that Mr. Lamond is qualified to serve as a director because of his extensive experience in important ecosystem partners, and his service on a number of boards provides an important perspective on operations, finance and corporate governance matters.

Margaret McLoughlin, Ph.D., has served on our board of directors since December 2015. From January 2014 to April 2019, Dr. McLoughlin served as an Executive Director in World Wide Business Development, at Pfizer Inc. focusing on venture investments, and from June 2018 to April 2019, she was a Partner in Pfizer Ventures, a venture capital arm of Pfizer Inc. focused on companies working in areas aligned with the future directions of Pfizer Inc. Dr. McLoughlin served as a director on the board of directors of 4D Molecular Therapeutics, System1 Biosciences and Adapsyn Biosciences. Dr. McLoughlin joined Pfizer Inc. in 2001 and prior to focusing on venture investments, had roles of increasing responsibility within Worldwide Business Development where she led transactions with multiple biotech companies, academic institutions and other large pharma companies. Prior to working at Pfizer Inc., Dr. McLoughlin served as a Director in Yale's Office of Cooperative Research for two years. Dr. McLoughlin served in various positions at Mallinckrodt Medical from 1992 to 1999, holding positions in Discovery Research, followed by Technology Planning. Dr. McLoughlin holds a B.S. in Chemistry from the University of California, Irvine and a Ph.D. in Chemistry from the University of California, Santa Barbara. We believe that Dr. McLoughlin is qualified to serve as a director because of her extensive experience in the biotechnology industry and her service on a number of boards, which provides an important perspective on operations and corporate governance matters, as well as her education in biotechnology.

Una Ryan, OBE, Ph.D., has served on our board of directors since January 2019. Dr. Ryan has served as a Managing Director at Golden Seeds LLC since 2012, a Partner at Astia Angel since 2012, and a Limited Partner at Breakout Ventures since 2016. She was Chairman of The Bay Area BioEconomy Initiative from 2012 to 2015. Dr. Ryan served as the President and Chief Executive Officer at Waltham Technologies, Inc. from 2008 to 2010. She served as the Chief Executive Officer, President and Chief Operating Officer of AVANT Immunotherapeutics Inc. from 1998 to 2008 (which then became known as Celldex, Inc). She also served as the President and Chief Executive Officer of Diagnostics for All, or DFA from 2009 to 2012 and as Director of Health Sciences at Monsanto Corporation from 1989 to 1993. Dr. Ryan serves on the board of directors of the following private companies: RenovoRx, Elemental Machines and Nativis, Inc. She also serves on the board of directors of the following non-profit entities: Cambridge in America, the University of Bristol Foundation and the San Francisco Art Institute. Dr. Ryan served as a director on the board of directors for AVANT Immunotherapeutics, Inc, AMRIGlobal, Inc, BayBio, MassBio, BIO, or Biotechnology Innovation Organization, New England Healthcare Institute, Board of Associates of the Whitehead Institute and Strategy & Policy Council of the MIT Center for Biomedical Innovation. Dr. Ryan holds a B.S. in Zoology, Microbiology, Chemistry from Bristol University and a Ph.D. in Cellular and Molecular Biology from Cambridge University. Dr. Ryan was awarded the Order of the British Empire for services to biotechnology. We believe that Dr. Ryan is qualified to serve as a director because of her extensive experience in the biotechnology industry and her service on a number of boards of companies, which provides an important perspective on operations and corporate governance matters.

Christopher J. Senner has served on our board of directors since March 2019. Mr. Senner has served as Executive Vice President and Chief Financial Officer for Exelixis, Inc. since 2015. Prior to joining Exelixis, Inc., Mr. Senner served as Vice President, Corporate Finance for Gilead Sciences, Inc., a biopharmaceutical company, from 2010 to 2015, where he was accountable for controllership, tax, treasury and corporate and operational financial planning. Mr. Senner previously spent 18 years at Wyeth, a pharmaceutical company acquired by Pfizer Inc. in 2009, in a variety of financial roles with increasing responsibility, most notably as Chief Financial Officer of Wyeth's United States pharmaceuticals business and the BioPharma business unit. Mr. Senner holds an undergraduate degree in Finance from Bentley College. We believe that Mr. Senner's extensive executive and professional experience in the biotechnology industry qualify him to serve as a director.

Kevin Young, CBE has served on our board of directors since January 2019. Mr. Young served as the Chief Operating Officer and Executive Vice President of Commercial Operations for Gilead Sciences, Inc. from 2004 to 2018. Mr. Young previously held positions at ICI Pharmaceuticals and Amgen, Inc., where Mr. Young was Head of the U.S. Inflammation Business Unit from 2001 to 2004. Mr. Young holds undergraduate and graduate degrees in Sports Science and Exercise from Liverpool John Moores University and the University of Nottingham, respectively, and has completed the Executive Program at the University of Michigan, School of Business Administration. Mr. Young was appointed a commander of the Most Excellent Order of the British Empire, recognizing his services to the healthcare and pharmaceutical industries. We believe that Mr. Young is qualified to serve as a director because of his extensive executive and professional experience in the biotechnology industry.

There are no family relationships among any of our directors or executive officers.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee is composed of Mr. David Lamond, who is the chair of our nominating and corporate governance committee, and Mr. Kevin Young, CBE, Margaret McLoughlin, Ph.D. and Una Ryan, OBE, Ph.D. The composition of our nominating and corporate governance committee meets the requirements for independence under current Nasdaq listing standards and SEC rules and regulations. Our nominating and corporate governance committee, among other things:

- identifies, evaluates and recommends nominees to our board of directors and committees of our board of directors;
- conducts searches for appropriate directors;
- evaluates the performance of our board of directors and of individual directors;
- considers and makes recommendations to the board of directors regarding the composition of the board and its committees;
- reviews developments in corporate governance practices;
- evaluates the adequacy of our corporate governance practices and reporting; and
- makes recommendations to our board of directors concerning corporate governance matters.

Our nominating and corporate governance committee has a written charter approved by our board of directors. A copy of the charter is available on the Investor Relations section of our website, which is located at https://ir.cortexyme.com/investor-relations, by clicking on "Governance Documents" in the "Governance" section of our website.

Nomination to the Board of Directors

Candidates for nomination to our board of directors are selected by our board of directors based on the recommendation of our nominating and corporate governance committee in accordance with its charter, our restated certificate of incorporation and restated bylaws, our Corporate Governance Guidelines and the criteria approved by our board of directors regarding director candidate qualifications. In recommending candidates for nomination, our nominating and corporate governance committee considers candidates recommended by directors, officers, employees, stockholders and others, using the same criteria to evaluate all candidates.

Our restated bylaws provide that stockholders may present nominations to be considered at an annual meeting by providing timely notice to our Secretary at our principal executive office. To be timely for our 2020 Annual Meeting, our Secretary must receive the written notice at our principal executive office no earlier than the one hundred twentieth (120th) day prior to the 2020 Annual Meeting and (ii) no later than the close of business on the later of the ninetieth (90th) day prior to the 2020 Annual Meeting, or the tenth (10th) day following the day on which public announcement is first made of the date of the 2020 Annual Meeting.

A stockholder's notice to the Secretary must set forth the information required by our restated bylaws. If a stockholder who has notified Cortexyme of such stockholder's intention to present a nomination for persons for election at an annual meeting does not appear to present such stockholder's proposal at such meeting, Cortexyme does not need to present the nomination of persons for election for vote at such meeting.

Audit Committee

Our audit committee is composed of Christopher J. Senner, who is the chair of our audit committee, Kevin Young, CBE and Una Ryan, OBE, Ph.D. The composition of our audit committee meets the requirements for independence under current Nasdaq listing standards and SEC rules and regulations. Each member of our audit committee is financially literate. In addition, our board of directors has determined that Mr. Senner and Ms. Ryan are audit committee financial experts within the meaning of Item 407(d) of Regulation S K of the Securities Act of 1933, as amended, or the Securities Act. This designation does not impose any duties, obligations or liabilities that are greater than those generally imposed on members of our audit committee and our board of directors.

Our audit committee, among other things:

- selects a firm to serve as the independent registered public accounting firm to audit our financial statements;
- helps to ensure the independence of the independent registered public accounting firm;
- discusses the scope and results of the audit with the independent registered public accounting firm, and reviews, with management and the independent accountants, our interim and year end operating results;
- develops procedures for employees to anonymously submit concerns about questionable accounting or audit matters;
- considers the adequacy of our internal accounting controls and audit procedures;
- reviews and approves any proposed transaction between our company and any related party; and
- approves the fees and other compensation to be paid to our independent registered public accounting firm, and pre approves all audit and non audit related services provided by our independent registered public accounting firm.

Our audit committee has a written charter approved by our board of directors. A copy of the charter is available on the Investor Relations section of our website, which is located at https://ir.cortexyme.com/investor-relations, by clicking on "Governance Documents" in the "Governance" section of our website.

Code of Business Conduct and Ethics

We have adopted a Code of Business Conduct and Ethics that applies to all of the members of our board of directors, officers and employees. Our Code of Business Conduct and Ethics is posted on the Investor Relations section of our website, which is located at https://ir.cortexyme.com/investor-relations, by clicking on "Governance Documents" in the "Governance" section of our website. We intend to satisfy the disclosure requirement under Item 5.05 of Form 8 K regarding amendment to, or waiver from, a provision of our Code of Business Conduct and Ethics by posting such information on our website at the location specified above.

Delinquent Section 16 Reports

Section 16(a) of the Exchange Act requires our directors, executive officers and any persons who own more than 10% of our common stock to file initial reports of ownership and reports of changes in ownership with the SEC. Based solely on our review of the copies of such forms filed with the SEC and written representations from the directors and executive officers, we believe that all Section 16(a) filing requirements were timely met in the year ended December 31, 2019 except for a Form 4 for each of Dr. McLoughlin, Mr. Young and Dr. Ryan with respect to shares of common stock that each director purchased on May 13, 2019 in our directed share program in connection with our IPO.

Item 11. Executive Compensation.

Executive Compensation

Our named executive officers for 2019, which consist of our principal executive officer and the next two most highly compensated executive officers, are:

Casey C. Lynch, our President and Chief Executive Officer;

Kristen Gafric, our Senior Vice President, Legal and Administration, and Secretary; and

Michael Detke, M.D., our Chief Medical Officer.

Summary Compensation Table

The following table provides information concerning compensation awarded to, earned by and paid to each of our named executive officers during 2018 and 2019:

Name and Principal Position	Year	Salary ($)	Bonus ($)(1)	Stock Option Awards ($)(2)	Non-Equity Incentive Plan Compensation ($)(3)	Total ($)
Casey C. Lynch	2019	415,577	—	—	144,375	559,952
Chief Executive Officer	2018	277,019	82,500	557,814	—	917,333
Kristen Gafric	2019	328,462	—	1,541,475	83,000	1,952,937
Senior Vice President, Legal and Administration, and Secretary						
Michael Detke, M.D.	2019	373,077	—	620,466	106,625	1,100,168
Chief Medical Officer						

(1) The amounts reported in this column represent performance-based cash incentives earned by Ms. Lynch based on 2018 performance.

(2) The amounts reported in this column reflect the aggregate grant date fair value for financial statement reporting purposes of stock options granted 2018 and 2019 as determined in accordance with FASB ASC Topic 718. These amounts reflect our accounting expense for these stock options and do not represent the actual economic value that may be realized by each named executive officer. There can be no assurance that these amounts will ever be realized. For information on the assumptions used in valuing these awards, refer to Note 9 to the historical financial statements included in this Annual Report on Form 10-K. As required by the SEC rules, the amounts shown exclude the impact of estimated forfeitures related to service-based vesting conditions.

(3) The amount reported in this column represent performance-based cash earned by each named executive officer under our Executive Incentive Bonus Plan for 2019

Executive Employment Arrangements

Each of our named executive officers was an at-will employee of the company for 2019. We have no employment agreements with our named executive officers.

Executive Incentive Bonus Plan

Our Executive Incentive Bonus Plan, or Bonus Plan, was adopted by our board of directors on April 9, 2019, and became effective on the day immediately prior to our IPO. The purpose of the Bonus Plan is to motivate and reward eligible officers and employees for their contributions toward the achievement of certain performance goals. The Bonus Plan is administered by the compensation committee, which has the discretionary authority to interpret the provisions of the Bonus Plan, including all decisions on eligibility to participate, the establishment of performance goals, the number of awards payable under the plan, and the payment of awards. The compensation committee, in its sole discretion and on such terms and conditions as it may provide, may delegate all or part of its authority and powers under the Bonus Plan to one or more directors and/or officers of the Company. Our compensation committee reviews and approves pursuant to the Bonus Plan the annual bonus opportunity and the specific goals, objectives to be achieved in order to earn such annual bonus for, and the amount of annual bonus earned by, each participant in our Bonus Plan, including our named executive officers. Our compensation committee has determined that each of our named executive officers is eligible to earn a bonus each year pursuant to our Bonus Plan equal to up to a specific percentage of their salary. The annual bonus opportunities for our names executive officers are tied to a set of specified goals and strategic objectives and we conduct an annual performance review to determine the attainment of such goals and objectives, the results of which are shared with our compensation committee. Our compensation committee makes the final determination of the level at which the specified goals and strategic objectives are achieved and the amount of annual bonus awards earned by each of our named executive officers. For 2019, bonuses were paid out based on the satisfaction of certain regulatory and clinical goals and strategic objectives.

Outstanding Equity Awards at Fiscal Year-End Table

The following table provides information regarding the outstanding stock option awards held by our named executive officers as of December 31, 2019.

Name	Grant Date(1)	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)(2)	Option Expiration Date
Casey C. Lynch	6/2/2017	33,264(3)	49,896(3)	0.46	6/1/2022
	10/30/2018	147,563(4)	324,641(4)	2.23	10/29/2028
Kristen Gafric	6/2/2017	11,488(5)	6,894(5)	0.41	6/1/2027
	1/11/2018	9,956(6)	8,426(6)	0.46	1/10/2028
	8/15/2019	17,187(7)	57,813(7)	28.71	8/14/2029
Michael Detke, M.D.	11/28/2018	35,845(8)	96,507(8)	2.23	11/27/2028
	2/6/2019	33,087(9)	99,264(9)	6.91	2/5/2029

(1) All stock options were granted under our 2019 Equity Incentive Plan (including stock options granted under our 2014 Stock Plan prior to its restatement as our 2019 Equity Incentive Plan).

(2) This column represents the fair market value of a share of our common stock on the date of grant, or, in the case of the stock option granted to Ms. Lynch on June 2, 2017, 110% of the fair market value of a share of our common stock on the date of grant, as determined by our board of directors.

(3) These option shares were part of a stock option grant covering 83,160 shares of our common stock. 1/48th of the stock option grant vested on July 13, 2017 and 1/48th of the grant vested and will vest on each monthly anniversary thereafter, subject to Ms. Lynch's continuous service through the applicable vesting date. In addition, if we terminate Ms. Lynch's employment without "cause," or if Ms. Lynch resigns for "good reason" (each as defined in a supplemental agreement applicable to Ms. Lynch's options), in either case, in connection with or following a change of control (as defined in our 2014 Stock Plan), then 100% of the then unvested shares subject to the stock option grant will vest effective immediately as of such termination or resignation or, if later, the closing of the change of control (the "Lynch Acceleration").

(4) These option shares were part of a stock option grant covering 472,204 shares of our common stock. 1/48th of the stock option grant vested on October 1, 2018 and 1/48th of the grant vested and will vest on each monthly anniversary thereafter, subject to Ms. Lynch's continuous service through the applicable vesting date. In addition, the Lynch Acceleration applies to these option shares prior to their full vesting.

(5) These option shares were part of a stock option grant covering 18,382 shares of our common stock. 1/48th of the stock option grant vested on July 13, 2017 and 1/48th of the grant vested and will vest on each monthly anniversary thereafter, subject to Ms. Gafric's continuous service through the applicable vesting date. In addition, if we terminate Ms. Gafric's employment without "cause," or if Ms. Gafric resigns for "good reason" (each as defined in a supplemental agreement applicable to Ms. Gafric's options), in either case, in connection with or following a change of control (as defined in our 2014 Stock Plan), then 100% of the then unvested shares subject to the stock option grant will vest effective immediately as of such termination or resignation or, if later, the closing of the change of control (the "Gafric Acceleration").

(6) These option shares were part of a stock option grant covering 18,382 shares of our common stock. 1/48th of the stock option grant vested on November 1, 2017 and 1/48th of the grant vested and will vest on each monthly anniversary thereafter, subject to Ms. Gafric's continuous service through the applicable vesting date. In addition, the Gafric Acceleration applies to these option shares prior to their full vesting.

(7) These option shares were part of a stock option grant covering 75,000 shares of our common stock. 1/48th of the stock option grant vested on September 15, 2019 and 1/48th of the grant vested and will vest on each monthly anniversary thereafter, subject to Ms. Gafric's continuous service through the applicable vesting date. In addition, the Gafric Acceleration applies to these option shares prior to their full vesting.

(8) These option shares were part of a stock option grant covering 132,352 shares of our common stock. 1/48th of the stock option grant vested on December 28, 2018 and 1/48th of the grant vested and will vest on each monthly anniversary thereafter, subject to Dr. Detke's continuous service through the applicable vesting date. In addition, if we terminate Dr. Detke's employment without "cause," or if Dr. Detke resigns for "good reason" (each as defined in a supplemental agreement applicable to Dr. Detke's options), in either case, in connection with or following a change of control (as defined in our 2014 Stock Plan), then 100% of the then unvested shares subject to the stock option grant will vest effective immediately as of such termination or resignation or, if later, the closing of the change of control (the "Detke Acceleration").

(9) These option shares were part of a stock option grant covering 132,351 shares of our common stock. 1/48th of the stock option grant vested on March 6, 2019 and 1/48th of the grant vested and will vest on each monthly anniversary thereafter, subject to Dr. Detke's continuous service through the applicable vesting date. In addition, the Detke Acceleration applies to these option shares prior to their full vesting.

Director Compensation

Director Compensation Table

The following table provides information concerning compensation awarded to, earned by and paid to each person who served as a non-employee member of our board of directors during the fiscal year ended December 31, 2019. Ms. Lynch and Dr. Dominy are not included in the table below, as they are employed as our Chief Executive Officer and Chief Scientific Officer, respectively, and receive no compensation for their service as directors. The compensation received by Ms. Lynch as an employee is shown in "Executive Compensation-Summary Compensation Table" above.

Name	Fees Earned or Paid in Cash ($)	Stock Option Awards ($)(1) (2)	Total ($)
David A. Lamond	33,750	—	33,750
Margaret McLoughlin, Ph.D.	33,000	1,039,164	1,072,164
Una Ryan, OBE, Ph.D.	42,375	430,879	473,254
Christopher J. Senner	37,500	704,617	742,117
Kevin Young, CBE	41,625	430,879	472,504

(1) The amounts reported in this column represent the aggregate grant date fair value for financial statement reporting purposes of stock options granted 2018 and 2019 as determined in accordance with FASB ASC Topic 718. These amounts reflect our accounting expense for these stock options and do not represent the actual economic value that may be realized by each non-employee director. There can be no assurance that these amounts will ever be realized. For information on the assumptions used in valuing these awards, refer to Note 9 to the historical financial statements included in this Annual Report on Form 10-K. As required by the SEC rules, the amounts shown exclude the impact of estimated forfeitures related to service-based vesting conditions.

(2) Our non-employee directors held the following number of stock options as of December 31, 2019:

Name	Shares Subject to Outstanding Stock Options
David A. Lamond	—
Margaret McLoughlin, Ph.D.	91,911
Una Ryan, OBE, Ph.D.	91,911
Christopher J. Senner	91,911
Kevin Young, CBE	91,911

Non-Employee Director Compensation Arrangements

We pay each non-employee director an annual cash retainer for service on the board of directors and an additional annual cash retainer for service on each committee on which the director is a member, which is paid quarterly in arrears. Our Lead Independent Director and the chairman of each committee will receive higher annual cash retainers for such service. The fees paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors of which the director is a member are as follows:

	Member Annual Cash Retainer	Lead/Chairperson Annual Cash
Board of Directors	$ 35,000	$ 45,000
Audit Committee	$ 7,500	$ 15,000
Compensation Committee	$ 5,000	$ 10,000
Nominating and Corporate Governance Committee	$ 4,000	$ 8,000

Pursuant to a policy adopted by our board of directors, each non-employee director who is initially appointed to our board of directors shall initially be granted a stock option to purchase 22,058 shares of our common stock. One-third of the shares subject to such initial stock option grant will vest on each anniversary of the date of grant, subject to the director's continued service as a member of our board of directors through each vesting date. Further, at the close of business on the date of each annual meeting of stockholders, each continuing non-employee director will be granted a stock option to purchase the total shares of our common stock set forth below:

- If the non-employee director's appointment to our board of directors was more than six (6) months prior to the annual meeting of our stockholders, the stock option will cover 11,029 shares of our common stock.
- If the non-employee director's appointment to our board of directors was between three (3) and six (6) months prior to the annual meeting of our stockholders, the stock option will cover 5,514 shares of our common stock.
- If the non-employee director's appointment to our board of directors was less than three (3) months prior to the annual meeting of our stockholders, the non-employee director will not receive a stock option on the date of the annual meeting of our stockholders.

100% of the shares subject to any such annual stock option grant will vest in full on the one-year anniversary of the grant date, subject to the director's continued service as a member of our board of directors through the vesting date.

All stock options granted to non-employee directors will be made pursuant to our 2019 Equity Incentive Plan and will vest in full immediately prior to, and contingent upon, the consummation of a change in control of our company, subject to the director's continued service as a member of our board of directors through the change in control.

We also reimburse our directors for their reasonable out-of-pocket expenses in connection with attending meetings of our board of directors and committees.

The non-employee director compensation program is intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors' interests with those of our stockholders.

Item 12. Security

Equity Compensation Plan Information

We currently maintain the following equity compensation plans that provide for the issuance of shares of our common stock to our officers and other employees, directors and consultants, each of which has been approved by our stockholders: our 2019 Equity Incentive Plan (the 2019 Plan which, prior to its restatement in connection with our IPO, was called the 2014 Stock Plan) and our 2019 Employee Stock Purchase Plan (the "ESPP").

The following table presents information as of December 31, 2019 with respect to compensation plans under which shares of our common stock may be issued.

Plan Category	(a) Number of securities to be issued upon exercise of outstanding options, warrants and rights	(b) Weighted-average exercise price of outstanding options, warrants and rights ($)	(c) Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column(a))
Equity compensation plans approved by security holders (1)	2,393,934 (2)	5.35	2,708,074 (3)
Equity compensation plans not approved by security holders	—	—	—
Total	2,393,934	5.35	2,708,074

(1) Includes our 2019 Plan and our ESPP. For a description of these plans, refer to Note 9 to the historical financial statements included in this Annual Report on Form 10-K.

(2) Includes stock options outstanding under the 2014 Plan (granted prior to the restatement of the plan as the 2019 Plan) and the 2019 Plan as of December 31, 2019.

(3) Includes 2,439,779 shares available for issuance under the 2019 Plan and 268,295 shares available for issuance under the ESPP. The number of shares reserved for issuance under the 2019 Plan increased automatically by 1,074,776 shares on January 1, 2020 and will increase automatically on January 1 of each year by a number of shares of common stock equal to the lesser of (i) 2,146,354 shares; (ii) 4% of the shares of common stock outstanding on the last day of the prior fiscal year; or (iii) such number of shares determined by our board of directors. Our compensation committee has not commenced or authorized any offerings pursuant to our ESPP, but may do so at a future time. The number of shares reserved for issuance under the ESPP increased automatically by 268,694 shares on January 1, 2020 and will increase automatically on January 1 of each year by the number of shares equal to the lessor of (1) 536,589 shares; (ii) 1% of the shares of common stock outstanding on the last day of the prior fiscal year; or (iii) such lesser number of shares determined by our board of directors.

Security Ownership of Certain Beneficial Owners and Management

The following table sets forth certain information with respect to the beneficial ownership of our common stock as of February 28, 2020 by:

- each stockholder known by us to be the beneficial owner of more than 5% of our common stock;
- each of our directors;
- each of our named executive officers; and
- all of our directors and executive officers as a group.

Beneficial ownership is determined in accordance with the rules of the SEC and generally includes any shares over which a person exercises sole or shared voting or investment power. Unless otherwise indicated below, to our knowledge, the persons and entities named in the table have sole voting and sole investment power with respect to all shares beneficially owned by them, subject to community property laws where applicable. Shares of our common stock subject to stock options that are currently exercisable or exercisable within 60 days of February 28, 2020 are deemed to be outstanding and to be beneficially owned by the person holding the stock options for the purpose of computing the percentage ownership of that person, but are not treated as outstanding for the purpose of computing the percentage ownership of any other person.

Percentage ownership of our common stock is based on 29,401,321 shares of our common stock outstanding on February 28, 2020. Unless otherwise indicated, the address of each of the individuals and entities named below is c/o Cortexyme, Inc., 269 East Grand Avenue, South San Francisco, CA 94080.

Name of Beneficial Owner	Common Stock	Options Exercisable within 60 days	Aggregate Number of Shares Beneficially Owned	%
5% Stockholders				
Entities affiliated with Pfizer Inc.(1)	3,249,973	—	3,249,973	11.1%
Entities affiliated with CTEPQ Partners LLC(2)	2,686,309	—	2,686,309	9.1%
Pierre R. and Christine E. Lamond and affiliated entities(3)	2,886,530	—	2,886,530	9.8%
SMALLCAP World Fund, Inc.(4)	2,442,914	—	2,442,914	8.3%
Takeda Ventures, Inc.(5)	2,679,802	—	2,679,802	9.1%
Named Executive Officers and Directors				
Casey C. Lynch(6)	1,240,580	238,556	1,479,136	5.0%
Kristen Gafric	330,882	52,111	382,993	1.3%
Michael Detke, M.D.	17,231	77,925	95,156	*
Stephen S. Dominy, M.D.(7)	1,436,911	178,405	1,615,316	5.5%
David A. Lamond(8)	1,955,165	—	1,955,165	6.6%
Margaret McLoughlin, Ph.D.	550	—	550	*
Una Ryan, OBE, Ph.D. (9)	2,875	38,296	41,171	*
Kevin Young, CBE	30,000	38,296	68,296	*
Christopher J. Senner	—	33,190	33,190	*
All executive officers and directors as a group (11 persons)	5,014,194	910,666	5,924,860	19.5%

* Represents beneficial ownership of less than one percent of the outstanding shares of our common stock.

(1) Based on information contained in a Schedule 13G filed with the SEC by Pfizer Inc. on May 22, 2019. Consists of (i) 624,205 shares held of record by Pfizer Inc. (“Pfizer”), (ii) 215,697 shares held of record by Pfizer Strategic Investment Holdings LLC (“PSIH”), a controlled affiliate of Pfizer and (iii) 2,410,071 shares held of record by Pfizer Ventures (US) LLC (“PVUS”), a controlled affiliate of Pfizer. The address for each of Pfizer, PSIH and PVUS is 235 East 42nd Street, New York, New York 10017.

(2) Based on information contained in a Schedule 13G/A filed with the SEC by CTEPQ Partners LLC (“CTEPQ”), EPQ LLC, CTYM PS (“CTYM”), Chad Boeding (“CD”), EPIQ Capital Group, LLC (“EPIQ”) on January 7, 2020. CTEPQ directly holds 936,309 Shares. CTYM directly holds 1,750,000 Shares. EPIQ acts as investment manager for CTEPQ and CTYM. Chad Boeding is the Managing Member of EPIQ and also controls entities that directly hold shares as follows: The Boeding Family Trust directly holds 13,173 shares, Wyntoon Partners LLC directly holds 120,070 shares, Austin Boeding UTMA directly holds 80 shares, Chad Boeding Roth IRA directly holds 6,164 shares, and Kristine Boeding Rollover IRA directly holds 1,000 shares. Each of CTEPQ, CTYM, Chad Boeding, and EPIQ (collectively, the “Reporting Persons”) may be deemed to be the beneficial owner of 2,686,309 shares. Each Reporting Person disclaims beneficial ownership of the shares not held directly by such Reporting Person. The address for each of CTEPQ, CTYM, CD and EPIQ is 1 Lombard Street, #200, San Francisco, CA 94111.

(3) Based on information contained in a Schedule 13G filed with the SEC by Pierre Lamond on September 30, 2019. Consists of (i) 961,510 shares held of record by Pierre R. and Christine E. Lamond Trust 11-22-85, (ii) 962,510 shares held of record by the Pierre R. Lamond 2019 Annuity Trust A dated March 4, 2019 and (iii) 962,510 shares held of record by the Christine E. Lamond 2019 Annuity Trust A dated March 4, 2019. Pierre R. Lamond is the trustee of Pierre R. and Christine E. Lamond Trust 11-22-85 and has sole voting and dispositive power with respect to the 961,510 shares held of record by Pierre R. and Christine E. Lamond Trust 11-22-85. Pierre R. Lamond is the trustee of the Pierre R. Lamond 2019 Annuity Trust A dated March 4, 2019 and has sole voting and dispositive power with respect to the 962,510 shares held of record by the Pierre R. Lamond 2019 Annuity Trust A dated March 4, 2019. Christine E. Lamond is the trustee of the Christine E. Lamond 2019 Annuity Trust A dated March 4, 2019 and has sole voting and dispositive power with respect to the 962,510 shares held of record by the Christine E. Lamond 2019 Annuity Trust A dated March 4, 2019.

(4) Based on information contained in a Schedule 13G/A filed with the SEC by Capital Research Global Investors on February 14, 2010. The shares are held of record by Capital Research Global Investors ("CRGI") on behalf of its client, SMALLCAP WORLD FUND, Inc. CRGI has sole voting and dispositive power over the shares. The address of SMALLCAP World Fund, Inc. is 333 S. Hope St., 53rd Floor, Los Angeles, California 90071.

(5) Based on information contained in a Schedule 13G filed with the SEC by Takeda Pharmaceutical Company Limited ("TPC"), Takeda Pharmaceuticals International AG ("TPIA"), Takeda Pharmaceuticals U.S.A, Inc. ("TPU") and Takeda Ventures, Inc. ("TVI") on May 20, 2019. TVI is a wholly-owned indirect subsidiary of TPC and TVI is owned directly by TPU, which is owned directly by TPC and TPIA, and TPIA is a wholly-owned direct subsidiary of TPC. The shares are held of record by TVI. The address of TVI is 435 Tasso Street, Suite 300, Palo Alto, California 94301.

(6) The shares of common stock consist of (i) 49,895 shares held of record by Casey C. Lynch, (ii) 1,098,774 shares of common stock held of record by Zachary J. Lynch and Casey C. Lynch, Trustees of the Zachary and Casey Lynch Living Trust dated February 24, 2009, and (iii) 91,911 shares of common stock held of record by the Casey C. Lynch 2019 Annuity Trust. Casey C. Lynch and Zachary Lynch are the trustees of the Zachary and Casey Lynch Living Trust dated February 24, 2009, and share voting and dispositive power with respect to the 1,098,774 shares held of record by Zachary J. Lynch and Casey C. Lynch, Trustees of the Zachary and Casey Lynch Living Trust dated February 24, 2009. Casey C. Lynch is the trustee of the Casey C. Lynch 2019 Annuity Trust and holds sole voting and dispositive power with respect to (a) 49,895 shares held of record by Casey C. Lynch and (b) 91,911 shares held of record by the Casey C. Lynch 2019 Annuity Trust.

(7) The shares of common stock consist of (i) 1,216,323 shares held of record by Stephen S. Dominy and Ylva K. Dominy, Trustees of the Dominy Family Trust, and (ii) 220,588 shares held of record by the Stephen Dominy 2019 Annuity Trust. Stephen S. Dominy and Ylva Dominy are trustees of the Dominy Family Trust 2016 and share voting and dispositive power with respect to the 1,216,323 shares held of record by Stephen S. Dominy and Ylva K. Dominy, Trustees of the Dominy Family Trust. Stephen S. Dominy is the trustee of the Stephen Dominy 2019 Annuity Trust and has sole voting and dispositive power with respect to the 220,588 shares held of record by the Stephen Dominy 2019 Annuity Trust.

(8) Based on information contained in a Schedule 13G/A filed with the SEC by David Lamond on February 11, 2020. Consists of (i) 301,829 shares held of record by David A. Lamond and (ii) 1,653,336 shares held of record by Blue Devil Trust dated 12/03/2010. Mr. Lamond is the trustee of the Blue Devil Trust dated 12/03/2010 and holds sole voting and dispositive power with respect to the shares held of record by Blue Devil Trust dated 12/03/2010. Mr. Lamond does not have voting and dispositive power with respect to the shares held of record by the Pierre R. and Christine E. Lamond Trust 11-22-85.

(9) Consists of 2,875 shares of common stock held of record by the Una S. Ryan Revocable Trust. Ms. Ryan is one of the trustees of the Una S. Ryan Revocable Trust and has shared voting and dispositive power with respect to the shares held of record by the Una S. Ryan Revocable Trust.

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

Certain Relationships and Related Party Transactions

Since January 1, 2019, the following are the only transactions or series of similar transactions to which we were or will be a party in which the amount involved exceeds $120,000 and in which any director, executive officer, beneficial holder of more than 5% of our capital stock or any member of their immediate family or any entity affiliated with any of the foregoing persons had or will have a direct or indirect material interest:

On May 13, 2019, Kevin Young, a member of our board of directors purchased 30,000 shares of our common stock at the initial public offering price of $17.00 per share for an aggregate purchase price of $510,000 in our directed share program in connection with our IPO.

On May 13, 2019, entities affiliated with Pfizer Inc., a beneficial holder of more than 5% of our capital stock, and SMALLCAP World Fund, a beneficial holder of more than 5% of our capital stock purchased 50,000 shares and 650,000 shares, respectively, of our common stock at the initial offering price of $17.00 per share for an aggregate purchase price of $850,000 and $11,050,000 in our IPO on the same terms as the other purchasers in the IPO.

On February 10, 2020, we issued and sold 30,000 shares of common stock at a purchase price of $50.00 per share for an aggregate purchase price of $1,500,000 in a private placement to an entity affiliated with David A. Lamond, a member of our board of directors, on the same terms as other purchasers in the private placement.

Review, Approval or Ratification of Transactions with Related Parties

Our written related party transactions policy states that our executive officers, directors, nominees for election as a director, beneficial owners of more than 5% of our common stock and any members of the immediate family of and any entity affiliated with any of the foregoing persons are not permitted to enter into a material related party transaction with us without the review and approval of our audit committee (or a committee composed solely of independent directors in the event it is inappropriate for our audit committee to review such transaction due to a conflict of interest). The policy provides that any request for us to enter into a transaction with an executive officer, director, nominee for election as a director, beneficial owner of more than 5% of our common stock or with any of their immediate family members or affiliates in which the amount involved exceeds $120,000 must be presented to our audit committee (or a committee composed solely of independent directors in the event it is inappropriate for our audit committee to review such transaction due to a conflict of interest) for review, consideration and approval. In approving or rejecting any such proposal, our audit committee (or a committee composed solely of independent directors in the event it is inappropriate for our audit committee to review such transaction due to a conflict of interest) considers the relevant facts and circumstances available and deemed relevant to the committee, including, but not limited to, whether the transaction is on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related party's interest in the transaction.

Independence of Directors

The Nasdaq listing rules generally require that a majority of the members of a listed company's board of directors be independent. In addition, the listing rules generally require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent.

In addition, audit committee members must also satisfy the independence criteria set forth in Rule 10A 3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act. In order to be considered independent for purposes of Rule 10A 3, a member of an audit committee of a listed company may not, other than in such member's capacity as a member of the audit committee, the board of directors or any other board committee (i) accept, directly or indirectly, any consulting, advisory or other compensatory fee from the listed company or any of its subsidiaries or (ii) be an affiliated person of the listed company or any of its subsidiaries.

Our board of directors conducts an annual review of the independence of our directors. Our board of directors has determined that none of the members of our board of directors other than Ms. Lynch and Dr. Dominy has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of the members of our board of directors other than Ms. Lynch and Dr. Dominy is "independent" as that term is defined under the rules of Nasdaq. Our board of directors has also determined that all members of our audit committee, compensation committee and nominating and corporate governance committee are independent and satisfy the relevant SEC and Nasdaq independence requirements for such committees.

Item 14. Principal Accounting Fees and Services.

We regularly review the services and fees from our independent registered public accounting firm. These services and fees are also reviewed with our audit committee annually. In addition to performing the audit of our financial statements, BDO USA, LLP provided various other services during the fiscal years ended December 31, 2019 and December 31, 2018. Our audit committee has determined that BDO USA, LLP's provision of these services, which are described below, does not impair BDO USA, LLP's independence from us. During the years ended December 31, 2019 and December 31, 2018, fees for services provided by BDO USA, LLP were as follows:

	Year Ended December 31,	
	2019	2018
Audit fees(1)	$ 817,990	$ 103,355
Tax fees(2)	78,776	—
Total fees	$ 896,766	$ 103,355

(1) Consists of fees rendered in connection with the audit of our financial statements, including audited financial statements presented in our Annual Report on Form 10-K, review of the interim financial statements included in our quarterly reports and services normally provided in connection with regulatory filings. Included in 2019 Audit fees is an aggregate of $0.5 million of fees billed in connection with our initial public offering, which closed in 2019. Audit fees in 2018 include fees related to the annual audit of the Company's financial statements.

(2) Consists of fees billed for professional services for tax compliance, tax advice and tax planning. These services include assistance regarding federal, state and international tax compliance, as well as technical tax advice related to federal and state income tax matters, assistance with sales tax and assistance with tax audits.

Policy on Audit Committee Pre-Approval of Audit and Permissable Non-Audit Services

Our audit committee's policy is to pre-approve all audit and permissible non-audit services provided by our independent registered public accounting firm, the scope of services provided by our independent registered public accounting firm and the fees for the services to be performed. These services may include audit services, audit-related services, tax services and other services. Pre-approval is detailed as to the particular service or category of services and is generally subject to a specific budget. Our independent registered public accounting firm and management are required to periodically report to the audit committee regarding the extent of services provided by our independent registered public accounting firm in accordance with this pre-approval, and the fees for the services performed to date.

All of the services relating to the fees described in the table above were approved by our audit committee.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this report:

1. Financial Statements

See Index to Financial Statements in Part II Item 8 of this Annual Report on Form 10-K.

2. 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.

3. Exhibits

The documents listed in the Exhibit Index are incorporated by reference or are filed with this report, in each case as indicated therein (numbered in accordance with Item 601 of Regulation S-K).

Item 16. Form 10-K Summary

None.

Exhibit Index

Exhibit No.	Exhibit title	Incorporated by reference				Filed or furnished herewith
		Form	File No.	Exhibit No.	Filing date	
3.1	Amended and Restated Certificate of Incorporation	8-K	001-38890	3.1	5/13/2019	
3.2	Amended and Restated Bylaws	8-K	001-38890	3.2	5/13/2019	
4.1	Specimen Stock Certificate	S-1/A	333-230853	4.1	4/29/2019	
4.2	Amended and Restated Investors' Rights Agreement, dated May 23, 2018, by and among the Registrant and certain of its stockholders.	S-1	333-230853	4.2	4/12/2019	
4.3	Description of Securities					X
10.1	Sub-Sublease Agreement by and between Cortexyme, Inc. and Verily Life Sciences LLC, dated June 18, 2018.	S-1	333-230853	10.1	4/12/2019	
10.2	Amendment No. 1 to Sub-Sublease by and between Cortexyme, Inc. and Verily Life Sciences LLC dated April 2, 2019.	10-Q	001-38890	10.1	8/9/2019	
10.3	Form of Indemnification Agreement between Cortexyme, Inc. and each of its officers and directors.	S-1/A	333-230853	10.2	4/29/2019	
10.4+	2014 Stock Plan, as amended as of November 28, 2018, and related forms of stock award agreements.	S-1	333-230853	10.3	4/12/2019	
10.5+	2019 Equity Incentive Plan and forms of stock award agreements thereunder.	S-1/A	333-230853	10.4	4/29/2019	
10.6+	2019 Employee Stock Purchase Plan.	S-1/A	333-230853	10.5	4/29/2019	
10.7+	Executive Incentive Bonus Plan.	S-1	333-230853	10.6	4/12/2019	
23.1	Consent of Independent Registered Public Accounting Firm					X
24.1	Power of Attorney (incorporated by reference to the signature page of this Annual Report on Form 10-K)					X
31.1	Certification of Chief Executive Officer pursuant to Rules 13a-14(a) and Rule 15d-14(a) of the Exchange Act					X
31.2	Certification of Chief Financial Officer pursuant to Rules 13a-14(a) and Rule 15d-14(a) of the Exchange Act					X
32.1*	Certification of Chief Executive Officer pursuant to Rule 13a-14(b) of the Exchange Act and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
32.2*	Certification of Chief Executive Officer pursuant to Rule 13a-14(b) of the Exchange Act and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
101.INS	XBRL Instance Document					X
101.SCH	XBRL Taxonomy Extension Schema Document					X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document					X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					X

* Furnished and not filed.

\+ Indicates a management contract or compensatory plan or arrangement.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Cortexyme, Inc.

Date: March 16, 2020

By: /s/ Casey C. Lynch

Casey C. Lynch
President, Chief Executive Officer and Chairman

POWER OF ATTORNEY

Each person whose signature appears below constitutes and appoints Casey C. Lynch, Christopher Lowe and Kristen Gafric, and each of them, as his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all 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 connection therewith, 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 agents, or any of them, or their or his substitutes, may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Casey C. Lynch **Casey C. Lynch**	President, Chief Executive Officer and Chairman of our Board of Directors (Principal Executive Officer)	March 16, 2020
/s/ Christopher Lowe **Christopher Lowe**	Chief Financial Officer (Principal Financial and Accounting Officer)	March 16, 2020
/s/ Stephen S. Dominy **Stephen S. Dominy, M.D.**	Director	March 16, 2020
/s/ David A. Lamond **David A. Lamond**	Director	March 16, 2020
/s/ Margaret McLoughlin **Margaret McLoughlin, Ph.D.**	Director	March 16, 2020
/s/ Una Ryan **Una Ryan, OBE Ph.D.**	Director	March 16, 2020
/s/ Christopher J. Senner **Christopher J. Senner**	Director	March 16, 2020
/s/ Kevin Young **Kevin Young, CBE**	Director	March 16, 2020

Exhibit 4.3

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

Cortexyme, Inc. ("we," "our," "us," or the "Company") has one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended ("1934 Act"): our common stock. The following summary of the terms of our common stock is based upon our amended and restated certificate of incorporation and our amended and restated bylaws. This summary does not purport to be complete and is subject to, and is qualified in its entirety by express reference to, the applicable provisions of our amended and restated certificate of incorporation and our amended and restated bylaws, which are filed as exhibits to our Annual Report on Form 10-K and are incorporated by reference herein. We encourage you to read our amended and restated certificate of incorporation, our amended and restated bylaws and the applicable provisions of the Delaware General Corporation Law ("DGCL") for more information.

Description of Common Stock

Under our amended and restated certificate of incorporation, we have authority to issue 100,000,000 shares of our common stock, par value $0.001 per share. As of December 31, 2019, 26,869,413 shares of our common stock were issued and outstanding. All shares of our common stock will, when issued, be duly authorized, fully paid and nonassessable.

Voting Rights

The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders. Cumulative voting for the election of directors is not provided for in our restated certificate of incorporation, which means the holders of a majority of our shares of common stock can elect all of the directors then standing for election.

Dividends

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive dividends, if any, as may be declared from time to time by the board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Rights and Preferences

Holders of common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future.

Description of Preferred Stock

Under our amended and restated certificate of incorporation, we have authority, subject to any limitations prescribed by law and without further stockholder approval, to issue from time to time up to 10,000,000 shares of preferred stock, par value $0.001 per share, in one or more series. As of December 31, 2019, we had no shares of preferred stock issued and outstanding.

Pursuant to our amended and restated certificate of incorporation, our board of directors has the authority to designate the rights, preferences, privileges and restrictions of each such series, including dividend rights, preferences, privileges and restrictions of each such series, including dividend rights, dividend rates, conversion rights, voting rights, terms of redemption, redemption prices, liquidation preferences, sinking fund terms and the number of shares constituting any series.

The issuance of preferred stock may have the effect of delaying, deferring or preventing a change in control of the company without further action by the stockholders. The issuance of redeemable convertible preferred stock with voting and conversion rights may also adversely affect the voting power of the holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In certain circumstances, an issuance of preferred stock could have the effect of decreasing the market price of the common stock.

Registration Rights

Based on the number of shares outstanding as of December 31, 2019, under our amended and restated investors' rights agreement, the holders of up to approximately 7.8 million shares of common stock, or their affiliates or transferees, have the right to require us to register their shares under the Securities Act so that those shares may be publicly resold, or to include their shares in any registration statement we file, in each case as described below.

The registration rights terminate with respect to the registration rights of an individual holder on the earliest to occur of May 8, 2024 (five years following our initial public offering), the liquidation, dissolution or indefinite cessation of the business operations of our company, or the closing of a deemed liquidation, dissolution or winding up of our company pursuant to our amended and restated certificate of incorporation, or with respect to any particular stockholder, such time after the effective date of the registration statement that such stockholder can sell all of its shares under Rule 144 of the Securities Act during any three-month period without registration.

Demand Registration Rights

The holders of at least 35% of the registrable securities may demand that we effect a registration under the Securities Act covering the public offering and sale of at least the number of registrable securities held by such stockholders having an anticipated aggregate offering price of at least $10,000,000. Upon any such demand we must effect the registration of such registrable securities that have been requested to register together with all other registrable securities that we may have been requested to register by other stockholders pursuant to the incidental registration rights described below. We are only obligated to effect two registrations in response to these demand registration rights.

Piggyback Registration Rights

If we register any securities for public sale, including pursuant to any stockholder-initiated demand registration, holders of such registrable securities will have the right to include their shares in the registration statement for such offering, subject to certain exceptions. The underwriters of any underwritten offering will have the right to limit the number of registrable securities to be included in the registration statement, subject to certain restrictions.

Form S-3 Registration Rights

We may be obligated to effect a registration on Form S-3 under the Securities Act. At any time after we are qualified to file a registration statement on Form S-3, the holders of registrable securities anticipated to have an aggregate sale price, net of underwriting discounts and commission, of at least $1,000,000 may request in writing that we effect a registration on Form S-3.

Expenses of Registration

We will pay all registration expenses related to any demand, piggyback or Form S-3 registration, including reasonable fees and disbursements of one special counsel for the holders of such registrable securities, other than underwriting fees, discounts or commissions (if any), which will be borne by the holders of such registrable securities.

Anti-Takeover Effects of Delaware Law and Our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

Our amended and restated certificate of incorporation and our amended and restated bylaws contain certain provisions that could have the effect of delaying, deterring or preventing another party from acquiring control of us. These provisions and certain provisions of Delaware law, which are summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate more favorable terms with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging a proposal to acquire us.

Undesignated Preferred Stock

As discussed above, our board of directors have the ability to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management of our company.

Limits on Ability of Stockholders to Act by Written Consent or Call a Special Meeting

Our amended and restated certificate of incorporation provides that our stockholders may not act by written consent, which may lengthen the amount of time required to take stockholder actions. As a result, a holder controlling a majority of our capital stock would not be able to amend our amended and restated bylaws or remove directors without holding a meeting of our stockholders called in accordance with our amended and restated bylaws.

In addition, our amended and restated bylaws provides that special meetings of the stockholders may be called only by the chairperson of the board, the Chief Executive Officer, the lead independent director, or at the request of a majority of our board of directors. Stockholders may not call a special meeting, which may delay the ability of our stockholders to force consideration of a proposal or for holders controlling a majority of our capital stock to take any action, including the removal of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of our board of directors or a committee of our board of directors. These provisions may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

Board Classification

Our board of directors is divided into three classes, one class of which is elected each year by our stockholders. The directors in each class will serve three-year terms. A third party may be discouraged from making a tender offer or otherwise attempting to obtain control of us as it is more difficult and time-consuming for stockholders to replace a majority of the directors on a classified board.

No Cumulative Voting

Our amended and restated certificate of incorporation and amended and restated bylaws do not permit cumulative voting in the election of directors. Cumulative voting allows a stockholder to vote a portion or all of its shares for one or more candidates for seats on the board of directors. Without cumulative voting, a minority stockholder may not be able to gain as many seats on our board of directors as the stockholder would be able to gain if cumulative voting were permitted. The absence of cumulative voting makes it more difficult for a minority stockholder to gain a seat on our board of directors to influence our board's decision regarding a takeover.

Amendment of Charter and Bylaws Provisions

The amendment of the above provisions of our amended and restated certificate of incorporation will require approval by holders of at least two thirds of our outstanding capital stock entitled to vote generally in the election of directors. The amendment of our amended and restated bylaws will require approval by the holders of at least two thirds of our outstanding capital stock entitled to vote generally in the election of directors.

Delaware Anti-Takeover Statute

We are subject to the provisions of Section 203 of the DGCL regulating corporate takeovers. In general, Section 203 prohibits a publicly held Delaware corporation from engaging, under certain circumstances, in a business combination with an interested stockholder for a period of three years following the date the person became an interested stockholder unless:

- prior to the date of the transaction, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, calculated as provided under Section 203; or
- at or subsequent to the date of the transaction, the business combination is approved by our board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation's outstanding voting stock. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We anticipate that Section 203 may also discourage attempts that might result in a premium over the market price for the shares of common stock held by stockholders.

The provisions of Delaware law and the provisions of our amended and restated certificate of incorporation and amended and restated bylaws, could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they might also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions might also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests.

Authorized but Unissued Shares

Our authorized but unissued shares of common stock and preferred stock will be available for future issuances without stockholder approval, except as required by the listing standards of the Nasdaq Global Select Market, and could be utilized for a variety of corporate purposes, including future offerings to raise additional capital, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could render more difficult or discourage an attempt to obtain control of the company by means of a proxy contest, tender offer, merger or otherwise.

Choice of Forum

Our amended and restated certificate of incorporation provides that, unless we consent to the selection of an alternative forum, to the fullest extent permitted by law, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (i) any derivative action or proceeding brought on behalf of us; (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees or agents to us or our stockholders; (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our amended and restated certificate of incorporation or amended and restated bylaws; or (iv) any action asserting a claim against us governed by the internal affairs doctrine; provided that, the exclusive forum provision will not apply to suits brought to enforce any liability or duty created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction; and provided further that, if and only if the Court of Chancery of the State of Delaware dismisses any such action for lack of subject matter jurisdiction, such action may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated certificate of incorporation also provides that the federal district courts of the United States of America will be the exclusive forum for the resolution of any complaint asserting a cause of action against us or any of our directors, officers, employees or agents and arising under the Securities Act. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any action, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in such action. For example, in December 2018, the Delaware Court of Chancery invalidated provisions in the certificates of incorporation of Delaware companies that purport to designate federal district courts as the exclusive forum in which a stockholder could bring a claim under the Securities Act. Consequently, we do not intend to enforce the federal forum selection provision in our amended and restated certificate of incorporation unless and until such time there is a final determination by the Delaware Supreme Court regarding the validity of provisions such as the federal forum selection provision. To the extent the Delaware Supreme Court makes a final determination that provisions such as the federal forum selection provision are not valid as a matter of Delaware law, we intend to amend our amended and restated certificate of incorporation to remove the federal forum selection provision.

Business Combinations with Interested Stockholders

Subject to certain exceptions, Section 203 of the DGCL prohibits a public Delaware corporation from engaging in a business combination (as defined in such section) with an "interested stockholder" (defined generally as any person who beneficially owns 15% or more of the outstanding voting stock of such corporation or any person affiliated with such person) for a period of three years following the time that such stockholder became an interested stockholder, unless (i) prior to such time the board of directors of such corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder; (ii) upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of such corporation at the time the transaction commenced (excluding for purposes of determining the voting stock of such corporation outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (A) by persons who are directors and also officers of such corporation and (B) by employee stock plans in which employee participants do not have the right

to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer); or (iii) at or subsequent to such time the business combination is approved by the board of directors of such corporation and authorized at a meeting of stockholders (and not by written consent) by the affirmative vote of at least 66 2/3% of the outstanding voting stock of such corporation not owned by the interested stockholder.

Limitation of Liability and Indemnification

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, and may indemnify our employees and other agents, to the fullest extent permitted by Delaware law.

Delaware law prohibits our amended and restated certificate of incorporation from limiting the liability of our directors for the following:

- any breach of the director's duty of loyalty to us or to our stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or unlawful stock repurchases or redemptions; and
- any transaction from which the director derived an improper personal benefit.

If Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law, as so amended. Our amended and restated certificate of incorporation does not eliminate a director's duty of care and, in appropriate circumstances, equitable remedies, such as injunctive or other forms of non-monetary relief, remain available under Delaware law. This provision also does not affect a director's responsibilities under any other laws, such as the federal securities laws or other state or federal laws. Under our amended and restated bylaws, we can purchase insurance on behalf of any person whom we are required or permitted to indemnify.

In addition to the indemnification required in our amended and restated certificate of incorporation and amended and restated bylaws, we have entered into an indemnification agreement with each member of our board of directors and each of our officers. These agreements provide for the indemnification of our directors and officers for certain expenses and liabilities incurred in connection with any action, suit, proceeding or alternative dispute resolution mechanism, or hearing, inquiry or investigation that may lead to the foregoing, to which they are a party or other participant, or are threatened to be made a party or other participant, by reason of the fact that they are or were a director, officer, employee, agent or fiduciary of our company, by reason of any action or inaction by them while serving as an officer, director, agent or fiduciary, or by reason of the fact that they were serving at our request as a director, officer, employee, agent or fiduciary of another entity. In the case of an action or proceeding by or in the right of our company, no indemnification will be provided for any claim where a court determines that the indemnified party is prohibited from receiving indemnification. We believe that these charter and bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers.

The limitation of liability and indemnification provisions in our restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. Moreover, a stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable. There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

Listing. Our common stock is listed on the Nasdaq Global Select Market under the symbol "CRTX."

Transfer Agent and Registrar. The transfer agent for our common stock is American Stock Transfer &Trust Company, LLC. Its address is 6201 15th Avenue, Brooklyn, NY 11219.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

Cortexyme, Inc.
South San Francisco, California

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-231307) of Cortexyme, Inc. of our report dated March 16, 2020, relating to the financial statements, which appears in this Form 10-K.

/s/ BDO USA, LLP
San Jose, California

March 16, 2020

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Casey C. Lynch, certify that:

1. I have reviewed this Annual Report on Form 10-K of Cortexyme, Inc.;

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

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

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

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

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

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

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

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

Date: March 16, 2020

By: /s/ Casey C. Lynch

Casey C. Lynch
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Christopher Lowe, certify that:

1. I have reviewed this Annual Report on Form 10-K of Cortexyme, Inc.;

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

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

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

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

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

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

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

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

Date: March 16, 2020

By: /s/ Christopher Lowe

Christopher Lowe
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

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

In connection with the Annual Report of Cortexyme, Inc. (the "Company") on Form 10-K for the period ended December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934 as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 16, 2020

By: /s/ Casey C. Lynch

Casey C. Lynch
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

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

In connection with the Annual Report of Cortexyme, Inc. (the "Company") on Form 10-K for the period ended December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934 as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 16, 2020

By: /s/ Christopher Lowe

Christopher Lowe
Chief Financial Officer
(Principal Financial and Accounting Officer)