Filed pursuant to Rule 424(b)(4)
Registration No. 333-230853

PROSPECTUS

4,412,000 Shares

Common Stock

This is the initial public offering of common stock of Cortexyme, Inc. Prior to this offering, there has been no public market for our common stock. The initial public offering price is $17.00 per share.

Our common stock has been approved for listing on the Nasdaq Global Select Market under the symbol "CRTX."

We are an "emerging growth company," as defined under the federal securities laws and, as such, we may elect to comply with certain reduced public company reporting requirements for this prospectus and future filings.

Investing in the common stock involves a high degree of risk. See the section entitled "Risk Factors" beginning on page 10 to read about factors you should consider before buying shares of our common stock.

	Per Share	Total
Initial public offering price	$ 17.00	$75,004,000
Underwriting discounts and commissions(1)	$ 1.19	$ 5,250,280
Proceeds, before expenses, to Cortexyme, Inc.	$ 15.81	$69,753,720

(1) See "Underwriting" for additional disclosure regarding underwriting discounts, commissions and estimated offering expenses.

To the extent the underwriters sell more than 4,412,000 shares of common stock, we have granted the underwriters a 30-day option to purchase up to 661,800 additional shares of common stock from us at the initial public offering price less the underwriting discounts and commissions.

Certain of our existing 5% stockholders and stockholders affiliated with certain of our directors (or their affiliates) have agreed to purchase, and we have directed allocations for, an aggregate of approximately $26.3 million of shares of our common stock in this offering at the initial public offering price and on the same terms as the other purchasers in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these persons or entities as they will on any other shares sold to the public in this offering.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock to purchasers on or about May 13, 2019.

Joint Book-Running Managers

BofA Merrill Lynch **Credit Suisse**

Co-Managers

Canaccord Genuity **JMP Securities**

The date of this prospectus is May 8, 2019

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Neither we nor the underwriters have authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus is accurate only as of its date regardless of the time of delivery of this prospectus or of any sale of our common stock.

For investors outside the United States, neither we nor the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus and any free writing prospectus related to this offering are required to inform themselves about and to observe any restrictions related to the offering of the shares of our common stock and the distribution of this prospectus and any such free writing prospectus outside of the United States.

PROSPECTUS SUMMARY

This summary highlights certain significant aspects of our business and this offering and is a summary of information contained elsewhere in this prospectus. This summary does not contain all the information that you should consider before deciding to invest in our common stock. You should read the entire prospectus carefully, including the sections titled "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations," "Business" and our historical financial statements and the related notes thereto included elsewhere in this prospectus, before making an investment decision. Unless the context otherwise requires, all references in this prospectus to "Cortexyme," the "company," "we," "our," "us" or similar terms refer to Cortexyme, Inc.

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 and expect top-line results by the end of 2021.

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 characteristic pathology observed in the brain of Alzheimer's patients, including amyloid beta production, inflammation and neurodegeneration. *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.

COR388 for the Treatment of Alzheimer's Disease

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 cerebral spinal fluid, or 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, such as Mean Mini-Mental State Exam, Cambridge Neuropsychological Test Automated Battery composite and Winterlight speech-based cognitive assessment. 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 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 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 plan to enroll approximately 570 mild to moderate Alzheimer's patients in our Phase 2/3 GAIN trial, or GingipAIN inhibitor for 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 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 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 tissue 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 historically have 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 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. To achieve this objective, we are pursuing the following strategies:

- Rapidly advance COR388 through clinical development in patients with Alzheimer's disease;

- Develop COR388 for other diseases where both human observational data and preclinical experiments support its therapeutic potential;

- Expand our portfolio by developing additional compounds, including gingipain inhibitors from our proprietary library; and

- Optimize value of COR388 and future drug candidates in major markets.

Our Team

We are led by a management team with deep scientific and drug development experience and a commitment to serving patients with Alzheimer's and other degenerative diseases. Collectively, our management team has a rich set of experiences both in academia and in industry, leading clinical programs for large biopharmaceutical companies and advancing clinical assets in venture-backed and public companies. We were

founded by our Chief Executive Officer, Casey C. Lynch, our Chief Scientific Officer, Stephen S. Dominy, M.D., and our Senior Vice President, Legal and Administration, and Secretary, Kristen Gafric and are joined by Leslie Holsinger, Ph.D., our Executive Vice President of Preclinical Development, Michael Detke, M.D., Ph.D., our Chief Medical Officer and Christopher Lowe, our Chief Financial Officer. Our leadership is complemented by a team of drug development experts, approximately two-thirds of whom hold Ph.D. or M.D. degrees. Together, our management team brings expertise across relevant disciplines, including neuroscience, infectious disease, immunology, oncology, translational science, medicinal chemistry, manufacturing and biomarker development.

Our company is supported by a group of investors that include both biopharmaceutical companies and institutional investors, and we have raised approximately $99.5 million in funding as of December 31, 2018. Our key investors are comprised of strategic investors, including Pfizer Ventures, Takeda Ventures and Verily Life Sciences, as well as Sequoia Capital, Breakout Labs, Breakout Ventures, Dolby Family Ventures, EPIQ Capital Group, the Lamond Family and Vulcan Capital, amongst others.

Risks Associated with our Business

- We are a clinical stage biopharmaceutical company with a limited operating history.
- Even if this offering is successful, 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.
- 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.
- 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.
- 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.
- 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 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 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 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.

- 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.

- We have identified material weakness in our internal control over financial reporting which could, if not remedied, result in material misstatements in our financial statements.

Implications of being an Emerging Growth Company

We qualify as an "emerging growth company," as defined in Section 2(a) of the Securities Act of 1933, as amended, or the Securities Act, as modified by the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As such, we are eligible to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies" including, but not limited to:

- an exemption from complying with the auditor attestation requirements of Section 404 of the Sarbanes Oxley Act of 2002, as amended, or Section 404;

- a requirement to have only two years of audited financial statements and only two years of related selected financial data and management's discussion and analysis of financial condition and results of operations disclosure;

- reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements; and

- an exemption from the requirement to seek non-binding advisory votes on executive compensation and new executive compensation arrangements entered into in connection with a merger, acquisition, consolidation, proposed sale or disposition of all or substantially all of our assets.

We have not made a decision regarding whether to take advantage of these exemptions. If we do take advantage of any of these exemptions, we do not know if some investors will find our common stock less attractive as a result. The result may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, Section 107 of the JOBS Act provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. In other words, an "emerging growth company" can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably opted out of the extended transition period for complying with new or revised accounting standards pursuant to Section 107(b) of the JOBS Act.

We could remain an "emerging growth company" for up to five years, or until the earliest of (a) the last day of the first fiscal year in which our annual gross revenues exceed $1.07 billion, (b) the date that we become a "large accelerated filer" as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, which would occur if the market value of our common stock that is held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter or (c) the date on which we have issued more than $1.0 billion in non-convertible debt during the preceding three-year period.

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 prospectus and should not be considered a part of this prospectus.

Trademarks

Cortexyme is a registered trademark of Cortexyme, Inc. All other brand names or trademarks appearing in this prospectus are the property of their respective holders. Solely for convenience, the trademarks and trade names in this prospectus 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.

The Offering

The following information assumes that the underwriters do not exercise their option to purchase additional shares in the offering. See "Underwriting."

Common stock offered by us	4,412,000 shares
Common stock to be outstanding after the offering	26,013,334 shares
Option to purchase additional shares of common stock	The underwriters have a 30-day option to purchase up to 661,800 additional shares of common stock at the public offering price, less underwriting discounts and commissions.
Use of proceeds	We estimate that the net proceeds to us from this offering will be approximately $67.6 million, based upon the initial public offering price of $17.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering to fund our global Phase 2/3 GAIN clinical trial for COR388, and to support future clinical and preclinical activities, manufacturing and development of our library of compounds, as well as for working capital and general corporate purposes, which may include the costs of operating as a public company. See "Use of Proceeds" for a more complete description.
Directed share program	At our request, the underwriters have reserved up to 7% of the shares offered by this prospectus for sale, at the initial public offering price, to certain persons associated with us. If these persons purchase reserved shares, it will reduce the number of shares available for sale to the general public. Any reserved shares that are not so purchased will be offered by the underwriters to the general public on the same terms as the other shares offered by this prospectus. For further information regarding our directed share program, see "Underwriting."
Listing	Our common stock has been approved for listing on the Nasdaq Global Select Market under the symbol "CRTX."
Risk factors	Investing in our common stock involves a high degree of risk. You should carefully read and consider the information set forth under "Risk Factors" and all other information in this prospectus before investing in our common stock.

Effective April 25, 2019, we effected a one-for-0.367647 reverse stock split, or the Reverse Stock Split, of our issued and outstanding common stock, redeemable convertible preferred stock, and stock options. We will make a cash payment to stockholders for all fractional shares which would otherwise be required to be issued as a result of the Reverse Stock Split.

Certain of our existing 5% stockholders and stockholders affiliated with certain of our directors (or their affiliates) have agreed to purchase, and we have directed allocations for, an aggregate of approximately $26.3 million of shares of our common stock in this offering at the initial public offering price and on the same terms as

the other purchasers in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these persons or entities as they will on any other shares sold to the public in this offering.

Except as otherwise indicated, all information in this prospectus is based upon 21,601,334 shares of our common stock outstanding as of December 31, 2018, assuming the conversion of all of our outstanding shares of redeemable convertible preferred stock as of December 31, 2018 into 18,161,027 shares of common stock and the exercise in full of an outstanding warrant to purchase 27,941 shares of common stock, as of December 31, 2018, upon the closing of this offering, and excludes:

- 1,885,504 shares of our common stock issuable upon the exercise of options to purchase shares of our common stock outstanding as of December 31, 2018, with a weighted-average exercise price of $1.57 per share;
- 525,728 shares of our common stock issuable upon exercise of options to purchase shares of our common stock granted after December 31, 2018, with a weighted-average exercise price of $7.99 per share;
- 2,682,942 shares of common stock reserved for future grant or issuance under our 2019 Equity Incentive Plan, or 2019 Plan, which share reserve will automatically increase each year, as more fully described in “Executive Compensation—Equity Incentive Plans;” and
- 268,295 shares of common stock reserved for issuance under our 2019 Employee Stock Purchase Plan, or 2019 ESPP, which share reserve will automatically increase each year, as more fully described in “Executive Compensation—Equity Incentive Plans.”

Except as otherwise indicated, all information in this prospectus reflects and assumes:

- a one-for-0.367647 reverse stock split of our capital stock on April 25, 2019 pursuant to which (i) every share of outstanding capital stock was converted and reconstituted into 0.367647 of a share of capital stock; (ii) the number of shares of common stock for which each outstanding option to purchase common stock is exercisable was proportionally decreased on a 0.367647-for-one basis; and (iii) the exercise price of each outstanding option to purchase common stock was proportionately increased on a one-for-0.367647 basis;
- the conversion upon the closing of this offering of all of our outstanding shares of redeemable convertible preferred stock into an aggregate of 18,161,027 shares of common stock;
- the exercise in full of an outstanding warrant to purchase 27,941 shares of common stock, as of December 31, 2018, upon the closing of this offering;
- the filing and effectiveness of our amended and restated certificate of incorporation and the adoption of our amended and restated bylaws upon the closing of this offering;
- no purchase by certain of our existing 5% stockholders and stockholders affiliated with certain of our directors (or their affiliates) who have agreed to purchase, and who we have directed allocations for, of up to approximately $26.3 million in shares of our common stock in this offering; and
- no exercise by the underwriters of their option to purchase additional shares of common stock from us in this offering.

Summary Financial Data

The following tables summarize our financial data for the periods and as of the dates indicated. We derived the summary statements of operations data for the years ended December 31, 2017 and 2018, and the summary balance sheet data as of December 31, 2018, from our audited financial statements and related notes thereto included elsewhere in this prospectus. Our historical results are not necessarily indicative of our future performance. The summary financial data included in this section are not intended to replace our financial statements and related notes thereto included elsewhere in this prospectus. You should read the following summary financial data together with our financial statements and related notes thereto included elsewhere in this prospectus and the sections titled "Selected Historical Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

(in thousands, except share and per share data)	Year Ended December 31, 2017	2018
Summary Statement of Operations Data:		
Operating expenses:		
Research and development	$ 9,099	$ 10,085
General and administrative	1,271	2,034
Net loss	(12,235)	(12,476)
Net loss per share	$ (3.70)	$ (3.71)
Pro forma net loss per share (unaudited)		(0.58)
Weighted average shares used in pro forma per share calculation (unaudited)(1)		21,551,160

(in thousands)	As of December 31, 2018 Actual	Pro Forma(1)	Pro Forma As Adjusted(2)
		(unaudited)	
Summary Balance Sheet Data:			
Cash, cash equivalents and short-term investments	$ 71,716	$ 71,717	$ 139,357
Working capital(3)	71,127	71,128	138,768
Total assets	72,877	72,878	140,518
Long-term obligations less current portion	—	—	
Redeemable convertible preferred stock	104,046	—	
Additional paid-in capital	245	104,273	171,872
Total stockholders' equity (deficit)	(32,626)	71,421	139,061

(1) Reflects (i) the conversion of all of our outstanding shares of redeemable convertible preferred stock into an aggregate of 18,161,027 shares of our common stock, (ii) the exercise in full of an outstanding warrant to purchase 27,941 shares of common stock upon the closing of this offering, and (iii) the filing and effectiveness of our amended and restated certificate of incorporation, in each case, immediately upon the closing of this offering. All common stock per share amounts have been adjusted retrospectively to reflect a one-for-0.367647 reverse stock split on April 25, 2019.

(2) Reflects the pro forma adjustments described in footnote (1) above and the sale and issuance of 4,412,000 shares of common stock by us in this offering, based upon the initial public offering price of $17.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

(3) We define working capital as current assets less current liabilities.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should consider carefully the risks and uncertainties described below, together with all of the other information in this prospectus, including our historical financial statements and related notes, before deciding whether to purchase shares of our common stock. If any of the following risks is realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. In that event, the price of our common stock could decline, and you could lose part or all of your investment.

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, 2017 and 2018, our net losses were $12.2 million and $12.5 million, respectively. We had an accumulated deficit of $32.8 million as of December 31, 2018.

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.

Even if this offering is successful, 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. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company.

Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. As of December 31, 2018, we had $71.7 million in cash, cash equivalents and short-term investments. As of March 31, 2019, we had cash, cash equivalents and short-term investments of $59.0 million, which excludes long-term investments of $5.7 million. We believe that our existing capital resources, together with the net proceeds from this offering, will be sufficient to fund our projected operations through 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 as of February 14, 2019. 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. Further, our lead drug candidate, COR388, has been tested in only nine Alzheimer's patients and 58 healthy volunteers as of February 14, 2019.

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; and
- inability to retain enrolled patients after a clinical trial is underway.

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., Celgene Corporation, 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.

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.

We have identified material weaknesses in our internal control over financial reporting which could, if not remediated, result in material misstatements in our financial statements.

Prior to this offering, we were a private company and had limited accounting and financial reporting personnel and other resources with which to address our internal controls and procedures. In connection with the audit of our consolidated financial statements for the years ended December 31, 2017 and 2018, our management identified material weaknesses in our internal control over financial reporting. A material weakness is defined as a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. Specifically, we identified material 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. We are developing a remediation plan designed to address these material weaknesses and other existing deficiencies. In addition, we have, and are in the process of, recruiting, hiring, and retaining additional financial reporting personnel to develop and implement appropriate internal controls and reporting procedures. If our remedial measures are insufficient to address the material weaknesses, or if additional material weakness or significant deficiencies in our internal control are discovered or occur in the future, our financial statements may contain material misstatements.

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 will 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 with our fiscal year ending the year after this offering is completed, 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 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. Prior to this offering, we have 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. 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.

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 may in the future 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 may 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 after this offering.

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:

- the 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, 2018, we were the owner of record of one issued U.S. patent relating to COR388 with claims directed to pharmaceutical compounds, pharmaceutical compositions containing these compounds, and methods of using these compounds in the treatment of various indications. We were also the owner of record of 24 pending U.S. and non-U.S. patent applications relating to COR388 in the areas of 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, as of December 31, 2018, we were the owner of record of one issued U.S. patent relating to our drug candidates other than COR388, with claims directed to pharmaceutical compounds, pharmaceutical compositions and methods of using these compounds in the treatment of various indications. We were also the owner of record of 33 pending U.S. and non-U.S. patent applications relating to such other drug candidates in these areas; as well as 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 scientific positions.

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 and This Offering

Our share price may be volatile, and you may be unable to sell your shares at or above the offering price.

The market price of our common stock is likely 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 addition, prior to this offering, there has been no public market for our common stock. Although our common stock has been approved for listing on the Nasdaq Global Select Market, an active trading market may not develop following the closing of this offering or, if developed, may not be sustained. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. If the market price of our common stock after this offering does not exceed the initial public offering price, you may not realize any return on your investment in us and may lose some or all of your investment. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in 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 after this offering, 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. Based on the number of shares of common stock outstanding as of December 31, 2018, upon the closing of this offering, we will have 26,013,334 shares of common stock outstanding, assuming no exercise of our outstanding options (and no exercise of the underwriters' option to purchase additional shares from us) or 26,675,134 shares of common stock if the underwriters' option to purchase additional shares is exercised in full.

All of the common stock sold in this offering will be freely tradable without restrictions or further registration under the Securities Act of 1933, as amended, or the Securities Act, except for any shares held by our affiliates as defined in Rule 144 under the Securities Act. The remaining 21,601,334 shares of common stock outstanding after this offering, based on shares outstanding as of December 31, 2018, will be restricted as a result of securities laws, lock-up agreements or other contractual restrictions that restrict transfers for at least 180 days after the date of this prospectus, subject to certain extensions. See also the section of this prospectus captioned “Shares Eligible for Future Sale.”

The underwriters may, in their sole discretion, release all or some portion of the shares subject to lock-up agreements with the underwriters prior to expiration of the lock-up period. See also the section of this prospectus captioned “Shares Eligible for Future Sale.” For more information regarding the lock-up agreements with the underwriters see the section of this prospectus captioned “Underwriting.”

The holders of 21,330,749 shares of common stock, or 98.75% based on shares outstanding on an as-converted basis as of December 31, 2018, will be entitled to rights with respect to registration of such shares under the Securities Act pursuant to a registration rights agreement between such holders and us. If such holders, by exercising their registration rights, sell a large number of shares, they could adversely affect the market price for our common stock. If we file a registration statement for the purpose of selling additional shares to raise capital and are required to include shares held by these holders pursuant to the exercise of their registration rights, our ability to raise capital may be impaired. We intend to file a registration statement on Form S-8 under the Securities Act to register 5,141,732 shares subject to outstanding stock options issued under the 2014 Plan and shares of common stock reserved for issuance under the 2019 Plan and the 2019 ESPP. Both the 2019 Plan and the 2019 ESPP provide for automatic increases in the shares reserved for issuance under the plans which could result in additional dilution to our stockholders. Once we register the shares under these plans, they can be freely sold in the public market upon issuance and vesting, subject to a 180-day lock-up period and other restrictions provided under the terms of the applicable plan and/or the equity award agreements entered into with participants in the plan.

Our management team may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a return.

Our management will have broad discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. Accordingly, investors will need to rely on our judgment with respect to the use of these proceeds. We intend to use the net proceeds from this offering to fund our global Phase 2/3 GAIN clinical trial for COR388, and to support future clinical and preclinical activities, manufacturing and development of our library of compounds, as well as for working capital and general corporate purposes, which may include the costs of operating as a public company. While we have no current agreements, commitments or understandings for any specific strategic acquisitions or in-licenses at this time, we may use a portion of the net proceeds for these purposes. For more information see, “Use of Proceeds.” The failure by our management to apply these funds effectively could adversely affect our ability to continue maintaining and expanding our business. Until the net proceeds are used, they may be placed in investments that do not produce significant income or that may lose value.

We have never paid dividends on our capital 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.

Upon the closing of this offering, our directors and executive officers and our affiliates will beneficially own, in the aggregate, approximately 32.32% of our outstanding capital stock (inclusive of shares purchased in this offering, and assuming no exercise of the underwriters' option to purchase additional shares). 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.

Because the public offering price of our common stock will be substantially higher than the net tangible book value per share of our outstanding common stock following this offering, new investors will experience immediate and substantial dilution.

The public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock immediately following this offering based on the total value of our tangible assets less our total liabilities. Therefore, if you purchase shares of our common stock in this offering, you will experience immediate dilution of approximately $11.65 per share, the difference between the initial public offering price of $17.00 per share, and the net tangible book value per share of our common stock as of December 31, 2018, after giving effect to the issuance of shares of our common stock in this offering. Furthermore, if the underwriters exercise their overallotment option, or outstanding options and warrants are exercised, you could experience further dilution. For a further description of the dilution that you will experience immediately after the offering, see the section of this prospectus captioned "Dilution."

Our failure to meet the continued listing requirements of the Nasdaq Global Select Market could result in a delisting of our common stock.

If, after listing, we fail to satisfy the continued listing requirements of the Nasdaq Global Select Market, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement or prevent future non-compliance with Nasdaq's listing requirements.

If securities or industry analysts do not publish research or reports about our business or publish negative reports about our business, our share price and trading volume could decline.

The trading market for our common stock will depend on the research and reports that securities or industry analysts publish about us or our business. Currently, we do not have any analyst coverage and we may not obtain analyst coverage in the future. In the event we obtain analyst coverage, we will not have any control over such analysts. If one or more of the analysts who cover us downgrade our shares or change their opinion of our shares, our share price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

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 to be in effect upon the closing of this offering will 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 to be in effect upon the closing of this offering 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 to be in effect upon the closing of this offering 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. For more information, see the section of this prospectus captioned “Description of Capital Stock—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 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 to be in effect upon the closing of this offering will 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 will 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.

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 intend 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;

- not 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) the last day of the fiscal year (a) following the fifth anniversary of the closing of this offering, (b) in which we have total annual gross revenue of at least $1.07 billion or (c) 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 (2) 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, this offering and 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans and expectations for our business operations and financial performance and condition. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “predict,” “potential,” “positioned,” “seek,” “should,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology.

We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy 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” and elsewhere in this prospectus regarding, among other things:

- 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;
- existing regulations and 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;
- the potential purchases of common stock by certain of our existing stockholders and their affiliated entities, including stockholders who are associated with certain of our directors, in this offering;
- potential claims relating to our intellectual property; and
- other risk factors included under “Risk Factors” in this prospectus.

We operate in a very competitive and rapidly changing environment. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained in this prospectus. The results, events and circumstances reflected in the forward-looking statements may not be achieved or occur, and actual results, events or circumstances could differ materially from those described in the forward-looking statements.

Forward-looking statements should not be read as a guarantee of future performance or results, and will not necessarily be accurate indications of the times at, or by, which such performance or results will be achieved. Forward-looking statements are based on information available at the time those statements are made and/or management’s good faith belief as of that time with respect to future events. While we believe that information provides a reasonable basis for these statements, that information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely on these statements.

Forward-looking statements speak only as of the date of this prospectus. You should not put undue reliance on any forward-looking statements. We assume no obligation to update forward-looking statements to reflect actual results, changes in assumptions or changes in other factors affecting forward-looking information, except to the extent required by applicable laws. If we update one or more forward-looking statements, no inference should be drawn that we will make additional updates with respect to those or other forward-looking statements.

You should read this prospectus and the documents that we reference in this prospectus and have filed with the Securities and Exchange Commission as exhibits to the registration statement of which this prospectus is a part with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

INDUSTRY AND MARKET DATA

This prospectus contains estimates, projections and other information concerning our industry, our business, and the markets for our drug candidates, including data regarding the estimated size of such markets and the incidence of certain medical conditions. We obtained the industry, market and similar data set forth in this prospectus from our internal estimates and research and from academic and industry research, publications, surveys, and studies conducted by third parties, including governmental agencies, including the following:

- The Alzheimer's Association, "2018 Alzheimer's Disease Facts and Figures;"
- The Alzheimer's Association, "2017 Alzheimer's Disease Facts and Figures;"
- Eke, P.I., Dye, B.A., Wei, L., Thornton-Evans, G.O., Genco, R.J. "Prevalence of Periodontitis in Adults in the United States: 2009 and 2010." *Journal of Dental Research*. Volume 91, Issue 10, August 2012;
- Pharmaceutical Research and Manufacturers of America, "2017 Medicines in Development for Alzheimer's Disease;"
- University of California San Francisco Memory and Aging Center, "Familial Alzheimer's Disease;" and
- World Health Organization, "Dementia fact sheet."

The content of the above sources, except to the extent specifically set forth in this prospectus, does not constitute a portion of this prospectus and is not incorporated herein. 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 independently verified the accuracy or completeness of the 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.

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of shares of our common stock in this offering will be approximately $67.6 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise in full their option to purchase additional shares, we estimate that the net proceeds from this offering will be approximately $78.1 million.

We intend to use the net proceeds from this offering to fund our global Phase 2/3 GAIN clinical trial for COR388, and to support future clinical and preclinical activities, manufacturing and development of our library of compounds, as well as for working capital and general corporate purposes, which may include the costs of operating as a public company.

We estimate that our current capital resources, along with the net proceeds from this offering, will be sufficient to fund our operating expenses and capital expenditure requirements through 2021, including through the completion and the announcement of the top-line results of our Phase 2/3 GAIN trial. However, the net proceeds from this offering, together with our current cash, will not be sufficient for us to fund the development of COR388 through regulatory approval, and we will need to raise additional capital to complete the development and commercialization of COR388. At this time, we cannot predict with certainty the amount of capital needed to complete the development and commercialization of COR388, but we anticipate seeking additional capital in the future to fund such capital needs through further equity offerings and/or debt borrowings. We cannot guarantee that we will be able to raise additional capital on reasonable terms or at all.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering or the amounts that we will actually spend on the uses set forth above.

The amounts and timing of our actual expenditures and the extent of our Phase 2/3 GAIN trial and research and development activities may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from any preclinical or clinical trials we may commence in the future, our ability to take advantage of expedited programs or to obtain regulatory approval for any other drug candidates we may identify and pursue, the timing and costs associated with the manufacture and supply of any other drug candidates we may identify and pursue for clinical development or commercialization, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

We intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination regarding the declaration and payment of dividends, if any, will be at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

CAPITALIZATION

The following table sets forth our cash, cash equivalents and short-term investments and capitalization as of December 31, 2018, after giving effect to a one-for-0.367647 reverse split of our capital stock, on:

- an actual basis;
- a pro forma basis, giving effect to (i) the conversion of all of our outstanding shares of our redeemable convertible preferred stock into an aggregate of 18,161,027 shares of our common stock, (ii) the exercise in full of an outstanding warrant to purchase 27,941 shares of common stock, and (iii) the effectiveness of our amended and restated certificate of incorporation, in each case, upon the closing of this offering; and
- a pro forma as adjusted basis, giving effect to (i) the pro forma adjustments set forth above and (ii) the sale and issuance of shares of our common stock by us in this offering, at the initial public offering price of $17.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with the section of this prospectus entitled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our historical financial statements and related notes thereto included elsewhere in this prospectus.

	As of December 31, 2018		
(In thousands, except share and per share data)	Actual	Pro Forma	Pro Forma As Adjusted
		(Unaudited)	
Cash, cash equivalents and short-term investments	$ 71,716	$ 71,717	$ 139,357
Redeemable convertible preferred stock, par value $0.001—18,439,076 shares authorized; 18,161,027 shares issued and outstanding, actual; no shares authorized, issued and outstanding, pro forma and pro forma as adjusted	104,046	—	—
Stockholders’ (deficit) equity:			
Preferred stock, $0.001 par value—no shares authorized, issued and outstanding, actual; 10,000,000 shares authorized, no shares issued and outstanding, pro forma and pro forma as adjusted			
Common stock, par value $0.001 – 24,794,114 shares authorized; 3,412,366 shares issued and outstanding, actual; 100,000,000 shares authorized, 21,601,334 shares issued and outstanding, pro forma; 100,000,000 shares authorized, 26,013,334 shares issued and outstanding, pro forma as adjusted	3	22	26
Additional paid-in capital	245	104,273	171,909
Accumulated other comprehensive loss	(49)	(49)	(49)
Accumulated deficit	(32,825)	(32,825)	(32,825)
Total stockholders’ (deficit) equity	(32,626)	71,421	139,061
Total capitalization	$ 71,420	$ 71,421	$ 139,061

Except as otherwise indicated, all information in this prospectus is based upon 21,601,334 shares of our common stock outstanding as of December 31, 2018, assuming the conversion of all of our outstanding shares of redeemable convertible preferred stock as of December 31, 2018 into 18,161,027 shares of common stock and the exercise in full of an outstanding warrant to purchase 27,941 shares of common stock, as of December 31, 2018, upon the closing of this offering, and excludes:

- 1,885,504 shares of our common stock issuable upon the exercise of options to purchase shares of our common stock outstanding as of December 31, 2018, with a weighted-average exercise price of $1.57 per share;
- 525,728 shares of our common stock issuable upon the exercise of options to purchase shares of our common stock granted after December 31, 2018, with a weighted-average exercise price of $7.99 per share;
- 2,682,942 shares of common stock reserved for future grants or issuance under our 2019 Plan, which share reserve will automatically increase each year, as more fully described in “Executive Compensation—Equity Incentive Plans;” and
- 268,295 shares of common stock reserved for future issuance under our 2019 ESPP, which share reserve will automatically increase each year, as more fully described in “Executive Compensation—Equity Incentive Plans.”

DILUTION

If you invest in our common stock, your interest will be diluted to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value (deficit) as of December 31, 2018 was $(32.6) million, or $(9.56) per share of common stock. Our historical net tangible book value (deficit) per share represents total tangible assets less total liabilities, less redeemable convertible preferred stock, divided by the number of our shares of common stock outstanding as of December 31, 2018.

Our pro forma net tangible book value (deficit) as of December 31, 2018, before giving effect to the issuance and sale of our shares of common stock in this offering, was $71.4 million, or $3.31 per share of our common stock. Our pro forma net tangible book value before the issuance and sale of our shares of common stock in this offering represents the amount of our total tangible assets reduced by the amount of our total liabilities and divided by the total number of shares of our common stock outstanding as of December 31, 2018, assuming the conversion of all of our outstanding shares of redeemable convertible preferred stock into 18,161,027 shares of our common stock and the exercise in full of an outstanding warrant to purchase 27,941 shares of common stock upon the closing of this offering.

After giving effect to our sale of 4,412,000 shares of our common stock in this offering at the initial public offering price of $17.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2018, after giving effect to a one-for-0.367647 reverse split of our capital stock on April 25, 2019, would have been $139.1, or $5.35 per share. This represents an immediate increase in net tangible book value of $2.04 per share to our existing stockholders and an immediate dilution of $11.65 per share to new investors purchasing shares of common stock in this offering. We determine dilution by subtracting the pro forma as adjusted net tangible book value per share after this offering from the amount of cash that a new investor paid for a share of common stock.

The following table illustrates this dilution on a per share basis:

Initial public offering price per share		$17.00
Historical net tangible book value per share as of December 31, 2018	$(9.56)	
Increase in pro forma net tangible book value per share	12.87	
Pro forma net tangible book value per share as of December 31, 2018	3.31	
Increase in pro forma net tangible book value per share attributable to new investors purchasing shares in this offering	$ 2.04	
Pro forma net tangible book value per share after this offering		5.35
Dilution per share to new investors in this offering		$11.65

The following table summarizes, as of December 31, 2018, on the pro forma as-adjusted basis described above, the difference between the existing stockholders and new investors with respect to the number of shares of common stock purchased from us, the total consideration paid to us and the average price per share paid or to be paid to us at the initial public offering price of $17.00 per share, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us:

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders	21,601,334	83.0%	$ 99,487,880	57.0%	$ 4.61
New investors	4,412,000	17.0%	$ 75,004,000	43.0%	$ 17.00
Total	26,013,334	100.0%	$174,491,880	100.0%	$ 6.71

(1) Certain of our existing 5% stockholders and stockholders affiliated with certain of our directors (or their affiliates) have agreed to purchase, and we have directed allocations for, an aggregate of approximately $26.3 million of shares of our common stock in this offering at the initial public offering price and on the same terms as the other purchasers in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these persons or entities as they will on any other shares sold to the public in this offering. The presentation in this table regarding ownership by existing stockholders does not give effect to any purchases in this offering by such investors.

If the underwriters exercise their option to purchase additional shares in full, the percentage of shares of our common stock held by existing stockholders would be 80.98% and the percentage of shares of our common stock held by new investors would be 19.02%.

Except as otherwise indicated, the above discussion and tables assume no exercise of the underwriters' option to purchase additional shares of common stock from us. If the underwriters exercise their option to purchase additional shares in full, the pro forma as-adjusted net tangible book value per share would be $5.61 per share, and the dilution per share to new investors in this offering would be $11.39 per share.

Except as otherwise indicated, all information in this prospectus is based upon 21,601,334 shares of our common stock outstanding as of December 31, 2018, assuming the conversion of all of our outstanding shares of redeemable convertible preferred stock as of December 31, 2018 into 18,161,027 shares of common stock and the exercise in full of an outstanding warrant to purchase 27,941 shares of common stock, as of December 31, 2018, upon the closing of this offering, and excludes:

- 1,885,504 shares of our common stock issuable upon the exercise of options to purchase shares of our common stock outstanding as of December 31, 2018, with a weighted-average exercise price of $1.57 per share;
- 525,728 shares of our common stock issuable upon the exercise of options to purchase shares of our common stock granted after December 31, 2018, with a weighted-average exercise price of $7.99 per share;
- 2,682,942 shares of common stock reserved for future grants or issuance under our 2019 Plan, which share reserve will automatically increase each year, as more fully described in "Executive Compensation—Equity Incentive Plans;" and
- 268,295 shares of common stock reserved for future issuance under our 2019 ESPP, which share reserve will automatically increase each year, as more fully described in "Executive Compensation—Equity Incentive Plans."

To the extent that any outstanding options are exercised, new options are issued under our equity incentive plans or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering.

SELECTED HISTORICAL FINANCIAL DATA

You should read the selected historical financial data set forth below in conjunction with our historical financial statements and related noted thereto included elsewhere in this prospectus and the information under the section "Management's Discussion and Analysis of Financial Condition and Results of Operations."

We derived the selected historical statements of operations data for the years ended December 31, 2017 and 2018 and the historical balance sheet data as of December 31, 2017 and 2018, from our audited historical financial statements appearing elsewhere in this prospectus. The selected historical financial data included in this section are not intended to replace the historical financial statements and related notes thereto included elsewhere in this prospectus. Our historical results are not necessarily indicative of our future performance.

Selected Historical Financial Data

(in thousands, except share and per share data)	Year Ended December 31, 2017	2018
Summary Statement of Operations Data:		
Operating expenses:		
Research and development	$ 9,099	$ 10,085
General and administrative	1,271	2,034
Net loss	(12,235)	(12,476)
Net loss per share	(3.70)	(3.71)

(in thousands)	As of December 31, 2017	2018
Summary Balance Sheet Data:		
Cash, cash equivalents and short-term investments	$ 7,343	$ 71,716
Working capital(1)	5,774	71,127
Total assets	7,718	72,877
Long-term obligations less current portion	7,171	—
Redeemable convertible preferred stock	17,178	104,046
Additional paid-in capital	66	245
Total stockholders' equity (deficit)	(20,280)	(32,626)

(1) We define working capital as current assets less current liabilities.

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 the section of this prospectus entitled "Selected Historical Financial Data" and our historical financial statements and related notes thereto included elsewhere in this prospectus. This discussion and other parts of this prospectus contain 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 section of this prospectus entitled "Risk Factors."

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 protease 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 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 and establishing our corporate infrastructure.

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, 2018, we had an accumulated deficit of $32.8 million. We incurred a net loss of $12.5 million in the year ended December 31, 2018. 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 issuance of convertible promissory notes and redeemable convertible preferred stock. From inception through December 31, 2018, we received net proceeds of approximately $99.5 million from the issuance of redeemable convertible preferred stock and convertible promissory notes. To date, we received net proceeds of $7.8 million from the sale and issuance of shares of our Series A redeemable convertible preferred stock in the year ended December 31, 2015 net proceeds of $8.0 million from the sales of our redeemable Series A convertible stock in the year ended December 31, 2016 net proceeds of $7.8 million from the sale and issuance of convertible promissory notes in the year ended December 31, 2017, net proceeds of $0.2 million from the sale and issuance of convertible promissory notes and net proceeds of $75.7 million from the sale and issuance of shares of our Series B redeemable convertible preferred stock in the year ended December 31, 2018. As of December 31, 2018, we had cash, cash equivalents and short-term investments of $71.7 million. As of March 31, 2019, we had cash, cash equivalents and short-term investments of $59.0 million, which excludes long-term investments of $5.7 million.

Our cash equivalents and short-term investments are held in money market funds, investments in corporate securities and government agency obligations.

We believe that our existing cash, cash equivalents and short-term investments, together with the net proceeds of this offering, 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. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company.

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, 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, and accounting services, 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 substantially as a result of staff expansion and additional occupancy costs, as well as costs associated with being a public company, including higher legal and accounting fees, investor relations costs, higher insurance premiums and other compliance costs associated with being a public company.

Interest Income

Interest and other income, net consists primarily of interest earned on our short-term investments in corporate notes and government agency notes.

Interest Expense

Interest and other expense, consists primarily of non-cash charges relating to expenses settled with the issuance of equity.

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.

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 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 is probable or the performance condition has been achieved. We account for awards to nonemployees using the fair value method. Awards to nonemployees are subject to periodic revaluation over their vesting terms and was not material for all periods presented. 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.

Prior to 2017, equity instruments issued to non-employees are accounted for in accordance with ASC 505-50 *Equity Based Payments to Non-Employees* and are recorded at their fair value on the measurement date and are subject to periodic adjustments as the underlying equity instruments vest. The fair value of options granted to consultants is expensed when vested. Non-employee stock-based compensation expense was not material for all periods presented.

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.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* (“ASU 2018-07”), to align the accounting for share-based payment awards issued to employees and nonemployees, particularly with regard to the measurement date and the impact of performance conditions. The new guidance requires equity-classified share-based payment awards issued to nonemployees to be measured on the grant date, instead of being remeasured through the performance completion date under the current guidance. For public entities, ASU 2018-07 is effective for fiscal years beginning after December 15, 2018. This update supersedes previous guidance for equity-based payments to nonemployees under Subtopic 505-50, Equity—Equity-Based Payments to Non-Employees. The Company chose to early adopt ASU 2018-07 effective for its financial statements starting January 1, 2017 and cumulative adjustment upon adoption was immaterial.

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.

The following assumptions were used to calculate the fair value of awards granted to employees, non-employees and directors during the periods indicated:

	Year Ended December 31,	
	2017	2018
Risk-free interest rate	1.83%-2.04%	2.39%-2.99%
Expected term (in years)	6.25	6.25
Volatility	63.0%	65.0%-70.0%
Dividend yield	0%	0%

We will continue to use judgment in evaluating the expected volatility, expected terms, and interest rates utilized for our stock-based compensation expense calculations on a prospective basis.

Stock-based compensation expense, net of actual forfeitures, is reflected in the statements of operations and comprehensive loss as follows (in thousands):

	Year Ended December 31,	
	2017	2018
Research and development	$ 32	$ 77
General and administrative	6	78
Total stock-based compensation	$ 38	$ 155

As of December 31, 2018, total unamortized stock-based compensation was $1.6 million.

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.

In the absence of a public trading market for our common stock, 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 the closing of this offering, our board of directors intends to determine 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, 2018, our total deferred tax assets were $8.0 million. Due to our lack of earnings history and uncertainties surrounding our ability to generate future taxable income, 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, 2017 and 2018

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

	Year Ended December 31,		Change	
	2017	2018	$	%
Operating expenses:				
Research and development	$ 9,099	$ 10,085	$ 986	11%
General and administrative	1,271	2,034	763	60%
Loss from operations	(10,370)	(12,119)	1,749	17%
Interest income	—	806	806	NA
Interest expense	(1,643)	(957)	(686)	(42)%
Changes in fair value of derivative liability	(222)	(206)	(16)	(7)%
Net loss	$ (12,235)	$ (12,476)	$ 241	2%

Research and Development Expenses

The following table summarizes our research and development expenses:

	Year ended December 31,	
	2017	2018
	(in thousands)	
Direct research and development expenses:		
COR388	$ 5,730	$ 6,066
Other direct research costs	665	736
Indirect research and development expenses:		
Personnel related (including stock-based compensation)	1,946	2,403
Facilities and other research and development expenses	758	880
Total research and development expenses	$ 9,099	$ 10,085

Research and development expenses were $9.1 million for the year ended December 31, 2017, compared to $10.1 million for the year ended December 31, 2018. The increase of $1.0 million was driven by an increase of $2.7 million in expenses for our lead product candidate, COR388, which entered into Phase 1 clinical trials, which increase was offset by a decrease of $2.4 million in preclinical and drug candidate manufacturing costs. In addition, we had an increase of $0.1 million in research and development expenses related to other preclinical programs currently in development. Personnel-related expenses, including stock-based compensation, increased by $0.5 million due to an increase in headcount.

General and Administrative Expenses

General and administrative expenses increased $0.8 million, or 60%, from $1.3 million for the year ended December 31, 2017 to $2.0 million for the year ended December 31, 2018. The increase in general and administrative expenses was primarily due to an increase of $0.6 million in personnel costs as a result of an increase in our employee headcount and an increase of $0.2 million in legal and accounting fees and other professional service fees.

Interest Income

Interest income, increased $0.8 million from $0 for the year ended December 31, 2018. The increase was due to interest income of $0.8 million as a result of increased average cash balances and rising interest rates on short term investments.

Interest Expense

Interest expense decreased $0.7 million, or 42%, from $1.6 million for the year ended December 31, 2017 to $1.0 million for the year ended December 31, 2018. The decrease was primarily due to a decrease in non-cash charges relating to interest and accretion of discount for convertible promissory notes payable.

Change in fair value of derivative liability

The change in fair value of derivative liability decreased $16,000, or 7%, from $222,000 for the year ended December 31, 2017 to $206,000 for the year ended December 31, 2018. The decrease is due to change in assumptions used in the fair value assessment and 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, 2018, we had an accumulated deficit of $32.8 million. As of December 31, 2018, we had cash, cash equivalents and short-term investments of $71.7 million.

Based on our existing business plan, we believe that our existing cash, cash equivalents, and short-term 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,	
	2017	2018
Net cash (used in) provided by:		
Operating activities	$ (9,827)	$ (11,695)
Investing activities	(77)	(46,754)
Financing activities	7,750	75,928
Net increase (decrease) in cash and cash equivalents	$ (2,154)	$ 17,479

Cash Used in Operating Activities

Net cash used in operating activities was $11.7 million for the year ended December 31, 2018 and $9.8 million for the year ended December 31, 2017.

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 operating activities in the year ended December 31, 2017 was primarily due to our net loss for the period of $12.2 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 $1.9 million, an increase in accounts payable and accrued liabilities of $0.5 million.

Cash Used in Investing Activities

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 $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.

Cash provided by financing activities was $7.8 million in the year ended December 31, 2017, which consisted of net proceeds of $7.8 million from the issuance of convertible notes.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2018 (in thousands):

	Total	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
Operating lease obligations[1]	$947	$ 367	$580	$—	$ —
Total contractual obligations	$947	$ 367	$580	$—	$ —

(1) Operating lease obligations represent future rent expense to be incurred for our current facility lease for the three-year term. The Company had issued 114,437 shares of its Series B redeemable convertible preferred stock in full satisfaction of rent expense for the term of the lease upon commencement of the lease period. No cash consideration was payable. The lease obligation above represents the recognition of rent expense on a straight-line basis and is determined based on the fair value of shares issued.

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.

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, 2018 and December 31, 2017.

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 are choosing 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 earliest of (1) the last day of our first fiscal year (a) following the fifth anniversary of the closing of this offering, (b) in which we have total annual gross revenue of at least $1.07 billion, or (ii) 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 (2) 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

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board, or FASB or other standard setting bodies and adopted by us as of the specified effective date. Unless otherwise discussed, the impact of recently issued standards that are not yet effective will not have a material impact on our financial statements upon adoption.

Recently Adopted Accounting Standards Updates

In May 2014, FASB issued ASU 2014-09, Revenue from Contracts with Customers (Topic 606), which will replace numerous requirements in U.S. GAAP, including industry-specific requirements, and provide companies with a single revenue recognition model for recognizing revenue from contracts with customers. The core principle of the new standard is that a company should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. On January 1, 2017, the Company early adopted the new accounting standard and all the related amendments. However, as the Company did not have any contracts with customers during 2017 or 2018, the adoption had no impact on the financial statements.

In November 2015, the FASB issued ASU No. 2015-17, *Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes* ("ASU 2015-17"). The standard requires that deferred tax assets and liabilities be classified as noncurrent on the balance sheet rather than being separated into current and noncurrent. ASU 2015-17 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2016. Early adoption is permitted, and the standard may be applied either retrospectively or on a prospective basis to all deferred tax assets and liabilities. Adoption of ASU 2015-17 did not have a material impact on the Company's financial position, results of operations and cash flows.

In January 2016, the FASB issued ASU No. 2016-01, "Financial Instruments - Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities" ("ASU 2016-01"). ASU 2016-01 requires equity investments (except those accounted for under the equity method or those that result in consolidation) to be measured at fair value with changes in fair value recognized in net income unless a policy election is made for investments without readily determinable fair values. Additionally, ASU 2016-01 requires public entities to use the exit price notion when measuring the fair value of financial instruments for measurement purposes and eliminates the requirement to disclose the method(s) and significant assumptions used to estimate the fair value of financial instruments measured at amortized cost on the balance sheet. Furthermore, it requires separate presentation of financial assets and financial liabilities by measurement category and form of financial asset on the balance sheet or the accompanying notes to the financial statements. ASU 2016-01 is effective for interim and annual periods beginning after December 15, 2017. Adoption of ASU 2016-01 did not have a material impact on the Company's financial position, results of operations and cash flows.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation—Stock Compensation (Topic 718)*: Improvements to Employee Share-Based Payment Accounting ("ASU 2016-09"). ASU 2016-09 requires, among other things, that excess tax benefits and tax deficiencies be recognized as income tax expense or benefit in the statement of operations rather than as additional paid-in capital, changes the classification of excess tax benefits from a financing activity to an operating activity in the statement of cash flows, and allows forfeitures to be accounted for when they occur rather than estimated. ASU 2016-09 became effective for the Company on January 1, 2017. Adoption of ASU 2016-09 did not have a material impact on the Company's financial position, results of operations and cash flows.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments* ("ASU 2016-15"), to address diversity in practice in how certain cash receipts and cash payments are presented and classified in the statement of cash flows. For public entities, the standard is effective for annual periods beginning after December 15, 2017, including interim periods within those fiscal years. The adoption of ASU 2016-15 did not have a material impact on the Company's financial position, results of operations and cash flows.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230)* ("ASU 2016-18"), which was intended to reduce diversity in practice in the classification and presentation of changes in restricted cash on the Statement of Cash Flows. ASU 2016-18 requires that the Statement of Cash Flows explain the change in total cash and equivalents and amounts generally described as restricted cash or restricted cash equivalents when reconciling the beginning-of-period and end-of-period total amounts. The standard also requires reconciliation between the total cash and cash equivalents and restricted cash presented on the Statement of Cash Flows and the cash and cash equivalents balance presented on the Balance Sheet. For public entities, ASU 2016-18 is effective for fiscal years beginning after December 15, 2017 and interim periods within those fiscal years and early adoption is permitted. The Company adopted the standard which resulted in 2017 restricted cash of $50,000 included in the reconciliation within the Statements of Cash Flows.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting* ("ASU 2017-09"), which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. The standard is effective for annual periods beginning after December 15, 2017, including interim periods within those fiscal years. Early adoption is permitted. The adoption of ASU 2017-09 did not have an impact on the Company's financial position, results of operations or cash flows.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07"), to align the accounting for share-based payment awards issued to employees and nonemployees, particularly with regard to the measurement date and the impact of performance conditions. The new guidance requires equity-classified share-based payment awards issued to nonemployees to be measured on the grant date, instead of being remeasured through the performance completion date under the current guidance. For public entities, ASU 2018-07 is effective for fiscal years beginning after December 15, 2018. This update supersedes previous guidance for equity-based payments to nonemployees under Subtopic 505-50, Equity—Equity-Based Payments to Non-Employees. The Company chose to early adopt ASU 2018-07 effective for its financial statements starting January 1, 2017 and cumulative adjustment upon adoption was immaterial.

Recently Issued Accounting Standards or Updates Not Yet Effective

In February 2016, the FASB issued ASU *No. 2016-02 (Topic 842), Leases.* ASU 2016-02 requires an entity to recognize assets and liabilities arising from a lease for both financing and operating leases. The ASU will also require new qualitative and quantitative disclosures to help investors and other financial statement users

better understand the amount, timing, and uncertainty of cash flows arising from leases. For public entities, ASU 2016-02 is effective for fiscal years beginning after December 15, 2018. Early adoption is permitted. The Company is in the process of evaluating the impact of adoption of ASU 2016-02 on its financial statements and currently believes the most significant change will be related to the recognition of lease liabilities and right-of-use assets on the balance sheet for real estate operating leases.

Quantitative and Qualitative Disclosures about Market Risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates or exchange rates. As of December 31, 2018, we had cash, cash equivalents, and short-term investments of $71.7 million, consisting of interest-bearing money market accounts, and investments in corporate notes and government agency securities, for which the fair market value would be affected by changes in the general level of United States interest rates. While we invest in short-term maturities and intend to hold these securities to maturity, an immediate 10% change in interest rates would have a material effect on the fair market value of our cash, cash equivalents and short-term investments, which we estimate to be approximately $0.4 million based upon current cash, cash equivalents and short-term investments,

We do not believe that inflation, interest rate changes, or exchange rate fluctuations had a significant impact on our results of operations for any periods presented herein.

BUSINESS

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 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.

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.

The following table identifies preclinical studies described in this prospectus relating to the presence of *P. gingivalis* in the human brain, the causal link between this bacteria and Alzheimer's disease pathology, and the activity of our gingipain inhibitors:

Study Name	Primary Purpose of Study
Human Brain Immunohistochemistry (IHC)	Demonstrate higher amount of *P. gingivalis gingipains* in the brain of Alzheimer's patient autopsy samples compared to controls and correlation to tau pathology
Human Brain PCR	Confirm presence of *P. gingivalis* specific DNA in Alzheimer's autopsy brains using PCR and sequencing
Human Cerebral Spinal Fluid (CSF) PCR	Demonstrate presence of *P. gingivalis* in the brain of live Alzheimer's patients through the detection of specific DNA fragments in cerebral spinal fluid
Oral Infection of Mice with *P. gingivalis*	Demonstrate that *P. gingivalis* infiltrates the brain and causes Alzheimer's disease pathology, including amyloid beta production, neuroinflammation, and neurodegeneration in orally infected wild type mice
Neuroprotection assay	Examine the impact of COR388 compared to other molecules on neuronal cell toxicity caused by *P. gingivalis* infection, using SH-SY5Y cells, which is a neuroblastoma cell line from human neural tissue commonly used in neuroscience research

Study Name	Primary Purpose of Study
Brain Injection of Gingipain Proteins into Mouse Brain, or Stereotactic Injection Study	Demonstrate toxicity of gingipains to neurons after injection into mouse brain
COR388 Dose Response in Mice Infected with *P. gingivalis*	Demonstrate COR388 blood exposures associated with efficacy in wild type mice infected with *P. gingivalis*
Identification of Gingipain Protease Substrates, tau and ApoE	Demonstrate the ability of gingipains to fragment proteins associated with Alzheimer's disease risk and pathology and the benefit of COR388 to reduce ApoE fragments in Alzheimer's patients

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.

Our Team

We are led by a management team with deep scientific and drug development experience and a commitment to serving patients with Alzheimer's and other degenerative diseases. Collectively, our management team has a rich set of experiences both in academia and in industry, leading clinical programs for large biopharmaceutical companies and advancing clinical assets in venture-backed and public companies. We were founded by our Chief Executive Officer, Casey C. Lynch, our Chief Scientific Officer, Stephen S. Dominy, M.D., and our Senior Vice President, Legal and Administration, and Secretary, Kristen Gafric and are joined by

Leslie Holsinger, Ph.D., our Executive Vice President of Preclinical Development, Michael Detke, M.D., Ph.D., our Chief Medical Officer and Christopher Lowe, our Chief Financial Officer. Our leadership is complemented by a team of drug development experts, approximately two-thirds of whom hold Ph.D. or M.D. degrees. Together, our management team brings expertise across relevant disciplines, including neuroscience, infectious disease, immunology, oncology, translational science, medicinal chemistry, manufacturing and biomarker development.

Our board of directors is comprised of our CEO and CSO and industry leaders that bring relevant biopharma and finance experience, including Margi McLoughlin, Ph.D., former Executive Director at Pfizer Ventures; David A. Lamond, President of En Pointe LLC; Kevin Young, CBE, former Chief Operating Officer of Gilead; Una Ryan, OBE, Ph.D., former Chief Executive Officer of AVANT Immunotherapeutics and Christopher J. Senner, Chief Financial Officer at Exelixis, Inc. Our clinical advisory board is comprised of scientific leaders in the fields of Alzheimer's, neurodegeneration and medicine, including Martin Farlow, M.D. and Marwan Sabbagh, M.D., who are directors of neuroscience institutes; Mark Brody, M.D., and Louis Kirby, M.D., who are founders of clinical research organizations specializing in neurodegenerative diseases; Eric Siemers, M.D., who was a fellow of Alzheimer's clinical development at Eli Lilly; David Munoz, M.D. and Mark Ryder, D.M.D., who are professors of pathology and orofacial sciences, respectively; and David Hosford, M.D, Ph.D., who is a regulatory expert and previous clinical reviewer of the FDA Division of Neurology Products.

Our company is supported by a group of investors that include both biopharmaceutical companies and institutional investors, and we have raised approximately $99.5 million in funding as of December 31, 2018. Our key investors are comprised of strategic investors, including Pfizer Ventures, Takeda Ventures and Verily Life Sciences, as well as Sequoia Capital, Breakout Labs, Breakout Ventures, Dolby Family Ventures, EPIQ Capital Group, the Lamond Family and Vulcan Capital, amongst others.

Overview of Alzheimer's Disease and Relationship to *P. gingivalis*

Significant Unmet Medical Need

Alzheimer's disease represents a significant unmet medical need and there are no marketed treatments that address the underlying cause of the disease. Alzheimer's disease is a progressive neurodegenerative disease that spreads throughout the brain and destroys memory and other important cognitive functions. 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. Alzheimer's disease can have a significant burden on family and caretakers. On average, caregivers devote approximately 22 hours per week or approximately 1,140 hours per year caring for patients. 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.

P. gingivalis Precedes and Is Correlated with Alzheimer's Disease Symptoms and Pathology

P. gingivalis is an asaccharolytic Gram-negative bacterium that secretes toxic virulence factor proteases known as gingipains. Evidence shows that brain infiltration by *P. gingivalis* precedes, and is correlated with, Alzheimer's disease symptoms and pathology. Significant evidence over the last decade has shown that a dysfunctional immune system in the brain is a risk factor linked to Alzheimer's disease. We believe that these genetic variations in essential immune pathways may cause a dysfunctional response to, or defective clearance of, *P. gingivalis* and gingipains in the brain.

Patients with Alzheimer's disease manifest with numerous pathologies, which we have found to be downstream of *P. gingivalis* infection. The disease mechanism of *P. gingivalis* and the therapeutic mechanism

for COR388, which blocks the downstream pathological effects of gingipains and *P. gingivalis*, are presented below in Figure 1.

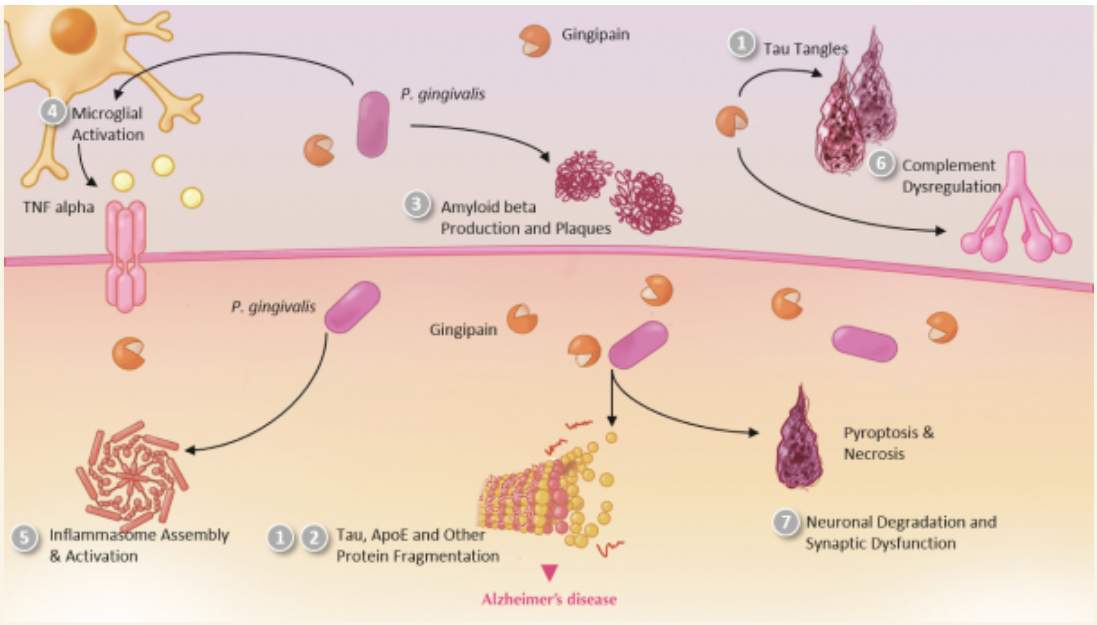

Figure 1. *P. gingivalis* infiltration of the brain and gingipain proteolytic activity affect the following characteristic pathology observed in the brain of Alzheimer's patients:

1. **Tau tangles**, also known as neurofibrillary tangles, are aggregates of hyperphosphorylated and fragmented tau protein usually found inside neurons. It has been demonstrated that tau is a target of gingipain proteolysis and that *P. gingivalis* infection for 22 weeks resulted in hyperphosphorylated tau tangles in the brains of mice.
2. **Apolipoprotein protein E**, or ApoE, is known to be fragmented in the Alzheimer's disease brain and fragmentation may lead to loss of function or toxicity. ApoE4 carriers have a higher risk of fragmentation and development of Alzheimer's disease compared to people with ApoE2 or ApoE3 alleles. ApoE is a target of gingipain proteolysis, with ApoE4 being a better gingipain target than ApoE2 and ApoE3. ApoE has many documented functions including in immune response
3. **Amyloid beta** production and plaque formation represent the abnormal accumulations of amyloid beta peptide. It has been demonstrated that amyloid beta is an antimicrobial peptide produced in response to infection, including infection by *P. gingivalis.*
4. **Microglial activation**, the process by which microglia, the immune cells of the brain, proliferate and are activated in the Alzheimer's disease brain and by *P. gingivalis.* Activated microglia can release inflammatory proteins in response to infection, such as tumor necrosis factor, or TNF, alpha.
5. **Inflammasomes**, a multiprotein intracellular complex that detects pathogenic microorganisms, are activated in the Alzheimer's disease brain in neurons and microglia, and by P. gingivalis infection. Inflammasomes activate pro-inflammatory cytokines and induce a form of cell death termed pyroptosis.
6. **Complement pathway**, a part of the innate immune system, is activated in the Alzheimer's disease brain. Bacterial infections, including *P. gingivalis*, are known to contribute to complement activation and dysregulation, as this pathway is a common component of the innate immune system's clearance of pathogens.
7. **Chronic neurodegeneration** represents the loss of neurons in the brain and, research has demonstrated that neurodegeneration spreads through the brain of Alzheimer's patients. *P. gingivalis* resides inside cells causing slowly progressive damage and death of neurons and other cells.

We believe the discovery of *P. gingivalis* and associated gingipains in the Alzheimer's disease brain, which we have observed to cause Alzheimer's pathology in animal models, provides a unique opportunity for successful upstream treatment of the underlying cause of Alzheimer's disease pathology in humans. We believe that previously unsuccessful approaches, like blocking production of amyloid beta, have been focusing on the downstream effects of infection rather than the underlying cause, which has led to the unsuccessful clinical development in the field.

Statistical Significance

In the description of our clinical trials and preclinical studies below, n represents the number of patients in a particular group and p or p-values represent the probability that random chance caused the result (e.g., a p-value = 0.001 means that there is a 0.1% probability that the difference between the placebo group and the treatment group is purely due to random chance). A p-value £ 0.05 is a commonly used criterion for statistical significance, and may be supportive of a finding of efficacy by regulatory authorities.

P. gingivalis and the Role of Gingipains

P. gingivalis is most commonly known as a cause of periodontal disease, which, like Alzheimer's disease, is an age-related degenerative condition. However, it is less commonly known that *P. gingivalis* can migrate from the mouth to other tissues in the body, including the brain, where we believe it causes degenerative conditions such as Alzheimer's disease. Furthermore, the presence of *P. gingivalis* has been observed in the brain of Alzheimer's disease patients with no concurrent periodontal disease, demonstrating that periodontal disease is a risk factor, but not a prerequisite, for Alzheimer's disease.

P. gingivalis secretes two different gingipain proteases, lysine gingipain, or Kgp, and arginine gingipain, or Rgp. Both are essential for *P. gingivalis* survival and pathogenicity. In January 2019, we co-authored a peer reviewed paper published in *Science Advances* that included research conducted by our co-authors at the University of Auckland. Based on that research, we reported the presence of higher levels of gingipains inside neurons in postmortem Alzheimer's disease brains relative to the presence observed in the brains of postmortem control patients (Figure 2 A, C). It is understood in the field that Alzheimer's disease pathology begins several decades prior to the manifestation of symptoms. Therefore, the presence of gingipains in some control patients is consistent with a disease initiating event. Both Rgp and Kgp load correlated strongly to Alzheimer's disease pathology as measured by tau load (Figure 2 B, D).

Gingipain levels in Alzheimer's disease brains correlates with Alzheimer's disease diagnosis and pathology, as demonstrated below in Figure 2.

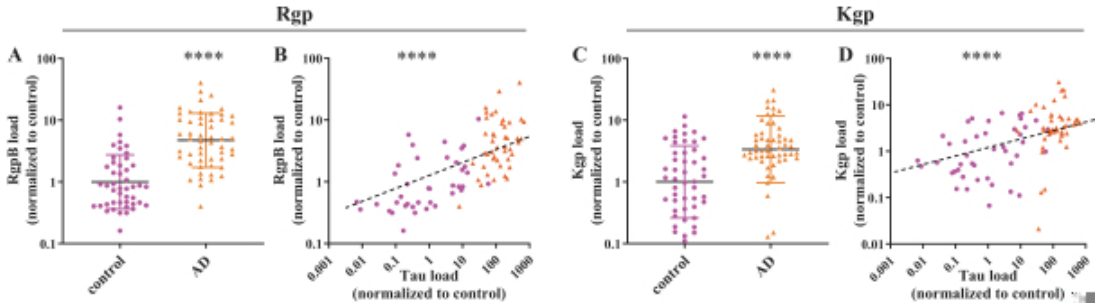

Figure 2. Greater than 90% of Alzheimer's patients had high gingipain levels in the brain (A and C). Rgp and Kgp are present in 96% and 91% of Alzheimer's disease brains, respectively, which is significantly higher than those observed in the brains of control patients. (B and D) Gingipain levels are correlated with Alzheimer's

pathology. (B) Spearman r = 0.674, n = 84. (D) Spearman r = 0.563, n = 89; AD = Alzheimer's Disease (**** p £ 0.0001).

In addition to the identification of *P. gingivalis* gingipains in the postmortem brain tissue of Alzheimer's disease subjects, we conducted a separate study where we identified bacterial DNA in the brain tissue of Alzheimer's patients from two separate gene sequences found only in *P. gingivalis* (16S and hmuY), confirming the presence of this specific bacteria.

Separately, we have developed a proprietary PCR method for detecting fragments of *P. gingivalis* DNA in CSF as a marker of bacterial infection within the central nervous system, or CNS, of human subjects. This method, which is not yet an FDA approved diagnostic test, detects fragments of bacterial DNA that are specifically found in *P. gingivalis* bacteria, recently shed or released from areas of the brain in contact with the CSF, which we believe is consistent with the presence of a CNS infection. Using this method, we identified fragmented bacterial DNA from *P. gingivalis* bacteria in the CSF of all nine mild to moderate Alzheimer's patients in our Phase 1b clinical trial, as well as in the CSF of all 50 mild to moderate Alzheimer's patients in a separate human observational study.

Examining CSF samples provides certain advantages relative to postmortem brain tissue, as CSF is readily available with a significant volume that can be sampled from live subjects in a clinical trial setting before and after treatment. Further, CSF generally circulates throughout the entire brain and, as such, may better indicate the bacterial DNA present throughout the brain and across the whole brain, as opposed to the bacterial DNA present on a specific small sample of brain tissue. However, there are also challenges inherent in the detection of fragments of *P. gingivalis* DNA in CSF that include:

- the DNA found is fragmented and represents a fraction of the genomic bacterial DNA present in the whole brain;
- the level of fragmented DNA is small and isolation of small amounts of DNA is subject to high variability;
- the fragmented DNA is a qualitative measure of the presence of a CNS infection, and while specific amounts of DNA can be identified in a specified volume of CSF, we cannot currently correlate it to a specific amount of bacteria present in the whole brain; and
- CSF is a biofluid that turns over regularly and will only contain DNA that has been released or shed within a specific timeframe.

P. gingivalis Infection Causes Alzheimer's Disease Pathology in Mice

We believe that the findings above in human brains and CSF, and the animal studies described below, suggest support for a causal relationship between *P. gingivalis* and Alzheimer's disease by satisfying several criteria for establishing disease causation by an infection. This criteria was originally described by Koch's Postulates and modified over time based on modern scientific discoveries. First, we have identified fragments of *P. gingivalis* DNA in the CSF of 59 Alzheimer's patients that we have reviewed with our current proprietary PCR method. Additionally, we have identified *P. gingivalis* gingipains and DNA in the brains of Alzheimer's disease patients and fewer gingipains in non-demented control brains. The presence of gingipains predates disease symptoms and correlates with severity of tau and ubiquitin pathology. Finally, researchers have demonstrated evidence of causation by reproducing Alzheimer's pathology in animal models after infection with *P. gingivalis*, as discussed in more detail below.

An important criterion for demonstrating causation by an infectious agent is to demonstrate that infection of an animal can reproduce the disease. One of the first studies in this regard was conducted by

researchers at University of Central Lancashire in ApoE genetic knockout mice, where it was shown that oral infection with *P. gingivalis* resulted in brain infection and activation of the complement pathway. In this model, *P. gingivalis* was shown to be unique in infecting the brain after oral infection, as two other oral bacteria inoculated into the oral cavity did not infect the brain. In another study, researchers at the National Center for Geriatrics and Gerontology in Japan, used a different model based on transgenic mice overexpressing the mutated human amyloid precursor protein and showed that oral infection with *P. gingivalis* impaired cognitive function and increased the deposition of amyloid beta plaques.

Researchers at the University of Illinois at Chicago, working independently of us, have demonstrated that oral infection of wild type mice with *P. gingivalis* for 22 weeks results in brain infiltration, neuroinflammation, amyloid beta production and plaque formation, tau phosphorylation and tau tangles, and neurodegeneration, as shown in figure 3.

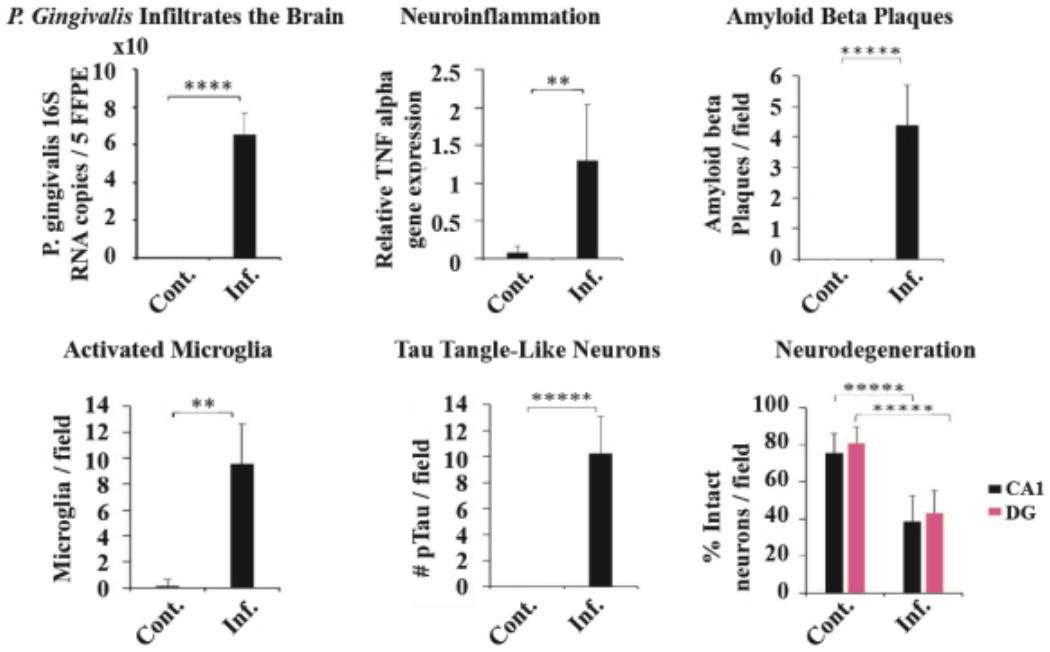

Figure 3. Results from 22-week oral infection with *P. gingivalis* of wild type mice. Adapted from Iliesvki et al. PLOS One 2018 (Cont. = control; Inf. = Infection; FFPE = formalin fixed paraffin embedded; pTau = phosphorylated Tau; ** p £ 0.01; **** p £ 0.0001; ***** p £ 0.00001).

Separately, in our January 2019 peer reviewed publication in *Science Advances*, we reported on a similar wild type mouse model of oral *P. gingivalis* infection. We found that oral infection of wild type mice with *P. gingivalis* results in *P. gingivalis* brain infection, neuroinflammation, loss of neurons in the hippocampus and increased production of amyloid beta. We further demonstrated that oral administration of small-molecule gingipain inhibitors to mice with an established *P. gingivalis* brain infection reduced the bacterial amount of *P. gingivalis* in the brain, reduced amyloid beta levels, protected neurons and reduced markers of neuroinflammation.

We believe this wild type mouse 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, which have historically not translated to successful disease modifying treatment in humans.

***Gingipains Are Responsible for Neurotoxicity of* P. gingivalis**

Gingipains have been shown to mediate the toxicity of *P. gingivalis* in many cell types, including neurons. In an in vitro study, human neuronal cells were infected with *P. gingivalis* and treated with test compounds in parallel. The results of the study indicated that infection with *P. gingivalis* for 48 hours results in approximately 40% cell death. As shown in Figure 4 below, this toxicity was blocked by gingipain inhibitors, including COR388, but not by common broad-spectrum antibiotics such as moxifloxacin and doxycycline, nor by semagacestat, a gamma-secretase inhibitor that blocks amyloid beta production.

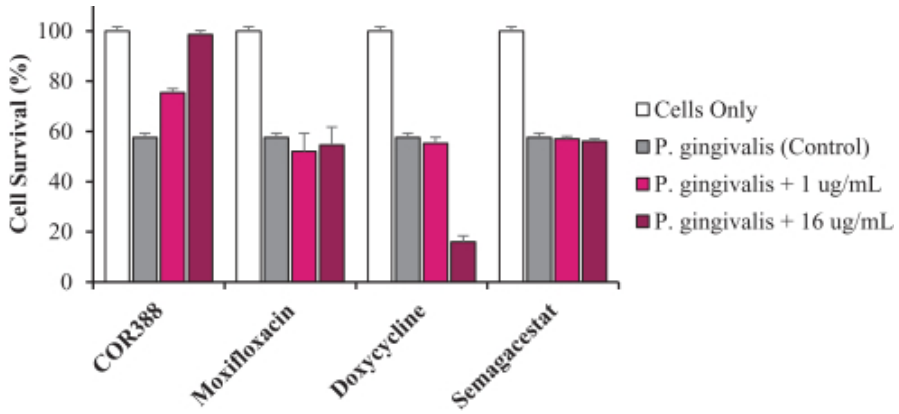

Figure 4. Human cells infected with *P. gingivalis* showed approximately 40% cell death, which was blocked by gingipain inhibitors, such as COR388, but not by broad-spectrum antibiotics nor by semagacestat.

In a separate study, injection of gingipains into the brain of wild type mice resulted in neurodegeneration within 7 days. Similar to the cell culture study, systemic gingipain inhibitors were effective in protecting neurons from gingipain-induced degradation. The exact mechanisms of *P. gingivalis* toxicity to neurons is under investigation. However, among the identified gingipain substrates we have documented, tau is a target of gingipain proteolysis and potentially contributes to the development and toxicity of tau tangles.

Gingipain Inhibition Reduces Pressure for Antibiotic Resistance

We believe that virulence factor inhibitors, such as COR388, have significant potential benefits over broad-spectrum antibiotics, including moxifloxacin and doxycycline. These highly-targeted inhibitors are intended to (i) not disrupt the normal bacterial microbiome, (ii) selectively target only *P. gingivalis* and (iii) have a mechanism of action less likely to generate pressure for antibiotic resistance. Potential for development of resistance was assessed in a typical assay involving the monitoring of the growth of the bacteria in the presence of drug. While no significant resistance to COR388 was detected, significant resistance with over 1,000-fold increase in the minimal inhibitory concentration, or MIC, was developed to moxifloxacin, a commonly used broad-spectrum antibiotic. While therapeutic resistance will continue to be monitored, these data are encouraging that resistance in human studies may be nonexistent or minimal.

COR388 – Our Differentiated Approach to the Treatment of Alzheimer's Disease

Our proprietary lead drug candidate, COR388, is an orally-administered, brain-penetrating small molecule gingipain inhibitor. In two Phase 1 clinical trials conducted to date, COR388 was well-tolerated in

healthy volunteers and Alzheimer's patients. 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 should be interpreted with caution because they were not all statistically significant. Furthermore, in our preclinical studies involving wild type mouse models, we observed that COR388 reduced bacterial load in the brain, reduced amyloid beta levels, protected neurons and reduced markers of neuroinflammation. We initiated our Phase 2/3 GAIN trial in mild to moderate Alzheimer's patients in April 2019 and expect top-line results by the end of 2021.

Pharmacological Properties and Preclinical Evidence

We designed COR388 to target a key upstream driver of Alzheimer's pathological pathways. Our clinical and preclinical studies demonstrated the presence of *P. gingivalis* in Alzheimer's patients that we tested, and we have observed in our preclinical data a causal relationship of *P. gingivalis* infection on developing neurodegenerative and neuroinflammatory disease pathology in animal models. In preclinical studies with *P. gingivalis*-infected mice, Kgp and Rgp inhibitors reduced the amount of *P. gingivalis* in mice brains and protected neurons in the hippocampus after oral administration. We found that neither the addition of an Rgp inhibitor nor a traditional antibiotic improved effectiveness over a Kgp inhibitor alone. Accordingly, we are developing COR388, an optimized Kgp inhibitor based on its favorable pharmacological properties, which include potency, selectivity, oral bioavailability and blood-brain barrier penetration.

Our preclinical studies of COR388 demonstrated dose-dependent reductions in infection measures when administered to mice with an established *P. gingivalis* brain infection. Doses of 10 mg/kg and 30 mg/kg both reduced *P. gingivalis* load, amyloid beta levels and TNF alpha levels in brain tissue relative to those observed in the infected control group. We also observed a dose-dependent, downward trend in blood levels of chemokine ligand 5, or CCL5 or RANTES, an inflammatory signaling protein that is elevated in the brain microvessels of

Alzheimer's patients. Importantly, COR388 was associated with maintenance of hippocampal interneurons in these studies. Summary results of these findings are presented below in Figure 5.

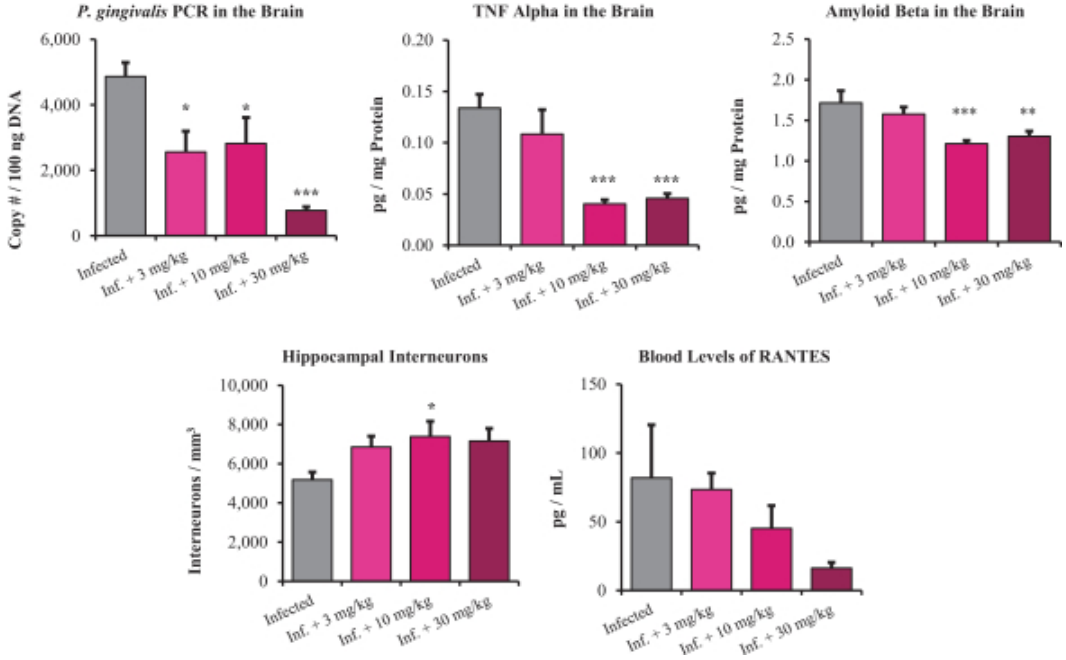

Figure 5. In preclinical studies, COR388 has demonstrated significant reductions in *P. gingivalis* load in the brain, TNF alpha, amyloid beta, as well as signs of neuronal preservation and a reduction in systemic inflammation depicted by levels of RANTES (Control = infected + 0 mg/kg COR388; 30 mg/kg = infected + 30 mg/kg COR388; 10 mg/kg = infected + 10 mg/kg COR388; 3 mg/kg = infected + 3 mg/kg COR388; pg = picogram; * p £ 0.05; ** p £ 0.01; *** p £ 0.001).

Our COR388 Clinical Results

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 reduced blood levels of RANTES and a reduction of fragments of ApoE in the CSF. In addition, data from the Alzheimer's patients treated with COR388 in our Phase 1b clinical trial showed improvements across several exploratory cognitive tests, including a statistically significant improvement in three measures on the WLA, relative to baseline, numerical but not statistically significant improvements in MMSE scores relative to baseline and placebo and improvements in several measures of cognitive function in the CANTAB relative to baseline and placebo that were not statistically significant.

Phase 1a Single Ascending Dose Study Results in Healthy Volunteers

In our Phase 1a SAD clinical study referred to as COR388-001, we treated 34 subjects with a single dose of COR388, at doses of 5 mg, 25 mg, 50 mg, 150 mg and 250 mg, or placebo. COR388 was found to be well-tolerated, with no increase in the incidence or severity of adverse events with increasing doses. There was only one treatment-emergent adverse event, or TEAE, that was considered related to study drug by the

investigator, a mild headache in the 25 mg cohort. Electrocardiograms, or ECGs, were closely monitored due to increases in the QRS duration and PR interval seen at very high doses in animal studies. While some subjects experienced transient small increases in the QRS duration and PR interval, there was variability in both placebo and COR388 patients, all readings were below the range considered abnormal and no readings were clinically significant, which means they did not result in the need to consider changes to the treatment of the patient. There were no discernable trends or abnormalities in the QTcF interval in this study or in animal studies. Summary results of these findings are presented below in Table 1.

Table 1. Drug related TEAEs in our Phase 1a study

	Placebo n=9	5 mg n=6	25 mg n=6	50 mg n=6	150 mg n=6	250 mg n=1
Mild Headache	0	0	1 (17%)	0	0	0

Phase 1b Multiple Ascending Dose Study Results in Healthy Older Volunteers and Alzheimer's Patients

In our Phase 1b MAD clinical study referred to as COR388-002, we treated 33 subjects across four dose cohorts. Cohorts 1-3 included 24 healthy older volunteers from 55 to 70 years of age who received 25 mg, 50 mg or 100 mg of COR388, or placebo, every 12 hours for 10 consecutive days. Cohort 4 included nine mild to moderate Alzheimer's patients who received 50 mg of COR388 or placebo every 12 hours for 28 days.

In healthy older volunteers, COR388 was found to be well-tolerated in this study. Adverse events for subjects treated with COR388 were infrequent, transient and mild to moderate in severity, and consistent with those treated with placebo. Four subjects administered COR388, or 22% of those treated with COR388, and two subjects administered placebo, or 33% of the placebo treated group, experienced at least one TEAE that was considered to be study-drug related or possibly study-drug related by the investigator. There were no clinically significant ECG events or abnormalities noted. While transient minor increases in the QRS duration and PR interval were seen in some subjects, there was variability in both placebo and COR388 patients, these readings were within the range expected for older subjects and no readings were clinically significant. In addition, there were no discernable trends in the QTcF interval. Summary results of these findings in healthy older volunteers are presented below in Table 2.

Table 2. Drug Related TEAEs: Cohorts 1-3 in Older Healthy Volunteers; 10 Days of Treatment

	Placebo n=6	25 mg n=6	50 mg n=6	100 mg n=6
Dizziness[1]	0	0	1 (17%)	1 (17%)
Dysgeusia[1]	1 (17%)	0	0	0
Nausea[1]	0	0	0	1 (17%)
Presyncope[2]	1 (17%)	0	0	0
Restlessness[1]	0	0	0	1 (17%)
Tachycardia[1, 3]	0	0	1 (17%)	0

[1] Mild AE severity, [2] Moderate AE severity. [3] AE consisted of six beats of transient tachycardia that occurred again 48 hours after stopping study drug and was at that time determined to be unrelated to study drug by the investigator. No serious adverse events were reported.

Cohort 4 enrolled nine mild to moderate Alzheimer's patients from 55 to 83 years of age with baseline MMSE scores between 14 and 25. These patients were allowed to stay on stable doses of background medications, including symptomatic Alzheimer's disease treatments, during the trial. COR388 was well-tolerated in Alzheimer's patients in this study. Two patients administered COR388, or 33% of those administered COR388, and two patients administered placebo, or 66% of the placebo treated group, experienced at least one mild to moderate TEAE that was considered to be study-drug related or possibly study-drug related by the

investigator. While some transient increases in the QRS duration and PR interval were seen, these readings were within the range expected for older subjects and were not clinically significant. Relative to placebo, there were no patterns in laboratory abnormalities or changes in ECGs, vital signs, physical examinations, or brain magnetic resonance imaging, or MRI, observed during these trials that would be deemed practically relevant to the treatment of the patient with COR388. Summary results of these findings in Alzheimer's patients are presented below in Table 3.

Table 3. Drug Related TEAE: Cohorts 4 in Alzheimer's Patients; 28 Days of Treatment

	Placebo n=3	50 mg n=6
Bradycardia[1]	1 (33%)	0
Orthostasis[1]	1 (33%)	0
Liver Enzyme Elevation[2]	0	1 (17%)
Pancreatic Enzyme Elevation[1]	0	1 (17%)
Transient QT Prolongation[1]	1 (33%)	1 (17%)

[1] Mild AE severity, [2] Moderate AE severity. No serious adverse events were reported.

Pharmacokinetic, Biomarker and Exploratory Cognitive Data from our Phase 1b MAD Study

Pharmacokinetics

In our Phase 1b MAD study, pharmacokinetic analysis of COR388 levels in human blood were generally consistent with, or higher than, blood levels in animal studies that were associated with reduced infection, reduced markers of inflammation and protection of neurons. Furthermore, COR388 was detected in the CSF at levels consistent with those observed in animal models, indicating potentially therapeutic levels of the drug were achieved in the CNS. Our proprietary method for detecting fragments of *P. gingivalis* DNA in CSF found fragmented DNA from *P. gingivalis* in the CSF of all nine Alzheimer's patients in our Phase 1b clinical trial, which is consistent with and suggests the presence of an infection in the CNS. COR388 was found to be rapidly absorbed after oral administration with a four to five-hour half-life, providing a profile that may allow for twice a day oral administration based on pharmacokinetic and irreversible binding properties of COR388.

Pharmacodynamic Markers

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 and ApoE. Levels of RANTES, an inflammatory marker, were significantly reduced in the blood of Alzheimer's patients after treatment with COR388 for 28 days, consistent with the dose response demonstrated in our preclinical study. Additionally, we have shown that ApoE, a target for gingipains, can be proteolytically cleaved into peptides consistent with those identified by others in the brain and by us in the CSF of Alzheimer's patients. In the Alzheimer's patients treated with COR388, fragments of ApoE in the CSF were reduced compared to placebo. Summary results of these findings in Alzheimer's patients are presented below in Figure 6.

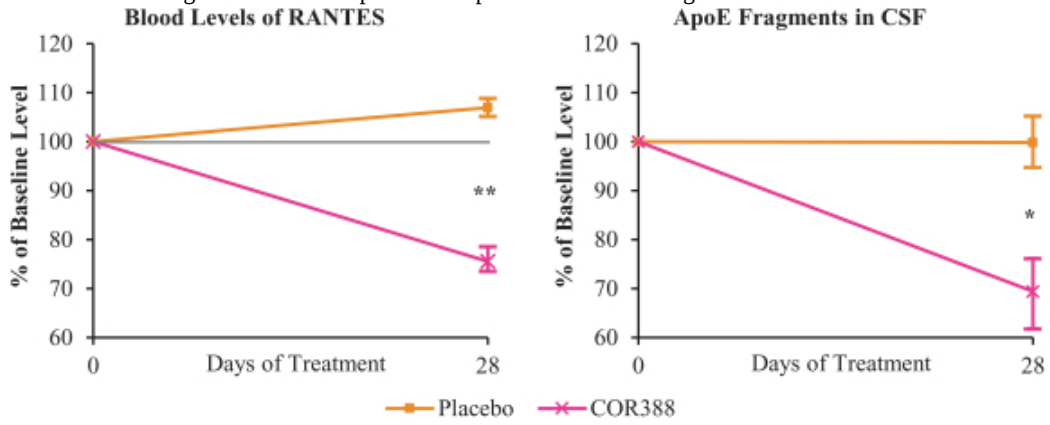

Figure 6. After 28 days of treatment with COR388, RANTES concentration in human blood and ApoE fragments generated by gingipains in CSF were significantly reduced (* p £ 0.05; ** p £ 0.01).

Exploratory Cognitive Testing

While the primary goals of our Phase 1a SAD and Phase 1b MAD trials were related to safety measures and assessment of human pharmacokinetics, we also observed improvements in some exploratory cognitive measures data from six Alzheimer's patients treated with COR388 in our Phase 1b MAD trial, as presented below. However, these improvements should be interpreted with caution because they were not all statistically significant.

- **Mini-Mental State Exam, or MMSE**: MMSE is a 30-point questionnaire commonly used in Alzheimer's trials to assess problems with memory and other cognitive functions, where people with MMSE scores of 14 to 25, enrolled in this study, represent a mild to moderate stage of disease. After treatment with COR388, MMSE scores increased from baseline, reflecting improvement. A difference of 1.7 and 1.2 points on the MMSE were seen in subjects treated with COR388 compared to those dosed with placebos on day 15 and day 28, respectively. This difference was not statistically significant.

- **Cambridge Neuropsychological Test Automated Battery, or CANTAB**: CANTAB is a computer-based cognitive assessment system that measures various aspects of cognitive function, including memory, attention and psychomotor skills. CANTAB is commonly used with Alzheimer's patients. We observed improvements for the Alzheimer's patients treated with COR388 from baseline and as compared to the placebo group on measures of episodic memory, working memory and psychomotor

speed. The improvement in the memory component of cognitive function, a composite combined score assessing both working memory as well as episodic memory, is shown in Figure 7B. An increase of 0.29 and 0.32 in this composite Z score from baseline was seen in subjects treated with COR388 on day 15 and day 28, respectively, indicating potential improvement over time. No such increase was observed in subjects dosed with placebos. The difference was not statistically significant.

- **Winterlight Speech-Based Cognitive Assessment, or WLA**: WLA is a new speech-based testing platform designed to detect cognitive impairment associated with dementia and mental illness. In the WLA utilized in our Phase 1b study, patients were asked to describe a picture in as much detail as possible, and their speech patterns were analyzed using 35 parameters available with Winterlight's speech analysis technology. Our results demonstrated statistically significant improvements from baseline after COR388 in three key measurements, previously shown in the literature to be some of the most important indicators of the presence and severity of Alzheimer's disease. The 32 other parameters either showed improvements that were not statistically significant, or showed no statistically significant changes over the course of the study. Additionally, the placebo group did not show any statistically significant improvements in any of the 35 measures. Parameters that showed statistically significant improvement from baseline after COR388 treatment included an increase in the use of prepositions and conjunctions, an increase in Content Units, or details identified in an image, and an increase in the number of Object Units identified in the image. Prepositions and conjunctions are words used to link and qualify how things are related to each other within an utterance and an increase in their use suggests an improvement in the quality and thoroughness of participant's picture descriptions. Prepositions and subordinating conjunctions represented, on average, 12% of all words contained within the transcript for the COR388 treatment group participants at Day 28, which is a statistically significant 5-point increase from Day 1 (p=0.001). The corresponding proportion for patients dosed with placebo was, on average, 9% of all words in the transcript at Day 28, which is a 0-point change from Day 1. For total Content Units, the COR388 treatment group reported, on average, 58% of all the image details at Day 28, which is a statistically significant 17-point increase from Day 1 (p=0.00008). In contrast, the placebo group reported 53% of all image details at Day 28, an insignificant increase of only six points from Day 1. For Object Units, the COR388 treatment group reported, on average, 69% of all objects (*e.g.*, "Books" and "Glasses") depicted in the image at Day 28, which is a statistically significant 23-point increase from Day 1 (p=0.00001). In contrast, the placebo group reported 57% of all depicted objects at Day 28, an insignificant increase of only 7 points from Day 1. In comparing subjects treated with COR388 versus subjects dosed with placebos, two of the measures (prepositions/conjunctions used and Object Units identified) were statistically significantly greater for COR388, one of the measures (prepositions/conjunctions used) remained statistically significantly greater with a conservative Bonferroni correction for multiple comparisons and one of the measures (Content Units identified) improved, but was not statistically significantly greater. The statistical analysis plan for WLA in the GAIN trial is still under finalization, but we plan to focus only on key parameters for demonstrating the effects of COR388 on Alzheimer's patients instead of all 35 speech analysis parameters.

Summary findings from these exploratory cognitive tests are presented below in Figure 7.

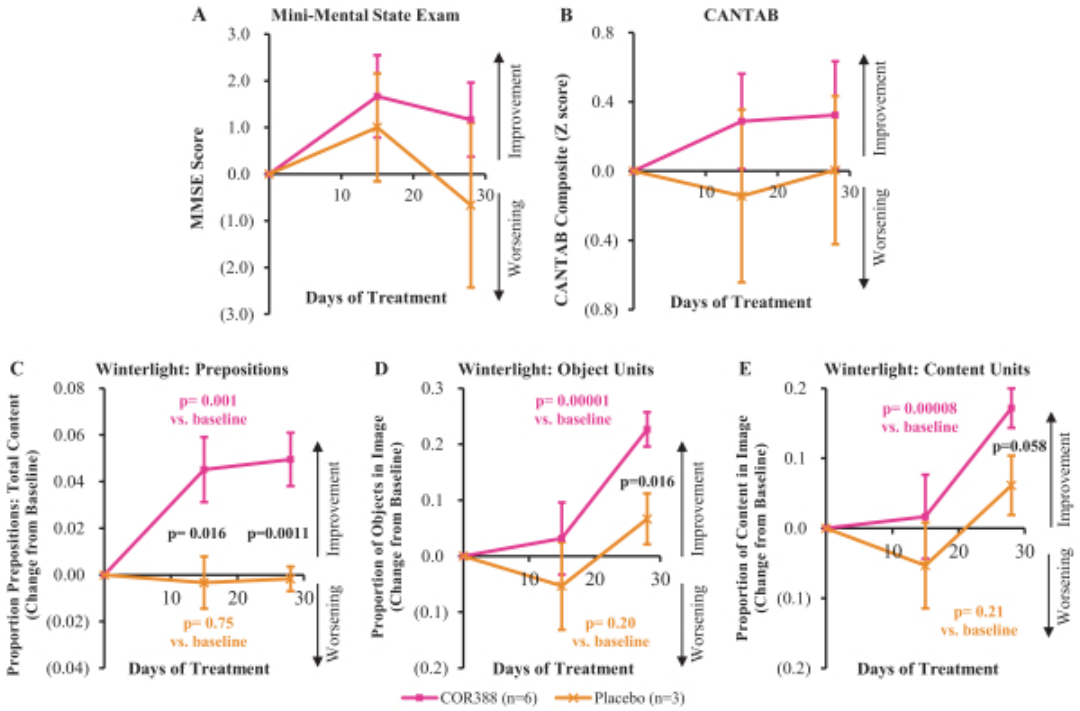

Figure 7. COR388 effects on selected cognitive tests (A) MMSE, (B) CANTAB Memory Composite of Cognitive Function, (C) WLA prepositions, encompassing analysis of prepositions and subordinating conjunctions, (D) WLA Object Units and (E) WLA Content Units.

Phase 2/3 Enabling Preclinical Safety and Chronic Toxicology

Safety pharmacology studies in appropriate preclinical species, mouse and dog, demonstrated large safety margins in cardiovascular, CNS, and respiratory safety studies: 12-fold in cardiovascular studies and 25-fold in CNS and respiratory studies over the top exposure planned in our Phase 2/3 GAIN trial. These safety margins were calculated by dividing the highest plasma concentration, or Cmax, at the "no adverse event level," or NOAEL, dose in the animal study by the projected Cmax for an 80 mg human dose. Standard six-to-nine-month chronic GLP toxicology studies in mice and dogs showed no adverse findings in clinical observations, behavior, clinical pathology laboratory parameters or histopathology. COR388 was observed to have a 24-fold therapeutic window between our top exposure planned in our Phase 2/3 GAIN trial and the NOAEL from mouse studies. Standard regulatory genotoxicity tests have been conducted with no evidence of genotoxicity.

Our Planned 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 22 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.

The primary endpoint will be the mean change in ADAS-Cog11 from baseline to the end of treatment period at 48 weeks. Secondary endpoints in all subjects will include: (i) change in Alzheimer's Disease Cooperative Study Group-Activities of Daily Living, or ADCS-ADL; and (ii) Change in Clinical Dementia Rating-Sum of Boxes, or CDR-SB. 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.

We also plan to invite placebo and treated patients who complete our Phase 2/3 GAIN trial to participate in an open label extension in which patients will receive either 40 mg or 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.

Pipeline Compounds

We have a library of small molecule protease inhibitors, including additional Kgp and Rgp inhibitors with structures that are distinct from COR388. The most advanced of these Kgp inhibitors 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 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 also 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. Accordingly, we plan to assess periodontal pocket depth as a secondary endpoint in our Phase 2/3 GAIN trial.

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 to begin our Phase 2/3 GAIN trial in Alzheimer's disease as currently planned and ongoing preclinical studies. Additional cGMP API campaigns are in process to ensure full supply for our Phase 2/3 GAIN trial including the potential open label extension.

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 is neat powder in a capsule and we believe its stability will mimic the stability of the drug substance, which has been demonstrated to be stable for 15 months at room temperature. Stability studies are ongoing and we are working with our CMOs to continue to optimize the drug candidate. Currently API is stored refrigerated, out of an abundance of caution while stability studies are ongoing, while the storage condition for the drug candidate 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 API, as well as drug candidate under cGMP protocols. The cGMP API manufacturing process is completed with a single vendor from readily available commercial starting materials and reagents. We do not currently have arrangements in place for redundant supply of bulk drug substance; however, this could easily be established by transferring the existing technology to any number of vendors as there are no proprietary technologies required for manufacturing. The drug candidate manufacturing is a simple capsule filling operation that could also be transferred to additional vendors as necessary. It is our intent to identify and qualify additional manufacturers to provide API and drug candidate manufacturing services prior to submission of a new drug application to the FDA for all drug candidates.

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., Celgene Corporation, 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 Regulation

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 2019. 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.

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.

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 Affordable Care Act, 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 Affordable Care Act, or 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. In addition, 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.

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. 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 March 31, 2019, we had 19 employees, including 14 in research and development and two in general and administrative functions. We also utilize seven consultants in various roles related to research and development. We believe our employee relations are good.

Legal Proceedings

We are not currently subject to any material legal proceedings.

Facilities

Our corporate headquarters are currently located in South San Francisco, California, where we sublease 3,185 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.

MANAGEMENT

Executive Officers and Directors

The names and ages of our executive officers and directors as of March 31, 2019, are as follows:

Name	Age	Position(s)
Executive Officers:		
Casey C. Lynch	45	President, Chief Executive Officer and Chairman of the Board
Christopher Lowe	51	Chief Financial Officer and Treasurer
Kristen Gafric	43	Senior Vice President, Legal and Administration, and Secretary
Michael Detke, M.D.	52	Chief Medical Officer
Stephen S. Dominy, M.D.	63	Chief Scientific Officer and Director
Leslie Holsinger, Ph.D.	53	Executive Vice President of Preclinical Development
Non-Employee Directors:		
David A. Lamond(2)	44	Director
Margi McLoughlin, Ph.D(2)(3).	56	Director
Una Ryan, OBE, Ph.D(1)(3).	77	Director
Christopher J. Senner(1)	51	Director
Kevin Young, CBE(1)(2)(3)	61	Director

(1) Member of audit committee
(2) Member of compensation committee
(3) Member of 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. He previously served on the board of Arrinex, a medical device company. 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.

Margi 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 University. 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.

Board of Directors

Our board of directors is currently comprised of seven members. Our amended and restated bylaws permit our board of directors to establish by resolution the authorized number of directors, and eight directors are currently authorized. Upon the closing of this offering our board of directors will consist of seven members with one vacancy in Class I, to be filled by the affirmative vote of a majority of the directors then in office. In addition, Una Ryan, OBE, Ph.D. was appointed as Lead Non-Management Director, effective upon the closing of this offering until the 2020 annual meeting of stockholders.

Voting Arrangements

The election of the members of our board of directors is currently governed by the amended and restated voting agreement that we entered into with certain holders of our common stock and certain holders of our redeemable convertible preferred stock in May 2018, as amended in December 2018 and March 2019, and the related provisions of our amended and restated certificate of incorporation. Pursuant to the voting agreement and these provisions, Drs. Dominy, McLoughlin, and Ryan, and Messrs. Lamond, Senner and Young and Ms. Lynch have been designated to serve on our board of directors.

- Dr. Margi McLoughlin (who was designated by Pfizer Ventures (US) LLC) and Mr. David A. Lamond (who was designated by the Pierre R. and Christine E. Lamond Trust 11-22-85) were elected by the holders of our redeemable convertible preferred stock;
- Ms. Casey C. Lynch and Dr. Stephen S. Dominy were elected by the holders of our common stock; and
- Dr. Una Ryan, Mr. Christopher J. Senner and Mr. Kevin Young were elected by the holders of our common stock and redeemable convertible preferred stock voting together as a single class on an as-converted basis.

The holders of our common stock and redeemable convertible preferred stock who are parties to our voting agreement are obligated to vote for such designees indicated above. The provisions of this voting agreement will terminate upon the closing of this offering and our certificate of incorporation will be amended and restated, after which there will be no further contractual obligations or charter provisions regarding the election of our directors.

Our directors hold office until their successors have been elected and qualified or appointed, or the earlier of their death, resignation or removal.

Classified Board

In connection with the closing of this offering, we will file our amended and restated certificate of incorporation which will provide that our board of directors will be divided into three classes, with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes of directors continuing for the remainder of their respective three-year terms. Upon the expiration of

the term of a class of directors, a director in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of our directors.

Our directors will be divided among the three classes as follows:

- the Class I directors will be Margi McLoughlin, Ph.D. and Una Ryan, OBE, Ph.D., and their terms will expire at the annual meeting of stockholders to be held in 2020;
- the Class II directors will be Kevin Young, CBE and David A. Lamond and their terms will expire at the annual meeting of stockholders to be held in 2021; and
- the Class III directors will be Casey C. Lynch, Stephen S. Dominy, M.D. and Christopher J. Senner and their terms will expire at the annual meeting of stockholders to be held in 2022.

In addition, our amended and restated bylaws and amended and restated certificate of incorporation will provide that, subject to the rights of any series of preferred stock, (i) only the board of directors may fill vacancies on the board of directors until the next annual meeting of stockholders and (ii) the number of our directors shall be fixed from time to time by a resolution of the majority of our board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the total number of directors.

This classification of the board of directors and the provisions described above may have the effect of delaying or preventing changes in our control or management. See “Description of Capital Stock—Anti-Takeover Effects of Delaware Law and Our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws.”

Role of the Board in Risk Oversight

One of the key functions of our board of directors is informed oversight of our risk management process. Our board of directors does not have a standing risk management committee, but rather administers this oversight function directly through the board of directors as a whole, as well as through its standing committees that address risks inherent in their respective areas of oversight. In particular, our board of directors is responsible for monitoring and assessing strategic risk exposure. Our audit committee is responsible for reviewing and discussing our major financial risk exposures and the steps our management has taken to monitor and control these exposures, including guidelines and policies with respect to risk assessment and risk management. Our audit committee also monitors compliance with legal and regulatory requirements. Our nominating and corporate governance committee monitors the effectiveness of our governance guidelines. Our compensation committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking.

Director Independence

In connection with this offering, our common stock has been approved for listing on the Nasdaq Global Select Market. Under Nasdaq rules, independent directors must comprise a majority of a listed company’s board of directors within a specified period of time after the closing of such company’s initial public offering. In addition, the Nasdaq rules require that, subject to specified exceptions, each member of a listed company’s audit, compensation, and nominating committees be independent. Audit committee members and compensation committee members must also satisfy the independence criteria set forth in Rule 10A-3 and Rule 10C-1, respectively, under the Exchange Act. Under Nasdaq rules, a director will only qualify as an “independent” director if, in the opinion of that company’s board of directors, that director does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director with the listed company.

In order to be considered independent for purposes of Rule 10A-3 and under Nasdaq rules, each member of the audit committee of a listed company may not, other than in his or her capacity as a member of such committee, the board of directors, or any other board committee: (i) accept, directly or indirectly, any consulting, advisory, or other compensatory fees from the listed company or any of its subsidiaries; or (ii) be an affiliated person of the listed company or any of its subsidiaries.

To be considered independent for purposes of Rule 10C-1 and under Nasdaq rules, the board of directors must affirmatively determine that each member of the compensation committee is independent, including a consideration of all factors specifically relevant to determining whether the director has a relationship to the company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (i) the source of compensation of such director, including any consulting, advisory or other compensatory fee paid by the company to such director; and (ii) whether such director is affiliated with the company, a subsidiary of the company or an affiliate of a subsidiary of the company.

Our board of directors undertook a review of its composition, the composition of its committees and the independence of our directors and considered whether any director has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. Based on information provided by each director concerning his or her background, employment, and affiliations, our board of directors has determined that all of our directors other than Casey C. Lynch and Stephen S. Dominy, M.D. do not have relationships that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the applicable rules and regulations of the Securities and Exchange Commission, and the listing and independence standards of the Nasdaq Global Select Market.

In making these determinations, our board of directors considered the current and prior relationships that each non-employee director has with us and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director, and the transactions involving them described in the section entitled "Certain Relationships and Related Party Transactions."

Committees of the Board of Directors

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee. The composition and responsibilities of each committee are described below. Immediately prior to the closing of this offering, copies of the charters for each committee will be available on the investor relations portion of our website at www.cortexyme.com. Members serve on these committees until their resignations or removal. The inclusion of our website in this prospectus does not include or incorporate by reference the information on our website into this prospectus.

Audit Committee

Following the closing of this offering, our audit committee will be comprised of Christopher J. Senner, Kevin Young, CBE and Una Ryan, OBE, Ph.D., with Mr. Senner serving as audit committee chair person. Our board of directors has determined that each of the members of our audit committee satisfies the requirements for independence and financial literacy under the current listing standards of the Nasdaq Global Select Market and the Securities and Exchange Commission rules and regulations, including Rule 10A-3. Our board of directors has also determined that Christopher J. Senner and Una Ryan, OBE, Ph.D. are each an audit committee financial expert within the meaning of Item 407(d) of Regulation S-K of the Securities Act.

Our audit committee will be responsible for, among other things:

- selecting a qualified firm to serve as independent registered public accounting firm to audit our financial statements;

- helping to ensure the independence and overseeing the performance of the independent registered public accounting firm;
- reviewing and discussing the scope and results of the audit with the independent registered public accounting firm, and reviewing, with management and the independent accountants, our interim and year-end operating results;
- reviewing our financial statements and our critical accounting policies and estimates;
- reviewing the adequacy and effectiveness of our internal controls;
- developing procedures for employees to submit concerns anonymously about questionable accounting, internal accounting controls, or audit matters;
- overseeing our policies on risk assessment and risk management;
- overseeing compliance with our code of business conduct and ethics;
- reviewing related-party transactions; and
- pre-approving all audit and all permissible non-audit services (other than de minimis non-audit services) to be performed by the independent registered public accounting firm.

Our audit committee will operate under a written charter, to be effective on the date of this offering, which satisfies the applicable rules of the Securities and Exchange Commission and the listing standards of the Nasdaq Global Select Market, and which will be available on our website upon the closing of this offering. All audit services to be provided to us and all permissible non-audit services, other than *de minimis* non-audit services, to be provided to us by our independent registered public accounting firm will be approved in advance by our audit committee.

Compensation Committee

Following the closing of this offering, our compensation committee will be comprised of David A. Lamond, Margi McLoughlin, Ph.D. and Kevin Young, CBE, each of whom will meet the requirements for independence under the listing standards of Nasdaq and the Securities and Exchange Commission rules and regulations. In addition, each member of our compensation committee will also be a non-employee director, as defined pursuant to Rule 16b-3 of the Exchange Act. David A. Lamond will be the chair of our compensation committee. Following the closing of this offering, the compensation committee will be responsible for, among other things:

- reviewing, approving and determining, or making recommendations to our board of directors regarding, the compensation of our executive officers, including our Chief Executive Officer;
- administering our equity compensation plans and agreements with our executive officers;
- reviewing, approving and administering incentive compensation and equity compensation plans;
- reviewing and approving our overall compensation philosophy; and
- making recommendations regarding non-employee director compensation to our full board of directors.

Our compensation committee will operate under a written charter, to be effective on the date of this offering, which satisfies the applicable rules of the Securities and Exchange Commission and the listing standards of the Nasdaq Global Select Market, and will be available on our website upon the closing of this offering.

Nominating and Corporate Governance Committee

Following the closing of this offering, our nominating and corporate governance committee will consist of Margi McLoughlin, Ph.D., Una Ryan, OBE, Ph.D. and Kevin Young, CBE, each of whom will meet the requirements for independence under the listing standards of Nasdaq and SEC rules and regulations. Kevin Young will be the chair of our nominating and corporate governance committee. Following the closing of this offering, the nominating and corporate governance committee will be responsible for, among other things:

- identifying, evaluating and selecting, or making recommendations to our board of directors regarding nominees for election to our board of directors and its committees;
- overseeing the evaluation and the performance of our board of directors and of individual directors;
- considering and making recommendations to our board of directors regarding the composition of our board of directors and its committees;
- overseeing our corporate governance practices;
- contributing to succession planning; and
- developing and making recommendations to our board of directors regarding corporate governance guidelines and matters.

Our nominating and corporate governance committee will operate under a written charter, to be effective on the date of this offering, which satisfies the applicable rules of the Securities and Exchange Commission and the listing standards of Nasdaq and will be available on our website upon the closing of this offering.

Compensation Committee Interlocks and Inside Participation

None of the members of our compensation committee is or has been an officer or employee of our company. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee (or other board of directors committee performing equivalent functions or, in the absence of any such committee, the entire board of directors) of any entity that has one or more executive officers serving on our board of directors or compensation committee. Certain members of our compensation committee are affiliated with entities that purchased our preferred stock. Please see “Certain Relationships and Related-Party Transactions—Equity Financings” for more information.

Non-Employee Director Compensation

Historically, we have neither had a formal compensation policy for our non-employee directors, nor have we had a formal policy of reimbursing expenses incurred by our non-employee directors in connection with their board service. However, we have reimbursed our non-employee directors for reasonable expenses incurred in connection with their attendance at board of directors or committee meetings and occasionally granted stock options to our non-employee directors. Except to the limited extent described below, we did not provide our non-employee directors, in their capacities as such, with any cash, equity or other compensation in fiscal 2018. Neither Casey C. Lynch, our President and Chief Executive Officer, nor Stephen S. Dominy, M.D., our Chief Scientific Officer, received compensation for services as a director. Compensation provided to Casey C. Lynch and Stephen S. Dominy, M.D. is discussed in the section titled “Executive Compensation.”

The following table sets forth information regarding compensation awarded, earned or paid for services rendered to us by our non-employee directors for fiscal 2018:

Name	Option Awards ($)(1)(2)	Total ($)
Current Non-Employee Directors		
David A. Lamond	—	—
Margi McLoughlin, Ph.D.	—	—
Una Ryan, OBE, Ph.D.(3)	—	—
Christopher J. Senner(4)	—	—
Kevin Young, CBE(5)	—	—
Former Non-Employee Directors		
Michael Martin, Ph.D.	—	—
Roger Quy, Ph.D.(6)	26,720(6)	26,720
Ilan Zipkin, Ph.D.	44,840	44,840

(1) The amounts reported in this column represent the aggregate grant date fair value for financial statement reporting purposes of stock options granted in fiscal 2018 under our 2014 Stock Plan, or 2014 Plan, as determined in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718, or 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 holder. 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 7 to the historical financial statements included at the end of this prospectus. As required by Securities and Exchange Commission rules, the amounts shown exclude the impact of estimated forfeitures related to service-based vesting conditions.
(2) The number of outstanding stock options held by each non-employee director and former non-employee director, as applicable, as of December 31, 2018 was as follows: Mr. Lamond (0), Dr. McLoughlin (0), Dr. Ryan (0), Mr. Senner (0), Mr. Young (0), Mr. Martin (0), Mr. Quy (36,764), and Mr. Zipkin (36,764).
(3) Dr. Ryan was appointed to the board of directors in January 2019.
(4) Mr. Senner was appointed to the board of directors in March 2019.
(5) Mr. Young was appointed to the board of directors in January 2019.
(6) As of December 31, 2018, Mr. Quy held outstanding stock options covering 36,764 shares, which included (i) an option to purchase 18,382 shares of common stock granted on March 23, 2016 and (ii) an option to purchase 18,382 shares of common stock granted on July 25, 2018. The option granted to Mr. Quy on July 25, 2018 was cancelled on January 23, 2019. The aggregate grant date fair value of the cancelled option was $26,720.

On April 9, 2019, our board of directors approved an outside director compensation policy that will become effective upon the closing of this offering. Under this policy, we will pay our directors who are not employees of the company 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 will be 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 Retainer
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

In addition, each non-employee director elected to our board of directors following the completion of this offering will, upon the date of his or her initial election or appointment to be a non-employee director, 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 following this offering, 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 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 3 and 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 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 following the closing of this offering are expected to be made pursuant to our 2019 Plan as more fully described in "Executive Compensation—Equity Incentive Plans" 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 will also continue to reimburse our non-employee directors for ordinary, necessary and reasonable out-of-pocket travel expenses to cover in-person attendance at, and participation in, Board and committee meetings.

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.

Director and Officer Indemnification Agreements

We have entered, and intend to continue to enter, into separate indemnification agreements with our directors and executive officers, in addition to the indemnification provided for in our amended and restated bylaws. These agreements, among other things, require us to indemnify our directors and executive officers for certain expenses, including attorneys' fees, judgments, penalties, fines and settlement amounts incurred by a director or executive officer in any action or proceeding arising out of their services as one of our directors or executive officers or as a director or executive officer of any other company or enterprise to which the person provides services at our request.

EXECUTIVE COMPENSATION

Overview

As an emerging growth company, we have opted to comply with the executive compensation disclosure rules applicable to "smaller reporting companies," as such term is defined in the rules promulgated under the Securities Act.

Our named executive officers for fiscal 2018, as determined in accordance with these rules, were:

- Casey C. Lynch, our President and Chief Executive Officer;
- Stephen S. Dominy, M.D., our Chief Scientific Officer; and
- Christopher Lowe, our Chief Financial Officer.

This discussion may contain forward-looking statements that are based on our current plans, considerations, expectations and determinations regarding future compensation programs. Actual compensation programs that we adopt following the closing of this offering may differ materially from the currently planned programs and arrangements summarized in this discussion.

Summary Compensation Table

The following table sets forth certain information regarding the compensation awarded to, earned by and paid to each of our named executive officers for fiscal 2018:

Name and Principal Position	Year	Salary ($)(1)	Bonus ($)(2)	Option Awards ($)(3)	Non-Equity Incentive Plan Compensation ($)	All Other Compensation ($)	Total ($)
Casey C. Lynch *President and Chief Executive Officer*	2018	277,019	82,500	557,814	—	—	917,333
Stephen S. Dominy, M.D. *Chief Scientific Officer*	2018	260,707	64,688	171,949	—	—	497,344
Christopher Lowe(4) *Chief Financial Officer and Treasurer*	2018	—	—	342,336	—	95,200(5)	437,536

(1) The amounts reported in this column represent salary earned by each of our named executive officers in fiscal year 2018.
(2) The amounts reported in this column represent performance-based cash incentives earned by each named executive officer based on fiscal year 2018 performance.
(3) The amounts reported in this column reflect the aggregate grant date fair value for financial statement reporting purposes of stock options granted in fiscal year 2018 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 7 to the historical financial statements included at the end of this prospectus. As required by the Securities and Exchange Commission rules, the amounts shown exclude the impact of estimated forfeitures related to service-based vesting conditions.
(4) In January 2019, Mr. Lowe became an employee of the company. From June 2018 until January 2019, Mr. Lowe was a consultant to the company, serving as our Interim Chief Financial Officer through his capacity as a partner at FLG Partners.
(5) This amount represents fees paid for Mr. Lowe's services pursuant to a consulting agreement entered into by and between FLG Partners, LLC and the company effective as of June 20, 2018.

Outstanding Equity Awards as of December 31, 2018

The following table provides information regarding the unexercised stock options held by each of our named executive officers as of December 31, 2018:

		Option Awards(1)			
Name	Grant Date	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	0(3)	83,159(3)	0.46	6/1/2022
	10/30/2018	29,512(4)	442,692(4)	2.23	10/29/2028
Stephen S. Dominy, M.D.	11/18/2016	83,159(5)	49,896(5)	0.41	11/17/2026
	10/30/2018	7,377(6)	110,674(6)	2.23	10/29/2028
Christopher Lowe	11/28/2018	0(7)	235,294(7)	2.23	11/27/2028

(1) All awards were granted under our 2014 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 Ms. Lynch's June 2, 2017 grant, 110% of 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 133,055 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 the 2014 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 472,205 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 133,055 shares of our common stock. 1/48th of the stock option grant vested on July 15, 2016 and 1/48th of the grant vested and will vest on each monthly anniversary thereafter, subject to Dr. Dominy's continuous service through the applicable vesting date. In addition, if we terminate Dr. Dominy's employment without "cause," or if Dr. Dominy resigns for "good reason" (each as defined in a supplemental agreement applicable to Dr. Dominy's options), in either case, in connection with or following a change of control (as defined in the 2014 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 "Dominy Acceleration").
(6) These option shares were part of a stock option grant covering 118,051 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 Dr. Dominy's continuous service through the applicable vesting date. In addition, the Dominy Acceleration applies to these option shares prior to their full vesting.
(7) These option shares were part of a stock option grant covering 235,294 shares of our common stock. 1/4th of the stock option grant will vest on November 15, 2019 and 1/48th of the grant will vest on each monthly anniversary thereafter, subject to Mr. Lowe's continuous service through the applicable vesting date. In addition, if we terminate Mr. Lowe's service without "cause," or if Mr. Lowe resigns for "good reason" (each as defined in the stock option agreement applicable to Mr. Lowe's options), in either case, in connection with or following a change of control (as defined in the 2014 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.

Executive Employment Arrangements

Each of our named executive officers was an at-will employee of the company for fiscal 2018, except Mr. Lowe. From June 2018 until January 2019, Mr. Lowe was a consultant to the company, serving as our interim Chief Financial Officer through his capacity as a partner at FLG Partners. We have no employment agreements or offer letters with our named executive officers.

Equity Incentive Plans

2019 Equity Incentive Plan

General. Our 2014 Stock Plan was amended, restated and re-named the 2019 Equity Incentive Plan, or 2019 Plan, by our board of directors on April 24, 2019 and our stockholders on April 25, 2019. The 2019 Plan became effective on the day immediately prior to the effectiveness of the registration statement of which this prospectus forms a part.

Share Reserve. The maximum aggregate number of shares that may be issued under the 2019 Plan is 5,131,549 shares of our common stock. In addition, the number of shares reserved for issuance under the 2019 Plan will be increased automatically on the first day of each fiscal year beginning with the 2020 fiscal year, by a number equal to the least of:

- 2,146,354 shares;
- 4% of the shares of common stock outstanding on the last day of the prior fiscal year; or
- such number of shares determined by our board of directors.

If an award expires, is forfeited or becomes unexercisable for any reason without having been exercised in full, or is surrendered pursuant to an exchange program, the unissued shares that were subject to the award will, unless the 2019 Plan is terminated, continue to be available under the 2019 Plan for issuance pursuant to future awards. In addition, any shares which are retained by the company upon exercise of an award in order to satisfy the exercise or purchase price for such award or any withholding taxes due with respect to such award will be treated as not issued and will continue to be available under the 2019 Plan for issuance pursuant to future awards. Shares issued under the 2019 Plan and later forfeited to the company due to the failure to vest or repurchased by the company at the original purchase price paid to the company for the shares (including, without limitation, upon forfeiture to or repurchase by the company in connection with a participant ceasing to be a service provider) will again be available for future grant under the 2019 Plan. To the extent an award under the 2019 Plan is paid out in cash rather than shares, such cash payment will not result in reducing the number of Shares available for issuance under the 2019 Plan.

Plan administration. Our board of directors has delegated its authority to administer the 2019 Plan to our compensation committee. Subject to the provisions of our 2019 Plan, the administrator has the power to determine the terms of awards, including the recipients, the exercise price, if any, the number of shares subject to each award, the fair market value of a share of our common stock, the vesting schedule applicable to the awards, together with any vesting acceleration, and the form of consideration, if any, payable upon exercise of the award and the terms of the award agreement for use under the 2019 Plan. The administrator also has the authority, subject to the terms of the 2019 Plan, to amend existing awards, to prescribe rules and to construe and interpret the 2019 Plan and awards granted thereunder and to institute an exchange program by which outstanding awards may be surrendered in exchange for awards of the same type which may have a lower exercise price or different terms, awards of a different type and/or cash subject to stockholder approval.

Eligibility. Employees, members of our board of directors who are not employees and consultants are eligible to participate in our 2019 Plan.

Non-employee directors. Our 2019 Plan provides that all non-employee directors will be eligible to receive all types of awards under our 2019 Plan except for incentive stock options. On April 9, 2019, our board of directors approved an outside director compensation policy that will become effective upon the closing of this offering pursuant to which our non-employee directors will be eligible to receive equity awards under our 2019 Plan as more fully described in “Management—Non-Employee Director Compensation.” In addition, in order to

provide a maximum limit on awards that can be provided to our non-employee directors under the 2019 Plan, our 2019 Plan provides that no non-employee director may receive awards under the 2019 Plan that, when combined with cash compensation received for service as a non-employee director, exceeds $1,000,000 in a calendar year. For purposes of this limit, the value of stock options and stock appreciation rights will be calculated using the Black-Scholes valuation methodology on the date of grant, and the value for all other types of awards will be determined by either (i) calculating the product of the fair market value per share on the date of grant and the aggregate number of shares subject to the award or (ii) calculating the product using an average of the fair market value over a number of trading days and the aggregate number of shares subject to the award.

Types of award. Our 2019 Plan provides for the grant of incentive stock options, within the meaning of Section 422 of the Code, to our employees and the employees of our subsidiaries, and for the grant of nonstatutory stock options, stock appreciation rights, restricted stock, restricted stock units, performance units, and performance shares to our employees, directors, and consultants and the employees and consultants of our subsidiaries.

Stock options. The administrator may grant incentive and/or non-statutory stock options under our 2019 Plan, provided that incentive stock options may only be granted to employees. The exercise price of such options must generally be equal to at least the fair market value of our common stock on the date of grant. The term of an option may not exceed 10 years; provided, however, that an incentive stock option held by a participant who owns more than 10% of the total combined voting power of all classes of our stock, or of certain of our subsidiary corporations, may not have a term in excess of five years and must have an exercise price of at least 110% of the fair market value of our common stock on the grant date. The administrator will determine the methods of payment of the exercise price of an option, which may include cash, shares or other property acceptable to the administrator. Subject to the provisions of our 2019 Plan, the administrator determines the remaining terms of the options (e.g., vesting). After the termination of service of an employee, director or consultant, the participant may exercise his or her option, to the extent vested, for the period of time stated in his or her option agreement. Generally, if termination is due to death or disability, the option will remain exercisable for 12 months. In the event of a termination for cause, options generally terminate immediately upon the termination of the participant for cause. In all other cases, the option will generally remain exercisable for three months following the termination of service. However, in no event may an option be exercised later than the expiration of its term. The maximum aggregate number of shares of our common stock that may be issued under the 2019 Plan pursuant to incentive stock options may not exceed the maximum number of shares reserved under the 2019 Plan and to the extent allowable under Section 422 of the Internal Revenue Code, or the Code, any other shares that become available for issuance or reissuance pursuant to the terms of the 2019 Plan.

Stock appreciation rights. Stock appreciation rights may be granted under our 2019 Plan. Stock appreciation rights allow the recipient to receive the appreciation in the fair market value of our common stock between the date of grant and the exercise date. Subject to the provisions of our 2019 Plan, the administrator determines the terms of stock appreciation rights, including when such rights vest and become exercisable and whether to settle such awards in cash or with shares of our common stock, or a combination thereof, except that the per share exercise price for the shares to be issued pursuant to the exercise of a stock appreciation right will be no less than 100% of the fair market value per share on the date of grant. The specific terms will be set forth in an award agreement.

Restricted stock. Restricted stock may be granted under our 2019 Plan. Restricted stock awards are grants of shares of our common stock that are subject to various restrictions, including restrictions on transferability and forfeiture provisions. Shares of restricted stock will vest and the restrictions on such shares will lapse, in accordance with terms and conditions established by the administrator. Such terms may include, among other things, vesting upon the achievement of specific performance goals determined by the administrator and/or continued service. The administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed. Recipients of restricted stock awards generally will have voting and dividend rights with respect to such shares upon grant without regard to vesting, unless the administrator

provides otherwise. Shares of restricted stock that do not vest for any reason will be subject to our right of repurchase or forfeited by the recipient and will revert to us. The specific terms will be set forth in an award agreement.

Restricted stock units. Restricted stock units may be granted under our 2019 Plan, and may include the right to dividend equivalents, as determined in the discretion of the administrator. Each restricted stock unit granted is a bookkeeping entry representing an amount equal to the fair market value of one share of our common stock. The administrator determines the terms and conditions of restricted stock units, including the vesting criteria, which may include achievement of specified performance criteria and/or continued service, and the form and timing of payment. The administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed. The administrator determines, in its sole discretion, whether an award will be settled in stock, cash or a combination of both. The specific terms will be set forth in an award agreement.

Performance units/performance shares. Performance units and performance shares may be granted under our 2019 Plan. Performance units and performance shares are awards that will result in a payment to a participant if performance goals established by the administrator are achieved and any other applicable vesting provisions are satisfied. The administrator will establish organizational or individual performance goals in its discretion, which, depending on the extent to which they are met, will determine the number and/or the value of performance units and performance shares to be paid out to participants. For purposes of such awards, the performance goals may be based on one or more of the following performance criteria and any adjustment(s) thereto, in each case as determined by the administrator: (i) sales or non-sales revenue; (ii) return on revenues; (iii) operating income; (iv) income or earnings including operating income; (v) income or earnings before or after taxes, interest, depreciation, and/or amortization; (vi) income or earnings from continuing operations; (vii) net income; (viii) pre-tax income or after-tax income; (ix) net income excluding amortization of intangible assets, depreciation and impairment of goodwill and intangible assets, and/or excluding charges attributable to the adoption of new accounting pronouncements; (x) raising of financing or fundraising; (xi) project financing; (xii) revenue backlog; (xiii) gross margin; (xiv) operating margin or profit margin; (xv) capital expenditures, cost targets, reductions and savings, and expense management; (xvi) return on assets (gross or net), return on investment, return on capital or invested capital, or return on stockholder equity; (xvii) cash flow, free cash flow, cash flow return on investment (discounted or otherwise), net cash provided by operations, or cash flow in excess of cost of capital; (xviii) performance warranty and/or guarantee claims; (xix) stock price or total stockholder return; (xx) earnings or book value per share (basic or diluted); (xxi) economic value created; (xxii) pre-tax profit or after-tax profit; (xxiii) strategic business criteria, consisting of one or more objectives based on meeting specified market penetration or market share, completion of strategic agreements such as licenses, funded collaborations, joint ventures, acquisitions, and the like, geographic business expansion, objective customer satisfaction or information technology goals, and/or intellectual property asset metrics; (xxiv) objective goals relating to divestitures, joint ventures, mergers, acquisitions, and similar transactions; (xxv) objective goals relating to staff management, results from staff attitude and/or opinion surveys, staff satisfaction scores, staff safety, staff accident and/or injury rates, compliance headcount, performance management, and completion of critical staff training initiatives; (xxvi) objective goals relating to projects, including project completion timing and/or achievement of milestones, project budget, and technical progress against work plans; and (xxvii) enterprise resource planning. However, awards issued to participants may take into account other factors (including subjective factors). In addition, performance goals may differ from participant to participant, performance period to performance period, and from award to award. Any criteria used may be measured, as applicable, (i) in absolute terms, (ii) in relative terms (including, but not limited to, any increase (or decrease) over the passage of time and/or any measurement against other companies or financial or business or stock index metrics particular to us), (iii) on a per share and/or share per capita basis, (iv) against our performance as a whole or against any of our affiliate(s), or a particular segment(s), a business unit(s) or a product(s) of ours or individual project company, (v) on a pre-tax or after-tax basis, and/or (vi) using an actual foreign exchange rate or on a foreign exchange neutral basis. After the grant of a performance unit or performance share, the administrator, in its sole discretion, may reduce or waive any performance objectives or other vesting provisions for such performance units or performance shares. Performance units shall have an initial dollar value established by the

administrator prior to the grant date. Performance shares shall have an initial value equal to the fair market value of our common stock on the grant date. The administrator, in its sole discretion, may pay earned performance units or performance shares in the form of cash, in shares, or in some combination thereof.

Non-transferability of awards. Unless the administrator provides otherwise, our 2019 Plan generally does not allow for the transfer of awards and only the recipient of an option or stock appreciation right may exercise such an award during his or her lifetime.

Certain adjustments. In the event of certain corporate events or changes in our capitalization, to prevent diminution or enlargement of the benefits or potential benefits available under the 2019 Plan, the administrator will make adjustments to one or more of the number, kind and class of securities that may be delivered under the 2019 Plan and/or the number, kind, class and price of securities covered by each outstanding award.

Liquidation or dissolution. In the event of our proposed winding up, liquidation or dissolution, the administrator will notify participants as soon as practicable and all awards will terminate immediately prior to the consummation of such proposed transaction.

Corporate transaction. Our 2019 Plan provides that in the event of certain significant corporate transactions, including: (1) a transfer of all or substantially all of our assets, (2) a merger, consolidation or other capital, reorganization or business combination transaction of the company with or into another corporation, entity or person, or (3) the consummation of a transaction, or series of related transactions, in which any person becomes the beneficial owner, directly or indirectly, of more than 50% of the company's then outstanding capital stock, each outstanding award will be treated as the administrator determines. Such determination, without the consent of any Participant, may provide that such awards will be (i) continued if we are the surviving corporation, (ii) assumed by the surviving corporation or its parent, (iii) substituted by the surviving corporation or its parent for a new award, (iv) canceled in exchange for a payment equal to the excess of the fair market value of our shares subject to such award over the exercise price or purchase price paid for such shares, or (v) in the case of options, participants may be given an opportunity to exercise options prior to the transaction and, if not exercised, such options may be terminated upon consummation of the transaction.

Change of control. The administrator may provide, in an individual award agreement or in any other written agreement between a participant and us that the stock award will be subject to additional acceleration of vesting and exercisability in the event of a change of control. Under the 2019 Plan, a "change of control" is generally (1) a merger, consolidation, or any other corporate reorganization in which our stockholders immediately before the transaction do not own, directly or indirectly, more than a majority of the combined voting power of the surviving entity (or the parent of the surviving entity), (2) the consummation of the sale, transfer or other disposition of all or substantially all of our assets, (3) an unapproved change in the majority of the board of directors during any 12-month period, and (4) the acquisition by any person or company of more than 50% of the total voting power of our then outstanding stock.

Clawback/recovery. Stock awards granted under the 2019 Plan will be subject to recoupment in accordance with any clawback policy we may be required to adopt pursuant to applicable law and listing requirements. In addition, the administrator may impose such other clawback, recovery or recoupment provisions in any stock award agreement as it determines necessary or appropriate.

Amendment or termination. Our board of directors has the authority to amend, suspend or terminate the 2019 Plan provided such action does not impair the existing rights of any participant. Our 2019 Plan will automatically terminate on April 23, 2029 unless we terminate it sooner. We will obtain stockholder approval of any amendment to our 2019 Plan as required by applicable law or listing requirements.

2014 Stock Plan

General. Our board of directors originally adopted, and our stockholders approved, our 2014 Stock Plan, or the 2014 Plan, on August 8, 2014 and December 4, 2014, respectively. The 2014 Plan was last amended on

November 28, 2018. Our 2014 Plan provides for the grant of incentive stock options to our employees (and employees of any parent or subsidiary of the company), and for the grant of non-statutory stock options and stock purchase rights to our employees, directors and consultants (and employees and consultants of any parent, subsidiary or affiliate of the company). On April 24, 2019 and April 25, 2019, our board of directors and our stockholders approved the amendment and restatement of our 2014 Plan as the 2019 Plan, which amendment and restatement became effective on the day immediately prior to the effectiveness of the registration statement of which this prospectus forms a part. The terms of the 2014 Plan as described herein will continue to govern the terms and conditions of the outstanding awards previously granted thereunder.

Share Reserve. We have reserved an aggregate of 2,973,736 shares that may be issued under our 2014 Plan. As of December 31, 2018, options to purchase 1,885,504 shares of our common stock were outstanding and 984,680 shares were available for future grants.

Plan Administration. Our board of directors has administered the 2014 Plan before this offering. Our board of directors has delegated its authority to administer the 2014 Plan to our compensation committee following this offering.

Types of Award. Our 2014 Plan provides for the grant of incentive stock options, nonstatutory stock options, and stock purchase rights.

Stock Options. Our board of directors granted incentive and/or non-statutory stock options under our 2014 Plan, provided that incentive stock options were only granted to employees. The exercise price of such options was generally equal to at least the fair market value of our common stock on the date of grant. The term of an option did not exceed 10 years; provided, however, that an incentive stock option held by a participant who owns more than 10% of the total combined voting power of all classes of our stock, or of certain of our subsidiary corporations, did not have a term in excess of 5 years and had an exercise price of at least 110% of the fair market value of our common stock on the grant date. Subject to the provisions of our 2014 Plan, the administrator determined the remaining terms of the options (e.g., vesting). After the termination of service of an employee, director or consultant, the participant may exercise his or her option, to the extent vested, for the period of time stated in his or her option agreement. Generally, if termination is due to death or disability, the option will remain exercisable for 12 months. In all other cases except for cause, the option will generally remain exercisable for 3 months following the termination of service. In the event of a termination for cause, the option will immediately terminate. However, in no event may an option be exercised later than the expiration of its term.

Stock purchase rights. Our board of directors granted stock purchase rights under our 2014 Plan. Stock purchase rights are rights to purchase our common stock that either are fully vested at grant or that will vest in accordance with terms and conditions established by the administrator, in its sole discretion. The administrator determined the number of shares that the participant may purchase, the price to be paid (if any) and the time in which the participant must accept the offer. The offer must be accepted by execution of a restricted stock purchase agreement in the form determined by the administrator. Once a stock purchase right is exercised, the participant has all the rights of a stockholder.

Non-transferability of Awards. Unless the administrator provides otherwise, our 2014 Plan generally does not allow for the transfer of awards and only the recipient of an option may exercise such an award during his or her lifetime.

Certain Adjustments. In the event of certain corporate events or changes in our capitalization, to prevent diminution or enlargement of the benefits or potential benefits available under the 2014 Plan, the administrator will make adjustments to one or more of the number, kind and class of securities that may be delivered under the 2014 Plan and/or the number, kind, class and price of securities covered by each outstanding award. *Dissolution or liquidation*. In the event of our dissolution or liquidation of the company, each option and stock purchase right

will terminate immediately prior to the consummation of such action, unless otherwise determined by the administrator.

Corporate Transaction. Our 2014 Plan provides that in the event of certain significant corporate transactions, including: (1) a transfer of all or substantially all of our assets, (2) a merger, consolidation or other capital, reorganization or business combination transaction of the Company with or into another corporation, entity or person, or (3) the consummation of a transaction, or series of related transactions, in which any person becomes the beneficial owner, directly or indirectly, of more than 50% of the Company's then outstanding capital stock, each outstanding award will be treated as the administrator determines.

Amendment or Termination. Our board of directors may amend or terminate the 2014 Plan at any time, provided such action does not materially and adversely affect the rights of any participant without his or her consent. In addition, stockholder approval must be obtained to the extent necessary and desirable to comply with applicable laws. Although our 2014 Plan will be amended and restated in the form of our 2019 Plan immediately prior to, and contingent upon, the effectiveness of this offering; our 2014 Plan will continue to govern the terms and conditions of awards previously granted under the 2014 Plan.

Employee Stock Purchase Plan

General. Our Employee Stock Purchase Plan, or 2019 ESPP, was adopted by our board of directors on April 24, 2019 and approved by our stockholders on April 25, 2019. The 2019 ESPP became effective on the day immediately prior to the effectiveness of the registration statement of which this prospectus forms a part. The 2019 ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of 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.

Share reserve. We have reserved 268,295 shares of our common stock for issuance under the 2019 ESPP. 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 least of:

- 536,589 shares;
- 1% of the shares of common stock outstanding on the last day of the prior fiscal year; or
- such lesser number of shares determined by our board of directors.

As of the date hereof, no shares of our common stock have been purchased under the 2019 ESPP.

Plan administration. The 2019 ESPP will be administered by our board of directors or a committee designated by our board of directors. Our board of directors has delegated its authority to administer the 2019 ESPP to our compensation committee.

Eligibility. Generally, all regular employees, including executive officers, employed by us or by any of our designated affiliates and certain non-U.S. service providers may participate in the 2019 ESPP.

Employees may have to satisfy one or more of the following service requirements before participating in the 2019 ESPP, as determined by the administrator, including: (1) being customarily employed for more than 20 hours per week, (2) being customarily employed for more than 5 months per calendar year, or (3) continuous employment with us or one of our affiliates for a period of time (not to exceed 2 years). No employee may purchase shares under the 2019 ESPP at a rate in excess of $25,000 worth of our common stock based on the fair

market value per share of our common stock at the beginning of an offering for each year such a purchase right is outstanding. Finally, no employee will be eligible for the grant of any purchase rights under the 2019 ESPP if immediately after such rights are granted, such employee has voting power over 5% or more of our outstanding capital stock measured by vote or value under Section 424(d) of the Code.

Non-U.S. service providers must provide bona fide services to the company and may be subject to additional eligibility criteria as the administrator may determine even if such criteria is not consistent with Section 423 of the Code.

Offerings. The 2019 ESPP is expected to be implemented through a series of offerings under which participants are granted purchase rights to purchase shares of our common stock on specified dates during such offerings. Under the 2019 ESPP, we may specify offerings with durations of not more than 27 months, and we may specify shorter purchase periods within each offering. Each offering will have one or more purchase dates on which shares of our common stock will be purchased for participants in the offering. An offering under the 2019 ESPP may be terminated under certain circumstances. The administrator will have the discretion to structure an offering so that if the fair market value of a share of our common stock on the first trading day of a new purchase period within that offering is less than or equal to the fair market value of a share of our common stock on the offering date for that offering, then that offering will terminate immediately as of that first trading day, and the participants in such terminated offering will be automatically enrolled in a new offering beginning on the first trading day of such new offering period. The administrator has not yet approved an offering under our 2019 ESPP and we are not certain whether or when this will occur.

Payroll deductions. Participants who are employees may contribute, normally through payroll deductions, up to 15% of their earnings (as defined by the board of directors in each offering) for the purchase of our common stock under the 2019 ESPP. Participants who are not employees will contribute on an after-tax basis in a manner determined by the administrator.

Unless otherwise determined by the administrator, common stock will be purchased for the accounts of participants in the 2019 ESPP at a price per share that is at least the lesser of (1) 85% of the fair market value of a share of our common stock on the first date of an offering, or (2) 85% of the fair market value of a share of our common stock on the date of purchase.

Certain adjustments. In the event that there occurs a change in our capital structure through such actions as a stock split, reverse stock split, stock dividend, combination, consolidation, recapitalization (including a recapitalization through a large nonrecurring cash dividend) or reclassification of our common stock, subdivision of our common stock, a rights offering, a reorganization, merger, spin-off, split-up, repurchase, or exchange of our common stock or other significant corporate transaction, or other change affecting our common stock, the administrator will make appropriate adjustments to: (1) the class(es) and maximum number of shares reserved under the 2019 ESPP, (2) the class(es) and maximum number of shares by which the share reserve may increase automatically each year, (3) the class(es) and number of shares and purchase price of all outstanding purchase rights, and (4) the class(es) and number of shares that are subject to purchase limits under ongoing offerings.

Dissolution or liquidation. In the event of our proposed winding up, liquidation or dissolution, any offering period then in progress will be shortened by setting a new purchase date and will terminate immediately prior to the consummation of such proposed dissolution or liquidation, unless provided otherwise by the administrator. The administrator will notify each participant that the purchase date has been changed and that the participant's purchase right will be exercised automatically on the new purchase date unless prior to such date the participant has withdrawn from the offering period.

Corporate transactions. The 2019 ESPP provides that in the event of certain significant corporate transactions, including: (1) a transfer of all or substantially all of our assets, (2) a merger, consolidation or other capital, reorganization or business combination transaction of the company with or into another corporation,

entity or person, or (3) the consummation of a transaction, or series of related transactions, in which any person becomes the beneficial owner, directly or indirectly, of more than 50% of the company's then outstanding capital stock, a successor corporation may assume or substitute each outstanding purchase right. If the successor corporation refuses to assume or substitute the purchase right, the offering period then in progress will be shortened, and a new purchase date will be set. The administrator will notify each participant that the purchase date has been changed and that the participant's purchase right will be exercised automatically on the new purchase date unless prior to such date the participant has withdrawn from the offering period.

Amendment or termination. The administrator has the authority to amend, suspend or terminate our 2019 ESPP, except that, subject to certain exceptions described in our 2019 ESPP, no such action may adversely affect any outstanding rights to purchase stock under our 2019 ESPP without the holder's consent. We will obtain stockholder approval of any amendment to our 2019 ESPP as required by applicable law or listing requirements.

Executive Incentive Bonus Plan

Our Executive Incentive Bonus Plan, or Bonus Plan, was adopted by our board of directors on April 9, 2019. The Bonus Plan became effective on the day immediately prior to the effectiveness of the registration statement of which this prospectus forms a part. 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.

Administration. The Bonus Plan will be administered by the compensation committee, which shall have 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.

Performance criteria. Commencing with our 2020 fiscal year, we expect the compensation committee to establish cash bonus targets and corporate performance metrics for a specific performance period or fiscal year pursuant to the Bonus Plan. Corporate performance goals may be based on one or more of the following criteria, as determined by our compensation committee and any adjustments thereto established by the compensation committee: (i) sales or non-sales revenue; (ii) return on revenues; (iii) operating income; (iv) income or earnings including operating income; (v) income or earnings before or after taxes, interest, depreciation, and/or amortization; (vi) income or earnings from continuing operations; (vii) net income; (viii) pre-tax income or after-tax income; (ix) net income excluding amortization of intangible assets, depreciation, and impairment of goodwill and intangible assets and/or excluding charges attributable to the adoption of new accounting pronouncements; (x) raising of financing or fundraising; (xi) project financing; (xii) revenue backlog; (xiii) gross margin; (xiv) operating margin or profit margin; (xv) capital expenditures, cost targets, reductions, and savings and expense management; (xvi) return on assets (gross or net), return on investment, return on capital or invested capital, or return on stockholder equity; (xvii) cash flow, free cash flow, cash flow return on investment (discounted or otherwise), net cash provided by operations, or cash flow in excess of cost of capital; (xviii) performance warranty and/or guarantee claims; (xix) stock price or total stockholder return; (xx) earnings or book value per share (basic or diluted); (xxi) economic value created; (xxii) pre-tax profit or after-tax profit; (xxiii) strategic business criteria, consisting of one or more objectives based on meeting specified market penetration or market share, completion of strategic agreements such as licenses, funded collaborations, joint ventures acquisitions, and the like, geographic business expansion, objective customer satisfaction or information technology goals, or intellectual property asset metrics; (xxiv) objective goals relating to divestitures, joint ventures, mergers, acquisitions, and similar transactions; (xxv) objective goals relating to staff management, results from staff attitude and/or opinion surveys, staff satisfaction scores, staff safety, staff accident and/or injury rates, compliance, headcount, performance management, or completion of critical staff training initiatives; (xxvi) objective goals relating to projects, including project completion, timing and/or achievement of

milestones, project budget, or technical progress against work plans; (xxvii) key regulatory objectives or milestones; and (xxviii) enterprise resource planning.

However, awards issued to participants may take into account other factors (including subjective factors). Performance goals may differ from participant to participant, performance period to performance period, and from award to award. Any criteria used may be measured, as applicable, (i) in absolute terms, (ii) in relative terms (including, but not limited to, any increase (or decrease) over the passage of time and/or any measurement against other companies or financial or business or stock index metrics particular to us), (iii) on a per share and/or share per capita basis, (iv) against our performance as a whole or against any of our affiliate(s), or a particular segment(s), a business unit(s) or a product(s) of ours or individual project company, (v) on a pre-tax or after-tax basis, and/or (vi) using an actual foreign exchange rate or on a foreign exchange neutral basis.

Service requirement. Unless otherwise determined by the compensation committee, a participant must be actively employed and in good standing with the Company on the date the award is paid. The compensation committee may make exceptions to this requirement in the case of retirement, death or disability, an unqualified leave of absence or under other circumstances, as determined by the compensation committee in its sole discretion.

Limits. The total awards under the Bonus Plan may not exceed $15 million in the aggregate during the applicable reliance period (within the meaning of Section 162(m)).

Amendment or Termination. The compensation committee may terminate the Bonus Plan at any time, provided such termination shall not affect the payment of any awards accrued under the Bonus Plan prior to the date of the termination. The compensation committee may, at any time, or from time to time, amend or suspend and, if suspended, reinstate, the Bonus Plan in whole or in part.

Perquisites, Health, Welfare and Retirement Benefits

Health and Welfare Benefits

Our named executive officers are eligible to participate in our employee benefit plans, including our medical, dental and vision plans, in each case on the same basis as all of our other employees.

Perquisites

We do not provide perquisites or personal benefits to our named executive officers. We do not make gross-up payments to cover our named executive officers' personal income taxes that may pertain to any of the compensation paid by us.

Retirement Benefits 401(k) Plan

We maintain a 401(k) defined contribution retirement plan for our eligible U.S. employees. Participants may make pre-tax and post-tax contributions to the plan from their eligible earnings, and we may make matching contributions and profit sharing contributions to eligible participants, in each case, up to the statutorily prescribed annual limits on contributions under the Internal Revenue Code. The 401(k) plan permits us to make matching contributions and profit sharing contributions to eligible participants. Contributions are allocated to each participant's individual account and are then invested in selected investment alternatives according to the participants' directions. The plan is intended to be qualified under Section 401(a) of the Internal Revenue Code, and the plan's trust is intended to be tax exempt. Income earned on pre-tax contributions made to the plan is not taxable to participants until withdrawn or distributed from the 401(k) plan.

Pension Benefits

None of our named executive officers participate in or have an account balance in any qualified or non-qualified defined benefit plan sponsored by us.

Nonqualified Deferred Compensation

We have not offered any nonqualified deferred compensation plans or arrangements or entered into any such arrangements with any of our named executive officers.

Rule 10b5-1 Sales Plans

We expect that some of our executive officers may enter into stock selling plans in accordance with Rule 10b5-1 of the Exchange Act, and our insider trading policy.

Registration Statements on Form S-8

We intend to file a registration statement on Form S-8 under the Securities Act to register all of the shares of common stock subject to outstanding stock options issued under our 2014 Plan or reserved for future issuance under our 2019 Plan and 2019 ESPP, which will be effective upon the consummation of this offering. This registration statement would cover approximately 5,141,732 shares. Shares registered under the registration statement will generally be available for sale in the open market after the 180-day lock-up period immediately following the date of this prospectus (as such period may be extended in certain circumstances).

Limitation of Liability and Indemnification of Directors and Officers

Our amended and restated certificate of incorporation, which will become effective upon the closing of this offering, will contain provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by Delaware law. Consequently, our directors will not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for the following:

- any breach of their duty of loyalty to our company or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases, or redemptions as provided in Section 174 of the Delaware General Corporation Law; or
- any transaction from which they derived an improper personal benefit.

Our amended and restated bylaws, which will become effective upon the closing of this offering, will provide that we shall indemnify, to the fullest extent permitted by law, any person who is or was a party or is threatened to be made a party to any action, suit or proceeding, by reason of the fact that he or she is or was one of our directors or officers or is or was serving at our request as a director or officer of another corporation, partnership, joint venture, trust or other enterprise. Our amended and restated bylaws will provide that we may indemnify to the fullest extent permitted by law any person who is or was a party or is threatened to be made a party to any action, suit or proceeding, by reason of the fact that he or she is or was one of our employees or agents or is or was serving at our request as an employee or agent of another corporation, partnership, joint venture, trust or other enterprise. Our amended and restated bylaws will also provide that we must advance expenses incurred by or on behalf of a director or officer in advance of the final disposition of any action or proceeding, subject to very limited exceptions.

Prior to the closing of this offering, we intend to obtain insurance policies under which, subject to the limitations of the policies, coverage is provided to our directors and officers against loss arising from claims made by reason of breach of fiduciary duty or other wrongful acts as a director or officer, including claims relating to public securities matters, and to us with respect to payments that may be made by us to these officers and directors pursuant to our indemnification obligations or otherwise as a matter of law.

Prior to the closing of this offering, we intend to enter into indemnification agreements with each of our directors and executive officers that may be broader than the specific indemnification provisions contained in the Delaware General Corporation Law. These indemnification agreements may require us, among other things, to indemnify our directors and executive officers against liabilities that may arise by reason of their status or service. These indemnification agreements may also require us to advance all expenses incurred by the directors and executive officers in investigating or defending any such action, suit or proceeding. We believe that these agreements are necessary to attract and retain qualified individuals to serve as directors and executive officers.

The underwriting agreement provides for indemnification by the underwriters of us and our officers, directors and employees for certain liabilities arising under the Securities Act, or otherwise.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling our company pursuant to the foregoing provisions, we have been informed that, in the opinion of the Securities and Exchange Commission, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

The following includes a summary of transactions since January 1, 2015, to which we have been a party in which the amount involved exceeded or will exceed $120,000, and in which any of our directors, executive officers or, to our knowledge, beneficial owners of more than 5% of our capital stock or any member of the immediate family of any of the foregoing persons had or will have a direct or indirect material interest, other than equity and other compensation, termination, change in control and other arrangements, which are described under "Executive Compensation." We also describe below certain other transactions with our directors, executive officers and stockholders.

Equity Financings

Series A Convertible Promissory Notes

Between November 2013 and May 2015, we entered into convertible note purchase agreements pursuant to which we issued $2.3 million in aggregate principal amount of convertible promissory notes, which we refer to as the Series A Convertible Promissory Notes. The Series A Convertible Promissory Notes accrued interest at a rate of 6% per year. The aggregate principal amount and accrued interest on the Series A Convertible Promissory Notes converted into shares of our Series A redeemable convertible preferred stock at a conversion price of $1.9067 per share, minus a discount, upon the closing of the initial tranche of our Series A redeemable convertible preferred stock financing in December 2015.

The following table summarizes the Series A Convertible Promissory Notes purchased by holders of more than 5% of our capital stock, and the conversion of such Series A Convertible Promissory Notes and accrued interest thereon into shares of our Series A redeemable convertible preferred stock.

Name of Stockholder*(1)	Series A Convertible Promissory Notes Principal Amount and Interest($)	Shares of Series A Redeemable Convertible Preferred Stock
David A. Lamond(2)	517,955.24	301,829
Pierre R. and Christine E. Lamond and affiliated entities(2)(3)	517,707.18	301,685

* Owners of more than 5% of our common stock.
(1) Additional details regarding these stockholders and their equity holdings are provided in this prospectus under the section "Principal Stockholders."
(2) Mr. David A. Lamond is a member of our board and was designated to our board by the Pierre R. and Christine E. Lamond Trust 11-22-85, but Mr. Lamond does not beneficially own any of the shares held by the Pierre R. and Christine E. Lamond Trust 11-22-85.
(3) Series A Convertible Promissory Note was purchased and held of record by Pierre R. and Christine E. Lamond Trust 11-22-85.

Sale of Series A Redeemable Convertible Preferred Stock

From December 2015 through September 2016, we sold an aggregate of 9,008,919 shares of our Series A redeemable convertible preferred stock at a purchase price of $1.9067 per share for an aggregate purchase price of $15.9 million. This included the conversion of the Series A Convertible Promissory Notes, with an aggregate conversion amount of approximately $2.4 million. The shares were issued in two tranches, with the first tranche of 4,660,730 shares closing in December 2015 and the second tranche of 4,348,189 shares closing in September 2016. Each share of our Series A redeemable convertible preferred stock will convert into one share of our common stock immediately prior to the closing of this offering in accordance with our certificate of incorporation.

The following table summarizes the Series A redeemable convertible preferred stock purchased by our directors, executive officers and beneficial holders of more than 5% of our capital stock. The terms of these

purchases, notwithstanding the conversion terms of the convertible promissory notes, were the same for all purchasers of Series A redeemable convertible preferred stock.

	Initial Closing		Second Closing			
Name of Stockholder*(1)	Shares of Series A Redeemable Convertible Preferred Stock	Aggregate Purchase Price ($)	Shares of Series A Redeemable Convertible Preferred Stock	Aggregate Purchase ($)	Total Shares Purchased	Aggregate Purchase Price ($)(6)
David Lamond(2)(3)	301,829	517,955.24	699,280	1,333,332.85	1,001,109	1,851,288.09
Entities affiliated with Pfizer Inc.(4)	961,510	1,833,332.31	1,398,561	2,666,666.39	2,360,071	4,499,998.70
Pierre R. and Christine E. Lamond and affiliated entities(2)(5)	1,263,195	2,351,039.49	699,280	1,333,333.35	1,962,475	3,684,372.84
Takeda Ventures, Inc.	961,510	1,833,332.31	1,398,561	2,666,666.39	2,360,071	4,499,998.70

* Owners of more than 5% of our common stock

(1) Additional details regarding these stockholders and their equity holdings are provided in this prospectus under the section "Principal Stockholders."

(2) Mr. David A. Lamond is a member of our board of directors and was designated to our board by the Pierre R. and Christine E. Lamond Trust 11-22-85, but Mr. Lamond does not beneficially own any of the shares held by the Pierre R. and Christine E. Lamond Trust 11-22-85.

(3) Consists of (i) 699,280 shares of Series A redeemable convertible preferred stock held of record by Blue Devil Trust dated 12/03/2010 and (ii) 301,829 shares of Series A redeemable convertible preferred stock held of record by David Lamond.

(4) Dr. McLoughlin is a member of our board of directors and was designated to our board by entities affiliated with Pfizer Inc., but Dr. McLoughlin does not beneficially own any of the shares held by entities affiliated with Pfizer Inc.

(5) Pierre R. and Christine E. Lamond Trust 11-22-85 purchased shares of Series A redeemable convertible preferred stock in December 2015 and September 2016, and subsequently transferred shares of Series A redeemable convertible preferred stock to affiliated entities. Shares owned prior to this offering consist of (i) 961,510 shares of Series A redeemable convertible preferred stock held of record by Pierre R. and Christine E. Lamond Trust 11-22-85, (ii) 500,482 shares of Series A redeemable convertible preferred stock held of record by the Pierre R. Lamond 2019 Annuity Trust A dated March 4, 2019 and (iii) 500,483 shares of Series A redeemable convertible preferred stock held of record by the Christine E. Lamond 2019 Annuity Trust A dated March 4, 2019.

(6) A portion of the consideration paid for the shares of Series A redeemable convertible preferred stock issued in the initial closing was funded through the conversion of the aggregate principal amount and accrued interest under the Series A Convertible Promissory Notes. See "Certain Relationships and Related Transactions—Series A Convertible Promissory Notes."

Series B Convertible Promissory Notes

From February 2017 through January 2018, we entered into convertible note purchase agreements pursuant to which we issued $8.0 million in aggregate principal amount of convertible promissory notes, which we refer to as the Series B Convertible Promissory Notes. The Series B Convertible Promissory Notes accrued interest at a rate of 8% per year. The aggregate principal amount and accrued interest on the Series B Convertible Promissory Notes converted into shares of our Series B redeemable convertible preferred stock at a conversion price of $9.6122 per share, minus a discount, upon the closing of the initial tranche of our Series B redeemable convertible preferred stock financing in May 2018.

The following table summarizes the Series B Convertible Promissory Note purchased by holders of more than 5% of our capital stock, and the conversion of such Series B Convertible Promissory Notes and accrued interest thereon into shares of our Series B redeemable convertible preferred stock.

Name of Stockholder*(1)	Series B Convertible Promissory Notes Principal Amount and Interest($)	Shares of Series B Redeemable Convertible Preferred Stock
Blue Devil Trust Date 12/03/2010(2)	1,105,777.10	143,798
Entities affiliated with Pfizer Inc.(3)	1,658,665.65	215,697
Takeda Ventures, Inc.	1,658,665.65	215,697
Pierre R. and Christine E. Lamond and affiliated entities(2)(4)	1,105,777.10	143,798

* Owners of more than 5% of our common stock.
(1) Additional details regarding these stockholders and their equity holdings are provided in this prospectus under the section "Principal Stockholders."
(2) Mr. David A. Lamond, a member of our board of directors, is the trustee of the Blue Devil Trust dated 12/03/2010. Mr. Lamond was designated to our board by the Pierre R. and Christine E. Lamond Trust 11-22-85, but Mr. Lamond does not beneficially own any of the shares held by the Pierre R. and Christine E. Lamond Trust 11-22-85.
(3) Dr. McLoughlin is a member of our board of directors and was designated to our board by entities affiliated with Pfizer Inc., but Dr. McLoughlin does not beneficially own any of the shares held by entities affiliated with Pfizer Inc.
(4) Series B Convertible Promissory Note was purchased and held of record by Pierre and Christine E. Lamond Trust 11-22-85.

Sale of Series B Redeemable Convertible Preferred Stock

Between May 2018 and July 2018, we sold an aggregate of 9,152,108 shares of our Series B redeemable convertible preferred stock at a purchase price of $9.6122 per share for an aggregate purchase price of $85.8 million. This included the conversion of the Series B convertible promissory notes with an aggregate conversion amount of approximately $8.8 million. Each share of our Series B redeemable convertible preferred stock will convert into one share of our common stock upon the closing of this offering in accordance with our certificate of incorporation.

The following table summarizes the Series B redeemable convertible preferred stock purchased by our directors, executive officers and beneficial holders of more than 5% of our capital stock. The terms of these purchases were the same for all purchasers of our Series B redeemable convertible preferred stock.

Name of Stockholder*(1)	Shares of Series B Redeemable Convertible Preferred Stock	Aggregate Purchase Price($)(2)
Blue Devil Trust dated 12/03/2010(3)	924,056	8,605,776.61
Entities affiliated with Pfizer Inc.(4)	839,902	7,658,662.43
Takeda Ventures, Inc.	319,731	2,658,663.94
Pierre R. and Christine E. Lamond and affiliated entities(3)(5)	924,055	8,605,776.61
SMALLCAP World Fund, Inc.	1,560,515	14,999,999.01

* owners of more than 5% of our common stock
(1) Additional details regarding these stockholders and their equity holdings are provided in this prospectus under the section "Principal Stockholders."
(2) A portion of the consideration paid for the shares of Series B redeemable convertible preferred stock issued in the initial closing was funded through the conversion of the aggregate principal amount and accrued interest under the Series B Convertible Promissory Notes. See "Certain Relationships and Related Transactions—Series B Convertible Promissory Notes."
(3) Mr. David A. Lamond, a member of our board of directors, is the trustee of the Blue Devil Trust dated 12/03/2010. Mr. Lamond was designated to our board by Pierre R. and Christine E. Lamond Trust 11-22-85, but Mr. Lamond does not beneficially own any of the shares held by Pierre R. and Christine E. Lamond Trust 11-22-85.
(4) Dr. McLoughlin is a member of our board of directors and was designated to our board by entities affiliated with Pfizer Inc., but Dr. McLoughlin does not beneficially own any of the shares held by entities affiliated with Pfizer Inc.

(5) Pierre R. and Christine E. Lamond Trust 11-22-85 purchased shares of Series B redeemable convertible preferred stock in May 2018, and subsequently transferred shares of Series B redeemable convertible preferred stock to affiliated entities. Shares owned prior to this offering consist of (i) 462,028 shares of Series B redeemable convertible preferred stock held of record by the Pierre R. Lamond 2019 Annuity Trust A dated March 4, 2019 and (ii) 462,027 shares of Series B redeemable convertible preferred stock held of record by the Christine E. Lamond 2019 Annuity Trust A dated March 4, 2019.

Directed Share Program

At our request, the underwriters have reserved up to 7% of the shares offered by this prospectus for sale, at the initial public offering price, to certain persons associated with us. The directed share program will not limit the ability of certain holders of more than 5% of our common stock, to purchase more than $120,000 in value of our common stock. We do not currently know the extent to which these related persons will participate in our directed share program, if at all, or to the extent they will purchase more than $120,000 in value of our common stock.

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and officers. The indemnification agreements and our certificate of incorporation and bylaws require us to indemnify our directors and officers to the fullest extent permitted by Delaware law. For more information regarding these indemnification agreements, see “Management—Limitation of Liability and Indemnification.”

Participation in this Offering

Certain of our existing 5% stockholders and stockholders affiliated with certain of our directors (or their affiliates) have agreed to purchase, and we have directed allocations for, an aggregate of approximately $26.3 million of shares of our common stock in this offering at the initial public offering price and on the same terms as the other purchasers in this offering.

Policies and Procedures for Related Party Transactions

Our board of directors intends to adopt a written related person transaction policy to set forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships in which we were or are to be a participant, the amount involved exceeds $120,000 and a related person had or will have a direct or indirect material interest, including, without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness or employment by us of a related person.

We believe that we have executed all of the transactions set forth under the section entitled “Policies and Procedures for Related Party Transactions” on terms no less favorable to us than we could have obtained from unaffiliated third parties. It is our intention to ensure that all future transactions between us and our officers, directors and principal stockholders and their affiliates, are approved by the audit committee of our board of directors, and are on terms no less favorable to us than those that we could obtain from unaffiliated third parties.

PRINCIPAL STOCKHOLDERS

The following table and footnotes set forth information regarding the beneficial ownership of our common stock as of March 31, 2019 and as adjusted to reflect the sale of the common stock offered by us under this prospectus by:

- each of our directors and named executive officers;
- all of our current directors and executive officers as a group; and
- each person who is known to us to beneficially own more than 5% of our common stock.

Except as otherwise noted, the address of each person listed in the table is c/o Cortexyme, Inc., 269 East Grand Avenue, South San Francisco, CA 94080. The table includes all shares of common stock issuable within 60 days of March 31, 2019 upon the exercise of options and other rights beneficially owned by the indicated stockholders on that date. Beneficial ownership is determined in accordance with the rules of the Securities and Exchange Commission and includes voting and investment power with respect to shares. To our knowledge, except under applicable community property laws or as otherwise indicated, the persons named in the table have sole voting and sole investment control with respect to all shares beneficially owned.

The applicable percentage of ownership for each stockholder is based on 21,755,889 shares of common stock outstanding as of March 31, 2019, which reflects the assumed conversion of all of our outstanding shares of redeemable convertible preferred stock and the exercise of an outstanding warrant to purchase shares of common stock. Percentage ownership of our common stock after the offering assumes the sale of shares by us in this offering. Shares of common stock issuable upon exercise of options and other rights beneficially owned are deemed outstanding for the purpose of computing the percentage ownership of the person holding these options and other rights, but are not deemed outstanding for computing the percentage ownership of any other person. The following table does not reflect any shares of our common stock that may be purchased pursuant to our directed share program described under “Underwriting—Directed Share Program.”

Certain of our existing 5% stockholders and stockholders affiliated with certain of our directors (or their affiliates) have agreed to purchase, and we have directed allocations for, an aggregate of approximately $26.3 million of shares of our common stock in this offering at the initial public offering price and on the same terms as the other purchasers in this offering. The figures in the table below do not reflect the purchase of the shares in this offering by these potential investors in the amounts they have agreed to purchase.

Name of Beneficial Owner	Shares beneficially owned prior to the offering: Common Stock	Options Exercisable within 60 days	Aggregate Number of Shares Beneficially Owned	%	Shares beneficially owned after the offering: Assuming no exercise of option to purchase additional shares	%	Assuming exercise of option to purchase additional shares	%
5% Stockholders								
Entities affiliated with Pfizer Inc.(1)	3,199,973	—	3,199,973	14.71%	3,199,973	12.23%	3,199,973	11.93%
Pierre R. and Christine E. Lamond and affiliated entities(2)	2,886,530	—	2,886,530	13.27%	2,886,530	11.03%	2,886,530	10.76%
SMALLCAP World Fund, Inc.(3)	1,560,515	—	1,560,515	7.17%	1,560,515	5.96%	1,560,515	5.82%
Takeda Ventures, Inc.(4)	2,679,802	—	2,679,802	12.32%	2,679,802	10.24%	2,679,802	9.99%
Named Executive Officers and Directors								
Casey C. Lynch(5)	1,240,580	92,560	1,333,140	6.10%	1,333,140	5.08%	1,333,140	4.95%
Christopher Lowe	—	—	—	*	—	*	—	*
Stephen S. Dominy, M.D.(6)	1,436,911	116,693	1,553,604	7.10%	1,553,604	5.91%	1,553,604	5.77%
David A. Lamond(7)	1,925,165	—	1,925,165	8.85%	1,925,165	7.36%	1,925,165	7.18%
Margi McLoughlin, Ph.D.(8)	3,199,973	—	3,199,973	14.71%	3,199,973	12.23%	3,199,973	11.93%
Una Ryan, OBE, Ph.D.	—	—	—	*	—	*	—	*
Kevin Young, CBE	—	—	—	*	—	*	—	*
Christopher J. Senner	—	—	—	*	—	*	—	*
All executive officers and directors as a group (11 persons)	8,133,511	333,638	8,467,149	38.85%	8,467,149	32.32%	8,467,149	31.52%

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

(1) Consists of (i) 624,205 shares of common stock issuable upon the conversion of shares of the redeemable convertible preferred stock held of record by Pfizer Inc. (“Pfizer”), (ii) 215,697 shares of common stock issuable upon the conversion of shares of the redeemable convertible preferred stock held of record by Pfizer Strategic Investment Holdings LLC (“PSIH”), a controlled affiliate of Pfizer and (iii) 2,360,071 shares of common stock issuable upon the conversion of shares of the redeemable convertible preferred stock 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) Consists of (i) 961,510 shares of common stock issuable upon the conversion of shares of the redeemable convertible preferred stock held of record by Pierre R. and Christine E. Lamond Trust 11-22-85, (ii) 962,510 shares of common stock issuable upon the conversion of shares of the redeemable convertible preferred stock held of record by the Pierre R. Lamond 2019 Annuity Trust A dated March 4, 2019 and (iii) 962,510 shares of common stock issuable upon the conversion of shares of the redeemable convertible preferred stock 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 of common stock issuable upon the conversion of shares of the redeemable convertible preferred stock 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 of common stock issuable upon the conversion of shares of the redeemable convertible preferred stock 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 of common stock issuable upon the conversion of shares of the redeemable convertible preferred stock held of record by the Christine E. Lamond 2019 Annuity Trust A dated March 4, 2019.

(3) Consists of 1,560,515 shares of common stock issuable upon the conversion of shares of the redeemable convertible preferred stock held of record by SMALLCAP World Fund, Inc. Julian N. Abdey, Noriko H. Chen, Peter Eliot, Brady L. Enright, Bradford F. Freer, Leo Hee, Roz Hongsaranagon, Claudia P. Huntington, Jonathan Knowles, Harold H. La, Aidan O’Connell, Andraz Razen, Gregory W. Wendt and Dylan Yolles, as portfolio managers, have voting and investment power over the securities held by SMALLCAP WORLD FUND, Inc. The address of SMALLCAP World Fund, Inc. is 333 S. Hope St., 53rd Floor, Los Angeles, California 90071.

(4) Consists of 2,679,802 shares of common stock issuable upon the conversion of shares of the redeemable convertible preferred stock held of record by Takeda Ventures, Inc., a controlled affiliate of Takeda Pharmaceutical Company Limited. The address of Takeda Ventures, Inc. is 435 Tasso Street, Suite 300, Palo Alto, California 94301.

(5) Consists of (i) 49,895 shares of common stock 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, (iii) 91,911 shares of common stock held of record by the Casey C. Lynch 2019 Annuity Trust and (iv) 92,560 shares subject to stock options issuable upon the exercise of options exercisable within 60 days after March 31, 2019. 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 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. 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 of common stock held of record by Casey C. Lynch and (b) 91,911 shares of common stock held of record by the Casey C. Lynch 2019 Annuity Trust.

(6) Consists of (i) 1,216,323 shares of common stock held of record by Stephen S. Dominy and Ylva K. Dominy, Trustees of the Dominy Family Trust, (ii) 220,588 shares of common stock held of record by the Stephen Dominy 2019 Annuity Trust and (iii) 116,693 shares subject to stock options issuable upon the exercise of options exercisable within 60 days after March 31, 2019. 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 of common stock 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 of common stock held of record by the Stephen Dominy 2019 Annuity Trust.

(7) Consists of (i) 301,829 shares of common stock issuable upon the conversion of shares of the redeemable convertible preferred stock held of record by David A. Lamond and (ii) 1,623,336 shares of common stock issuable upon the conversion of shares of the redeemable convertible preferred stock 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.

(8) Dr. McLoughlin is a member of our board of directors and was designated to our board by entities affiliated with Pfizer Inc., but does not have voting and dispositive power with respect to the shares held of record by entities affiliated with Pfizer Inc.

DESCRIPTION OF CAPITAL STOCK

Description of Capital Stock

The following is a description of the material terms of our amended and restated certificate of incorporation and amended and restated bylaws as each will be in effect as of the closing of this offering, and of specific provisions of Delaware law. The following description is intended as a summary only and is qualified in its entirety by reference to our amended and restated certificate of incorporation, our amended and restated bylaws and the Delaware General Corporation Law, or DGCL. Copies of our amended and restated certificate of incorporation and amended and restated bylaws have been filed as exhibits to the registration statement of which this prospectus is a part.

General

Immediately following the closing of this offering, our authorized capital stock will consist of 100,000,000 shares of common stock, $0.001 par value per share, and 10,000,000 shares of preferred stock, $0.001 par value per share, all of which preferred stock will be undesignated. The following information reflects the filing of our amended and restated certificate of incorporation and the conversion of all outstanding shares of our preferred stock into shares of common stock immediately prior to the closing of this offering.

Upon the closing of this offering and based on 21,601,334 shares of our common stock outstanding as of December 31, 2018, 26,013,334 shares of our common stock will be outstanding, assuming the conversion of all outstanding shares of our redeemable convertible preferred stock into 18,161,027 shares of our common stock immediately prior to the closing of this offering and the exercise in full of an outstanding warrant to purchase 27,941 shares of common stock, as of December 31, 2018, upon the closing of this offering. As of December 31, 2018, we had 68 stockholders of record.

Effective April 25, 2019, we effected a one-for-0.367647 reverse stock split, or the Reverse Stock Split, of our issued and outstanding common stock, convertible preferred stock, and stock options. We will make a cash payment to stockholders for all fractional shares which would otherwise be required to be issued as a result of the Reverse Stock Split.

Common Stock

As of December 31, 2018, we had 21,601,334 shares of common stock issued and outstanding assuming the conversion of all outstanding shares of our redeemable convertible preferred stock into 18,161,027 shares of our common stock as if such conversion had occurred on December 31, 2018 and the exercise in full of an outstanding warrant to purchase 27,941 shares of common stock, as of December 31, 2018, upon the closing of this offering.

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 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. For more information, see the section of this prospectus captioned “Dividend Policy.”

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.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are, and the shares of common stock to be issued pursuant to this offering, when paid for, will be fully paid and nonassessable.

Preferred Stock

As of December 31, 2018, there were 18,161,027 shares of redeemable convertible preferred stock outstanding, which will convert, upon the closing of this offering, into 18,161,027 shares of our common stock. After the closing of this offering, the board of directors will have the authority, without further action by the stockholders, to issue up to 10,000,000 shares of preferred stock, $0.001 par value per share, in one or more series. The board of directors will also have 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. As of the closing of the offering, no shares of redeemable convertible preferred stock will be outstanding. We currently have no plans to issue any shares of redeemable convertible preferred stock.

Warrants

As of December 31, 2018, we had an outstanding warrant to purchase 27,941 shares of our common stock at an exercise price of $0.03 per share. The warrant was exercised in full in April 2019.

Options

As of December 31, 2018, we had outstanding options to purchase 1,885,504 shares of our common stock under our 2014 Plan and 984,680 shares remained available for future awards.

Registration Rights

Based on the number of shares outstanding as of December 31, 2018, under our amended and restated investors' rights agreement, the holders of up to approximately 21.3 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 five years following the consummation of this 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

At any time after one hundred eighty (180) days after this offering, 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

In connection with this offering, certain holders were entitled to, and the necessary percentage of holders waived, their rights to notice of this offering and to include their shares of registrable securities in this offering. If we register any securities for public sale in another offering, 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 registrable securities to be included in the registration statement, subject to certain restrictions.

Form S-3 Registration Rights

Following this offering, we may be obligated under our registration rights agreement 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, which will be in effect upon the closing of this offering, will 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 will 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 will provide 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 bylaws or remove directors without holding a meeting of our stockholders called in accordance with our bylaws.

In addition, our amended and restated bylaws will provide 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 will 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

Upon the closing of the offering, our board of directors will be 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. For more information on the classified board, see "Management—Board of Directors." A third party may be discouraged from making a tender offer or otherwise attempting to obtain control of us as it is it 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 will 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 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, as amended upon the closing of this offering, 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 Nasdaq, 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 will 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 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 will 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. 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.

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, each to be in effect upon the closing of this offering, will 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, to be in effect after the closing of this offering, will 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 will also be empowered to 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 amended and restated certificate of incorporation and amended and restated bylaws, to be in effect after the closing of this offering, 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.

Transfer Agent and Registrar

Upon the closing of this offering, the transfer agent and registrar for our common stock will be American Stock Transfer & Trust Company, LLC. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, NY 11219, and its telephone number is (718) 921-8124.

Listing

Our common stock has been approved for listing on the Nasdaq Global Select Market under the trading symbol "CRTX."

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no market for our common stock. Future sales of substantial amounts of common stock in the public market could adversely affect prevailing market prices. Furthermore, since only a limited number of shares will be available for sale shortly after this offering because of certain contractual and legal restrictions on resale, sales of substantial amounts of our common stock in the public market after the restrictions lapse could adversely affect the prevailing market price and our ability to raise equity capital in the future.

Upon the closing of the offering, we will have outstanding 26,013,334 shares of common stock (or 26,675,134 shares if the option to purchase additional shares is exercised in full). Of these shares, all of the shares sold in this offering will be freely transferable without restriction or further registration under the Securities Act, except that any shares purchased by one of our "affiliates," as that term is defined in Rule 144 under the Securities Act, may be sold only in compliance with the limitations described below, and any shares purchased by any of our affiliates pursuant to our directed share program will be subject to the lock-up agreements described below. The remaining shares of common stock held by our existing stockholders are "restricted securities" as defined in Rule 144. Restricted shares may be sold in the public market only if registered under the Securities Act or if they qualify for an exemption from registration, including, among others, the exemptions provided by Rules 144 and 701 promulgated by the SEC under the Securities Act. As a result of the contractual 180-day lock-up period described in "Underwriting—No Sales of Similar Securities" and the provisions of Rules 144 and 701, these shares will be available for sale in the public market as follows:

- beginning on the date of this prospectus, the shares of common stock sold in this offering including certain shares sold under our directed share program that are not subject to a 180-day lock-up will be immediately available for sale in the public market;
- beginning 181 days after the date of this prospectus, 21,601,334 additional shares of common stock plus shares sold under our directed share program that are subject to a 180-day lock-up, may become eligible for sale in the public market upon the satisfaction of certain conditions, of which 15,260,358 shares would be held by affiliates and subject to the volume and other restrictions of Rule 144, as described below; and
- the remainder of the shares of common stock will be eligible for sale in the public market from time to time thereafter, subject in some cases to the volume and other restrictions of Rule 144, as described below.

Lock-Up Agreements

We, our executive officers, directors and holders of substantially all of our common stock and securities convertible into or exchangeable for our common stock, have agreed or will agree that, subject to certain exceptions, for a period of 180 days from the date of this prospectus, we and they will not, without the prior written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated and Credit Suisse Securities (USA) LLC, dispose of or hedge any shares or any securities convertible into or exchangeable for shares of our capital stock. Merrill Lynch, Pierce, Fenner & Smith Incorporated and Credit Suisse Securities (USA) LLC may, in their sole discretion, release any of the securities subject to these lock-up agreements at any time. See "Underwriting—No Sales of Similar Securities."

Rule 144

In general, under Rule 144, as currently in effect, an affiliate who beneficially owns shares that were purchased from us, or any affiliate, at least six months previously, is entitled to sell, upon the expiration of the lock-up agreement described in "Underwriting," within any three-month period beginning 180 days after the date of this prospectus, a number of shares that does not exceed the greater of 1% of our then-outstanding shares of common stock, which will equal approximately 260,133 shares immediately after this offering, (or 266,751 shares if the option to purchase additional shares is exercised), or the average weekly trading volume of our

common stock on the Nasdaq Global Select Market during the four calendar weeks preceding the filing of a notice of the sale with the SEC. Sales under Rule 144 by our affiliates or persons selling shares on behalf of our affiliates are also subject to certain manner of sale provisions, notice requirements and the availability of current public information about us. The sale of these shares, or the perception that sales will be made, may adversely affect the price of our common stock after this offering because a great supply of shares would be, or world be perceived to be, available for sale in the public market.

Following this offering, a person that is not an affiliate of ours at the time of, or at any time during the three months preceding, a sale and who has beneficially owned restricted securities within the meaning of Rule 144 for at least six months may sell shares subject only to the availability of current public information about us, and any such person who has beneficially owned restricted shares of our common stock for at least one year may sell shares without restriction.

We are unable to estimate the number of shares that will be sold under Rule 144 since this will depend on the market price for our common stock, the personal circumstances of the stockholder and other factors.

Rule 701

In general, under Rule 701, as currently in effect, any of our employees, directors, officers, consultants or advisors who purchased shares from us pursuant to Rule 701 in connection with a compensatory stock or option plan or other written agreement before the effective date of this offering is entitled to resell such shares 90 days after the effective date of this offering in reliance on Rule 144, without having to comply with the holding period requirements or other restrictions contained in Rule 144.

The Securities and Exchange Commission has indicated that Rule 701 will apply to typical stock options granted by an issuer pursuant to Rule 701 before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after the date of this prospectus. Securities issued in reliance on Rule 701 are restricted securities and, subject to the contractual lock-up restrictions described above, beginning 90 days after the date of this prospectus, may be sold by persons other than “affiliates,” as defined in Rule 144, subject only to the manner of sale provisions of Rule 144 and by “affiliates” under Rule 144 without compliance with its one-year minimum holding period requirement.

Registration Statements on Form S-8

We intend to file a registration statement on Form S-8 under the Securities Act to register all of the shares of common stock subject to outstanding stock options under our 2014 Plan or reserved for future issuance under our 2019 Plan and 2019 ESPP, which will be effective upon the consummation of this offering. This registration statement would cover approximately 5,141,732 shares. Shares registered under the registration statement will generally be available for sale in the open market after the 180-day lock-up period immediately following the date of this prospectus (as such period may be extended in certain circumstances). See “Certain Relationships and Related-Party Transactions—Amended and Restated Investors’ Rights Agreement.”

Registration Rights

Beginning 180 days after the date of this prospectus, subject to certain exceptions and automatic extensions in certain circumstances, certain holders of shares of our common stock will be entitled to the rights described under “Description of Capital Stock—Registration Rights.” Registration of these shares under the Securities Act would result in these shares becoming freely tradeable without restriction under the Securities Act immediately upon effectiveness of the registration.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

This section discusses the material U.S. federal income tax consequences of the ownership and sale, exchange or other taxable disposition of our common stock sold pursuant to this offering to a "non-U.S. holder" (as defined below). This discussion does not provide a complete analysis of all potential tax considerations. The information provided below is based upon provisions of the Internal Revenue Code of 1986, as amended, or Code, Treasury regulations promulgated thereunder, administrative rulings and judicial decisions currently in effect. These authorities may change at any time, possibly on a retroactive basis, or the Internal Revenue Service, or IRS, might interpret the existing authorities differently. In either case, the U.S. federal income tax considerations of owning or disposing of our common stock could differ from those described below. As a result, we cannot assure you that the U.S. federal income tax considerations described in this discussion will not be challenged by the IRS or will be sustained by a court if challenged by the IRS.

This discussion does not address the tax considerations arising under the alternative minimum tax, the net investment income tax, the laws of any state, local or non-U.S. jurisdiction, or under U.S. federal gift and estate tax laws. In addition, this discussion does not address tax considerations applicable to an investor's particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

- banks, insurance companies or other financial institutions;
- partnerships or entities or arrangements treated as partnerships or other pass-through entities for U.S. federal income tax purposes (or investors in such entities);
- corporations that accumulate earnings to avoid U.S. federal income tax;
- tax-exempt or governmental organizations or tax-qualified retirement plans;
- real estate investment trusts or regulated investment companies;
- controlled foreign corporations or passive foreign investment companies;
- persons who acquired our common stock pursuant to the exercise of an employee stock option or otherwise as compensation for services;
- brokers or dealers in securities or currencies;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- persons that own, or are deemed to own, more than 5% of our capital stock (except to the extent specifically set forth below);
- certain former citizens or long-term residents of the United States;
- persons who hold our common stock as a position in a hedging transaction, "straddle," "conversion transaction" or other risk reduction transaction;
- persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, for investment purposes); or
- persons deemed to sell our common stock under the constructive sale provisions of the Code.

In addition, if a partnership or entity classified as a partnership for U.S. federal income tax purposes is a beneficial owner of our common stock, the tax treatment of a partner in the partnership or an owner of the entity will depend upon the status of the partner or owner and the activities of the partnership or entity. Accordingly, this discussion does not address U.S. federal income tax considerations applicable to partnerships that hold our common stock, and partners in such partnerships should consult their tax advisors.

Investors considering the purchase of our common stock should consult their own tax advisors regarding the application of the U.S. federal income, gift and estate tax laws to their particular situations and the consequences of non-U.S., state or local laws, and tax treaties.

Non-U.S. Holder Defined

For purposes of this section, a "non-U.S. holder" is any holder of our common stock, other than an entity taxable as a partnership for U.S. federal income tax purposes, that is not:

- an individual who is a citizen or resident of the United States for U.S. federal income tax purposes;
- a corporation, or other entity taxable as a corporation for U.S. federal income tax purposes, created or organized under the laws of the United States, any state therein or the District of Columbia or otherwise treated as such for U.S. federal income tax purposes;
- a trust that (1) is subject to the primary supervision of a U.S. court and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable Treasury regulations to be treated as a U.S. person; or
- an estate whose income is subject to U.S. federal income tax regardless of source.

Distributions

We do not anticipate making any distributions on shares of our common stock in the foreseeable future. If we do make any distributions on shares of our common stock, however, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Distributions in excess of our current and accumulated earnings and profits will constitute a return of capital that is applied against and reduces, but not below zero, a non-U.S. holder's adjusted tax basis in shares of our common stock. Any remaining excess will be treated as gain realized on the sale, exchange or other taxable disposition of our common stock. See "Material U.S. Federal Income Tax Considerations for Non-U.S. Holders—Sale of Common Stock."

Subject to the discussion below regarding the Foreign Account Tax Compliance Act, or FATCA, and backup withholding, any distribution made to a non-U.S. holder on our common stock that is not effectively connected with a non-U.S. holder's conduct of a trade or business in the United States will generally be subject to U.S. withholding tax at a 30% rate. The withholding tax might not apply, however, or might apply at a reduced rate, under the terms of an applicable income tax treaty between the United States and the non-U.S. holder's country of residence. You should consult your tax advisors regarding your entitlement to benefits under a relevant income tax treaty. Generally, in order for us or our paying agent to withhold tax at a lower treaty rate, a non-U.S. holder must certify its entitlement to treaty benefits. A non-U.S. holder generally can meet this certification requirement by providing an IRS Form W-8BEN, W-8BEN-E (or any successor form to the IRS Form W-8BEN or W-8BEN-E) to us or our paying agent. If the non-U.S. holder holds the stock through a financial institution or other agent acting on the non-U.S. holder's behalf, the non-U.S. holder will be required to provide appropriate documentation to the agent. The non-U.S. holder's agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. If you are eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty, you may obtain a refund or credit from the IRS of any excess amounts withheld by filing an appropriate claim for a refund with the IRS in a timely manner.

Distributions received by a non-U.S. holder that are effectively connected with a U.S. trade or business conducted by the non-U.S. holder, and, if required by an applicable income tax treaty between the United States and the non-U.S. holder's country of residence, are attributable to a permanent establishment maintained by the non-U.S. holder in the United States, are not subject to the 30% U.S. withholding tax. To obtain this exemption, a non-U.S. holder must provide us with an IRS Form W-8ECI properly certifying such exemption. Such effectively connected distributions, although not subject to U.S. withholding tax, are generally taxed at the same graduated rates applicable to U.S. persons, net of certain deductions and credits. In addition to the graduated tax described above, distributions received by corporate non-U.S. holders that are effectively connected with a U.S. trade or business of the corporate non-U.S. holder may also be subject to a "branch profits tax" equal to 30% of its effectively connected earnings and profits for the taxable year, as adjusted for certain items, although an applicable income tax treaty between the United States and the non-U.S. holder's country of residence might provide for a lower rate.

Sale of Common Stock

Subject to the discussion below regarding FATCA and backup withholding, non-U.S. holders will generally not be subject to U.S. federal income tax on any gains realized on the sale, exchange or other taxable disposition of our common stock unless:

- the gain (1) is effectively connected with the conduct by the non-U.S. holder of a U.S. trade or business and (2) if required by an applicable income tax treaty between the United States and the non-U.S. holder's country of residence, is attributable to a permanent establishment (or, in the case of an individual, a fixed base) maintained by the non-U.S. holder in the United States (in which case the special rules described below apply);

- the non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of the sale, exchange or other taxable disposition of our common stock, and certain other requirements are met (in which case the gain would be subject to a flat 30% tax, or such reduced rate as may be specified by an applicable income tax treaty, which may be offset by certain U.S.-source capital losses, even though the individual is not considered a resident of the United States, provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses); or

- the rules of the Foreign Investment in Real Property Tax Act, or FIRPTA, treat the gain as effectively connected with a U.S. trade or business.

The FIRPTA rules may apply to a sale, exchange or other taxable disposition of our common stock if we are at the time of the sale, exchange, or other taxable disposition, or were within the shorter of the five-year period preceding the disposition and the non-U.S. holder's holding period, a "United States real property holding corporation," or USRPHC. In general, we would be a USRPHC if the fair market value of our "U.S. real property interests" comprised at least half of the fair market value of our business assets and our U.S. and non-U.S. real property interests. If we are or become a USRPHC, as long as our common stock is regularly traded on an established securities market, such common stock will be treated as "U.S. real property interests" subject to the FIRPTA rules only if a non-U.S. holder actually owns or constructively holds more than 5% of our outstanding common stock at any time within the shorter of the five-year period preceding the disposition and the non-U.S. holder's holding period. Currently, we believe we are not, and do not anticipate becoming, a USRPHC.

If any gain from the sale, exchange or other taxable disposition of our common stock (1) is effectively connected with a U.S. trade or business conducted by a non-U.S. holder and, (2) if required by an applicable income tax treaty between the United States and the non-U.S. holder's country of residence, is attributable to a permanent establishment (or, in the case of an individual, a fixed base) maintained by such non-U.S. holder in the United States, then the gain generally will be subject to U.S. federal income tax at the same graduated rates

applicable to U.S. persons, net of certain deductions and credits. If the non-U.S. holder is a corporation, under certain circumstances, that portion of its earnings and profits that is effectively connected with its U.S. trade or business, subject to certain adjustments, generally would be subject to a "branch profits tax." The branch profits tax rate is equal to 30% of its effectively connected earnings and profits for the taxable year, as adjusted for certain items, although an applicable income tax treaty between the United States and the non-U.S. holder's country of residence might provide for a lower rate.

Backup Withholding and Information Reporting

Payments of dividends on our common stock will not be subject to backup withholding, provided the non-U.S. holder certifies its non-U.S. status, such as by furnishing a valid IRS Form W-8BEN, W-8BEN-E or W-8ECI (and we or our paying agent do not have actual knowledge or reason to know the holder is a U.S. person or that the conditions of any other exemption are not, in fact, satisfied), or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any dividends on our common stock paid to the non-U.S. holder, regardless of whether any tax was actually withheld. Copies of these reports may be made available to tax authorities in the country where the non-U.S. holder resides. In addition, proceeds of the sale or other taxable disposition of our common stock within the United States or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting if the applicable withholding agent receives the certification described above or the non-U.S. holder otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker that does not have certain enumerated relationships with the United States generally will not be subject to backup withholding or information reporting. The backup withholding rate is currently 24%.

Backup withholding is not an additional tax. Any amounts withheld from a payment to a holder of our common stock under the backup withholding rules can be credited against any U.S. federal income tax liability of the holder and may entitle the holder to a refund from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Foreign Account Tax Compliance Act, or FATCA

FATCA imposes U.S. federal withholding tax of 30% on certain types of U.S. source "withholdable payments" (including dividends and the gross proceeds from the sale, exchange or other taxable disposition of U.S. stock) to "foreign financial institutions", which are broadly defined for this purpose, and other non-U.S. entities in connection with the failure to comply with certain certification and information reporting requirements regarding U.S. account holders or owners of such institutions or entities. The obligation to withhold under FATCA applies to any dividends on our common stock. While withholding under FATCA would have applied also to gross proceeds from the sale, exchange or other taxable disposition of our common stock paid after December 31, 2018 and to certain "passthru" payments received with respect to instruments held through foreign financial institutions after the date on which applicable final Treasury regulations are issued, recently proposed Treasury regulations eliminate FATCA withholding on payments of gross proceeds entirely and limit FATCA withholding on these "passthru" payments to those payments made two years after the date on which applicable final Treasury regulations are issued. Taxpayers generally may rely on these proposed Treasury regulations until final Treasury regulations are issued. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock.

The preceding discussion of U.S. federal income tax considerations is for general information only. It is not tax advice. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state, local and non-U.S. tax consequences of the sale, exchange or other taxable disposition of our common stock, including the consequences of any proposed change in applicable laws.

UNDERWRITING

Merrill Lynch, Pierce, Fenner & Smith Incorporated and Credit Suisse Securities (USA) LLC are acting as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

Underwriter	Number of Shares
Merrill Lynch, Pierce, Fenner & Smith Incorporated	1,875,100
Credit Suisse Securities (USA) LLC	1,654,500
Canaccord Genuity LLC	441,200
JMP Securities LLC	441,200
Total	4,412,000

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officer's certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus and to dealers at that price less a concession not in excess of $0.714 per share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares.

	Per Share	Without Option	With Option
Public offering price	$ 17.00	$ 17.00	$ 17.00
Underwriting discount	$ 1.19	$ 1.19	$ 1.19
Proceeds, before expenses, to us	$ 15.81	$ 69,753,720	$80,216,778

The expenses of the offering, not including the underwriting discount, payable by us are estimated to be approximately $2.1 million. We have also agreed to reimburse the underwriters for certain of their expenses incurred in connection with, among others, the review and clearance by the Financial Industry Regulatory Authority, Inc. in an amount of up to $40,000.00.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to 661,800 additional shares at the public offering price, less the underwriting discount. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We, our executive officers and directors and our other existing security holders have agreed not to sell or transfer any common stock or securities convertible into, exchangeable for, exercisable for, or repayable with common stock, for 180 days after the date of this prospectus without first obtaining the written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated and Credit Suisse Securities (USA) LLC. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly

- offer, pledge, sell or contract to sell any common stock,
- sell any option or contract to purchase any common stock,
- purchase any option or contract to sell any common stock,
- grant any option, right or warrant for the sale of any common stock,
- lend or otherwise dispose of or transfer any common stock,
- request or demand that we file or make a confidential submission of a registration statement related to the common stock, or
- enter into any swap or other agreement that transfers, in whole or in part, the economic consequence of ownership of any common stock whether any such swap or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for or repayable with common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

Nasdaq Global Select Market Listing

Our common stock has been approved for listing on the Nasdaq Global Select Market under the symbol "CRTX."

Before this offering, there has been no public market for our common stock. The initial public offering price will be determined through negotiations between us and the representatives. In addition to prevailing market conditions, the factors to be considered in determining the initial public offering price are:

- the valuation multiples of publicly traded companies that the representatives believe to be comparable to us,
- our financial information,
- the history of, and the prospects for, our company and the industry in which we compete,

- an assessment of our management, its past and present operations, and the prospects for, and timing of, our future revenues,
- the present state of our development,
- the likelihood of approval of our drug candidates, and
- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for the shares may not develop. It is also possible that after the offering the shares will not trade in the public market at or above the initial public offering price.

The underwriters do not expect to sell more than 5% of the shares in the aggregate to accounts over which they exercise discretionary authority.

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. “Covered” short sales are sales made in an amount not greater than the underwriters’ option to purchase additional shares described above. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. “Naked” short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the closing of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Directed Share Program

At our request, the underwriters have reserved up to 7% of the shares offered by this prospectus for sale, at the initial public offering price, to certain persons associated with us. If these persons purchase reserved shares, it will reduce the number of shares available for sale to the general public. Any reserved shares that are not so purchased will be offered by the underwriters to the general public on the same terms as the other shares offered by this prospectus.

Indications of Interest

Certain of our existing 5% stockholders and stockholders affiliated with certain of our directors (or their affiliates) have agreed to purchase, and we have directed allocations for, an aggregate of approximately $26.3 million of shares of our common stock in this offering at the initial public offering price and on the same terms as the other purchasers in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these persons or entities as they will on any other shares sold to the public in this offering.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

Some of the underwriters and their affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

European Economic Area

In relation to each member state of the European Economic Area, no offer of ordinary shares which are the subject of the offering has been, or will be made to the public in that Member State, other than under the following exemptions under the Prospectus Directive:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the representatives for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of ordinary shares referred to in (a) to (c) above shall result in a requirement for the Company or any representative to publish a prospectus pursuant to Article 3 of the Prospectus Directive, or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person located in a Member State to whom any offer of ordinary shares is made or who receives any communication in respect of an offer of ordinary shares, or who initially acquires any ordinary shares will be deemed to have represented, warranted, acknowledged and agreed to and with each representative and the Company that (1) it is a "qualified investor" within the meaning of the law in that Member State implementing Article 2(1)(e) of the Prospectus Directive; and (2) in the case of any ordinary shares acquired by it as a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, the ordinary shares acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Member State other than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the representatives has been given to the offer or resale; or where ordinary shares have been acquired by it on behalf of persons in any Member State other than qualified investors, the offer of those ordinary shares to it is not treated under the Prospectus Directive as having been made to such persons.

The Company, the representatives and their respective affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgments and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly, any person making or intending to make an offer in that Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the Company or any of the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the Representatives have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the Company or the representatives to publish a prospectus for such offer.

For the purposes of this provision, the expression an "offer of ordinary shares to the public" in relation to any ordinary shares in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the ordinary shares to be offered so as to enable an investor to decide to purchase or subscribe the ordinary shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (as amended) and includes any relevant implementing measure in each Member State.

The above selling restriction is in addition to any other selling restrictions set out below.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "Order") and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Notice to Prospective Investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to Prospective Investors in the Dubai International Financial Centre

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or DFSA. This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for the prospectus. The shares to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus you should consult an authorized financial advisor.

Notice to Prospective Investors in Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission, or ASIC, in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the “Corporations Act”), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons (the “Exempt Investors”) who are “sophisticated investors” (within the meaning of section 708(8) of the Corporations Act), “professional investors” (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under Section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Notice to Prospective Investors in Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to Prospective Investors in Japan

The shares have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, "Japanese Person" shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, the shares were not offered or sold or caused to be made the subject of an invitation for subscription or purchase and will not be offered or sold or caused to be made the subject of an invitation for subscription or purchase, and this prospectus or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares, has not been circulated or distributed, nor will it be circulated or distributed, whether directly or indirectly, to any person in Singapore other than (i) to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time (the "SFA")) pursuant to Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

(a) to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(b) where no consideration is or will be given for the transfer;

(c) where the transfer is by operation of law; or

(d) as specified in Section 276(7) of the SFA.

Notice to Prospective Investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

LEGAL MATTERS

The validity of the issuance of our common stock offered in this prospectus will be passed upon for us by Orrick, Herrington & Sutcliffe LLP, 1000 Marsh Road, Menlo Park, California 94025. Latham & Watkins LLP, 140 Scott Drive, Menlo Park, California 94025, is acting as counsel for the underwriters in connection with this offering. Certain investment funds affiliated with Orrick, Herrington & Sutcliffe LLP own shares of our preferred stock which will be converted into an aggregate of 10,403 shares of common stock upon the closing of this offering.

EXPERTS

The financial statements as of December 31, 2018 and 2017 and for each of the two years in the period ended December 31, 2018 included in this prospectus have been so included in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, as stated in their report appearing elsewhere herein, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the Securities and Exchange Commission a registration statement on Form S-1 under the Securities Act with respect to this offering of our common stock. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement, some items of which are contained in exhibits to the registration statement as permitted by the rules and regulations of the Securities and Exchange Commission. For further information with respect to us and our common stock, we refer you to the registration statement, including the exhibits and the financial statements and notes filed as a part of the registration statement. Statements contained in this prospectus concerning the contents of any contract or any other document are not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, please see the copy of the contract or document that has been filed. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. The exhibits to the registration statement should be referenced for the complete contents of these contracts and documents.

Upon the closing of the offering, we will be subject to the informational requirements of the Exchange Act and will file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission. You can read our filings with the Securities and Exchange Commission, including the registration statement, at the Securities and Exchange Commission’s website at www.sec.gov. We also maintain a website at http://www.cortexyme.com. Upon the closing of the offering, you may access, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendment to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after such material is electronically filed with, or furnished to, the Securities and Exchange Commission. However, the information contained on or accessible through our website is not part of this prospectus or the registration statement of which this prospectus forms a part, and potential investors should not rely on such information in deciding to purchase our common stock in this offering.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Board of Directors and Stockholders
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, 2017 and 2018, the related statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' deficit, and cash flows for each of the two years in the period ended December 31, 2018, 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, 2017 and 2018, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2018**,** in conformity with accounting principles generally accepted in the United States of America.

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 4, 2019, except for the "Reverse Stock Split" paragraph of Note 2, as to which the date is April 29, 2019

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		Pro Forma December 31, 2018 (unaudited)
	2017	2018	
ASSETS			
Current assets:			
Cash and cash equivalents	$ 7,343	$ 24,872	$ 24,873
Short-term investments	—	46,844	46,844
Restricted cash	50	—	—
Prepaid expenses and other current assets	144	868	868
Total current assets	7,537	72,584	72,585
Property and equipment, net	122	283	283
Other assets	59	10	10
Total assets	$ 7,718	$ 72,877	$ 72,878
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT			
Current liabilities:			
Accounts payable	$ 517	$ 495	$ 495
Other accrued liabilities	688	962	962
Accrued interest payable	558	—	—
Total current liabilities	1,763	1,457	1,457
Convertible promissory notes — related parties, net of discount	4,686	—	—
Convertible promissory notes, net of discount	2,485	—	—
Derivative liability	1,886	—	—
Total liabilities	10,820	1,457	1,457
Commitments and contingencies (Note 6)			
Series A redeemable convertible preferred stock, par value $0.001, 9,008,931 shares authorized, 9,008,919 shares issued and outstanding as of December 31, 2017 and 2018, respectively; liquidation preference of $17,178 at December 31, 2017 and 2018, respectively; no shares issued and outstanding, pro forma (unaudited)	17,178	17,178	—
Series B redeemable convertible preferred stock, par value $0.001, 9,430,145 shares authorized, Nil and 9,152,108 shares issued and outstanding as of December 31, 2017 and 2018, respectively; liquidation preference of Nil and $87,972 at December 31, 2017 and 2018, respectively; no shares issued and outstanding, pro forma (unaudited)	—	86,868	—
Stockholders' equity (deficit):			
Common stock, $0.001 par value, 14,705,880 and 24,794,114 shares authorized, 3,361,016 and 3,412,366 issued and outstanding as of December 31, 2017 and 2018, respectively, 21,601,334 shares issued and outstanding, pro forma (unaudited)	3	3	22
Additional paid in capital	66	245	104,273
Accumulated other comprehensive loss	—	(49)	(49)
Accumulated deficit	(20,349)	(32,825)	(32,825)
Total stockholders' equity (deficit)	(20,280)	(32,626)	71,421
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 7,718	$ 72,877	$ 72,878

See accompanying notes to the financial statements

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

	Year ended December 31,	
	2017	2018
Operating expenses:		
Research and development	$ 9,099	$ 10,085
General and administrative	1,271	2,034
Total operating expenses	10,370	12,119
Loss from operations	(10,370)	(12,119)
Interest income	—	806
Interest expense	(1,643)	(957)
Change in fair value of derivative liability	(222)	(206)
Net loss	$ (12,235)	$ (12,476)
Other comprehensive loss, net of tax:		
Unrealized loss on available for sale securities	—	(49)
Comprehensive loss	$ (12,235)	$ (12,525)
Net loss per share - basic and diluted	$ (3.70)	$ (3.71)
Weighted-average shares of common stock outstanding — basic and diluted	3,302,979	3,362,192
Proforma net loss per-share basic and diluted (unaudited)		$ (0.58)
Pro forma weighted-average shares of common stock outstanding — basic and diluted (unaudited)		21,551,160

See accompanying notes to the financial statements

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

	Series A Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Common Stock		Additional Paid in Capital	Accumulated Deficit	Other Comprehensive Loss	Shareholders' Deficit
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at January 1, 2017	9,008,919	$17,178	—	$ —	3,361,016	$ 3	$ 27	$ (8,114)	$ —	$ (8,084)
Vesting of early exercise stock options	—	—	—	—	—	—	1	—	—	1
Stock based compensation	—	—	—	—	—	—	38	—	—	38
Net Loss	—	—	—	—	—	—	—	(12,235)	—	(12,235)
Balance at December 31, 2017	9,008,919	17,178	—	—	3,361,016	3	66	(20,349)	—	(20,280)
Issuance of Series B redeemable convertible preferred stock in exchange for cash, 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 at December 31, 2018	9,008,919	$17,178	9,152,108	$86,868	3,412,366	$ 3	$ 245	$ (32,825)	$ (49)	$ (32,626)

See accompanying notes to the financial statements

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

	Year Ended December 31, 2017	2018
Cash flows from operating activities:		
Net loss	$ (12,235)	$ (12,476)
Adjustments to reconcile net loss to net cash used in operating activities:		
Non-cash interest expense related to convertible promissory notes	558	263
Non-cash rent expense	—	153
Stock based compensation	38	155
Depreciation and amortization	45	51
Accretion of discount on convertible promissory notes payable	1,085	694
Amortization of discount on available-for-sale investments	—	(351)
Change in the fair value of derivative liability	222	206
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	37	(690)
Other assets	(18)	50
Accounts payable	223	(23)
Other accrued liabilities	218	273
Net cash used in operating activities	(9,827)	(11,695)
Cash flows from investing activities:		
Purchase of short-term investments	—	(55,242)
Proceeds from maturities of short-term investments	—	8,700
Purchases of property and equipment	(77)	(212)
Net cash used in investing activities	(77)	(46,754)
Cash flows from financing activities:		
Proceeds from issuance of convertible promissory notes	7,750	250
Proceeds from issuance of preferred stock, net of issuance costs	—	75,688
Proceeds from issuance of common stock upon exercise of stock options	—	24
Deferred initial public offering costs	—	(34)
Net cash provided by financing activities	7,750	75,928
Net increase / (decrease) in cash, cash equivalents and restricted cash	(2,154)	17,479
Cash, cash equivalents and restricted cash at beginning of period	9,547	7,393
Cash, cash equivalents and restricted cash at end of period	$ 7,393	$ 24,872
Cash paid in period for		
Income Taxes	$ 1	$ 1
Non-cash investing and financing activities:		
Issuance of Series B redeemable convertible stock for facility lease	—	1,100
Issuance of Series B redeemable convertible preferred stock in connection with conversion of convertible promissory notes and accrued interest	—	11,027

See accompanying notes to the financial statements

CORTEXYME, INC.
NOTES TO 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.

Liquidity and Capital Resources

The Company has incurred losses and negative cash flows from operations since inception and had an accumulated deficit of $32.8 million as of December 31, 2018. Since inception through December 31, 2018, the Company has funded operations primarily with the net proceeds of the convertible promissory notes and from the issuance of redeemable convertible preferred stock. The Company expects to incur substantial operating losses for the next several years and will need to obtain additional financing in order to launch and commercialize any drug candidates for which it receives regulatory approval. As of December 31, 2018, the Company had cash, cash equivalents, and short-term investments of $71.7 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 these financial statements. If the Company is not able to secure adequate additional funding, the Company may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, or suspend or curtail planned programs. Any of these actions could materially harm the Company's business, results of operations and future prospects. There can be no assurance that such financing will be available at all or at terms acceptable to the Company.

Note 2. Summary of Significant Accounting Policies

Basis of Presentation

The financial statements and accompanying notes have been prepared in accordance with generally accepted accounting principles in the United States of America ("U.S. GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented.

Use of Estimates

The preparation of the Company's financial statements in conformity with U.S. 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 and stock-based awards and other issuances, valuation of derivative instruments, accruals for research and development costs, useful lives of long-lived assets, and uncertain tax positions. 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.

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.

Unaudited Pro Forma Balance Sheet Information

The unaudited pro forma balance sheet information as of December 31, 2018 assumes the conversion of all outstanding shares of redeemable convertible preferred stock into 18,161,027 shares of the Company's common stock and the related reclassification of the carrying value of the redeemable convertible preferred stock to permanent equity and the exercise in full of an outstanding warrant to purchase 27,941 shares of common stock upon closing of the Company's planned initial public offering ("IPO"). Shares of common stock issued in the IPO and any related net proceeds are excluded from the pro forma information.

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 Short-Term 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. Short-term investments are investments in marketable securities with maturities of greater than three months at the time of purchase. Collectively, cash equivalents and short-term investments are considered available-for-sale and are recorded at fair value. Unrealized gains and losses are recorded in accumulated other comprehensive loss in the statements of redeemable convertible preferred stock and stockholders' 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.

Restricted Cash

Restricted cash at December 31, 2017, comprises cash balances primarily held as collateral in connection with the Company's use of bank issued credit cards. This collateral balance was no longer required in 2018.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the statement of financial position that sum to the total of the same such amounts shown in the statement of cash flows (in thousands):

	December 31,	
	2017	2018
Cash and cash equivalents	$7,343	$24,872
Restricted cash	50	—
Total cash, cash equivalents and restricted cash shown in the statement of cash flows	$7,393	$24,872

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 and short-term investments are financial instruments that potentially subject the Company to concentrations of credit risk. The Company invests in money market funds, treasury bills and notes, government bonds, commercial paper and corporate notes. The Company limits its credit risk associated with cash equivalents and short-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, 2017 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 will be reclassified to additional paid-in capital upon the closing of the IPO. No amounts were deferred as of December 31, 2017. The Company deferred $34,000 as of December 31, 2018, which is included in prepaid expense and other assets in the accompanying balance sheets. In the event the IPO is aborted, including postponement of 90 days or greater, all capitalized deferred offering costs will be expensed.

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. Expenses related to clinical studies are generally accrued based on time and materials incurred by the service providers and in accordance with the contracts. This process involves reviewing open contracts and purchase orders, communicating with applicable personnel to identify 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 accrued 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 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.

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 ASC 718, Compensation—Stock Compensation ("ASC 718"). 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. In June 2018, the FASB issued ASU 2018-07, Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting, which aligns accounting for share-based payments issued to

nonemployees to that of employees under the existing guidance of Topic 718, with certain exceptions. This update supersedes previous guidance for equity-based payments to nonemployees under Subtopic 505-50, Equity—Equity-Based Payments to Non-employees. The Company early adopted this ASU effective January 1, 2017. Non-employee stock-based compensation expense was $2,000 and $30,000 for the years ended December 31, 2017 and 2018, respectively.

Redeemable Convertible Preferred Stock

The Company records all shares of convertible preferred stock at their respective fair values less issuance costs on the dates of issuance. The convertible preferred stock is recorded outside of stockholders' 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 demand redemption of the stock. In the event of a change of control of the Company, proceeds received from the sale of such shares will be 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 have converted their shares of convertible preferred stock into shares of common stock. The Company has 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.

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.

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 2017 and 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 are 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 are outstanding. In May 2018, the convertible promissory notes including the redemption premium were converted into Series B redeemable convertible preferred stock. See Note 9 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 Loss

The Company is required to report all components of comprehensive loss, including net loss, in the financial statements in the period in which they are recognized. Comprehensive 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 loss from its available-for-sale securities during the year ended December 31, 2018, which is considered other comprehensive 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, 2017 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.

Emerging Growth Company Status

The Company is an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. The Company has elected to not use this extended transition period for complying with certain new or revised accounting standards that have different effective dates for public and private companies.

Recent Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board (FASB), or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise discussed, the impact of recently issued standards that are not yet effective will not have a material impact on the Company's financial statements upon adoption.

In February 2016, the FASB issued Accounting Standards Update ("Update" or "ASU") No. 2016-02, *Leases (Topic 842)* ("ASU 2016-02"), which supersedes ASC Topic 840, *Leases (Topic 840)* and provides principles for the recognition, measurement, presentation and disclosure of leases for both lessees and lessors. The FASB has continued to clarify this guidance through the issuance of additional ASUs. ASU 2016-02 requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease, respectively. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than twelve months regardless of classification. Entities may make an accounting policy election to not recognize lease assets and liabilities for leases with a term of 12 months or less. The standard is effective for the Company for annual reporting periods beginning after December 15, 2018 and for interim periods within those fiscal years. Early adoption is permitted for all entities. The Company is in the process of evaluating the impact of adoption of the ASU on its financial statements and currently believe the most significant change will be related to the recognition of lease liabilities and right-of-use assets on the balance sheet for real estate operating leases.

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 Company is currently evaluating the impact that the adoption of ASU 2017-11 will have on its financial statements.

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* ("ASU 2018-13"). The new guidance modifies the disclosure requirements in Topic 820 as follows:

- Removals: the amount of and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy; the policy for timing of transfers between levels; and the valuation processes for Level 3 fair value measurements.

- Modifications: for investments in certain entities that calculate net asset value, an entity is required to disclose the timing of liquidation of an investee's assets and the date when restrictions from redemption might lapse only if the investee has communicated the timing to the entity or announced the timing publicly; and the amendments clarify that the measurement uncertainty disclosure is to communicate information about the uncertainty in measurement as of the reporting date.

- Additions: the changes in unrealized gains and losses for the period included in other comprehensive income for recurring Level 3 fair value measurements held at the end of the reporting period; and the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements.

This guidance is effective for all entities for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. The amendments on changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and the narrative description of measurement uncertainty should all be applied prospectively for only the most recent interim or annual period presented in the initial year of adoption. All other amendments should be applied retrospectively to all periods presented upon their effective date. Early adoption is permitted. An entity is permitted to early adopt any removed or modified disclosures upon issuance of ASU 2018-13 and delay adoption of the additional disclosures until their effective date. The Company is currently evaluating the impact of the new guidance on its financial statements.

Recently Adopted Accounting Pronouncements

In May 2014, FASB issued ASU 2014-09, Revenue from Contracts with Customers (Topic 606), which will replace numerous requirements in U.S. GAAP, including industry-specific requirements, and provide companies with a single revenue recognition model for recognizing revenue from contracts with customers. The core principle of the new standard is that a company should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. On January 1, 2017, the Company early adopted the new accounting standard and all the related amendments. However, as the Company did not have any contracts with customers during 2017 or 2018, the adoption had no impact on the financial statements.

In November 2015, the FASB issued ASU No. 2015-17, *Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes* ("ASU 2015-17"). The standard requires that deferred tax assets and liabilities be classified as noncurrent on the balance sheet rather than being separated into current and noncurrent. ASU 2015-17 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2016. Early adoption is permitted, and the standard may be applied either retrospectively or on a prospective basis to all deferred tax assets and liabilities. Adoption of ASU 2015-17 did not have a material impact on the Company's financial position, results of operations and cash flows.

In January 2016, the FASB issued ASU No. 2016-01, "Financial Instruments - Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities" ("ASU 2016-01"). ASU 2016-01 requires equity investments (except those accounted for under the equity method or those that result in consolidation) to be measured at fair value with changes in fair value recognized in net income unless a policy election is made for investments without readily determinable fair values. Additionally, ASU 2016-01 requires public entities to use the exit price notion when measuring the fair value of financial instruments for measurement purposes and eliminates the requirement to disclose the method(s) and significant assumptions used to estimate the fair value of financial instruments measured at amortized cost on the balance sheet. Furthermore, it requires separate presentation of financial assets and financial liabilities by measurement category and form of financial asset on the balance sheet or the accompanying notes to the financial statements. ASU 2016-01 is effective for interim and annual periods beginning after December 15, 2017. Adoption of ASU 2016-01 did not have a material impact on the Company's financial position, results of operations and cash flows.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation – Stock Compensation (Topic 718)*: Improvements to Employee Share-Based Payment Accounting ("ASU 2016-09"). ASU 2016-09 requires, among other things, that excess tax benefits and tax deficiencies be recognized as income tax expense or benefit in the statement of operations rather than as additional paid-in capital, changes the classification of excess tax benefits from a financing activity to an operating activity in the statement of cash flows, and allows forfeitures to be accounted for when they occur rather than estimated. ASU 2016-09 became effective for the Company on January 1, 2017. Adoption of ASU 2016-09 did not have a material impact on the Company's financial position, results of operations and cash flows.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments* ("ASU 2016-15"), to address diversity in practice in how certain cash receipts and cash payments are presented and classified in the statement of cash flows. For public entities, the standard is effective for annual periods beginning after December 15, 2017, including interim periods within those fiscal years. The adoption of ASU 2016-15 did not have a material impact on the Company's financial position, results of operations and cash flows.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230)* ("ASU 2016-18"), which was intended to reduce diversity in practice in the classification and presentation of changes in restricted cash on the Statement of Cash Flows. ASU 2016-18 requires that the Statement of Cash Flows explain the change in total cash and equivalents and amounts generally described as restricted cash or restricted cash equivalents when reconciling the beginning-of-period and end-of-period total amounts. The standard also requires reconciliation between the total cash and cash equivalents and restricted cash presented on the Statement of Cash Flows and the cash and cash equivalents balance presented on the Balance Sheet. For public entities, ASU 2016-18 is effective for fiscal years beginning after December 15, 2017 and interim periods within those fiscal years and early adoption is permitted. The Company adopted the standard which resulted in 2017 restricted cash of $50 included in the reconciliation within the Statements of Cash Flows.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting* ("ASU 2017-09"), which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. The standard is effective for annual periods beginning after December 15, 2017, including interim periods within those fiscal years. Early adoption is permitted. The adoption of ASU 2017-09 did not have an impact on the Company's financial position, results of operations or cash flows.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation – Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07"), to align the accounting for share-based payment awards issued to employees and nonemployees, particularly with regard to the measurement date and the impact of performance conditions. The new guidance requires equity-classified share-based payment awards issued to nonemployees to be measured on the grant date, instead of being remeasured through the performance completion date under the current guidance. For public entities, ASU 2018-07 is effective for fiscal years beginning after December 15, 2018. This update supersedes previous guidance for equity-based payments to nonemployees under Subtopic 505-50, Equity—Equity-Based Payments to Non-Employees. The Company chose to early adopt ASU 2018-07 effective for its financial statements starting January 1, 2017 and the cumulative adjustment upon adoption was immaterial.

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. The fair value of convertible promissory notes was approximately $9.7 million as of December 31, 2017 due to the redemption premium on debt conversion feature.

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, 2017 and 2018.

A summary of the assets and liabilities carried at fair value in accordance with the hierarchy defined above is as follows (in thousands):

	Fair Value Measurements at December 31, 2017			
	Total	Level 1	Level 2	Level 3
Liabilities:				
Derivative liability	$ 1,886	$ —	$ —	$ 1,886
Total Liabilities	$ 1,886	$ —	$ —	$ 1,886

	Fair Value Measurements at December 31, 2018			
	Total	Level 1	Level 2	Level 3
Assets:				
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 assets	$ 60,457	$ 11,815	$ 48,642	$ —

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

	December 31, 2017	December 31, 2018
Fair value at beginning of period	$ —	$ 1,886
Bifurcated derivative liability	1,664	113
Change in fair value	222	206
Conversion of promissory notes to Series B redeemable convertible preferred stock	—	(2,205)
Fair value at end of period	$1,886	$ —

Note 4. Cash, cash equivalents and short-term 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, 2017	December 31, 2018
Cash and cash equivalents		
Cash	$ 7,343	$ 11,259
Money market funds	—	11,815
Commercial Paper	—	1,798
Total cash and cash equivalents	**$ 7,343**	**$ 24,872**
Short-term investments		
Commercial paper	—	12,562
Corporate notes	—	16,111
Government notes	—	8,979
Asset backed securities	—	9,192
Total short-term investments	**$ —**	**$ 46,844**

The investments are classified as available-for-sale securities. At December 31, 2018 the balance in the Company's accumulated other comprehensive income 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, 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, 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, 2018			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Assets:				
Money market funds	$ 11,815	$ —	$ —	$ 11,815
Commercial paper	14,362	—	(2)	14,360
Corporate notes	16,129	—	(18)	16,111
Government notes	8,980	—	(1)	8,979
Asset backed securities	9,220	—	(28)	9,192
Total assets	$ 60,506	$ —	$ (49)	$ 60,457

	December 31, 2018
Classified as (with contractual maturities):	
Cash equivalents (due within 90 days)	$ 13,613
Short-term investments (due within one year)	46,844
	$ 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,	
	2017	2018
Prepaid expenses	$ 51	$ 47
Prepaid research and development expenses	90	753
Other assets	3	68
	$144	$868

Property and equipment, net

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

	December 31,	
	2017	2018
Lab Equipment	$166	$378
Less: accumulated depreciation	(44)	(95)
Property and equipment, net	$122	$283

Depreciation expense was $45,000 and $51,000 for the years ended December 31, 2017 and 2018, respectively.

Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31,	
	2017	2018
Personnel expenses	$312	$483
Research and development expenses	314	380
Professional fees	56	75
Other	6	24
	$688	$962

Note 6. 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.

Leases

In June 2018, the Company entered into a three-year lease agreement 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 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.

100% of the issued shares were initially subject to a repurchase option. 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 3 years. The scheduled release of shares will cease immediately on the occurrence of a termination event.

In the event of a termination of the lease for any reason other than (i) a material, uncured default of the tenant or (ii) the voluntary or involuntary liquidation, dissolution or winding up of the tenant, the Company has an irrevocable exclusive option for a period of three months from the termination to repurchase any unvested shares. In the event of (i) or (ii) above or an acquisition or initial public offering of the tenant, any unvested shares will fully and immediately vest, and any repurchase option will lapse in respect to any unvested shares.

The Company recognizes rent expense on a straight line basis. As of December 31, 2018, 98,543 unvested shares were subject to the repurchase option representing $947,000 of future rent expense to be recognized over the remaining term of 31 months on a straight-line basis over the respective lease period. Rent expense incurred for the years ended December 31, 2017 and 2018 was $335,000 and $387,000, respectively.

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, 2018

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 7. Redeemable Convertible Preferred Stock and Stockholders' Deficit

The Company's Certificate of Incorporation, as amended and restated, authorizes the Company to issue 24,794,114 shares, of $0.001 par value common stock. 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 all classes of redeemable preferred stock outstanding. The Company has never declared any dividends on common stock. As of December 31, 2017 and 2018, the Company had reserved common stock, on an if-converted basis, for issuance as follows:

	December 31,	
	2017	2018
Redeemable convertible preferred stock	9,008,919	18,161,027
Common stock options issued and outstanding	769,409	1,885,504
Common stock warrants	27,941	27,941
Shares available for issuance under 2014 Stock Plan	138,272	984,680
Total	9,944,541	21,059,152

As of December 31, 2017, 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

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

Significant terms of the Series A and B redeemable convertible preferred stock as of December 31, 2018 (collectively, the "Preferred Stock") are as follows:

Dividends

The holders of Preferred Stock are entitled to receive non-cumulative dividends prior and in preference to any declaration or payment of dividends on common stock, when and if declared by the Board of Directors, at the rate of $0.15259 for Series A and $0.7692 per share for Series B, as adjusted for stock splits, dividends, reclassifications or the like, per annum. After payment of the above dividends to holders of Preferred Stock, any additional dividends will be distributed pro rata amongst the holders of the Preferred Stock and Common Stock on an as-if converted to common stock basis. No dividends have been declared or paid as of December 31, 2018.

Voting

The holders of the Preferred Stock are entitled to voting rights equal to the number of shares of common stock into which each share of the Preferred Stock could be converted. The holders of the Preferred Stock, voting as a separate class, are entitled to elect two members of the Board of Directors. The holders of Common Stock, voting as a separate class, are entitled to elect two members of the Board of Directors. The remaining member of the Board of Directors will be elected by the holders of the Preferred Stock and Common Stock, voting together as a single class and on an as-converted basis.

Liquidation

In the event of any liquidation, dissolution, or winding up of the Company, either voluntary or involuntary, the holders of the Preferred Stock shall be entitled to receive on a pari passu basis and in preference to any distribution to the common shareholders, the greater of their stated liquidation preference or the amount such holders would have received had they converted their preferred stock into common stock immediately prior to such dissolution. For each series of Preferred Stock, the stated liquidation preference per share is equal to $1.9067 and $9.6122 per share, respectively, plus any declared but unpaid dividends. Any remaining assets shall be distributed among the holders of common stock pro rata, based on the number of shares of common stock held by each.

Conversion

Each share of Preferred Stock is convertible, at the option of the holder, into the number of shares of common stock that result from dividing the applicable original share price per share by the applicable conversion price per share at the time of conversion, as adjusted for stock splits, stock dividends, reclassification and the like. At December 31, 2017 and 2018, the conversion price equaled the original share price. Each share of Preferred Stock shall automatically convert upon the earlier of (i) a vote of at least 60% of the then-outstanding shares of Preferred Stock or, (ii) a public offering of the Company's common stock which results in gross proceeds of at least $40.0 million.

At December 31, 2018, the conversion price for each share of Series A and Series B is $1.9067 and $9.6122, respectively.

Redemption

At any time after May 23, 2025, and within sixty days of receipt by the Company of a written request of from the holders of 60% of the then outstanding shares of Series A and Series B voting as a single class, the Company will redeem all shares of Series A and Series B in three annual installments. The redemption price for each share of Series A and Series B will be $1.9067 and $9.6122, respectively, plus all declared but unpaid dividends.

Protection Provisions

The holders of the Preferred Stock have certain protective provisions. As long as at least 2,000,000 shares of the Preferred Stock remain outstanding, the Company cannot, without the approval of at least 60% of the holders of shares of the Preferred Stock then outstanding, take any action that: (i) consummates a liquidation, dissolution or winding up of the Company; (ii) amends, alters or repeals any provision of the Certificate of Incorporation or Bylaws of the Company; (iii) creates or authorizes any capital stock having the rights, preferences or privileges senior or on a parity with the Preferred Stock; (iv) reclassifies, amends or alters any existing securities of the Company to have the rights, preferences or privileges senior or on a parity with the Preferred Stock; (v) results in redemption, repurchase, payment or declaration of dividends or other distributions with respect to shares of Preferred Stock or common stock other than permitted repurchases and dividends; (vi) results in the Company incurring indebtedness of more than $250,000; (vii) increases or decreases the authorized number of shares of Preferred Stock; (viii) amends or adopts any equity compensation plans, unless previously approved by the Board of Directors; (ix) increases or decreases the members of the Board of Directors; or (x) results in holding capital stock in a subsidiary that is not wholly-owned by the Company or otherwise results in the sale of capital stock of a subsidiary of the Company.

Common Stock

The Company is authorized to issue 24,794,114 shares of common stock with a par value of $0.001 per share. As of December 31, 2017, and 2018, the Company had 3,361,016 and 3,412,366 shares issued and outstanding respectively.

The Company has issued restricted common stock to founders and certain employees of the Company that is subject to vesting as determined by the Board of Directors. These common stock holders entered into stock purchase agreements with the Company, which allow the Company to repurchase the shares of common stock from those holders at the original issuance price, if the holders cease to provide services to the Company. The Company's right to repurchase the common stock generally lapses over a period of 48 months. Any shares subject to repurchase by the Company are not deemed, for accounting purposes, to be outstanding until those shares vest. At December 31, 2017, and 2018, 1,102 and 0 shares of common stock were subject to repurchase at $0.001 per share, respectively. The Company recognizes the measurement date fair value of the restricted stock over the vesting period as compensation expense.

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 classified as equity and remains outstanding at December 31, 2018.

Note 8. Stock Option Plan

In 2014, the Company adopted the 2014 Stock Plan (the 2014 Plan) under which 2,973,736 shares of the Company's common stock have been reserved for issuance to employees, directors and consultants.
Under the 2014 Plan, the Board of Directors may grant incentive stock options or non-statutory stock options. Incentive stock options may only be granted to Company employees. The exercise price of incentive stock options and non- statutory stock options will be no less than 100% of the fair value per share of the Company's common stock on the grant date. If an individual owns capital stock representing more than 10% of the outstanding shares, the price of each share will be at 110% of the fair value. Fair value is determined by the Board of Directors. Options expire after ten years (five years for stockholders owning greater than 10% of all classes of stock). For options that have been exercised prior to vesting, the Company has a repurchase option exercisable upon the voluntary or involuntary termination of the purchaser's employment with the Company for any reason.

In 2017 and 2018, the Company recognized $38,000 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, 2018 is $1.57 million to be recognized over a remaining weighted average requisite service period of 3.7 years.

Stock option activity under the 2014 Plan is as follows:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (Years)	Aggregate Intrinsic Value
Balance at December 31, 2016	**594,445**	$ 0.37	—	1,107,581
Options granted	202,537	0.44	—	—
Options exercised	—	—	—	—
Options cancelled	(27,573)	0.40	—	—
Balance at December 31, 2017	**769,409**	0.39	8.89	1,418,954
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 vested and expected to vest to December 31, 2018	1,885,504	$ 1.57	9.07	$1,252,496
Options exercisable at December 31, 2018	439,004	$ 0.57	8.02	$ 730,331

Aggregate intrinsic value represents the difference between the Company's estimated fair value of its common stock and the exercise price of outstanding options. The total intrinsic value of options exercised was $91,000 for the year ended December 31, 2018. During the year ended December 31, 2018, the weighted-average grant-date fair value of the options vested was $0.54 per share. The weighted-average grant date fair value of options granted during the years ended December 31, 2017 and 2018 was $0.44 and $2.08 per share, respectively.

The following table summarizes employee and non-employee stock-based compensation expense for the years ended December 31, 2017 and 2018 and also the allocation within the statements of operations and comprehensive loss (in thousands):

	2017	2018
General and administrative expense	$ 6	$ 78
Research and development expense	32	77
	$38	$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, 2017 and 2018.

	2017	2018
Fair value of common stock	0.163	0.766
Expected volatility	63.0%	69.6%
Expected Dividends	—	—
Expected Term (in years)	6.25	6.25
Risk Free Interest Rate	1.87%	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. Because there has been no public market for the Company's common stock, the board of directors has 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. The board of directors intended 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, 2017 and 2018, there was a total of $117,000 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 $37,000 and $102,000.

Note 9. 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 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.

As of December 31, 2017, the estimated fair value of the embedded derivatives was determined assuming a probability of 90% that a qualified financing would occur and a zero probability that a change in control would occur. As a result, the Company increased the fair value of the embedded derivative liability to $1.9 million and recorded a change in fair value of derivative liability of $222,000.

The following table summarizes convertible promissory notes as of December 31, 2017 and 2018 (in thousands):

	December 31, 2017	2018
Convertible notes payable, due on February 1, 2019 interest at 8.0% per annum	$7,750	$—
Less: unamortized debt discount	(579)	—
Derivative liability at fair value	1,886	—
Total convertible notes payable, net of discount	$9,057	$—

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.

Note 10. 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. There are no amounts payable to the stockholder as at December 31, 2018.

As described more fully 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 leased facility. During 2018, 15,893 shares vested under the agreement.

Under the terms of the convertible promissory notes described in Note 9, 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.

Note 11. Income taxes

From inception through 2018, 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, 2018 and 2017.

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, 2017	2018
Federal statutory income tax rate	35.00%	21.00%
State income taxes	4.85%	6.24%
Non-deductible expenses and others	(0.47)%	(1.02)%
Non-deductible expenses related to the convertible promissory notes	(5.33)%	(1.96)%
Change in valuation allowance	(16.05)%	(24.26)%
Remeasurement of federal tax-rate change	(18.00)%	—
	— %	— %

As of December 31, 2017 and 2018, the components of the Company's deferred tax assets are as follows (in thousands):

	Year ended December 31, 2017	2018
Deferred tax asset:		
Federal and State net operating loss carryforwards	$ 4,845	$ 8,010
Total deferred tax asset	4,845	8,010
Deferred tax liabilities:		
Property and equipment	(14)	(70)
Less valuation allowance	(4,831)	(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 consolidated balance sheets. The valuation allowance increased by approximately $1.9 million and $3.1 million respectively for the years ended December 31, 2017 and 2018.

At December 31, 2018, the Company has net operating loss carryforwards for federal income tax purposes of approximately $28.2 million that begin to expire in 2034, and federal research tax credits of approximately $0.4 million that begin to expire in 2036. The Company also has state net operating loss carryforwards of approximately $29.8 million that begin to expire in 2034. 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.

On December 22, 2017, the U.S. government enacted a comprehensive tax reform legislation, commonly referred to as the Tax Cuts and Jobs Act (the "Tax Reform Act"). The Tax Reform Act makes broad and complex changes to the US tax code including but not limited to, (1) reducing the U.S. federal corporate tax rate from 35% to 21%; (2) requiring companies to pay a one-time transition tax on certain repatriated earnings of foreign subsidiaries, which has no impact to the Company; (3) generally eliminating US federal income taxes on dividends from foreign subsidiaries; (4) requiring a current inclusion in US federal income of certain earnings of controlled foreign corporations; (5) creating a new limitation on deductible interest expense; and (6) changing rules related to the uses and limitations of net operating loss carryforwards created in tax years beginning after December 31, 2017.

Reduction of U.S. federal corporate tax rate - The Tax Reform Act reduces the corporate tax rate to 21 percent, effective January 1, 2018. Consequently, the Company accounted for the reduction of $2.2 million of deferred tax assets with an offsetting adjustment to the valuation allowance for the year ended December 31, 2017.

Uncertain Tax Positions

The Company follows the provisions of the FASB Accounting Standards Codification (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 consolidated 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 2018, remain open to U.S. federal and California state tax examinations. There were no interest or penalties accrued at December 31, 2017 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,	
	2017	2018
Beginning balance	$ —	$ 171
Additions for tax positions taken in a prior year	62	—
Additions for tax positions taken in a current year	109	185
Ending balance	$ 171	$ 356

Note 12. 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,	
	2017	2018
Numerator:		
Net loss	$ (12,235)	$ (12,476)
Denominator		
Weighted average common shares outstanding	3,302,979	3,362,192
Net loss per share, basic and diluted	$ (3.70)	$ (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,	
	2017	2018
Series A convertible preferred stock	9,008,919	9,008,919
Series B convertible preferred stock	—	9,152,108
Options issued and outstanding	769,409	1,885,504
Warrants	27,941	27,941
	9,806,269	20,074,472

Unaudited Pro Forma Basic and Diluted Net Loss Per Share

The unaudited pro forma basic and diluted loss per share for the year ended December 31, 2018 gives effect to the conversion of all shares of convertible preferred stock upon the closing of the planned IPO by treating all shares of convertible preferred stock as if they had been converted to common stock at the beginning of the earliest period presented, or the date of the original issuance, if later. Shares to be sold in the planned IPO are excluded from the unaudited pro forma basic and diluted net loss per share calculation (in thousands except for share and per share amounts):

	December 31, 2018
Numerator:	
Net loss and proforma net loss	$ (12,476)
Denominator	
Shares used to compute net loss per share, basic and diluted	3,362,192
Pro forma adjustments to reflect assumed effect of conversion of convertible preferred stock	18,188,968
Shares used to compute pro forma net loss per share, basic and diluted	21,551,160
Pro forma net loss per share, basic and diluted	$ (0.58)

Note 13. 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, 2017 and 2018.

Note 14. Subsequent Events

The Company has completed an evaluation of all subsequent events through March 4, 2019 to ensure that these financial statements include appropriate disclosure of events both recognized in the financial statements and events which occurred but were not recognized in the financial statements. The Company has concluded that no subsequent event has occurred that requires disclosure.

4,412,000 Shares

Common Stock

PROSPECTUS

BofA Merrill Lynch

Credit Suisse

Canaccord Genuity

JMP Securities

May 8, 2019

Through and including June 2, 2019 (the 25th day after the date of this prospectus), all dealers effecting transactions in the common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to any unsold allotment or subscription.