UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-K

(Mark One)

☑ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the Fiscal Year Ended December 31, 2018
or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from _____ to _____

Commission File Number: 000-29959

Cassava Sciences, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**91-1911336**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification Number)*

7801 N. Capital of Texas Highway, Suite 260, Austin, TX 78731
(512) 501-2444
(Address, including zip code, of registrant's principal executive offices and telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act: Common Stock, $0.001 par value

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

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

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

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates was $11,955,662 computed by reference to the last sales price of $2.06 as reported on the Nasdaq Capital Market, as of the last business day of the Registrant's most recently completed second fiscal quarter, June 30, 2018. The number of shares outstanding of the Registrant's common stock on March 22, 2019 was 17,219,300.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement for its 2019 Annual Meeting of Stockholders (the "Proxy Statement"), to be filed with the Securities and Exchange Commission, are incorporated by reference to Part III of this Form 10-K Report.

CASSAVA SCIENCES, INC.

FORM 10-K
INDEX

PART I

This annual report contains certain statements that are considered forward-looking statements within the meaning of the Private Securities Reform Act of 1995. We intend that such statements be protected by the safe harbor created thereby. Forward-looking statements relate to expectations, beliefs, projections, future plans and strategies, anticipated events or trends and similar expressions concerning matters that are not historical facts. In some cases, you can identify forward-looking statements by terms such as "anticipate," "believe," "could," "estimate," "expect," "intend," "may," "plan," "potential," "should," "will" and "would" or the negatives of these terms or other comparable terminology.

The forward-looking statements are based on our beliefs, assumptions and expectations of our future performance, taking into account all information currently available to us. Forward-looking statements involve risks and uncertainties and our actual results and the timing of events may differ significantly from the results discussed in the forward-looking statements. Examples of such forward-looking statements include, but are not limited to statements about

- Our ability to initiate, conduct or complete clinical studies with PTI-125 or PTI-125Dx, our product candidates targeted at Alzheimer's disease and other neurodegenerative diseases, including our anticipated timeline for initiating a Phase IIb study of PTI-125;
- any potential benefits of our product candidates, such as PTI-125 or PTI-125Dx, including the potential ability of PTI-125 to prevent or reverse amyloid-related damage or PTI-125Dx to diagnose Alzheimer's disease;
- discussions with potential strategic partners for the development and commercialization of our product candidates;
- the utility of protection, or the sufficiency, of our intellectual property;
- potential competitors or competitive products;
- expected future sources of revenue and capital and increasing cash needs;
- market acceptance of our potential product candidates;
- expectations regarding trade secrets, technological innovations, licensing agreements and outsourcing of certain business functions;
- expenses increasing or fluctuations in our financial or operating results;
- operating losses and anticipated operating and capital expenditures;
- expectations regarding the issuance of shares of common stock to employees pursuant to equity compensation awards, net of employment taxes;
- our ability to maintain compliance with the ongoing listing requirements for the Nasdaq Capital Market;
- anticipated hiring and development of our internal systems and infrastructure;
- the sufficiency of our current resources to fund our operations over the next 12 months; and
- assumptions and estimates used for our disclosures regarding stock-based compensation.

Such forward-looking statements and our business are subject to numerous risks and uncertainties that you should consider before investing in our Company. These risks are described more fully in the section titled "Risk Factors." These risks include, but are not limited to, the following:

- We are in the early stages of clinical drug development and have a limited operating history in our business targeting Alzheimer's disease and no products approved for commercial sale.
- We have incurred significant net losses in each period since our inception and anticipate that we will continue to incur net losses for the foreseeable future.
- Development of biopharmaceutical products is a highly uncertain undertaking and involves a substantial degree of risk.
- We will need to obtain substantial additional financing to complete the development and any commercialization of our product candidates.
- Research and development of biopharmaceutical products is inherently risky. Our business is heavily dependent on the successful development of our product candidates.
- We may not be successful in our efforts to continue to develop product candidates or to develop commercially successful products.
- We may not be successful in our efforts to expand indications for product candidates.
- We are concentrating a substantial portion of our research and development efforts on the diagnosis and treatment of Alzheimer's disease, an area of research that has recorded many clinical failures.
- We may encounter substantial delays in our clinical trials or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.
- Our clinical trials may fail to demonstrate evidence of the safety and efficacy of our product candidates, which would prevent, delay, or limit the scope of regulatory approval and the commercialization of our product candidates.
- We may be unable to protect our intellectual property rights or trade secrets.
- We may be subject to third-party claims of intellectual property infringement.
- We may not succeed in our maintenance or pursuit of licensing rights or third-party intellectual property necessary for the development of our product candidates.
- Enacted or future legislation or regulatory actions may adversely affect our product pricing, or limit the reimbursement we may receive for our products.
- A significant breakdown, security breach or interruption affecting our internal computer systems, or those used by our third-party research collaborators, may compromise the confidentiality of our financial or proprietary information, result in material disruptions of our products and operations and adversely affect our reputation.
- We may be unsuccessful at hiring and retaining qualified personnel.
- We may not be successful in transitioning our business operations from our prior focus on analgesic drug development to a new focus on drug development for neurodegeneration, such as Alzheimer's disease.

We cannot assure you that we will realize the results or developments we expect or anticipate or, even if substantially realized, that they will result in the consequences or affect us or our operations in the way we expect. The forward-looking

statements included in this Annual Report on Form 10-K are made only as of the date hereof. We undertake no obligation to publicly update or revise any forward-looking statement as a result of new information, future events or otherwise, except as otherwise required by law.

All information in this Annual Report on Form 10-K has been retroactively adjusted to reflect the ratio of a 7-for-1 reverse stock split that took effect on May 10, 2017, except as otherwise described or as required by law.

Item 1. *Business*

Overview

Cassava Sciences, Inc. is a clinical-stage drug development company. Our expertise is to develop new product candidates and to guide these through various regulatory and development pathways in preparation for their potential commercialization. Since our inception, we have generally focused our drug development efforts on disorders of the central nervous system. We are currently conducting a Phase II clinical program for patients with Alzheimer's disease. By necessity, the conduct of drug development is complex, lengthy, expensive and risky. The U.S. Food and Drug Administration (the "FDA") has not yet established the safety or efficacy of our product candidates.

Our overall strategy is to leverage our unique scientific/clinical platform to develop a first-in-class program for neurodegeneration. Our goal is to address Alzheimer's disease and other neurodegenerative diseases, particularly those with a strong neuroinflammation component, with PTI-125, our drug product candidate and a diagnostic product candidate, PTI-125Dx, to detect Alzheimer's disease.

We seek to develop and gain regulatory approval for PTI-125 for the treatment of Alzheimer's disease and PTI-125Dx for the diagnosis of Alzheimer's disease. The following is a summary of our clinical-stage biopharmaceutical assets:

PTI-125 – PTI-125 is the name of our product candidate for the treatment of Alzheimer's disease. This proprietary small molecule drug represents an entirely new target to treat Alzheimer's disease. PTI-125 benefits from a strong scientific rationale, peer-reviewed publications in prestigious academic journals and multiple peer-reviewed research grant awards from the National Institutes of Health ("NIH"), the primary agency of the U.S. government for biomedical research.

In 2018, we initiated a Phase II clinical program in patients with Alzheimer's disease using PTI-125. Our Phase II clinical program with PTI-125 is substantially funded by research grant awards from the NIH. PTI-125 was discovered and designed in-house and was characterized by our academic collaborators during research activities that were conducted from approximately 2008 to date. We own exclusive, worldwide rights to PTI-125, without royalty obligations to any third party.

PTI-125Dx – We are developing PTI-125Dx as a blood-based biomarker/diagnostic to detect Alzheimer's disease. The goal of PTI-125Dx is to make the detection of Alzheimer's disease as simple as getting a blood test. This clinical-stage program is substantially funded by research grant awards from the NIH. PTI-125Dx was discovered and designed in-house and was characterized by our academic collaborators during research activities that were conducted from approximately 2008 to date. We own exclusive, worldwide rights to PTI-125Dx, without royalty obligations to any third party.

Our scientific approach is different.

For over 100 years, scientists have ascribed various neurodegenerative diseases to pathological proteins that misfold. Misfolded proteins are also altered or they aggregate, such as amyloid and tau in the case of Alzheimer's disease. Destruction of neuronal synapses, accelerated nerve cell death, and dysfunction of the brain support cells, are all widely believed to be a direct consequence of misfolded proteins.

Historically, the drug industry has attempted to treat Alzheimer's disease by developing drugs that block the synthesis of, or remove or dis-aggregate, beta amyloid and, more recently, tau. Essentially, the prevailing doctrine said that amyloid must be cleared out of the brain. This scientific approach – known as the amyloid hypothesis - has been repeatedly tested by our competitors in late stage clinical trials using a variety of antibody backbones, epitopes, target conformations, biomarkers and in various stages of disease. Such studies have all failed to yield therapeutic benefit for patients with Alzheimer's disease. More recently, experimental efforts have been proposed to ramp up the brain's immune system in people with Alzheimer's disease to remove amyloid or tau, an approach known as immunotherapy. Current attempts to use immunotherapy to treat

Alzheimer's disease may yet work, but for over 20 years this approach has also consistently failed due to lack of efficacy and/or for safety reasons. For example, older adults who receive active immunotherapy treatment often show reduced responsiveness of the immune system, and patients who do improve sometimes develop a life-threatening brain inflammation called aseptic meningitis. More generally, even when active or passive immunization against amyloid beta has reduced the brain's amyloid load, such effects resulted in no therapeutic benefit to patients with Alzheimer's disease.

Since drug innovation is a trial-and-error process, clinical failures represent important learning opportunities. In the case of Alzheimer's disease, we believe the biopharmaceutical industry's track record of persistent failure reflects a need to consider more recent and innovative approaches regarding the neurobiology of Alzheimer's disease. We believe such scientific approaches may broaden the range of possible treatment approaches.

Over the last ten years, we have developed a new and promising scientific approach for the treatment and diagnosis of neurodegeneration, particularly Alzheimer's disease.

Importantly, we do not seek to clear amyloid out of the brain. Our approach is to stabilize a critical protein in the brain.

"Proteopathy" refers to a disease in which a protein becomes structurally abnormal, assembles and aggregates, and therefore loses its normal function and disrupts or injures the function of surrounding cells, tissues and organs. Through years of basic research, we have identified a structurally altered protein in the brain. We believe our experimental evidence demonstrates that this proteopathy plays a critical role in the development of neurodegenerative diseases, including the neurodegeneration observed in Alzheimer's disease. Using scientific insight and advanced tools in biochemistry, bioinformatics and imaging, we have elucidated this protein dysfunction. We have engineered a family of high-affinity small molecules to target the structurally altered protein and restore the protein to its normal shape and function. This family of small molecules, including PTI-125, was designed in-house and characterized by our academic collaborators.

The target of PTI-125 is an altered form of a scaffolding protein called filamin A ("FLNA"). Altered FLNA causes a cascade of toxic effects in the brain. Altered FLNA is a proteopathy, which means that this protein is no longer capable of executing a stable, beneficial and protective role and instead becomes harmful and destructive to the brain. By reversing the alteration of FLNA, its pathology ceases to adversely affect surrounding cells in the brain. In animal models of disease, restoring normal FLNA resulted in a multitude of therapeutic effects, including normalizing neurotransmission, decreasing neuroinflammation and restoring memory and cognition. By restoring function to multiple receptors and exerting powerful anti-inflammatory effects, we believe our approach has potential to slow the progression of neurodegeneration in humans. Thus, we have designed product candidates, such as PTI-125, with the goal of slowing or, potentially, even reversing the deterioration of brain cells. We believe the ability to simultaneously improve many vital functions in the brain represents a new, different and crucial approach to address neurodegeneration.

Importantly, since PTI-125 has a unique mechanism of action, we believe its potential therapeutic effects may be additive or synergistic with that of other therapeutic candidates aimed at the treatment of neurodegeneration.

Our mission is to detect and treat Alzheimer's disease.

Our lead therapeutic product candidate, called PTI-125, is initially aimed at Alzheimer's disease. PTI-125 is a small molecule drug with a novel mechanism of action. This drug candidate has demonstrated both cognitive improvement and slowing of disease progression in animal models of disease. PTI-125 is in Phase II clinical stage of development, with substantial support from the *National Institute on Aging* ("NIA"), a division of the NIH.

The target of PTI-125 is an altered form of filamin A ("FLNA"). FLNA is a scaffold protein that is widely found throughout the body. The function of a scaffold protein is to bring multiple other proteins together for them to interact. However, an altered, and highly toxic, form of FLNA is found in the Alzheimer's brain. Altered FLNA contributes to Alzheimer's disease by disrupting the normal function of neurons, leading to neurodegeneration and brain inflammation. Our product candidate, PTI-125, is aimed at countering the altered and toxic form of FLNA in the brain, thus restoring the normal function of this critical protein.

PTI-125 binds to altered FLNA with very high affinity. In doing so, PTI-125 restores the normal shape of FLNA and the normal function of three brain receptors: the alpha-7 nicotinic acetylcholine receptor; the N-methyl-D-aspartate ("NMDA") receptor; and the insulin receptor. These receptors have pivotal roles in brain cell survival, cognition and memory. In animal

models, treatment with PTI-125 resulted in dramatic improvements in brain health, such as reduced amyloid and tau deposits, improved insulin receptor signaling and improved learning and memory. In addition, PTI-125 has another beneficial treatment effect of significantly reducing inflammatory cytokines in the brain. In animal models of disease, treatment with PTI-125 abolished IL-6 production and suppressed TNF-alpha and IL-1beta levels by 86% and 80%, respectively, illustrating a powerful anti-neuroinflammatory effect.

Our science is published in peer-reviewed academic journals. In addition, our research has been supported by the NIH under multiple research grant awards. Each grant was awarded following an in-depth, competitive, peer-reviewed evaluation of our approach for scientific and technical merit by a panel of outside experts in the field. Strong, long-term support from the NIH has allowed us to advance our two product candidates for neurodegeneration, PTI-125 and PTI-125Dx, into clinical development.

Overview of Alzheimer's disease.

Alzheimer's disease is a progressive neurodegenerative disorder that affects cognition, function and behavior. Most cases of Alzheimer's disease are age-related. Alzheimer's disease has become markedly more common with the aging of the U.S. population. Over 44 million individuals worldwide suffered from dementia in 2014, and approximately 34 million individuals are affected by Alzheimer's disease, according to *Alzheimer's Disease International*. The prevalence of Alzheimer's disease is widely expected to increase over time, with 13.8 million people age 65 and older projected to have the disease by 2050 in the U.S., up from 5.6 million in 2019. This projection does not include Alzheimer's disease patients under the age of 65, who currently account for approximately 3% of the overall Alzheimer's disease population according to the Alzheimer's Association.

In addition to its debilitating effect on patients' cognition, memory and day-to-day functioning, Alzheimer's disease places a significant burden on the healthcare system. According to the Alzheimer's Association, the aggregate cost of care in 2018 for patients with Alzheimer's disease and other types of dementia in the U.S. was estimated to be $234 billion, over half of which is borne by the Medicare system. If the prevalence of Alzheimer's disease nearly triples in the U.S. between now and 2050, as is widely believed will happen, there is potential for the disease to cause a major financial drain on the national economy.

Alzheimer's disease is often grouped into three categories based on severity: mild, moderate and severe. Although the relative prevalence of each of these categories is not well-defined in the literature, a report published by the Alzheimer's Society, a leading care and research charity in the United Kingdom for individuals and families that suffer from dementia, estimates that between 70% and 90% of all Alzheimer's disease patients age 65 and older have mild-to-moderate Alzheimer's disease.

Currently marketed drug therapies for Alzheimer's disease are limited in scope and therapeutic effect.

There are no disease-modifying drug therapies to treat Alzheimer's disease. The FDA has not approved any new drugs for Alzheimer's disease since 2003. Currently marketed drug therapies focus solely on treating symptoms, mostly in patients with mild-to-moderate Alzheimer's disease. At the time of diagnosis, patients are initiated on a class of drugs called cholinesterase inhibitors. The Alzheimer's brain has low levels of a neurotransmitter called acetylcholine. Cholinesterase inhibitors prevent an enzyme in the brain, called acetylcholinesterase, from breaking down acetylcholine. Currently marketed cholinesterase inhibitors include donepezil (marketed by Eisai Co., Ltd. and Pfizer, Inc. as Aricept®), rivastigmine (marketed by Novartis AG as Exelon®) and galantamine (marketed by Janssen Pharmaceuticals, Inc. as Razadyne®). Cholinesterase inhibitors may enhance cognition for some patients for several months, after which the targeted brain receptors are desensitized, and drug efficacy is lost.

Our science is based on stabilizing a critical protein in the brain.

Our scientific approach is to treat neurodegeneration by targeting an altered form of a scaffolding protein called filamin A ("FLNA"). Scaffolding proteins are essential for cell function because they participate in virtually every process within the cell. If their function is impaired, the consequences can be devastating. Technological advances in medicine and improvements in lifestyle are making our lives longer. But with age, genetic mutations and other factors conspire against healthy cells, resulting in altered proteins. Sometimes a cell can rid itself of altered proteins. However, when disease changes the shape and function of critical proteins, multiple downstream processes are impaired. There are many clinical conditions

in which proteins become structurally altered and impair the normal function of cells, tissues and organs, leading to disease. Conversely, restoring altered proteins back to health – which is called proteostasis – is a well-accepted therapeutic strategy in clinical medicine.

Accumulation of altered proteins is common in age-related brain disorders. The most common is Alzheimer's disease. Altered proteins observed in the aging brain include hyperphosphorylated tau and beta amyloid, both hallmarks of Alzheimer's disease. Our scientists and outside collaborators have demonstrated that an altered, and highly toxic, form of the scaffolding protein FLNA exists in the Alzheimer's brain. Critically, altered FLNA enables the toxicity of both beta amyloid and tau proteins. This toxic cascade impairs brain health, leading to worsening symptoms of Alzheimer's disease over time. In addition to impairing brain cell function, altered FLNA enables persistent inflammation in the Alzheimer's brain. We have shown that altered FLNA also promotes neuroinflammation via toll-like receptor 4 ("TLR4"), an immune receptor that causes release of pro-inflammatory cytokines. Our therapeutic approach is designed to counteract these brain pathologies by restoring altered FLNA protein back to its normal, non-diseased conformation with PTI-125. Treatment with PTI-125 has been shown to restore the normal function of three brain receptors critical to brain cell survival, cognition and memory, i.e., the alpha-7 nicotinic acetylcholine receptor; the NMDA receptor; and the insulin receptor. Treatment with PTI-125 has also been shown to dramatically reduce inflammatory cytokine levels in brains of mice with Alzheimer's disease mutations, thus reducing the neuroinflammation that also characterizes Alzheimer's disease.

PTI-125 is our proprietary drug for the treatment of Alzheimer's disease.

We believe there is experimental evidence for improving brain health by restoring altered FLNA with PTI-125, our lead product candidate. PTI-125 is a proprietary small molecule drug that represents an entirely new scientific approach to treat neurodegeneration. Published studies have demonstrated that PTI-125 targets an altered form of a protein called FLNA that is widely found in the Alzheimer's brain. Altered FLNA causes neuronal dysfunction, neuronal degeneration and neuroinflammation. Our drug therapy, PTI-125, is aimed at countering the toxic shape of FLNA by reverting it back to its native, healthy confirmation. Importantly, PTI-125 is not dependent on clearing amyloid from the brain. The following is a summary profile of PTI-125.

IND submission to FDA.

Over the past ten years, we successfully conducted basic research, and in vitro and preclinical studies in support of an Investigational New Drug ("IND") submission to the FDA for PTI-125, including requisite studies around safety pharmacology, genetic toxicology and bioanalytical methods. In 2017 we filed an IND submission to the FDA for PTI-125.

Clinical safety of PTI-125 in a Phase I study.

Following FDA acceptance of our IND in 2017, we then investigated the safety, dosing and pharmacokinetic profile of PTI-125 in healthy human volunteers. The design of our first-in-human Phase I study was based on regulatory feedback, clinical and scientific rationale and observations from previously conducted preclinical and in vitro studies. In a Phase I study, PTI-125 was evaluated in 24 healthy human volunteers in a single-site in the U.S. for safety, tolerability and pharmacokinetics. Study subjects were administered a single oral dose of 50, 100 or 200 mg of PTI-125. The drug was well-tolerated. Importantly, in this study PTI-125 showed no treatment-related adverse effects and no dose-limiting safety findings. Pharmacokinetic measurements demonstrated that PTI-125, a small molecule, was rapidly absorbed, with no accumulation. Dose-proportionality outcomes were observed over the entire dose range of 50 to 200 mg. Full results of this Phase I study were presented at the 10th Annual International Conference on Clinical Trials on Alzheimer's Disease, in Boston, MA in 2017.

Given the absence of dose-limiting effects in healthy adults in a Phase I study, a strong scientific rationale, and multiple peer-reviewed publications and research grant awards, we believe this program demonstrated favorable proof-of-principle for the development of PTI-125 in Alzheimer's disease. In 2018, we mapped out, in collaboration with outside science advisors and medical experts, a strategic clinical plan to advance PTI-125 into a comprehensive Phase II clinical development program.

Phase II clinical development program for PTI-125.

The general objective of our Phase II program with PTI-125 is to gain an initial estimate of the safety, tolerability and biological activity of this drug candidate in patients with Alzheimer's disease. We believe meaningful Phase II data may also enable us to seek one or more strategic collaborations with pharmaceutical or biotechnology companies.

Our Phase II program for PTI-125 is staged in two parts. In part one, we initiated a Phase IIa safety study in the fourth quarter of 2018. In part two, we expect to initiate a Phase IIb study in approximately the second half of 2019.

The first part of our Phase II clinical development program consists of an open-label pharmacokinetics and safety study. In this Phase IIa safety study, 12 patients with mild-to-moderate Alzheimer's disease will be exposed to PTI-125 twice-daily over a continuous four-week period. Certain pharmacokinetics parameters will be measured (e.g. half-life, clearance, peak and trough concentrations in blood, as well as the brain to blood ratio shortly after dosing). Additional clinical endpoints for our Phase IIa study include objective measurements of safety and tolerability and, potentially, confirmation of target engagement via certain biomarkers of neurodegeneration and neuroinflammation consistent with Alzheimer's disease.

The second part of our Phase II clinical development program consists of a randomized, placebo-controlled study. In this Phase IIb study, 36 patients with mild-to-moderate Alzheimer's disease will be either exposed to PTI-125 or a placebo twice-daily over a continuous three-month period. The clinical endpoints for the Phase IIb study are objective measurements of safety and tolerability, and, potentially, confirmation of target engagement via relevant biomarkers of neurodegeneration and neuroinflammation, and cognitive testing.

By design, and based on feedback from our scientific collaborators, our Phase II program aims to enroll a limited number of patients (N=12 and N=36, for our Phase IIa study and Phase IIb study, respectively). Consequently, we do not expect our Phase II program to generate data that is generally considered 'statistically significant' (i.e., $p<0.05$) on parameters of interest.

PTI-125Dx is our blood-based diagnostic to detect Alzheimer's disease.

Our initial diagnostic effort is focused on detecting Alzheimer's disease from a small sample of blood, possibly years before the overt appearance of clinical symptoms. The goal of PTI-125Dx is to make the detection of Alzheimer's disease as simple as getting a blood test. We are developing PTI-125Dx as a fast, accurate and quantitative blood-based biomarker/diagnostic to detect and monitor Alzheimer's disease. If successful, we believe PTI-125Dx has potential to make obsolete many of the current approaches for diagnosing Alzheimer's disease.

Over the past ten years, we discovered that altered FLNA is a hallmark feature of brain pathology in patients with Alzheimer's disease. We believe PTI-125Dx, which is a complex and unique detection system for altered FLNA, can reveal early traces of the disease, potentially even before the overt appearance of disease symptoms, such as memory loss. In September 2017, we announced a $1.8 million research grant award from the NIH for PTI-125Dx. The NIH awarded us this research grant following a confidential, competitive and in-depth evaluation of PTI-125Dx technology for scientific and technical merit. This is a technical milestone-based grant award that will enable us to work collaboratively with leaders in the field to develop and test on clinical samples a blood-based diagnostic for Alzheimer's disease.

A diagnostic, which is also sometimes also called a biomarker, is a measurement of a biological indicator of disease. A deep understanding of the biology of disease is required to identify and develop a diagnostic. A valid diagnostic has certain baseline characteristics to be functional and useful for clinical practice. It must detect disease in patients with disease and, conversely, not detect disease in healthy subjects; it must preferably be quantitative; and it must show some biological information related to disease. Collectively, the ability to selectively detect disease indicators can be useful to provide diagnostic information (i.e., detect the disease) or prognostic information (i.e., predict the course of disease).

Currently, the most definitive method to diagnose Alzheimer's disease is through autopsy after death, which is not particularly helpful. Methods to detect Alzheimer's disease in the living years may be expensive, invasive, subjective, risky or uncomfortable. Importantly, because of the expense and invasiveness of current tests, most people are not tested until they show obvious cognitive decline. Current approaches for diagnosing Alzheimer's disease include measurement of amyloid-β (specifically, $A\beta_{42}$), total tau ("T-tau") or phosphorylated tau ("P-tau") levels in cerebrospinal fluid ("CSF"); structural neuroimaging techniques, including magnetic resonance imaging ("MRI") or computerized tomography ("CT"); positron-emission tomography ("PET") imaging of brain amyloid (AmyVid®); and batteries of cognitive tests. Usually, a combination of more than one test is often necessary to provide a working diagnosis. When such tests and techniques are used in

combination, the totality of data can be sensitive and specific for the detection of Alzheimer's disease. In practice, however, such tests and techniques are only used after the overt appearance of symptoms, such as memory loss.

We believe there is a profound need for a blood-based diagnostic test for Alzheimer's disease. A quick, simple, inexpensive test may provide advantages to the medical community and to society at large. Advantages may include confirming the presence of Alzheimer's disease when cognition is mildly impaired, or conversely, to rule out Alzheimer's disease when memory loss occurs. Other potential benefits include discriminating Alzheimer's disease from other root causes of dementias; stratifying patients by stage of Alzheimer's disease; selection and enrollment of the appropriate patients into studies with experimental product candidates; and better alignment of a patient's specific diagnosis with a targeted therapeutic.

It is widely accepted that in Alzheimer's disease, pathological changes in the brain occur at least 10-15 years before clinical symptoms become apparent. These "pre-symptomatic" changes include depositions in the brain containing beta amyloid and tau. Our long-term goal with PTI-125Dx is to identify people with Alzheimer's disease, potentially long before clinical symptoms occur. In such a case, it may then be possible to cease - or at least slow down - brain damage before it is too late. Importantly, a non-invasive screen for latent Alzheimer's disease prior to the appearance of symptoms could be conducted as a general health screen, not just in patients at risk by family history or in patients already showing cognitive impairment. Once a disease-modifying treatment is found, early detection will be important. Early detection may also enable the approval of a disease-modifying treatment, as some people believe one reason for clinical trial failures in Alzheimer's disease is that treatment is started too late to make a difference in the course of the disease.

Moreover, with repeat measurements over time, PTI-125Dx may provide a probability of cognitive decline or disease progression. Even if PTI-125Dx does not provide a precise cutoff numerical value for Alzheimer's disease, we believe it may be important to incorporate data from PTI-125Dx into the overall diagnostic framework for neurodegeneration, including Alzheimer's disease. As with any method of detecting disease, some people may embrace a way to detect Alzheimer's disease long before clinical symptoms appear, while others may prefer not to know – at least until a treatment is found.

We own worldwide rights to our neurodegeneration program.

We own intellectual property, including patents, patent applications, technology, trade secrets and know-how in the U.S. and other countries. The protection of patents, designs, trademarks and other proprietary rights that we own or license is critical to our success and competitive position. We consider the overall protection of our patents and other intellectual property rights to be of material value and act to protect these rights from infringement.

We seek to protect our technology by, among other methods, filing and prosecuting U.S. and foreign patents and patent applications with respect to our technology and products and their uses. The focus of our patent strategy is to secure and maintain intellectual property rights to technology for our program in neurodegeneration.

PTI-125 and PTI-125Dx were both discovered and designed in-house and were characterized by our academic collaborators during research activities that were conducted from approximately 2008 to date. We own exclusive, worldwide rights to these drug assets and related technologies, without royalty obligations to any third party. Our intellectual property protection in this area currently runs through 2034, plus extensions, and includes six issued patents and related patent filings and applications.

Our Development Team

Our product development team is led by seasoned professionals with a proven track record of innovation in drug discovery and development, as well as substantial business expertise. Our Founder and Chief Executive Officer, Remi Barbier, has over 25 years of biopharmaceutical industry experience and has led teams responsible for pioneering several pharmaceutical innovations, including abuse deterrent opioid drugs; the clinical development of the pain drugs REMOXY® and FENROCK™; and other programs in neuroscience and other therapeutics areas. Before founding Cassava Sciences (formerly known as Pain Therapeutics, Inc.), he held leadership roles and was founder or co-founder of four life science companies, three of which are now publicly traded. Our Chief Medical Officer, Nadav Friedmann Ph.D., M.D., has eight prior FDA drug approvals and previously served as CEO of Daiichi Pharmaceuticals USA and Head of Johnson & Johnson's Biotechnology Research Center. Lindsay Burns, Ph.D., VP, Neuroscience, worked on the development of several product candidates in neuroscience and other therapeutics areas while at Neurex (acquired by Elan Pharmaceuticals) and Abgenix (acquired by Amgen). Michael Zamloot, SVP of Technology Operations, has four prior FDA drug approvals and has worked in drug operations and supply chain

management at Boehringer Mannheim (acquired by Roche Diagnostics), Athena Neuroscience (acquired by Elan Pharmaceuticals) and Ciba-Geigy (acquired by Novartis).

Our team is further supported by a group of scientific advisors that share our commitment to advancing new treatments for Alzheimer's disease. Some of the leading experts in the field who advise us include:

- Jeff Cummings, MD, Director of Cleveland Clinic Lou Ruvo Center for Brain Health and Professor of Neurotherapeutics and Drug Development, Cleveland Clinic.
- Hoau-Yan Wang, PhD, Tenured Associate Medical Professor at CUNY Medical School; co-lead scientist on discovery & development of PTI-125.
- Steven E. Arnold, M.D., Translational Neurology Head of the Interdisciplinary Brain Center, Massachusetts General Hospital, Harvard Medical School.
- Barbara Sahakian, FBA, FMedSci, Professor of Clinical Neuropsychology at the Department of Psychiatry and Medical Research Council /Wellcome Trust Behavioral and Clinical Neuroscience Institute, University of Cambridge.
- Trevor William Robbins, CBE FRS FMedSci, Professor of Cognitive neuroscience and former Head of the Department of Psychology at the University of Cambridge.

Our Strategy

Our goal is to develop product candidates to diagnose and treat neurodegeneration, such as Alzheimer's disease. Key elements of our business strategy to achieve this mission include:

- building a lean company that is narrowly focused on developing innovative product candidates for Alzheimer's disease and other areas of neurodegeneration;
- validating our unique scientific approach with competitive research grants and publishing our scientific data in peer-reviewed journals;
- applying our development capabilities to advance our product candidates through clinical proof-of-concept studies and beyond;
- using our expertise and experience to continue to focus on discovering new indications and product candidates, validated by experimental evidence and leading experts in the field;
- continuing to outsource preclinical studies, clinical trials and formulation development activities in order to allow more efficient deployment of our resources

We also conduct basic research and development in collaboration with academic and other partners. Our research and development expenses were $3.0 million and $7.6 million for the year ended December 31, 2018 and 2017, respectively. See *"Item 7 Management's Discussion and Analysis of Financial Condition and Results of Operations*" for additional details regarding our research and development activities.

Competition

The drug discovery and development industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face potential competition from many different sources, including pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize, such as PTI-125 or PTI-125Dx, may compete with existing therapies and new therapies that may become available in the future.

Our competitors may have significantly greater financial resources, an established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing-approved products. These competitors also compete with us in recruiting and retaining qualified scientific and technical personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring or developing technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of PTI-125, and any other product candidates that we develop to address neurodegenerative disorders, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition, patience and physician acceptance and the availability of reimbursement from government and other third-party payors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products.

Our competitors are large pharmaceutical companies that are developing product candidates for Alzheimer's disease, including Eisai; Biogen; Eli Lilly; Janssen; Merck; Novartis; Allergan; Amgen; Roche; Genentech; and others. Small to mid-size companies that are developing product candidates for Alzheimer's disease are also a source of intense competition for us, including Alector, Inc; Alzheon, Inc.; AC Immune; Proclara Biosciences; Tau Rx Therapeutics; vTv Therapeutics; Avanir; AZTherapeutics; Axsome Therapeutics; Anavex Life Sciences; Charsire Biotechnology; Neurotrope Bioscience; Cognition Therapeutics; Cortexyme: M3 Biotechnology; NeuroTherapeia; PharmatrophiX; Tetra Discovery; Yumanity Therapeutics; and others. Competing product candidates are in various stages of development, from pre-clinical research to Phase III.

In recent years, we have observed ramped-up worldwide efforts aimed at developing blood-based techniques to detect and monitor Alzheimer's disease. The key competitive factors affecting the success of PTI-125Dx, and any other product candidates that we develop to diagnose neurodegeneration, if approved, are likely to be their measure of accuracy, such as specificity and sensitivity, as well as their convenience, patience acceptance, price and the availability of reimbursement from government and other third-party payors. Our competitors in the diagnostic area are pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. For example, in 2019, a team of researchers at King's College (London, England) announced they had identified a panel of blood proteins that may identify asymptomatic patients who may be expected to develop neuropathology. Also, in 2019, an international consortium of researchers led by the Center for Neurodegenerative Diseases (Tubingen, Germany) published data showing that a protein called 'neurofilament light chain' may be a non-specific biomarker for neuropathology. Also, in 2018, researchers at the Center for Development of Advanced Medicine for Dementia (Aichi Prefecture, Japan) announced that they had identified a panel of blood-based biomarkers that may help detect and monitor Alzheimer's disease. Despite increased research effort, the field has generally been hampered by lack of reproducibility and an unclear path on how to move academic discoveries into clinical utilization.

In addition to blood-based techniques to detect Alzheimer's disease, competitors are examining the use of novel tracing agents and imaging techniques to map the course of neurodegeneration. In 2012 the FDA approved Amyvid® (Eli Lilly Pharmaceuticals), which is a radioactive diagnostic agent for brain imaging of amyloid plaque. Amyvid's can rule out Alzheimer's disease but does not confirm its presence. That is, a negative scan means little or no plaque is present; however, a positive scan does not necessarily indicate Alzheimer's disease. In addition, Amyvid cannot be used to stage Alzheimer's disease because some people take years to show cognitive decline after amyloid plaque develops, while other others rapidly develop advanced Alzheimer's disease within months. Amyvid has had modest clinical utilization due to its high cost, lack of reimbursement, need for specialized training, all of which resulting in the product making an overall limited contribution to a clinical diagnosis. Other companies that have announced development programs for new imaging techniques include 3SCAN, Inc. (San Francisco, CA), which uses detailed representations of anatomical structures to make non-invasive maps of the brain; Alzeca Biosciences, Inc. (Houston, TX), which employs targeted MRI agents to detect neurodegeneration; BioArtic AB (Stockholm, Sweden), which is studying the use of certain amyloid beta proteins to diagnose neurodegeneration; and others.

Manufacturing

We do not own or lease any manufacturing facilities. We outsource formulation, manufacturing and related activities to third parties. For the foreseeable future, we will continue to rely on third parties to conduct certain quality control and assurance testing, shipping or storage of our product candidates.

We currently rely on contract development and manufacturing organizations ("CDMOs") for the manufacture of all our materials for preclinical studies and clinical trials and expect to continue to do so for preclinical studies, clinical trials, and for commercial supply of any product candidates that we may develop. We currently have established relationships with several CDMOs for the manufacturing of our product candidates.

Our suppliers must comply with current good manufacturing practices ("cGMP") enforced by the FDA and other government agencies such as the U.S. Drug Enforcement Administration ("DEA"). Our suppliers are subject to unannounced inspection by regulators, including pre-approval inspections by the FDA and the DEA, to ensure they are in strict compliance with government regulations and standards. Our suppliers may be forced to stop producing, storing, shipping or testing our drug products if they fall out of compliance with government regulations and standards.

We have no control over our suppliers' compliance, or lack thereof, with the multitude of regulations and standards that affect our drug products. We cannot control decisions by our suppliers that affect their ability or willingness to continue to supply us on acceptable terms, or at all.

We may not be able to replace a commercial supplier on commercially reasonable terms, or at all. Replacing any of our commercial suppliers will be expensive and time consuming. Further, if any of our product candidates are approved for commercialization, our suppliers may encounter difficulties in achieving high volumes of production to satisfy commercial demands. Failure by any of our suppliers to perform as expected could delay or prevent commercialization of our product candidates or result in shortages, cost overruns, or other problems and would materially harm our business.

Strategic Shift Away from Analgesic Drug Development

Historically, our focus was on analgesic drug development. During that time, we conceived, formulated, developed, tested and patented various analgesic drug candidates with robust abuse-deterrent properties, including REMOXY® ER (extended-release oxycodone capsules CII) and FENROCK™ (transdermal fentanyl patch CII).

In late 2018, we announced a strategic shift away from analgesic drug development. In March 2019, we announced an intention to rebrand the Company around neurodegenerative diseases, such as Alzheimer's disease. Our rebranding plan includes a new company name, logo, NASDAQ ticker symbol and website.

On March 20, 2019, we gave Durect Corporation, a prior collaborator, written notice of termination of a licensing agreement for REMOXY. This action effectively ends our development of REMOXY. We continue to conduct certain pre-clinical activities with FENROCK, a product candidate that we own without royalty obligations to any third-party. Our FENROCK related activities are substantially funded by NIH. Now that our primary focus on our product candidates for neurodegeneration, we anticipate providing updates regarding our activities on FENROCK only if and when material developments occur.

Government Regulation

Government authorities in the U.S. at the federal, state and local level and in other countries regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug and diagnostic products. Generally, before a new drug or diagnostic can be marketed, considerable data demonstrating its quality, safety and efficacy and/or specificity 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 U.S., the FDA regulates drugs under the Food, Drug, and Cosmetic Act ("FDCA"). Both drugs and diagnostics also are subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the

subsequent compliance with appropriate federal, state, local and foreign statutes and regulations 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. Any agency or judicial enforcement action could have a material adverse effect on us.

Any future product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the U.S. The NDA process generally involves the following:

- Completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with good laboratory practice;
- Submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- Approval by an independent institutional review board ("IRB") or ethics committee before each trial may be initiated;
- Performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, code of good clinical practice ("cGCP"), requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- Submission to the FDA of an NDA;
- A determination by the FDA within 60 days of its receipt of an NDA to accept the filing for review;
- Satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug will be produced to assess compliance with cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- Potential FDA audit of the preclinical study and/or clinical trial sites that generated the data in support of the NDA;
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the U.S.; and
- Compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy ("REMS"), and the potential requirement to conduct post-approval studies.

The data required to support an NDA are generated in two distinct developmental stages: preclinical and clinical. The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for any future product candidates will be granted on a timely basis, or at all.

Preclinical Studies and IND

The preclinical developmental stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. As sponsor, we must submit the results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before human clinical trials may begin.

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as in vitro and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of

preclinical studies is subject to federal regulations and requirements, including cGCP regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, 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. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin.

Clinical Trials

The clinical stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with cGCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside of the U.S. may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA. The FDA may accept a well-designed and well-conducted foreign clinical trial not conducted under an IND if the trial was conducted in accordance with cGCP requirements and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials in the U.S. generally are conducted in three sequential phases, known as Phase I, Phase II and Phase III, and may overlap.

- Phase I clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, tolerability and safety of the drug.

- Phase II clinical trials involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified, and a preliminary evaluation of efficacy is conducted.

- Phase III clinical trials generally involve many patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. These trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA. Written safety reports and the investigators for serious and unexpected adverse events, or any other findings suggesting a significant risk to humans exposed to the drug must be submitted to the FDA.

Phase I, Phase II, and Phase III clinical trials may not be completed successfully within any specified period, if at all. 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 or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated check-points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal studies and must 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 product and, among other things, companies must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that our product candidates do not undergo unacceptable deterioration over their shelf life.

NDA Review Process

Following completion of the clinical trials, data is analyzed to assess whether the investigational product is safe and effective for the proposed indicated use or uses. The results of preclinical studies and clinical trials are then submitted to the FDA as part of an NDA, along with proposed labeling, chemistry and manufacturing information to ensure product quality and other relevant data. In short, the NDA is a request for approval to market a drug for one or more specified indication and must contain proof of safety and efficacy for a drug's purity and potency. The application may include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from several alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of FDA. FDA approval of an NDA must be obtained before a drug may be marketed in the U.S.

Under the Prescription Drug User Fee Act ("PDUFA"), as amended, each NDA must be accompanied by a user fee. FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's fiscal year 2019 fee schedule, effective through September 30, 2019, the user fee for an application requiring clinical data, such as an NDA, is approximately $2.6 million. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all submitted NDAs before it accepts them for filing and may request additional information rather than accept the NDA for filing. The FDA must decide on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has 10 months, from the filing date, in which to complete its initial review of a new molecular-entity NDA and respond to the applicant, and six months from the filing date of a new molecular-entity NDA designated for priority review. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often extended by FDA requests for additional information or clarification.

Before approving an NDA, the FDA may conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities fully comply with cGMP requirements and are adequate to assure consistent production of the product within required specifications. The FDA also may audit data from clinical trials to ensure compliance with cGCP requirements. Additionally, the FDA may refer applications for novel product candidates which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions on approval. The FDA likely will reanalyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. After the FDA evaluates an NDA, it will issue either an approval letter or a Complete Response Letter ("CRL"). An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A CRL indicates that the FDA's review of the application is complete and the application cannot be approved in its present form. A CRL usually describes the specific

deficiencies in the NDA identified by the FDA. The CRL may require additional clinical data, additional pivotal Phase III clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the applicant may either resubmit the NDA, addressing all the deficiencies identified in the CRL, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

Advertising and Promotion

The FDA and other federal regulatory agencies closely regulate the marketing and promotion of drugs through, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet. None of our product candidates can be commercially promoted before receiving FDA approval. After approval, product promotion can include only those claims relating to safety and effectiveness that are consistent with the labeling approved by the FDA. Healthcare providers are permitted to prescribe drugs for "off-label" uses — that is, uses not approved by the FDA and therefore not described in the drug's labeling — because the FDA does not regulate the practice of medicine. However, FDA regulations impose stringent restrictions on manufacturers' communications regarding off-label uses. Failure to comply with applicable FDA requirements and restrictions in this area may subject us to adverse publicity and enforcement action by the FDA, the U.S. Department of Justice, or the Office of the Inspector General of the HHS, as well as state authorities. This could subject us to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which we promote or distribute our product candidates.

Post-Approval Requirements

After a product candidate receives regulatory approval, it is often subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to drug listing and registration, recordkeeping, periodic reporting, product sampling and distribution, adverse event reporting and advertising, marketing and promotion restrictions.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-market testing, known as Phase 4 testing, or a REMS, or surveillance to monitor the effects of an approved product that is also a known drug of abuse, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, drug manufacture, packaging, and labeling procedures must continue to conform to cGMP after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration subjects entities to periodic announced or unannounced inspections by the FDA or these state agencies, during which the agency inspects manufacturing facilities to assess compliance with cGMP. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with cGMP. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered. In addition, other regulatory actions may be taken, including, among other things, warning letters, the seizure of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations, refusal to approve pending applications or supplements to approved applications, civil penalties, and criminal prosecution.

The FDA may require post-approval studies and clinical trials if the FDA finds that scientific data, including information regarding related drugs, deem it appropriate. The purpose of such studies would be to assess a known serious risk or signals of serious risk related to the drug or to identify an unexpected serious risk when available data indicate the potential for a serious risk. The FDA may also require a labeling change if it becomes aware of new safety information that it believes should be included in the labeling of a drug.

The Hatch-Waxman Amendments

Orange Book Listing

In seeking approval for our product candidates through an NDA, we will be required to list with the FDA each patent whose claims cover the drug product. Upon receiving regulatory approval, each of the patents listed in the application for this drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known

as the "Orange Book". Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated NDA, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredient in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, preclinical or clinical tests to prove the safety or efficacy of their drug product. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to make certain certifications to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a section viii statement certifying that its proposed ANDA label does not contain (or carves out) any language regarding the patented method-of-use rather than make certifications concerning a listed method-of-use patent. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant. The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Exclusivity

Upon NDA approval of a new chemical entity, or NCE, which is a drug that contains no active moiety that has been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity during which the FDA cannot receive any ANDA seeking approval of a generic version of that drug or any Section 505(b)(2) NDA that relies on the FDA's findings regarding that drug. A drug may obtain a three-year period of exclusivity for a change to the drug, such as the addition of a new indication to the labeling or a new formulation, during which the FDA cannot approve an ANDA or any Section 505(b)(2) NDA, if the supplement includes reports of new clinical trials (other than bioavailability clinical trials) essential to the approval of the supplement.

An ANDA may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period.

Section 505(b)(2) NDAs

Generally, drug products obtain FDA marketing approval pursuant to an NDA or an ANDA. A third alternative is a Section 505(b)(2) NDA, which enables the applicant to rely, in part, on data not developed by the applicant, such as the FDA's findings of safety and efficacy in the approval of a similar product or published literature in support of its application.

Section 505(b)(2) NDAs may provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from clinical trials not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference. If the Section 505(b)(2) applicant can establish that reliance on the FDA's previous findings of safety and efficacy is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical trials of the new product. The FDA may also require companies to perform additional clinical trials or provide additional materials to support the change from the approved product. The FDA may then approve the new product candidate for all, or some, of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

To the extent that the Section 505(b)(2) applicant is relying on the FDA's findings of safety and effectiveness for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. Therefore, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired; until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired; and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant. In the interim period, the FDA may grant tentative approval. Tentative approval indicates that the FDA has determined that the applicant meets the standards for approval as of the date that the tentative approval is granted. Final regulatory approval can only be granted if the FDA is assured that there is no new information that would affect final regulatory approval. As with traditional NDAs, a Section 505(b)(2) NDA may be eligible for three-year marketing exclusivity, assuming the NDA includes reports of new clinical trials (other than bioavailability clinical trials) essential to the approval of the NDA.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, clinical trial sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to post certain information regarding the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

DEA Regulatory Requirements

Certain product candidates are regulated as a controlled substance under the Controlled Substances Act, or CSA. CSA establishes registration, security, recordkeeping, reporting, storage, distribution, importation, exportation and other requirements administered by the DEA. The DEA regulates the handling of controlled substances through a closed chain of distribution. This control extends to the equipment and raw materials used in their manufacture and packaging of a controlled substance in order to prevent loss and diversion into illicit channels of commerce.

Controlled substances under the CSA are subject to a high degree of regulation. Schedule II drugs are subject to the strictest requirements for registration, security, recordkeeping and reporting. Also, distribution and dispensing of these drugs are highly regulated. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription.

Annual registration is required for any facility that manufactures, distributes, dispenses, imports or exports any controlled substance. The registration is specific to the particular location, activity and controlled substance schedule. For example, separate registrations are needed for import and manufacturing, and each registration will specify which schedules of controlled substances are authorized.

The DEA typically inspects a facility to review its security measures prior to issuing a registration. Security requirements vary by controlled substance schedule, with the most stringent requirements applying to Schedule II substances. Required security measures include background checks on employees and physical control of inventory through measures such as cages, surveillance cameras and inventory reconciliations. Records must be maintained for the handling of all controlled substances, and periodic reports made to the DEA, for example distribution reports for Schedule II controlled substances, Schedule III substances that are narcotics, and other designated substances. Reports must also be made for thefts or losses of any controlled substance, and to obtain authorization to destroy any controlled substance. In addition, special permits and notification requirements apply to imports and exports of narcotic drugs.

To enforce these requirements, the DEA conducts periodic inspections of registered establishments that handle controlled substances. Failure to maintain compliance with applicable requirements, particularly as manifested in loss or diversion, can result in administrative, civil or criminal enforcement action that could have a material adverse effect on our business, results of operations and financial condition. The DEA may seek civil penalties, refuse to renew necessary registrations or initiate administrative proceedings to revoke those registrations. In certain circumstances, violations could result in criminal

proceedings. In addition, individual states also independently regulate controlled substances. We and our contract manufacturers will be subject to state regulation on distribution of these products.

Other Regulatory Requirements

We may be subject to federal, state and local environmental laws and regulations, including the Environmental Protection Act and the Clean Air Act. Although we believe that our safety procedures for handling and disposing of controlled materials comply with the standards prescribed by state and federal regulations, accidental contamination or injury from these materials may occur. In the event of such an occurrence, we could be held liable for any damages that result and any such liability could exceed our resources.

We may also be subject to regulations under other federal, state, and local laws, including the Occupational Safety and Health Act, national restrictions on technology transfer, and import, export, and customs regulations. It is possible that any portion of the regulatory framework under which we operate may change and that such change could have a negative impact on our current and anticipated operations. Failure to comply with these requirements could result, among other things, in suspension of regulatory approval, recalls, injunctions or civil or criminal sanctions.

Third-Party Payor Coverage and Reimbursement

The commercial success of our product candidates, if approved, will depend, in part, upon the availability of coverage and adequate reimbursement from third-party payors at the federal, state and private levels. Third-party payors include governmental programs such as Medicare or Medicaid, private insurance plans and managed care plans. These third-party payors may deny coverage or reimbursement for our product candidates in whole or in part if they determine that our product candidates are not medically appropriate or necessary. Also, third-party payors attempt to control costs by limiting coverage through the use of formularies and other cost-containment mechanisms and the amount of reimbursement for particular procedures or drug treatments.

Some third-party payors also require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, these requirements or any announcement or adoption of such proposals could have a material adverse effect on our ability to obtain adequate prices for our approved product candidates to operate profitably.

Reverse Stock Split

On May 4, 2017, following stockholder approval, our board of directors (the "Board") approved a reverse stock split at a ratio of 7-for-1. On May 4, 2017, we filed with the Secretary of State of the State of Delaware a Certificate of Amendment to the Company's Amended and Restated Certificate of Incorporation to effect the 7-for-1 reverse stock split of our outstanding shares of common stock. The number of outstanding shares of common stock on the date of the reverse split was reduced from 46.1 million to 6.6 million shares. Our common stock began trading on the Nasdaq Global Market on a split-adjusted basis when the market opened for trading on May 10, 2017. As a result, all common stock share amounts included in this Annual Report on Form 10-K have been retroactively reduced by a factor of seven, and all common stock per share amounts have been increased by a factor of seven, with the exception of our common stock par value.

Incorporation

We were incorporated in Delaware in May 1998 as Pain Therapeutics, Inc. On March 26, 2019, the Company changed its name to Cassava Sciences, Inc.

Employees

As of December 31, 2018, we had 9 employees. We engage numerous consultants to perform services on retainer, per diem or an hourly basis.

Available Information

We file electronically with the Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of the site is http://www.sec.gov.

You may obtain a free copy of our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and amendments to those reports on the day of filing with the SEC on our website at http://www.cassavasciences.com, by contacting our corporate offices by calling 512-501-2450 or by sending an e-mail message to IR@cassavasciences.com.

Item 1A. ***Risk Factors***

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as other information contained in this Annual Report on Form 10-K, including our financial statements and the related notes and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations, and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment.

Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations and the market price of our common stock.

Risks Related to Our Business, Financial Condition, and Capital Requirements

We may not be successful in transitioning away from our prior focus on analgesic drug development.

We believe our future success is dependent upon our ability to successfully develop product candidates for neurodegeneration, such as Alzheimer's disease. Importantly, in the fourth quarter of 2018, we announced the initiation of a strategic reorganization away from our historical focus on analgesic drug development, and in March 2019, we announced that we are no longer developing REMOXY and changed our Company name to Cassava Sciences, Inc. Going forward, and for the foreseeable future, we anticipate that our product candidates for neurodegeneration will be the principal focus of our business operations and such efforts will consume the vast majority of our resources. We may not be successful in transitioning to the development of product candidates for neurodegeneration, such as Alzheimer's disease, in which case our business, results of operations and financial condition will suffer, and we may need to cease our operations.

We may not be successful in developing our new product candidates in neurodegeneration.

Our product candidates in neurodegeneration are still in the early stages of development and will take several more years to develop and must undergo extensive clinical and scientific validations. Even if we are successful in developing any of our product candidates through clinical and scientific validation, we may not be able to develop a drug or a diagnostic that:

- meets applicable regulatory standards, in a timely manner or at all;
- successfully competes with other technologies and tests;
- avoids infringing the proprietary rights of others;
- are adequately reimbursed by third-party payors;
- can be performed at commercial levels or at reasonable cost; or
- can be successfully marketed

To the extent we are not successful in developing our new product candidates in neurodegeneration, our results of operations and business will be materially adversely affected.

We have a limited operating history in our business targeting Alzheimer's disease and no history of product approvals for commercial sale, which may make it difficult to evaluate our current business and predict our future success and viability.

We are an early clinical-stage biopharmaceutical company with a limited operating history in our business targeting Alzheimer's disease. Since we commenced operations in May 1998, we have had no product candidates approved for commercial sale and have not generated any revenue from product sales. Drug development is a highly uncertain undertaking and involves a substantial degree of risk. To date, we have not initiated or completed a pivotal clinical trial involving Alzheimer's disease, obtained marketing approval for any product candidates, or conducted sales and marketing activities necessary for successful product commercialization. Our long operating history as a company without product revenue makes any assessment of our future success and viability subject to significant uncertainty.

We will continue to encounter risks and difficulties frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields. We have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not successfully address these risks and difficulties, our business, results of operations and financial condition will suffer materially.

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

We have incurred net losses in each reporting period since our inception, including a net loss of $6.6 million for the year ended December 31, 2018. As of December 31, 2018, we had an accumulated deficit of $164.0 million.

We have invested significant financial resources in research and development activities for product candidates. We do not expect to generate revenue from product sales for several years, if at all. The amount of our future net losses will depend, in part, on the level of our future expenditures and revenue. Moreover, our net losses may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indicator of our future performance.

We expect to continue to incur significant expenses and higher operating losses for the foreseeable future. We anticipate that our expenses will increase substantially as we:

- continue our research and discovery activities;
- advance our current and any future product candidates through preclinical and clinical development;
- initiate and conduct additional preclinical, clinical, or other studies for our product candidates;
- work with our CDMO's to scale up the manufacturing processes for our product candidates;
- seek regulatory approvals and marketing authorizations for our product candidates;
- obtain, maintain, protect, defend and enforce our intellectual property portfolio;
- attract, hire, and retain qualified personnel;
- provide additional internal infrastructure to support our continued research and development operations and any planned commercialization efforts in the future;
- experience any delays or encounter other issues related to our operations; and
- meet the requirements and demands of being a public company.

Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. In any quarter, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

We have no product revenues and may never achieve revenues or profitability based on product revenues.

We have no products approved for commercial sale. To obtain revenues from the sales of our product candidates that are significant or large enough to achieve profitability, we must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, manufacturing, and marketing product candidates with significant commercial value. This is a significant endeavor that few early-stage biopharmaceutical companies can successfully achieve. Our ability to generate revenue and achieve profitability depends on many factors, including:

- completing research and preclinical and clinical development of our product candidates;
- obtaining regulatory approvals and marketing authorizations for product candidates for which we successfully complete clinical development;
- developing a sustainable and scalable manufacturing process for our product candidates, as well as establishing and maintaining commercially viable supply relationships with third parties that can provide adequate products and services to support clinical activities and commercial demand for our product candidates;
- identifying, assessing, acquiring, and/or developing new product candidates;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- addressing any competing technological and market developments;
- maintaining, protecting, expanding, and enforcing our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

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

We will require additional capital to fund our operations and to complete the development of our product candidates. A failure to obtain this necessary capital on acceptable terms, or at all, could force us to delay, limit, reduce, or terminate our commercialization efforts, product development, or other operations.

Our operations have required substantial amounts of cash since inception, and we expect our expenses to increase significantly in the foreseeable future. To date, we have financed our operations primarily through the sale of equity securities, research grants and payments received from prior third-party collaborations. Developing our product candidates and conducting clinical trials for the treatment of neurodegenerative diseases, including Alzheimer's disease, will require substantial amounts of capital. We will also require a significant amount of capital to commercialize any approved products.

As of December 31, 2018, we had cash and cash equivalents of $19.8 million. Based on our current operating plan, we believe that our existing cash and cash equivalents will be sufficient to fund our projected operations for at least the next 12 months. Our estimate as to how long we expect our existing cash and cash equivalents to be available to fund our operations is based on assumptions that may prove inaccurate, and we could use our available capital resources sooner than we currently expect. In addition, 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.

We will require additional capital for the further development of our product candidates. Additional capital may not be available when we need it, or on terms acceptable to us or at all. We have no committed source of additional capital. If

adequate capital is not available to us on a timely basis, we may be required to significantly delay, limit, reduce or terminate our research and development programs or the commercialization of product candidates, if approved, or be unable to continue or expand our operations, or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition, results of operations, and growth prospects and cause the price of our common stock to decline.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise additional funds through collaborations, strategic alliances, or licensing arrangements with pharmaceutical partners, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates, or grant licenses on terms that may not be favorable to us.

Global credit and financial market conditions could negatively impact the value of our portfolio of cash equivalents, short-term investments or long-term investments and our ability to meet our financing objectives.

Our cash and cash equivalents are generally maintained in highly liquid investments with remaining maturities of 90 days or less at the time of purchase. Our short-term investments, if any, consist primarily of readily marketable debt securities with original maturities of greater than 90 days from the date of purchase but remaining maturities of less than one year from the balance sheet date. Our long-term investments, if any, consist primarily of readily marketable debt securities with maturities in one year or beyond from the balance sheet date. While, as of the date of this filing, we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents, short-term investments or long-term investments since December 31, 2018, no assurance can be given that deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents, short-term investments or long-term investments or our ability to meet our financing objectives.

New accounting pronouncements and legislative actions may significantly impact our future financial position or results of operations.

Future changes in financial accounting standards may cause adverse, unexpected fluctuations in the timing of the recognition of revenues or expenses and may affect our financial position or results of operations. New pronouncements and varying interpretations of existing pronouncements have occurred with frequency, and may occur again in the future, which may require us to make changes in our accounting policies in the future. Compliance with changing regulation of corporate governance and public disclosure may result in additional expenses. Changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002 ("SOX"), new SEC regulations, PCAOB pronouncements and Nasdaq rules, are creating uncertainty for companies such as ours and insurance, accounting and auditing costs are high as a result of this uncertainty and other factors. We are committed to maintaining high standards of corporate governance and public disclosure. As a result, we intend to invest all reasonably necessary resources to comply with evolving standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention to compliance activities.

Risks Related to the Discovery, Development, and Commercialization of Our Product Candidates

Research and development of biopharmaceutical products is very risky. Our business is heavily dependent on the successful development of our product candidates, which are in the early stages of development. We cannot give any assurance that any of our product candidates will receive regulatory approval, which is necessary before they can be commercialized.

We are at the early stages of development of our product candidates. To date, we have invested substantial effort and financial resources to identify, procure intellectual property for, and develop our programs in neurodegeneration, including conducting preclinical studies and early-stage clinical trials for our product candidates, PTI-125 and PTI-125Dx, and providing general and administrative support for these operations. Our future success is dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates, and we may fail to do so for many reasons, including the following:

- our product candidates may not successfully complete preclinical studies or clinical trials;

- a product candidate may, on further study, be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- our competitors may develop therapeutics that render our product candidates obsolete or less attractive;
- the product candidates that we develop may not be sufficiently covered by intellectual property for which we hold exclusive rights;
- the product candidates that we develop may be covered by third parties' patents or other intellectual property or exclusive rights;
- the market for a product candidate may change so that the continued development of that product candidate is no longer reasonable or commercially attractive;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- if a product candidate obtains regulatory approval, we may be unable to establish sales and marketing capabilities, or successfully market such approved product candidate, to gain market acceptance; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, if applicable.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

We may not be successful in our efforts to further develop our current product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. Each of our product candidates is in the early stages of development and will require significant additional clinical development, management of preclinical, clinical, and manufacturing activities, regulatory approval, adequate manufacturing supply, a commercial organization, and significant marketing efforts before we generate any revenue from product sales, if at all.

We have never completed a product development program in neurodegeneration. None of our product candidates in neurodegeneration have advanced into late-stage development and it may be years before any such trial is initiated, if at all. Further, we cannot be certain that any of our product candidates will be successful in clinical trials. We may in the future advance product candidates into clinical trials and terminate such trials prior to their completion.

If any of our product candidates successfully complete clinical trials, we may seek regulatory approval to market our product candidates in the U.S., the European Union, and in additional foreign countries where we believe there is a viable commercial opportunity. We may never receive regulatory approval to market any product candidates even if such product candidates successfully complete clinical trials, which would adversely affect our viability. To obtain regulatory approval in countries outside the U.S., we would need to comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, manufacturing and controls, clinical trials, commercial sales, pricing, and distribution of our product candidates. Even if we are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our business, financial condition, results of operations, and our growth prospects could be negatively affected.

Even if we receive regulatory approval to market any of our product candidates, whether for the treatment of neurodegenerative diseases or other diseases, we cannot provide assurance that any such product candidate will be successfully commercialized, widely accepted in the marketplace or more effective than other commercially available alternatives.

Investment in biopharmaceutical product development involves significant risk that any product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, and become commercially viable. We cannot provide any assurance that we will be able to successfully advance any of our product candidates through the development process or, if approved, successfully commercialize any of our product candidates.

We only have two product candidates in clinical development for neurodegeneration and we may not be successful in our efforts to continue to create additional product candidates. If we fail to successfully identify and develop additional product candidates, our commercial opportunity may be limited.

Identifying, developing, obtaining regulatory approval, and commercializing additional product candidates for the treatment of neurodegenerative diseases requires substantial funding and is prone to the risks of failure inherent in drug development. We cannot provide any assurance that we will be able to successfully identify or acquire additional product candidates, advance any additional product candidates through the development process, or assemble sufficient resources to identify, acquire, develop additional product candidates. If we are unable to successfully identify, acquire, develop, and commercialize additional product candidates, our commercial opportunity may be limited.

Early indications of safety from a Phase I clinical trial with PTI-125 may not predict the results of later trials

Results of a Phase I clinical trial with PTI-125 demonstrated safety, tolerability and pharmacokinetics in 24 healthy subjects exposed to 50-200 mg in a single ascending dose study. However, this was a small, "first-in-human" Phase I study designed to assess the initial safety characteristics of PTI-125 in healthy subjects and this study was not designed to evaluate safety, tolerability and efficacy of PTI-125 in patients. Additional large, well-controlled, multi-dose studies will be required to evaluate the safety, tolerability and efficacy of PTI-125 to treat patients with any indication, including Alzheimer's disease. There can be no assurance that such future studies will demonstrate the safety, tolerability or efficacy of PTI-125. The failure of PTI-125 to show safety, tolerability or efficacy in any future clinical trials would significantly harm our business.

We have never obtained FDA approval for a diagnostic test and we may not be able to secure such approval in a timely manner or at all.

We are developing a blood-based diagnostic test for Alzheimer's disease, which will require FDA approval prior to commercialization. Our diagnostic product candidate, marketing, sales and development activities and manufacturing processes are subject to extensive and rigorous regulation by the FDA pursuant to the FDCA, by comparable agencies in foreign countries, and by other regulatory agencies and governing bodies. Under the FDCA, a diagnostic must receive FDA clearance or approval before it can be commercially marketed in the U.S. The process of obtaining marketing approval or clearance from the FDA or by comparable agencies in foreign countries for new products could:

- take a significant period of time;
- require the expenditure of substantial resources;
- involve rigorous pre-clinical testing, as well as increased post-market surveillance;
- require changes to products; and
- result in limitations on the indicated uses of products.

If we do not compete effectively with scientific and commercial competitors, we may not be able to successfully develop our diagnostic test for Alzheimer's disease.

The field of clinical laboratory testing is highly competitive. Tests that are developed are characterized by rapid technological change. Our competitors in the U.S. and abroad are numerous and include, among others, major diagnostic companies, reference laboratories, molecular diagnostic firms, universities and other research institutions. Most of our potential competitors have considerably greater financial, technical, marketing and other resources than we do, which may allow these competitors to discover important biological markers and determine their function before we do. We could be adversely affected if we do not discover proteins or biomarkers and characterize their function, develop diagnostic and pharmaceutical and clinical services based on these discoveries, obtain required regulatory and other approvals and launch these tests and their related services before our competitors. We also expect to encounter significant competition with respect to any diagnostic tests that we may develop or commercialize. Those companies that bring to market new diagnostic tests before we do may achieve a significant competitive advantage in marketing and commercializing their tests. We may not be able to develop additional diagnostic tests successfully and we may not obtain or enforce patents covering these tests that

provide protection against our competitors. Moreover, our competitors may succeed in developing diagnostic tests that circumvent our technologies or tests. Furthermore, our competitors may succeed in developing technologies or tests that are more effective or less costly than those developed by us or that would render our technologies or tests less competitive or obsolete. We expect competition to intensify in the fields in which we are involved as technical advances in these fields occur and become more widely known and changes in intellectual property laws generate challenges to our intellectual property position.

Our blood-based diagnostic to detect Alzheimer's disease, called PTI-125Dx, relies on the use of research antibodies that we source from commercial vendors. Research antibodies are not consistently available or reliable, and we will need to develop our own proprietary antibodies to advance our diagnostic program.

PTI-125Dx relies on the use of commercially available antibodies, which are complex molecules that can recognize and bind to an intended protein. Consistent use of commercially available antibodies is not feasible due to the presence of certain technical flaws, such as improper validation, significant batch-to-batch variations or inconsistent storage, any of which can jeopardize our studies and experiments. Because antibody underperformance can be a significant drain on time and resources, we have initiated plans to develop and validate our own, fit-for-purpose antibody for use with PTI-125Dx and such technical activities are on-going. The complexity of developing our own antibody gives rise to a combination of technical issues that are challenging to solve, and we cannot be certain that we will be able to successfully complete any of these activities, in which case our program may be harmed.

We are heavily dependent on the success of PTI-125 and PTI-125Dx, our product candidates which are still under clinical development. If these product candidates do not receive regulatory approval, our business may be harmed.

Since inception, we have not succeeded in getting regulatory approval for our product candidates and we may never do so. In recent years we have invested a significant portion of our efforts and financial resources in the development of PTI-125 and PTI-125Dx for the treatment and detection of Alzheimer's disease, respectively. Our future success is substantially dependent on our ability to successfully complete clinical development and obtain regulatory approval for our product candidates, which may never occur. We expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to PTI-125 and PTI-125Dx. This will require additional clinical development, management of clinical and manufacturing activities, regulatory approval in one or more national jurisdictions and obtaining commercial-scale manufacturing supply. Substantial investment and significant efforts will be required before we can generate any revenues from any commercial sales. We cannot be certain that we will be able to successfully complete any of these activities.

We may not be successful in our efforts to expand indications for approved product candidates.

Our drug development strategy is to clinically test and seek regulatory approval for our product candidates in indications in which we believe there is the most evidence that we will be able to generate proof-of-concept data. We may then expand to clinical testing in other medical indications. Conducting clinical trials for additional indications for our product candidates requires substantial technical, financial, and human resources and is prone to the risks of failure inherent in drug development. We cannot provide any assurance that we will be successful in our effort to obtain regulatory approval for our product candidates for additional indications even if we obtain approval for our initial indications.

We have concentrated a substantial portion of our research and development efforts on the treatment and detection of Alzheimer's disease, an area of research that has seen significant failure rates. Further, our product candidates are based on new scientific approaches and novel technology, which makes it difficult to predict the time and cost of product candidate development.

We currently focus a substantial portion of our research and development efforts on addressing Alzheimer's disease. Collectively, efforts by biopharmaceutical companies in the field of neurodegenerative diseases have seen many failures and limited success in drug development. For example, there are no therapeutic options available to reverse Alzheimer's disease, or even to halt its progress. Our future success is highly dependent on the successful development of our product candidates for treating Alzheimer's disease. Developing and, if approved, commercializing our product candidates for treatment of Alzheimer's disease subjects us to many challenges, including obtaining regulatory approval from the FDA and other regulatory authorities who have only a limited set of precedents to rely on. We cannot be sure that our approach will yield satisfactory therapeutic products that are safe and effective, scalable, or profitable.

Our Phase II clinical trials with PTI-125 in patients with Alzheimer's disease are not designed to show a statistically meaningful difference between those patients who receive placebo and those who receive drug product.

Clinical research data is often analyzed with statistical probability ("p-value") to address the question of whether a clinical observation is related to a treatment effect, a random effect or something else. This, in turn, requires a clinical study to incorporate a sufficiently large sample patient population to infer the appropriate statistical analysis. By design, our Phase II clinical program with PTI-125 does not include a sufficiently large patient population to generate statistical probability on clinical observations. This feature may make it difficult for investors to properly interpret whether clinical observations in our Phase II studies with PTI-125, if any, are important or meaningful. Conversely, our clinical studies may generate statistically meaningful data (i.e., $p<0.05$) that has trivial or no clinical importance. In general, the distinction between statistical significance and clinical significance is a complex area of research that continues to evolve and may be subject to differences of opinion among scientists, clinicians and other professionals.

We may encounter substantial delays in our clinical trials or may not be able to conduct or complete our clinical trials on the timelines we expect, if at all.

Clinical testing is expensive, time consuming, and subject to uncertainty. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. We cannot be sure that submission of an IND or a clinical trial application ("CTA") will result in the FDA or European Medicines Agency ("EMA"), as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, safety or other issues may arise that could suspend or terminate such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our future clinical trials may not be successful. Events that may prevent successful or timely initiation or completion of clinical trials include:

- inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials;
- delays in confirming target engagement, patient selection, or other relevant biomarkers to be utilized in preclinical and clinical product candidate development;
- delays in reaching a consensus with regulatory agencies on study design;
- delays in reaching an agreement on acceptable terms with prospective contract research organizations ("CROs") and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in identifying, recruiting, and training suitable clinical investigators;
- delays in obtaining required IRB approval for each clinical trial site;
- imposition of a temporary or permanent clinical hold by regulatory agencies for a number of reasons, including:
- after review of an IND or amendment, CTA or amendment, or equivalent application or amendment;
- as a result of a new safety finding that presents unreasonable risk to clinical trial participants;
- a negative finding from an inspection of our clinical trial operations or study sites; or
- the finding that the investigational protocol or plan is clearly deficient to meet its stated objectives;
- delays in identifying, recruiting, and enrolling suitable patients to participate in our clinical trials, and delays caused by patients withdrawing from clinical trials, or failing to return for post-treatment follow-up;
- difficulty collaborating with patient groups and investigators;

- failure by our CROs, other third parties, or us to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA's or any other regulatory authority's cGCPs requirements, or applicable EMA or other regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- the cost of clinical trials of our product candidates being greater than we anticipate;
- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon product development programs; and
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing.

Any inability to successfully initiate or complete clinical trials could result in additional costs to us or impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may be required to, or we may elect, to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the data safety monitoring board for such trial or by the FDA, EMA, or any other regulatory authority, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA, or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions, or lack of adequate funding to continue the clinical trial.

We may in the future advance product candidates into clinical trials and terminate such trials prior to their completion, which could adversely affect our business.

Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay, or potentially jeopardize our ability to commence product sales and generate revenue. 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 the denial of regulatory approval of our product candidates.

We may encounter difficulties enrolling patients in our clinical trials, and our clinical development activities could thereby be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll enough patients who remain in the trial until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons, including:

- the size and nature of the patient population;
- the patient eligibility criteria defined in the protocol, including biomarker-driven identification and/or certain highly-specific criteria related to stage of disease progression, which may limit the patient populations eligible for our clinical trials to a greater extent than competing clinical trials for the same indication that do not have biomarker-driven patient eligibility criteria;
- the size of the study population required for analysis of the trial's primary endpoints;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- competing clinical trials for similar therapies or targeting patient populations meeting our patient eligibility criteria;
- clinicians' and patients' perceptions as to the potential advantages and side effects of the product candidate being studied in relation to other available therapies and product candidates;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will not complete such trials, for any reason.

Our clinical trials may fail to demonstrate substantial evidence of the safety and efficacy of our product candidates, which would prevent, delay, or limit the scope of regulatory approval and commercialization.

Before obtaining regulatory approvals for any of our product candidates, we must demonstrate through lengthy, complex, and expensive preclinical experiments and clinical trials that our product candidates are both safe and effective for use in an intended population. Each product 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 product candidates may not be predictive of the results of early-stage or later-stage clinical trials, and results of early clinical trials of our product 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 product 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. Open-label extension studies may also extend the timing and cost of a clinical trial substantially. Product 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. Many companies in the biopharmaceutical 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 neurodegenerative diseases, where failure rates historically have been higher than in many other disease areas. Most product candidates that begin clinical trials are never approved by regulatory authorities for commercialization.

We have limited experience in designing clinical trials in neurodegeneration and may be unable to design and execute a clinical trial to support marketing approval. We cannot be certain that our current clinical trials or any other future clinical trials will be successful. Additionally, any safety concerns observed in any one of our clinical trials in our targeted indications

could limit the prospects for regulatory approval of our product candidates in those and other indications, which could have a material adverse effect on our business, financial condition, and results of operations.

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 product candidates for approval. 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 product candidates. Even if regulatory approval is secured for any of our product candidates, the terms of such approval may limit the scope and use of our product candidates, which may also limit its commercial potential.

The market opportunities for PTI-125 and PTI-125Dx, if approved, may be smaller than we anticipate.

If our clinical development programs succeed, we expect to seek regulatory approval of PTI-125 and PTI-125Dx for patients with Alzheimer's disease. Our projections of the number of patients with Alzheimer's disease is based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, patient foundations and market research, and may prove to be incorrect. The actual number of patients may turn out to be lower than expected. Additionally, the potential patient population for our current programs or future product candidates may be limited. Even if we obtain significant market share for any product candidate, if approved, if the potential target populations are smaller than anticipated, we may never achieve profitability without obtaining marketing approval for additional indications.

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, any of which may harm our business operations.

The development and commercialization of new product candidates is highly competitive. Moreover, the neurodegenerative field is characterized by intense and increasing competition, and a strong emphasis on intellectual property. We may face competition with respect to any of our product 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.

Several large pharmaceutical and biotechnology companies are currently pursuing the development of products for the treatment of neurodegenerative diseases, including Alzheimer's disease. Many of these 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 products than we do.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop. Furthermore, currently approved products could be discovered to have application for treatment of neurodegenerative disease indications, which could give such products significant advantages over any of our product candidates. Our competitors also may obtain FDA, EMA, or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, products or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, we could face litigation or other proceedings with respect to the scope, ownership, validity, and/or enforceability of our patents relating to our competitors' products and our competitors may allege that our products infringe, misappropriate, or otherwise violate their intellectual property. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

The manufacture of our product candidates is complex, and we may encounter difficulties in production. If we or any of our third-party manufacturers encounter such difficulties, or fail to meet rigorously enforced regulatory standards, our ability to provide supply of our product candidates for clinical trials or our products 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 product candidates are complex, expensive, highly-regulated, and subject to multiple risks. Further, as product 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 product 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 product candidates, or supply commercial products, if approved, we will need to manufacture them in large quantities. Our CDMOs may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If our CDMOs are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing, and clinical trials of that product candidate may be delayed or become infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. The same risk 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 products that we may develop is subject to FDA, EMA, and foreign regulatory authority approval processes, 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 cGMP on an ongoing basis. If we or our third-party manufacturers are unable to reliably produce products to specifications acceptable to the FDA, EMA, or other regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CDMOs will be able to manufacture the approved product to specifications acceptable to the FDA, EMA, or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, 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 product candidates, 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 our product candidates receive regulatory approval, we and our collaborators will be subject to ongoing FDA obligations and continued regulatory review, such as continued safety reporting requirements, and we and our collaborators may also be subject to additional FDA post-marketing obligations or new regulations, all of which may result in significant expense and limit our and our collaborators' ability to commercialize our potential drugs.

Any regulatory approvals that our product candidates receive may also be subject to limitations on the indicated uses for which the drug may be marketed or contain requirements for potentially costly post-marketing follow-up studies. In addition, if the FDA approves any of our product candidates, the labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping for the drug will be subject to extensive regulatory requirements. The subsequent discovery of previously unknown problems with the drug, including but not limited to adverse events of unanticipated severity or frequency, or the discovery that adverse events previously observed in preclinical research or clinical trials that were believed to be minor actually constitute much more serious problems, may result in restrictions on the marketing of the drug, and could include withdrawal of the drug from the market.

The FDA's policies may change, and additional government regulations may be enacted that could prevent or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. If we are not able to maintain regulatory compliance, we may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution. Any of these events could prevent us from marketing our drugs and our business could suffer.

We may not succeed at in-licensing product candidates or technologies to expand our product pipeline.

We may not successfully in-license product candidates or technologies to expand our product pipeline. The number of such candidates and technologies is limited. Competition among large pharmaceutical companies and biopharmaceutical companies for promising product candidates and technologies is intense because such companies generally desire to expand their product pipelines through in-licensing. If we fail to carry out such in-licensing and expand our product pipeline, our potential future revenues may suffer.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

The regulatory cycles of the FDA, EMA, and comparable foreign regulatory authorities are lengthy, time consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.

The time required to obtain approval by the FDA, EMA, and comparable foreign regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials, and depends upon numerous factors, including the type, complexity, and novelty of the product candidates involved. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical, or other studies. The FDA has not approved a new drug for Alzheimer's disease since 2003. We have not obtained regulatory approval for any product candidate, including our product candidates aimed at Alzheimer's disease, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Applications for our product candidates could fail to receive regulatory approval in an initial or subsequent indication for many reasons, including but not limited to the following:

- the FDA, EMA, or comparable foreign regulatory authorities may disagree with the design, implementation, or results of our clinical trials;
- the FDA, EMA, or comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities, or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- we may be unable to demonstrate to the FDA, EMA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio when compared to the standard of care is acceptable;
- the FDA, EMA, or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a new drug application ("NDA"), or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA, EMA, or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures, and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, EMA, or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and growth prospects.

Our product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.

We have not yet completed long term safety studies with PTI-125 to determine if this product candidate is safe for humans. Adverse events or other undesirable side effects caused by PTI-125 could cause us or regulatory authorities to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA, or other comparable foreign regulatory authorities.

Drug-related side effects could affect patient recruitment, the ability of enrolled patients to complete the study, and/or result in potential product liability claims. We are required to maintain product liability insurance pursuant to certain of our development and commercialization agreements. We may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. A successful product liability claim or series of claims brought against us could adversely affect our results of operations, business, and reputation. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical trial participants, costs due to related litigation, distraction of management's attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates, and decreased demand for our product candidates, if approved for commercial sale.

Our employees, independent contractors, consultants, commercial partners, and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud, misconduct, or other illegal activity by our employees, independent contractors, consultants, commercial partners, and vendors. Misconduct by these parties could include intentional, reckless, and negligent conduct that fails to:

- comply with the laws of the FDA, EMA, and other comparable foreign regulatory authorities;
- provide true, complete, and accurate information to the FDA, EMA, and other comparable foreign regulatory authorities;
- comply with manufacturing standards we have established;
- comply with healthcare fraud and abuse laws in the U.S. and similar foreign fraudulent misconduct laws; or
- report financial information or data accurately or to disclose unauthorized activities to us.

Activities subject to laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. Further, it is not always possible to identify and deter misconduct by employees and third parties, 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 be in compliance with such laws. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Risks Related to Our Reliance on Third Parties

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 product 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 cGCPs 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 product candidates we may develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

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, including with the shipment of any drug supplies, could delay clinical development or marketing approval of any product candidates we may develop or commercialization of our product candidates, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of materials for our research programs, preclinical studies, clinical trials, and for commercialization of any product candidates that we may develop. This reliance on third parties carries and may increase the risk that we will not have sufficient quantities of such materials, product candidates, or any product candidates that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.

We do not have any manufacturing facilities. We currently rely on CDMOs for all of the manufacture of our materials for preclinical studies and clinical trials and expect to continue to do so for preclinical studies, clinical trials, and for commercial supply of any product candidates that we may develop. We currently have established relationships with several CDMOs for the manufacturing of our product candidates. We may be unable to establish any further agreements with CDMOs or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on CDMOs entails additional risks, including:

- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting; and
- the inability to produce required volume in a timely manner and to quality standards.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the U.S. Our failure, or the failure of our CDMOs, to comply with applicable regulations could result in clinical holds on our trials, sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures, or recalls of product candidates or product candidates, operating restrictions, and criminal prosecutions,

any of which could significantly and adversely affect supplies of our product candidates and harm our business, financial condition, results of operations, and growth prospects.

Any product candidates that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future third-party manufacturers could delay clinical development or marketing approval. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer and may incur added costs and delays in identifying and qualifying any such replacement. Furthermore, securing and reserving production capacity with contract manufacturers may result in significant costs.

Our current and anticipated future dependence upon others for the manufacture of any product candidates we may develop may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis.

We depend on third-party suppliers for key raw materials used in our manufacturing processes, and the loss of these third-party suppliers or their inability to supply us with adequate raw materials could harm our business.

We rely on third-party suppliers for the supply of the raw materials required for the production of our product candidates, and we expect to continue to rely on third party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of raw materials involve several risks, including limited control over pricing, availability, quality, and delivery schedules. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our competitors who are larger than we are. We do not have long-term supply agreements, and we purchase our required drug product on a development manufacturing services agreement or purchase order basis. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for any product candidates we develop, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the U.S. and other countries with respect to our proprietary product candidates and other technologies we may develop. We seek to protect our proprietary position by filing patent applications in the U.S. and abroad relating to our core programs and product candidates, as well as other technologies that are important to our business. Given that the development of our product candidates is at an early stage, our intellectual property portfolio with respect to certain aspects of our product candidates is also at an early stage. For example, we have filed or intend to file patent applications on aspects of our technology and core product candidates; however, there can be no assurance that any such patent applications will issue as granted patents. Furthermore, in some cases, we have only filed provisional patent applications on certain aspects of our technology and product candidates and each of these provisional patent applications is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of the filing date of the applicable provisional patent application. Any failure to file a non-provisional patent application within this timeline could cause us to lose the ability to obtain patent protection for the inventions disclosed in the associated provisional patent applications.

Furthermore, in some cases, we may not be able to obtain issued claims covering compositions relating to our core programs and product candidates, as well as other technologies that are important to our business, and instead may need to rely on filing patent applications with claims covering a method of use and/or method of manufacture for protection of such

core programs, product candidates, and other technologies. There can be no assurance that any such patent applications will issue as granted patents, and even if they do issue, such patent claims may be insufficient to prevent third parties, such as our competitors, from utilizing our technology. Any failure to obtain or maintain patent protection with respect to our core programs and product candidates could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

If any of our patent applications do not issue as patents in any jurisdiction, we may not be able to compete effectively.

Changes in either the patent laws or their interpretation in the U.S. and other countries may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our patents with respect to our product candidates. With respect to our intellectual property related to our product candidates, we cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors or other third parties.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, or enforce 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 in time to obtain patent protection. Although we enter into nondisclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, CDMOs, consultants, advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in any of our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

U.S. intellectual property rights around diagnostic methods is a complex and evolving area of law and effective patent claims may not be available to us for our diagnostic product candidate, PTI-125Dx.

The legal system for intellectual property around diagnostic methods is highly complex, remains uncertain and continues to evolve. In the U.S., patent courts have struggled to define a clear means of patent eligibility for modern age diagnostics. Case law interpretations from the U.S. Supreme Court has left certain important scientific advances in the area of diagnostics without effective patent claims. In 2012, the Supreme Court held that a simple process involving correlations between blood test results and patient health is not eligible for patent claims because such processes incorporate "laws of nature". Since then, different outcomes from different courts, including Federal Circuit, district court and Patent Trial and Appeal Board decisions, have continued to create a sometimes vague or conflicting legal framework for determining the eligibility of patent claims for diagnostic methods. As a result, we cannot be certain how PTI-125Dx fits into the current U.S. legal framework for obtaining effective patent claims. Furthermore, claims for diagnostic methods can be complicated to enforce. In order for patent infringement to occur with a protected diagnostic, the patented method must generally either be performed by one person in its entirety or performed by multiple parties all under the control or direction of a single party. Accordingly, even if effective patent claims are issued for PTI-125Dx, it may not be practical, possible or even desirable to enforce potential infringement claims around this product candidate.

If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical technology and product candidates would be adversely affected.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our product candidates or other technologies or which effectively prevent others from commercializing competitive technologies and product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents to which we have rights may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether product candidates or other technologies will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and growth prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patents may be challenged in the courts or patent offices in the U.S. and abroad. We may be subject to a third-party pre-issuance submission of prior art to the United States Patent and Trademark Office ("USPTO") or become involved in opposition, derivation, revocation, reexamination, post-grant and inter partes review, or interference proceedings or other similar proceedings challenging our patent rights. An adverse determination in any such submission, proceeding, or litigation could reduce the scope of, or invalidate or render unenforceable, such patent rights, allow third parties to commercialize our product candidates or other technologies and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our priority of invention or other features of patentability with respect to our patents and patent applications. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our product candidates and other technologies. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. If we are unsuccessful in any such proceeding or other priority or inventorship dispute, we may be required to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other priority or inventorship disputes. Such licenses may not be available on commercially reasonable terms or at all or may be non-exclusive. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture, and commercialization of one or more of the product candidates we may develop. The loss of exclusivity or the narrowing of our owned and licensed patent claims could limit our ability to stop others from using or commercializing similar or identical technology and products.

In addition, given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

Filing, prosecuting, and defending patents on our product candidates and other technologies in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the U.S.

Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products, and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the U.S. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary 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, could put 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 and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by government 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 government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the U.S. over the lifetime of our owned or licensed patents and applications. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of the patent laws in the U.S. could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the U.S., the first to invent the claimed invention was entitled to the patent, while outside the U.S., the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act (the "America Invents Act") enacted in September 2011, the U.S. transitioned to a first inventor to file system in which, assuming that other requirements for patentability 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. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Since patent applications in the U.S. and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we were the first to either (i) file any patent application related to our product candidates or other technologies or (ii) invent any of the inventions claimed in our patents or patent applications.

The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. 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. Because of a lower evidentiary standard in USPTO proceedings as compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents 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 growth prospects.

In addition, the patent positions of companies in the development and commercialization of pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways

that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

Issued patents covering our product candidates and other technologies could be found invalid or unenforceable if challenged in court or before administrative bodies in the U.S. or abroad.

If we initiated legal proceedings against a third party to enforce a patent covering our product candidates or other technologies, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be 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 raise claims challenging the validity or enforceability of our patents before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, inter partes review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of, or amendment to our patents in such a way that they no longer cover our product candidates or other technologies. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we or our licensing partners and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates or other technologies. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations, and growth prospects.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, our business may be materially harmed.

Depending upon the timing, duration, and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman Act"). The Hatch-Waxman Act permits a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A 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 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 extensions as compensation for patent term lost during regulatory review processes are also available in certain foreign countries and territories, such as in Europe under a Supplementary Patent Certificate. However, we may not be granted an extension in the U.S. and/or foreign countries and territories because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing 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 a patent term extension or the term of any such extension is shorter than what we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and growth prospects could be materially harmed.

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

We may be subject to claims that former employees, scientific collaborators or other third parties have an interest in our patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of employees, consultants, or others who are involved in developing our product candidates or other technologies. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership of our patents, trade secrets, or other intellectual property. If the defense of any such claims fails, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates and other technologies. 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. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for our product candidates and other technologies, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology, and other proprietary information and to maintain our competitive position. We consider trade secrets and know-how to be one of our primary sources of intellectual property. Trade secrets and know-how can be difficult to protect. We expect our trade secrets and know-how to over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel from academic to industry scientific positions.

We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, CDMOs, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants as well as train our employees not to bring or use proprietary information or technology from former employers to us or in their work, and remind former employees when they leave their employment of their confidentiality obligations. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite our efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. 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 U.S. are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

We may not be successful in obtaining necessary rights to our product candidates or other technologies.

Many pharmaceutical companies, biotechnology companies, and academic institutions that compete with us in the field of neurodegeneration therapy may have patents filed and are likely filing patent applications potentially relevant to our business. In order to avoid infringing these third-party patents, we may find it necessary or prudent to obtain licenses to such patents from such third-party intellectual property holders. We may also require licenses from third parties for certain technologies for use with future product candidates. In addition, with respect to any patents we co-own with third parties, we may wish to obtain licenses to such co-owner's interest to such patents. However, we may be unable to secure such licenses or otherwise acquire any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for our future product candidates. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

We may be subject to claims that our employees, consultants, or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants, and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors and potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. 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 or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

Third-party claims of intellectual property infringement, misappropriation, or other violation against us may prevent or delay the development and commercialization of our product candidates and other technologies.

The field of developing innovations for neurodegenerative diseases is highly competitive and dynamic. Due to the focused research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is in flux, and it may remain uncertain in the future. Additionally, the technology used in our product candidates is still in an early stage and no products utilizing similar technology have yet reached the market. As such, there may be significant intellectual property related litigation and proceedings relating to our, and other third party, intellectual property and proprietary rights in the future.

Our commercial success depends in part on our ability to develop, manufacture, market, and sell any product candidates that we develop and to use our proprietary technologies without infringing, misappropriating, and otherwise violating the patents and other intellectual property rights of third parties. There is a substantial amount of complex litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may become party to, or threatened with, such actions in the future, regardless of their merit. As discussed above, recently, due to changes in U.S. law referred to as patent reform, new procedures including inter partes review and post-grant review have been implemented. As stated above, this reform adds uncertainty to the possibility of challenge to our patents in the future.

Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates and other technologies may give rise to claims of infringement of the patent rights of others. Although we believe that we do not infringe on any third parties' patents or other intellectual property, we cannot assure you that our product candidates and other technologies that we have developed, are developing or may develop in the future will not infringe existing or future patents owned by third parties. We may not be aware of patents that have already been issued to a third party, such as a competitor in the fields in which we are developing product candidates, who might assert infringement of patents it may hold by our current or future product candidates or other technologies, including claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover our product candidates or other technologies. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates or other technologies, could be found to be infringed by our product candidates or other technologies. In addition, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates or other technologies may infringe.

Third parties may have patents or obtain patents in the future and claim that the manufacture, use or sale of our product candidates or other technologies infringes upon these patents. In the event that any third-party claims that we infringe their patents or that we are otherwise employing their proprietary technology without authorization and initiates litigation against us, even if we believe such claims are without merit, a court of competent jurisdiction could hold that such patents are valid, enforceable and infringed by our product candidates or other technologies. In this case, the holders of such patents may be able to block our ability to commercialize the applicable product candidate or technology unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be held invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all. Even if we are able to obtain a license, the license would likely obligate us to pay license fees or royalties or both, and the rights granted to us might be nonexclusive, which could result in our competitors gaining access to the same intellectual property. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize our product candidates or other

technologies, or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business.

Defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and other employee resources from our business, and may impact our reputation. In the event of a successful claim of infringement against us, we may be enjoined from further developing or commercializing our infringing product candidates or other technologies. In addition, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties, and/or redesign our infringing product candidates or technologies, which may be impossible or require substantial time and monetary expenditure. In that event, we would be unable to further develop and commercialize our product candidates or other technologies, which could harm our business significantly.

Engaging in litigation to defend against third parties alleging that we have infringed, misappropriated, or otherwise violated their patents or other intellectual property rights is very expensive, particularly for a company of our size, and time-consuming. Some of our competitors may be able to sustain the costs of litigation or administrative proceedings more effectively than we can because of greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings against us could impair our ability to compete in the marketplace. The occurrence of any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe on our patents or the patents of our licensing partners, or we may be required to defend against claims of infringement. In addition, our patents or the patents of our licensing partners also may become involved in inventorship, priority, or validity disputes. To counter or defend against such claims can be expensive and time consuming. In an infringement proceeding, a court may decide that a patent in which we have an interest is invalid or unenforceable, the other party's use of our patented technology falls under the safe harbor to patent infringement, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. 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.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. 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 and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Intellectual property rights do not necessarily address all potential threats.

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 products that are similar to our product candidates or utilize similar technology but that are not covered by the claims of the patents that we may own;
- we might not have been the first to make the inventions covered by the issued patent or pending patent application that we own now or in the future;

- we 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 owned intellectual property rights;
- it is possible that our current or future pending patent applications will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;
- our competitors or other third parties 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 products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and growth prospects.

Risks Related to Our Operations

We are a small company. We are highly dependent on our key personnel, and if we are not successful in attracting, motivating, and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract, motivate, and retain highly qualified managerial, scientific, and medical personnel. We are highly dependent on our management, particularly our Chief Executive Officer, Remi Barbier, and our scientific and technical personnel. The loss of the services provided by any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to find suitable replacements, could result in delays in the development of our product candidates and harm our business.

Competition for skilled personnel is intense and the turnover rate can be high, which may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. We expect that we may need to recruit talent from outside of our region in Austin, TX, and doing so may be costly and difficult.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided equity option grants that vest over time. The value to employees of these equity grants that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. If we are unable to attract and incentivize quality personnel on acceptable terms, or at all, it may cause our business and operating results to suffer.

If our current research collaborators or scientific advisors terminate their relationships with us or develop relationships with a competitor, our ability to continue our business operations could be adversely affected.

We have relationships with research collaborators at academic and other institutions who conduct research at our request. These research collaborators are not our employees. As a result, we have limited control over their activities and, except as otherwise required by our collaboration agreements, can expect only limited amounts of their time to be dedicated to our activities. Our ability to discover drugs and biomarkers involved in human disease and validate and commercialize diagnostic tests will depend in part on the continuation of these collaborations. If any of these collaborations are terminated, we may not

be able to enter into other acceptable collaborations. In addition, our existing collaborations may not be successful. Our research collaborators and scientific advisors may have relationships with other commercial entities, some of which could compete with us. Our research collaborators and scientific advisors sign agreements which provide for the confidentiality of our proprietary information and the results of studies conducted at our request. We may not, however, be able to maintain the confidentiality of our technology and other confidential information related to all collaborations. The dissemination of our confidential information could have a material adverse effect on our business.

We will need to grow the size and capabilities of our organization, and we may experience difficulties in managing this growth.

As our development plans and strategies develop, we may need to add a significant number of additional managerial, operational, financial, and other personnel. Future growth will impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, retaining, and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and FDA review process for our current and future product candidates, while complying with our contractual obligations to contractors and other third parties;
- expanding our operational, financial and management controls, reporting systems, and procedures; and
- managing increasing operational and managerial complexity.

Our future financial performance and our ability to continue to develop and, if approved, commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth. Our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to manage these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors, and consultants to provide certain services. There can be no assurance that the services of these independent organizations, advisors, and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, if at all.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop our product candidates and, accordingly, may not achieve our research, development, and commercialization goals.

Our internal computer systems, or those used by our third-party research institution collaborators, CROs or other contractors or consultants, may fail or suffer other breakdowns, cyberattacks, or information security breaches that could compromise the confidentiality, integrity, and availability of such systems and data, result in material disruptions of our development programs and business operations, risk disclosure of confidential, financial, or proprietary information, and affect our reputation.

In the ordinary course of our business, we collect and store sensitive data, including legally protected patient health information, personally identifiable information about our employees, intellectual property, and proprietary business information. We manage and maintain our applications and data utilizing on-site systems. These applications and data encompass a wide variety of business-critical information including research and development information, commercial information and business and financial information. Despite the implementation of security measures, our internal computer systems and those of our current or future CROs and other contractors and consultants may be vulnerable to damage from computer viruses and unauthorized access. As the cyber-threat landscape evolves, these attacks are growing in frequency, sophistication, and intensity, and are becoming increasingly difficult to detect. Such attacks could include the use of key loggers or other harmful and virulent malware, including ransomware or other denials of service, and can be deployed through

malicious websites, the use of social engineering, and/or other means. If a breakdown, cyberattack, or other information security breach were to occur and cause interruptions in our operations, it could result in a misappropriation of confidential information, including our intellectual property or financial information, and 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 product candidates and other third parties for the manufacture of our product 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, financial, or proprietary information, including data related to our personnel, we could incur liability or risk disclosure of confidential, financial, or proprietary information, and the further development and commercialization of our product candidates could be delayed. There can be no assurance that we and our business counterparties will be successful in efforts to detect, prevent, or fully recover systems or data from all breakdowns, service interruptions, attacks, or breaches of systems that could adversely affect our business and operations and/or result in the loss of critical or sensitive data, which could result in financial, legal, business, or reputational harm to us.

Our business involves environmental risks that may result in liability for us.

In connection with our research and development activities, we, and our collaborators and vendors, are subject to federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials, biological specimens, chemicals and wastes. Although we believe that we comply with such applicable laws, regulations and policies in all material respects and have not been required to correct any material noncompliance, we may incur significant costs to comply with environmental and health and safety regulations in the future. Although we believe that our safety procedures for handling and disposing of controlled materials comply with the standards prescribed by state and federal regulations, accidental contamination or injury from these materials may occur. In the event of such an occurrence, we could be held liable for any damages that result and any such liability could exceed our resources.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our third-party research institution collaborators, CROs, CDMOs, suppliers, and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, and other natural or man-made disasters or business interruptions, for which we are partly uninsured. In addition, we rely on our third-party research institution collaborators for conducting research and development of our product candidates, and they may be affected by government shutdowns or withdrawn funding. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third party manufacturers to produce and process our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

Most of our operations are located in a single office facility in Austin, TX. Damage or extended periods of interruption to our corporate, development, or research facilities due to fire, natural disaster, power loss, communications failure, unauthorized entry, or other events could cause us to cease or delay development of some or all of our product candidates. Our insurance might not cover all losses under such circumstances and our business may be seriously harmed by such delays and interruption.

Social media platforms present risks and challenges.

As social media continues to expand, it also presents us with new challenges. The inappropriate or unauthorized use of our confidential information on media platforms could cause brand damage or information leakage, which would cause legal or regulatory problems for us. In addition, negative, inappropriate or inaccurate posts or comments about us or our product candidates on social media internet sites could quickly and irreversible damage our reputation, brand image and goodwill. Further, the accidental or intentional disclosure of non-public sensitive information by our workforce or others through media channels could lead to information loss or could lead to legal problems for us.

The comprehensive tax reform bill of 2017 could adversely affect our business and financial condition.

On December 22, 2017, the Tax Cuts and Jobs Act (the "Tax Act"), was enacted. The Tax Act makes broad and complex changes to the U.S. tax code, with many of its provisions effective for tax years beginning on or after January 1, 2018. The Tax Act, among other things, contains significant changes to corporate taxation, including a permanent reduction of the corporate income tax rate, a partial limitation on the deductibility of business interest expense, a limitation of the deduction for net operating loss carryforwards to 80% of current year taxable income, an indefinite net operating loss carryforward, immediate deductions for certain new investments instead of deductions for depreciation expense over time, the modification or repeal of many business deductions and credit, and puts into effect the migration from a "worldwide" system of taxation to a territorial system. We continue to examine the impact this legislation may have on our business. The overall impact of the Tax Act is evolving, and our business operations and financial condition could be adversely affected.

Risks Related to the Ownership of Our Common Stock

We do not know whether a market will continue to develop for our common stock or what the market price of our common stock will be, and, as a result, it may be difficult to sell shares of our common stock.

If a market for our common stock is not sustained, it may be difficult to sell shares of our common stock at an attractive price or at all. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations and progression of our product pipeline may not meet the expectations of public market analysts and investors, and, as a result of these and other factors, the price of our common stock may fall.

The market price of our common stock may be volatile, which could result in substantial losses for investors who purchase our shares.

Some of the factors that may cause the market price of our common stock to fluctuate include:

- the success of existing or new competitive products or technologies;
- the timing and results of clinical trials for our current product candidates and any future product candidates that we may develop;
- failure or discontinuation of any of our product development and research programs;
- results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our research programs, clinical development programs, or product candidates that we may develop;

- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders, or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- market conditions in the pharmaceutical and biotechnology sectors; and
- general economic, industry, and market conditions.

In recent years, the stock market in general, Nasdaq, and the markets for early stage companies and pharmaceutical and biotechnology companies, has experienced significant price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common stock, regardless of our actual operating performance. Following periods of such volatility in the market price of a company's securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management's attention and resources from our business.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We do not currently have and may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock could decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock or if we fail to meet their operating results estimates for us, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances, and licensing arrangements. We, and indirectly, our stockholders, will bear the cost of issuing and servicing such securities. Because our decision to issue debt or equity securities in any future offering will depend on market conditions and other factors beyond our control, we cannot predict or estimate the amount, timing, or nature of any future offerings. To the extent that we raise additional capital through the sale of equity or debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell, or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additionally, any future collaborations we enter into with third parties may provide capital in the near term but limit our potential cash flow and revenue in the future. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us.

If we are unable to maintain effective internal controls, our business, financial position, and results of operations could be adversely affected.

As a public company, we are subject to reporting and other obligations under the Securities Exchange Act of 1934, as amended ("Exchange Act"), including the requirements of Section 404 of SOX, which require annual management assessments of the effectiveness of our internal control over financial reporting.

The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by SOX. These reporting and other obligations place significant demands on our management and administrative and operational resources, including accounting resources.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the U.S. Any failure to maintain effective internal controls could have an adverse effect on our business, financial position, and results of operations.

We are a smaller reporting company and we cannot be certain if the reduced disclosure requirements applicable to smaller reporting companies will make our common stock less attractive to investors.

We are currently a "smaller reporting company" as defined in the Exchange Act, and are thus allowed to provide simplified executive compensation disclosures in our filings, are exempt from the provisions of Section 404(b) of SOX requiring that an independent registered public accounting firm provide an attestation report on the effectiveness of internal control over financial reporting and have certain other reduced disclosure obligations with respect to our SEC filings. We will remain a "smaller reporting company" until the aggregate market value of our outstanding common stock held by non-affiliates as of the last business day our recently completed second fiscal quarter is $250 million or more. We cannot predict whether investors will find our common stock less attractive because of our reliance on any of 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 cannot ensure that there will be an active, liquid trading market for our common stock, as we have in the past and may in the future fail to meet all applicable listing requirements and, our common stock may be delisted from The Nasdaq Capital Market, which could have an adverse impact on the liquidity and market price of our common stock.

Our common stock is currently listed on The Nasdaq Capital Market, which has qualitative and quantitative listing criteria that we must meet in order to remain listed on Nasdaq.

Until August 2018, we were listed on the Nasdaq Global Market and have in the past temporarily fallen out of compliance with Nasdaq listing standards and there can be no assurance that we will continue to meet the appropriate Nasdaq listing requirements in the future.

On March 13, 2018, we received a notice from the staff of The Nasdaq Stock Market LLC (the "Staff") that we were not in compliance with Nasdaq Listing Rule 5450, setting forth the requirements for continued listing on Nasdaq. Nasdaq Listing Rule 5450 requires, among other things, that we meet one of the three standards under Nasdaq Listing Rule 5450(b); the Equity Standard; the Market Value Standard; or the Total Asset/Total Revenue Standard. The Staff notice stated that we were not in compliance with Nasdaq Listing Rule 5450(b)(2)(A) (under the Market Value Standard), as the minimum market value of our common stock had been below $50 million for 30 consecutive business days. In addition, the Staff notice stated that we did not meet the requirements under Nasdaq Listing Rule 5450(b)(3)(A) (under the Total Asset/Total Revenue Standard).

On April 26, 2018, following ten consecutive business days during which the market value of our common stock was $50 million or greater, we regained compliance with Nasdaq Listing Rule 5450(b)(2)(A).

On August 8, 2018, we received a letter from the Listing Qualifications Department of Nasdaq notifying us that our application to transfer our Nasdaq listing from the Nasdaq Global Select Market to The Nasdaq Capital Market had been

approved. Our common stock was transferred to The Nasdaq Capital Market the opening of business on August 13, 2018 under the symbol "PTIE." On March 28, 2019, our common stock symbol was changed to "SAVA". This transfer of our listing to The Nasdaq Capital Market or any other similar future transfers could adversely affect the liquidity of our common stock. Any such event could make it more difficult to dispose of, or obtain accurate quotations for the price of, our common stock, and there also would likely be a reduction in our coverage by securities analysts, if any, and the news media, which could cause the price of our common stock to decline further. We may also face other material adverse consequences in such event, such as negative publicity, a decreased ability to obtain additional financing, diminished investor and/or employee confidence, and the loss of business development opportunities, some or all of which may contribute to a further decline in our stock price.

If future events cause our common stock to be delisted, the liquidity of our common stock would be adversely affected, investors may not be able to sell their shares quickly or at the latest market price if trading in our stock is not active, and the market price of our common stock could decrease.

Anti-takeover provisions in our charter documents and Delaware law may prevent or delay removal of incumbent management or a change of control.

Anti-takeover provisions of our amended and restated certificate of incorporation and amended and restated bylaws and Delaware law may have the effect of deterring or delaying attempts by our stockholders to remove or replace management, engage in proxy contests and effect changes in control. The provisions of our charter documents include:

- a classified board so that only one of the three classes of directors on our Board is elected each year;
- elimination of cumulative voting in the election of directors;
- procedures for advance notification of stockholder nominations and proposals;
- the ability of the Board to amend our bylaws without stockholder approval; and
- the ability of the Board to issue up to 10,000,000 shares of preferred stock without stockholder approval upon the terms and conditions and with the rights, privileges and preferences as the Board may determine.

In addition, as a Delaware corporation, we are subject to Delaware law, including Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years following the date that the stockholder became an interested stockholder unless certain specific requirements are met as set forth in Section 203.

These provisions, alone or together, could have the effect of deterring or delaying changes in incumbent management, proxy contests or changes in control.

Our share ownership is concentrated, and our officers, directors and principal stockholders can exert significant control over matters requiring stockholder approval.

Due to their combined stock holdings, our officers, directors and principal stockholders (i.e., stockholders holding greater than 5% of our common stock) acting collectively may have the ability to exercise significant influence over matters requiring stockholder approval including the election of directors and approval of significant corporate transactions. In particular, Remi Barbier, our founder, Chairman of the Board, President and Chief Executive Officer, owns or controls a significant amount of the voting power of our outstanding capital stock. This concentration of ownership may delay or prevent a change in control of the Company and may make some transactions, including but not limited to any merger, consolidation, or sale of substantially all of our assets, more difficult or impossible to complete without the support of key stockholders.

Publicly available information regarding stockholders' ownership may not be comprehensive because the SEC does not require certain large stockholders to publicly disclose their stock ownership positions.

If the fair value of our stock increases and outstanding performance awards vest, we expect to use substantial amounts of cash to fund employee tax liabilities.

We have performance awards outstanding. If these performance awards vest, we expect to issue our employees shares of our common stock net of statutory employment taxes. This net issuance results in fewer shares issued and uses our cash to fund such taxes. The use of cash could be substantially higher, depending on the fair value of our common stock on the date the performance awards vest. If our use of cash to fund these taxes is substantial, our cash balance could substantially decline and our stock price could also decline.

We may in the future seek to fund the cash used for performance awards through the sale of our common stock. However, we may not be successful in selling shares of our common stock to fund the cash used for performance awards. If the number of shares we sell to fund the cash used for performance awards is significant, our stock price could decline.

Our operating results may fluctuate from quarter to quarter and this fluctuation may cause our stock price to decline.

Our quarterly operating results have fluctuated in the past and are likely to fluctuate in the future. Factors contributing to these fluctuations include, among other items, the timing and enrollment rates of clinical trials for our product candidates, our need for clinical supplies and the valuation of stock-based compensation. Thus, quarter-to-quarter comparisons of our operating results may not be indicative of what to expect in the future. As a result, in some future quarters our clinical, financial or operating results may not meet the expectations of securities analysts and investors and could result in a decline in the price of our stock.

We may sell additional equity or debt securities to fund our operations, which may result in dilution to our stockholders and impose restrictions on our business.

In order to raise additional capital to support our operations, we may sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock including under our ATM Agreement (as defined below), which could result in dilution our stockholders. On February 8, 2018, we entered into the Capital on Demand™ Sales Agreement, or the ATM Agreement, with JonesTrading Institutional Services LLC ("JonesTrading"), for the offer and sale up to $16.9 million of shares of our common stock, from time to time in one or more public offerings of our common stock, with JonesTrading acting as agent. Such transactions are to be made pursuant to a shelf registration statement that was declared effective by the SEC on July 31, 2017. On August 16, 2018, we filed a prospectus supplement, dated August 15, 2018, limiting sales under such ATM Agreement to up to $7.0 million of shares of our common stock and suspending sales under our ATM Agreement. We have sold a total of $4.1 million of our common stock under the ATM Agreement, before offering expenses.

On August 17, 2018, we completed an offering of common stock and issuance of warrants. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in prior offerings, and investors purchasing our shares or other securities in the future could have rights superior to existing shareholders. The price per share at which we sell additional shares of our common stock or securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in prior offerings.

Organizational Risks

We may not be successful in implementing the reorganization of our business.

In late 2018, we announced a strategic reorganization from a focus on analgesic drug development to neurodegenerative drug development. If we are unsuccessful in the execution of our new strategic reorganization, our business, financial condition, results of operations and prospects will be materially adversely affected.

The success of our business will depend upon our ability to develop and commercialize drug and diagnostic assets that target Alzheimer's disease, as well as others that we may develop or in-license in the future. There can be no assurance that we will be able to continue to implement the reorganization successfully or that we will realize the projected benefits of this initiative. If we do not successfully execute our strategic reorganization, our financial results will be adversely affected. Even if we execute this strategic reorganization as planned, we may not yield the anticipated benefits. Moreover, our continued implementation of our strategic reorganization may entail such actions as a reduction in headcount or other savings initiatives

and diversion of resources from other drugs currently in our pipeline which may have a material adverse effect on our business and profitability. Furthermore, our financial condition and results of operations following the strategic reorganization may not be comparable to the financial condition and results of operations reflected in our historical financial statements and historical financial information may not be indicative of our future financial performance.

We have broad discretion in the use of the net proceeds from any of our financing transactions and may not use them effectively.

Our management has broad discretion in the application of the net proceeds from our financing transactions, and investors will not have the opportunity to assess whether the net proceeds are being used appropriately. Our management could spend the net proceeds from offerings in ways that may vary substantially from their intended use, do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from our financing transactions in a manner that does not produce income or that loses value.

Risks Relating to Commercialization

We currently have no in-house capabilities to manufacture or commercialize our product candidates and we rely on third-party commercial drug manufacturers for clinical drug supplies. If we are unable to develop our own manufacturing, sales, marketing and distribution capabilities, or if we are not successful in contracting with third parties for these services on favorable terms, or at all, our product revenues could be disappointing.

We rely on various third-parties to manufacture, fill, label, store, test and ship our product candidates. We plan to continue to outsource formulation, manufacturing and related activities. These suppliers must comply with cGMP regulations enforced by the FDA and other government agencies and DEA regulations, and are subject to ongoing periodic unannounced inspection, including preapproval inspections by the FDA and DEA and corresponding state and foreign government agencies to ensure strict compliance with cGMP and other standards. These manufacturers may subsequently be stopped from producing, manufacturing, filling, labeling, storing, testing and shipping our product candidates due to their non-compliance with federal, state or local regulations. We do not have control over our suppliers' compliance with these regulations and standards and we cannot control decisions by our suppliers that affect their ability or willingness to continue to supply us on acceptable terms, or at all.

Disputes in the past have arisen with some of these third-parties with respect to fulfilling certain conditions and obligations. There can be no guarantee that such disputes will not arise again in the future, which may lead to termination of an agreement. If an agreement is terminated, we would not be able to commercialize our product candidates until another manufacturer is identified and we have entered into a manufacturing agreement with such manufacturer. We may not be able to replace a commercial supplier on commercially reasonable terms, or at all. Replacing any of our commercial suppliers would be expensive and time consuming. Failure by any of our suppliers to perform as expected could delay or prevent the commercialization or potential regulatory approval of our product candidates for an extended period of time, result in shortages, cost overruns or other problems and would materially harm our business.

We currently have no sales, marketing or distribution capabilities. We have not established commercial strategies regarding any of our product candidates. In order to commercialize our products, if any are approved by the FDA, we will either have to develop such capabilities internally or collaborate with third parties who can perform these services for us.

If we decide to commercialize any of our drugs ourselves, we may not be able to

- hire and retain the necessary experienced personnel;
- build sales, marketing and distribution operations in a cost-effective manner which are capable of successfully launching new drugs;
- obtain access to adequate numbers of physicians to prescribe our products; or
- generate sufficient product revenues.

In addition, establishing such operations on our own will take time and involve significant expense. If our commercial operations lack complementary products, we may not be able to compete in a cost-effective manner with competitors with more products to sell. If we engage third-party collaborators to perform any commercial operations, our future revenues may depend significantly upon the performance of those collaborators.

If we decide to enter into new co-promotion or other licensing arrangements with third parties, we may be unable to locate acceptable collaborators because the number of potential collaborators is limited and because of competition from others for similar alliances. Even if we are able to identify one or more acceptable new collaborators, we may not be able to enter into any collaborative arrangements on favorable terms, or at all.

In addition, due to the nature of the market for our product candidates, it may be necessary for us to license all or substantially all of our product candidates to a single collaborator, thereby eliminating our opportunity to commercialize these other products independently. If we enter into any such new collaborative arrangements, our revenues are likely to be lower than if we marketed and sold our products ourselves.

In addition, any revenues we receive would depend upon our collaborators' efforts which may not be adequate due to lack of attention or resource commitments, management turnover, change of strategic focus, business combinations or other factors outside of our control. Depending upon the terms of our collaboration, the remedies we have against an under-performing collaborator may be limited. If we were to terminate the relationship, it may be difficult or impossible to find a replacement collaborator on acceptable terms, or at all.

If physicians and patients do not accept and use our drugs, we will not achieve sufficient product revenues and our business will suffer.

Even if the FDA approves our drugs, physicians and patients may not accept and use them. Acceptance and use of our drugs will depend on a number of factors including:

- when the drug is launched into the market and related competition;
- approved label claims;
- perceptions by members of the healthcare community, including physicians, about the safety and effectiveness of our drugs;
- perceptions by physicians regarding the cost benefit of our product candidates;
- published studies demonstrating the cost-effectiveness of our drugs relative to competing products;
- availability of reimbursement for our products from government or healthcare payers;
- our or our collaborators' ability to implement a risk management plan prior to the distribution of any Schedule II drug; and
- effectiveness of marketing and distribution efforts by us and other licensees and distributors.

Because we expect to rely on sales generated by our current lead product candidates for substantially all of our revenues for the foreseeable future, the failure of any of these drugs to find market acceptance would harm our business and could require us to seek additional financing.

Our ability to market and promote our product candidates will be determined and limited by FDA-approved labeling.

The commercial success of our product candidates will depend upon our ability to obtain FDA-approved labeling describing their features. Our failure to achieve FDA approval of product labeling containing such information will prevent us from advertising and promoting the key features of our product candidates in order to differentiate them from other similar products. This would make our products less competitive in the market.

Risks Related to Government Regulation

If we fail to comply with the complex federal, state, local and foreign laws and regulations that apply to our business, we could suffer severe consequences that could materially and adversely affect our operating results and financial condition.

Our operations are subject to extensive federal, state, local and foreign laws and regulations, all of which are subject to change. These laws and regulations currently include, among other things:

- The Clinical Laboratory Improvement Amendments ("CLIA") of 1988, which are United States federal regulatory standards that apply to all clinical laboratory testing performed on humans in the United States, requires that laboratories obtain certification from the federal government, and state licensure laws;
- FDA laws and regulations;
- The Health Insurance Portability and Accountability Act ("HIPAA"), which imposes comprehensive federal standards with respect to the privacy and security of protected health information and requirements for the use of certain standardized electronic transactions, including penalties for violators, enforcement authority to state attorneys general and requirements for breach notification;
- state laws regulating testing and protecting the privacy of test results, as well as state laws protecting the privacy and security of health information and personal data and mandating reporting of breaches to affected individuals and state regulators;
- the federal anti-kickback law, or the Anti-Kickback Statute, which prohibits knowingly and willfully offering, paying, soliciting, receiving, or providing remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual, or the furnishing, arranging for, or recommending of an item or service that is reimbursable, in whole or in part, by a federal health care program;
- the federal False Claims Act ("FCA"), which imposes liability on any person or entity that, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment to the federal government;
- the federal Civil Monetary Penalties Law, which prohibits, among other things, the offering or transfer of remuneration to a Medicare or state health care program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies;
- other federal and state fraud and abuse laws, such as anti-kickback laws, prohibitions on self-referral, and false claims acts, which may extend to services reimbursable by any third-party payor, including private insurers;
- the federal Physician Payments Sunshine Act, which requires manufacturers to track and report to the federal government certain payments and other transfers of value made to physicians and teaching hospitals and ownership or investment interests held by physicians and their immediate family members;

- Section 216 of the federal Protecting Access to Medicare Act of 2014 ("PAMA"), which requires applicable laboratories to report private payer data in a timely and accurate manner beginning in 2017 and every three years thereafter (and in some cases annually);

- state laws that impose reporting and other compliance-related requirements; and

- similar foreign laws and regulations that will apply to us in foreign countries in which we may choose to operate in the future.

Enacted and future legislation may increase the difficulty and cost for us to commercialize our product candidates and may reduce the prices we are able to obtain for our product candidates.

Legislative and regulatory changes and future changes regarding the healthcare system could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities or affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In the U.S., the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (the "Medicare Modernization Act") established the Medicare Part D program and provided authority for limiting the number of drugs that will be covered in any therapeutic class thereunder. The Medicare Modernization Act, including its cost reduction initiatives, could limit the coverage and reimbursement rate that we receive for any of our approved products. Private payors may follow Medicare coverage policies and payment limitations in setting their own reimbursement rates resulting in similar limits in payments from private payors.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, among other things, imposes a significant annual fee on companies that manufacture or import branded prescription product candidates. It also contains substantial provisions intended to, among other things, broaden access to health insurance, reduce or constrain the growth of health care spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, and impose additional health policy reforms, any of which could have a material adverse effect on our business. A significant number of provisions are not yet, or have only recently become, effective, but the Affordable Care Act may result in downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

The Affordable Care Act, as well as other healthcare reform measures that have been and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product, and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may compromise our ability to generate revenue, attain profitability or commercialize our products.

The Affordable Care Act is a highly complex piece of legislation that continues to evolve. We do not and cannot understand or anticipate the full impact and potential implications of the Affordable Care Act on our business or on our drugs.

Our relationships with customers and payors will be subject to applicable anti-kickback, fraud and abuse, transparency, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm, administrative burdens, and diminished profits and future earnings.

Healthcare providers, physicians and payors play a primary role in the recommendation and prescription of any product candidates for which we may obtain marketing approval. Our future arrangements with payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any product candidates for which we may obtain marketing approval. Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. Restrictions under applicable federal, state and foreign healthcare laws and regulations may affect our ability to operate and expose us to areas of risk, including:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, offering, 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 under federal and state healthcare programs such as Medicare and Medicaid. 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;

- the FCA, which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA;

- HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute to defraud any healthcare benefit program or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and its implementing regulations, which also imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- federal laws requiring drug manufacturers to report information related to payments and other transfers of value made to physicians and other healthcare providers, as well as ownership or investment interests held by physicians and their immediate family members, including under the federal Open Payments program, commonly known as the Sunshine Act, as well as other state and foreign laws regulating marketing activities; and

- state and foreign equivalents of each of the above laws, including state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers; state laws which require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restricting payments that may be made to healthcare providers; 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 often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Nonetheless, it is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations.

Government agencies may establish and promulgate usage guidelines that could limit the use of our product candidates.

Government agencies, professional and medical societies, and other groups may establish usage guidelines that apply to our product candidates. These guidelines could address such matters as usage and dose, among other factors. Application of such guidelines could limit the clinical use or commercial appeal of our product candidates.

Risks Relating to Manufacturing

We do not own any manufacturing facilities and we rely on third-party commercial drug manufacturers for clinical drug supply.

We do not own any manufacturing facilities. We plan to continue to outsource formulation, manufacturing and related activities. We rely on a limited number of third-party suppliers to formulate, manufacture, fill, label, ship or store all of our product candidates. These suppliers must comply with current cGMP regulations enforced by the FDA and other government agencies and DEA regulations, and are subject to ongoing periodic unannounced inspection, including preapproval inspections by the FDA and DEA and corresponding state and foreign government agencies to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards. These manufacturers may subsequently be stopped from producing, storing, shipping or testing our drug products due to their non-compliance with federal, state or local regulations. We do not have control over our suppliers' compliance with these regulations and standards. We cannot control decisions by our suppliers that affect their ability or willingness to continue to supply us on acceptable terms, or at all. We may not be able to replace a commercial supplier on commercially reasonable terms, or at all. Replacing any of our commercial suppliers would be expensive and time consuming. Failure by any of our suppliers to perform as expected could delay or prevent commercialization of our product candidates or result in shortages, cost overruns, or other problems and would materially harm our business.

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

None.

Item 2. ***Properties***

We lease approximately 6,000 square feet of office space pursuant to a non-cancelable operating lease in Austin, TX that expires in December 2020, which is used for the development of novel drugs. We believe that our facilities are adequate and suitable for our current needs.

Item 3. ***Legal Proceedings***

None.

Item 4. ***Mine Safety Disclosures***

Not applicable.

PART II

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

Market Price of Dividends of the Registrants Common Equity and Related Stockholder Matters

Our common stock is quoted on Nasdaq, under the symbol "SAVA."

We currently expect to retain future earnings, if any, for use in the operation and expansion of our business and, notwithstanding our special non-dividend distributions in December 2012 (of $0.75 per share of common stock totaling $34.0 million) and December 2010 (of $2.00 per share of common stock totaling $85.7 million), we have not paid and do not anticipate paying any cash dividends in the foreseeable future. As of January 17, 2019, there were approximately 26 holders of record of our common stock.

Item 6. ***Selected Financial Data***

Not applicable.

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

This discussion and analysis should be read in conjunction with our financial statements and accompanying notes included elsewhere in this report. Operating results are not necessarily indicative of results that may occur in future periods.

Overview

Cassava Sciences, Inc. is a clinical-stage drug development company. Our expertise is to develop new product candidates and to guide these through various regulatory and development pathways in preparation for their potential commercialization. Since our inception, we have generally focused our drug development efforts on disorders of the central nervous system. We are currently conducting a Phase II clinical program for patients with Alzheimer's disease. By necessity, the conduct of drug development is complex, lengthy, expensive and risky. The U.S. Food and Drug Administration (the "FDA") has not yet established the safety or efficacy of our product candidates.

Our overall strategy is to leverage our unique scientific/clinical platform to develop a first-in-class program for neurodegeneration. Our goal is to address Alzheimer's disease and other neurodegenerative diseases, particularly those with a strong neuroinflammation component, with PTI-125, our drug product candidate and a diagnostic product candidate, PTI-125Dx, to detect Alzheimer's disease.

We seek to develop and gain regulatory approval for PTI-125 for the treatment of Alzheimer's disease and PTI-125Dx for the diagnosis of Alzheimer's disease. The following is a summary of our clinical-stage biopharmaceutical assets:

PTI-125 – PTI-125 is the name of our product candidate for the treatment of Alzheimer's disease. This proprietary small molecule drug represents an entirely new target to treat Alzheimer's disease. PTI-125 benefits from a strong scientific rationale, peer-reviewed publications in prestigious academic journals and multiple peer-reviewed research grant awards from the National Institutes of Health ("NIH"), the primary agency of the U.S. government for biomedical research.

In 2018, we initiated a Phase II clinical program in patients with Alzheimer's disease using PTI-125. Our Phase II clinical program with PTI-125 is substantially funded by research grant awards from the NIH. PTI-125 was discovered and designed in-house and was characterized by our academic collaborators during research activities that were conducted from approximately 2008 to date. We own exclusive, worldwide rights to PTI-125, without royalty obligations to any third party.

PTI-125Dx – We are developing PTI-125Dx as a blood-based biomarker/diagnostic to detect Alzheimer's disease. The goal of PTI-125Dx is to make the detection of Alzheimer's disease as simple as getting a blood test. This clinical-stage program is substantially funded by research grant awards from the NIH. PTI-125Dx was discovered and designed in-house and was characterized by our academic collaborators during research activities that were conducted from approximately 2008 to date. We own exclusive, worldwide rights to PTI-125Dx, without royalty obligations to any third party.

Our scientific approach is different.

For over 100 years, scientists have ascribed various neurodegenerative diseases to pathological proteins that misfold. Misfolded proteins are also altered or they aggregate, such as amyloid and tau in the case of Alzheimer's disease. Destruction of neuronal synapses, accelerated nerve cell death, and dysfunction of the brain support cells, are all widely believed to be a direct consequence of misfolded proteins.

Historically, the drug industry has attempted to treat Alzheimer's disease by developing drugs that block the synthesis of, or remove or dis-aggregate, beta amyloid and, more recently, tau. Essentially, the prevailing doctrine said that amyloid must be cleared out of the brain. This scientific approach – known as the amyloid hypothesis - has been repeatedly tested by our competitors in late stage clinical trials using a variety of antibody backbones, epitopes, target conformations, biomarkers and in various stages of disease. Such studies have all failed to yield therapeutic benefit for patients with Alzheimer's disease. More recently, experimental efforts have been proposed to ramp up the brain's immune system in people with Alzheimer's disease to remove amyloid or tau, an approach known as immunotherapy. Current attempts to use immunotherapy to treat Alzheimer's disease may yet work, but for over 20 years this approach has also consistently failed due to lack of efficacy and/or for safety reasons. For example, older adults who receive active immunotherapy treatment often show reduced responsiveness of the immune system, and patients who do improve sometimes develop a life-threatening brain inflammation

called aseptic meningitis. More generally, even when active or passive immunization against amyloid beta has reduced the brain's amyloid load, such effects resulted in no therapeutic benefit to patients with Alzheimer's disease.

Since drug innovation is a trial-and-error process, clinical failures represent important learning opportunities. In the case of Alzheimer's disease, we believe the biopharmaceutical industry's track record of persistent failure reflects a need to consider more recent and innovative approaches regarding the neurobiology of Alzheimer's disease. We believe such scientific approaches may broaden the range of possible treatment approaches.

Over the last ten years, we have developed a new and promising scientific approach for the treatment and diagnosis of neurodegeneration, particularly Alzheimer's disease.

Importantly, we do not seek to clear amyloid out of the brain. Our approach is to stabilize a critical protein in the brain.

"Proteopathy" refers to a disease in which a protein becomes structurally abnormal, assembles and aggregates, and therefore loses its normal function and disrupts or injures the function of surrounding cells, tissues and organs. Through years of basic research, we have identified a structurally altered protein in the brain. We believe our experimental evidence demonstrates that this proteopathy plays a critical role in the development of neurodegenerative diseases, including the neurodegeneration observed in Alzheimer's disease. Using scientific insight and advanced tools in biochemistry, bioinformatics and imaging, we have elucidated this protein dysfunction. We have engineered a family of high-affinity small molecules to target the structurally altered protein and restore the protein to its normal shape and function. This family of small molecules, including PTI-125, was designed in-house and characterized by our academic collaborators.

The target of PTI-125 is an altered form of a scaffolding protein called filamin A ("FLNA"). Altered FLNA causes a cascade of toxic effects in the brain. Altered FLNA is a proteopathy, which means that this protein is no longer capable of executing a stable, beneficial and protective role and instead becomes harmful and destructive to the brain. By reversing the alteration of FLNA, its pathology ceases to adversely affect surrounding cells in the brain. In animal models of disease, restoring normal FLNA resulted in a multitude of therapeutic effects, including normalizing neurotransmission, decreasing neuroinflammation and restoring memory and cognition. By restoring function to multiple receptors and exerting powerful anti-inflammatory effects, we believe our approach has potential to slow the progression of neurodegeneration in humans. Thus, we have designed product candidates, such as PTI-125, with the goal of slowing or, potentially, even reversing the deterioration of brain cells. We believe the ability to simultaneously improve many vital functions in the brain represents a new, different and crucial approach to address neurodegeneration.

Importantly, since PTI-125 has a unique mechanism of action, we believe its potential therapeutic effects may be additive or synergistic with that of other therapeutic candidates aimed at the treatment of neurodegeneration.

Our mission is to detect and treat Alzheimer's disease.

Our lead therapeutic product candidate, called PTI-125, is initially aimed at Alzheimer's disease. PTI-125 is a small molecule drug with a novel mechanism of action. This drug candidate has demonstrated both cognitive improvement and slowing of disease progression in animal models of disease. PTI-125 is in Phase II clinical stage of development, with substantial support from the *National Institute on Aging* ("NIA"), a division of the NIH.

The target of PTI-125 is an altered form of filamin A ("FLNA"). FLNA is a scaffold protein that is widely found throughout the body. The function of a scaffold protein is to bring multiple other proteins together for them to interact. However, an altered, and highly toxic, form of FLNA is found in the Alzheimer's brain. Altered FLNA contributes to Alzheimer's disease by disrupting the normal function of neurons, leading to neurodegeneration and brain inflammation. Our product candidate, PTI-125, is aimed at countering the altered and toxic form of FLNA in the brain, thus restoring the normal function of this critical protein.

PTI-125 binds to altered FLNA with very high affinity. In doing so, PTI-125 restores the normal shape of FLNA and the normal function of three brain receptors: the alpha-7 nicotinic acetylcholine receptor; the N-methyl-D-aspartate ("NMDA") receptor; and the insulin receptor. These receptors have pivotal roles in brain cell survival, cognition and memory. In animal models, treatment with PTI-125 resulted in dramatic improvements in brain health, such as reduced amyloid and tau deposits, improved insulin receptor signaling and improved learning and memory. In addition, PTI-125 has another beneficial treatment effect of significantly reducing inflammatory cytokines in the brain. In animal models of disease, treatment with PTI-125

abolished IL-6 production and suppressed TNF-alpha and IL-1beta levels by 86% and 80%, respectively, illustrating a powerful anti-neuroinflammatory effect.

Our science is published in peer-reviewed academic journals. In addition, our research has been supported by the NIH under multiple research grant awards. Each grant was awarded following an in-depth, competitive, peer-reviewed evaluation of our approach for scientific and technical merit by a panel of outside experts in the field. Strong, long-term support from the NIH has allowed us to advance our two product candidates for neurodegeneration, PTI-125 and PTI-125Dx, into clinical development.

Our science is based on stabilizing a critical protein in the brain.

Our scientific approach is to treat neurodegeneration by targeting an altered form of a scaffolding protein called filamin A ("FLNA"). Scaffolding proteins are essential for cell function because they participate in virtually every process within the cell. If their function is impaired, the consequences can be devastating. Technological advances in medicine and improvements in lifestyle are making our lives longer. But with age, genetic mutations and other factors conspire against healthy cells, resulting in altered proteins. Sometimes a cell can rid itself of altered proteins. However, when disease changes the shape and function of critical proteins, multiple downstream processes are impaired. There are many clinical conditions in which proteins become structurally altered and impair the normal function of cells, tissues and organs, leading to disease. Conversely, restoring altered proteins back to health – which is called proteostasis – is a well-accepted therapeutic strategy in clinical medicine.

Accumulation of altered proteins is common in age-related brain disorders. The most common is Alzheimer's disease. Altered proteins observed in the aging brain include hyperphosphorylated tau and beta amyloid, both hallmarks of Alzheimer's disease. Our scientists and outside collaborators have demonstrated that an altered, and highly toxic, form of the scaffolding protein FLNA exists in the Alzheimer's brain. Critically, altered FLNA enables the toxicity of both beta amyloid and tau proteins. This toxic cascade impairs brain health, leading to worsening symptoms of Alzheimer's disease over time. In addition to impairing brain cell function, altered FLNA enables persistent inflammation in the Alzheimer's brain. We have shown that altered FLNA also promotes neuroinflammation via toll-like receptor 4 ("TLR4"), an immune receptor that causes release of pro-inflammatory cytokines. Our therapeutic approach is designed to counteract these brain pathologies by restoring altered FLNA protein back to its normal, non-diseased conformation with PTI-125. Treatment with PTI-125 has been shown to restore the normal function of three brain receptors critical to brain cell survival, cognition and memory, i.e., the alpha-7 nicotinic acetylcholine receptor; the NMDA receptor; and the insulin receptor. Treatment with PTI-125 has also been shown to dramatically reduce inflammatory cytokine levels in brains of mice with Alzheimer's disease mutations, thus reducing the neuroinflammation that also characterizes Alzheimer's disease.

Financial Overview

We have yet to generate any revenues from product sales. We have an accumulated deficit of $164.0 million at December 31, 2018. These losses have resulted principally from costs incurred in connection with research and development activities, salaries and other personnel-related costs and general corporate expenses. Research and development activities include costs of preclinical and clinical trials as well as clinical supplies associated with our product candidates. Salaries and other personnel-related costs include non-cash stock-based compensation associated with options and other equity awards granted to employees and non-employees. Our operating results may fluctuate substantially from period to period as a result of the timing of preclinical activities, enrollment rates of clinical trials for our product candidates and our need for clinical supplies.

We believe that our cash and cash equivalents at December 31, 2018, will enable us to fund our operating expenses for at least the next 12 months. In addition, we may seek in the future to fund our operations through additional public or private equity or debt financings or other sources. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. If we are unable to obtain financing or reach profitability, the related lack of liquidity will have a material adverse effect on our operations and future prospects.

We expect to continue to use significant cash resources in our operations for the next several years. Our cash requirements for operating activities and capital expenditures may increase substantially in the future as we:

- conduct preclinical and clinical trials for our product candidates;
- seek regulatory approvals for our product candidates;
- develop, formulate, manufacture and commercialize our product candidates;
- implement additional internal systems and develop new infrastructure;
- acquire or in-license additional products or technologies, or expand the use of our technology;
- maintain, defend and expand the scope of our intellectual property; and
- hire additional personnel.

Product revenue will depend on our ability to receive regulatory approvals for, and successfully market, our product candidates. If our development efforts result in regulatory approval and successful commercialization of our product candidates, we will generate revenue from direct sales of our drugs and/or, if we license our drugs to future collaborators, from the receipt of license fees and royalties from sales of licensed products. We conduct our research and development programs through a combination of internal and collaborative programs. We rely on arrangements with universities, our collaborators, CROs and clinical research sites for a significant portion of our product development efforts.

We focus substantially all our research and development efforts on research and development in the areas of neurology. The following table summarizes expenses which have been reduced for reimbursements received for NIH grants (in thousands):

	Years ended December 31,	
	2018	2017
Research and development expenses - gross	$ 6,016	$ 9,024
Less: Reimbursement from NIH grants	3,047	1,409
Research and development expenses - net	$ 2,969	$ 7,615

Research and development expenses include compensation, contractor fees and supplies as well as allocated common costs. Contractor fees and supplies generally include expenses for preclinical studies and clinical trials and costs for formulation and manufacturing activities. Other common costs include the allocation of common costs such as facilities. During the year ended December 31, 2018 and 2017, we received $3.0 million and $1.4 million from research grants from the NIH. These reimbursements were recorded as a reduction to our research and development expenses.

Our abuse-deterrent technology has been applied across certain of our portfolio of product candidates. Data, know-how, personnel, clinical results, research results and other matters related to the research and development of any one of our product candidates also relate to, and further the development of, our other product candidates. As a result, costs allocated to a specific drug candidate may not necessarily reflect the actual costs surrounding research and development of such drug candidate due to cross application of the foregoing.

Estimating the dates of completion of clinical development, and the costs to complete development, of our product candidates would be highly speculative, subjective and potentially misleading. Pharmaceutical products take a significant amount of time to research, develop and commercialize. The clinical trial portion of the development of a new drug alone usually spans several years. We expect to reassess our future research and development plans based on our review of data we receive from our current research and development activities. The cost and pace of our future research and development activities are linked and subject to change.

Critical Accounting Policies

The preparation of our financial statements in accordance with U.S. generally accepted accounting principles requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues, expenses and interest income in our financial statements and accompanying notes. We evaluate our estimates on an ongoing basis, including those estimates related to agreements and research collaborations. We base our estimates on historical experience and various other assumptions that we believe 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 may differ from these estimates under different assumptions or conditions. The following items in our financial statements require significant estimates and judgments:

- *Stock-based compensation*. We recognize non-cash expense for the fair value of all stock options and other share-based awards. We use the Black-Scholes option valuation model to calculate the fair value of stock options, using the single-option award approach and straight-line attribution method. For options granted to employees and directors, we recognize the resulting fair value as expense on a straight-line basis over the vesting period of each respective stock option, generally four years. For options granted to non-employees, we remeasure the fair value expense using Black-Scholes each reporting period.

- We have granted share-based awards that vest upon achievement of certain performance criteria, or performance awards. We multiply the number of performance awards by the fair market value of our common stock on the date of grant to calculate the fair value of each award. We estimate an implicit service period for achieving performance criteria for each award. We recognize the resulting fair value as expense over the implicit service period when we conclude that achieving the performance criteria is probable. We periodically review and update as appropriate our estimates of implicit service periods and determinations on achievement of the performance criteria. Performance awards vest and common stock is issued upon achievement of the performance criteria.

- *Income Taxes.* We make estimates and judgments in determining the need for a provision for income taxes, including the estimation of our taxable income or loss for each full fiscal year. We have accumulated significant deferred tax assets that reflect the tax effects of net operating loss and tax credit carryovers and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Realization of deferred tax assets is dependent upon future earnings, if any. We are uncertain as to the timing and amount of any future earnings. Accordingly, we offset these deferred tax assets with a valuation allowance. We may in the future determine that our deferred tax assets will likely be realized, in which case we will reduce our valuation allowance in the quarter in which such determination is made. If the valuation allowance is reduced, we may recognize a benefit from income taxes in our statement of operations in that period. We classify interest recognized in connection with our tax positions as interest expense, when appropriate.

Recent Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*. The core principle of Topic 842 is that a lessee should recognize the assets and liabilities that arise from leases. For operating leases, a lessee is required to recognize a right-of-use asset and a lease liability, initially measured at the present value of the lease payments, in the statement of financial position. This ASU is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. The Company is evaluating the effect that the adoption of this ASU will have on its financial statements. The Company currently expects that its operating lease commitment for its office space will be subject to the new standard and recognized as right-of-use asset and operating lease liability upon adoption of ASU 2016-02, which will increase the total assets and total liabilities that it reports relative to such amounts prior to adoption.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820) - Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"), which is designed to improve the effectiveness of disclosures by removing, modifying and adding disclosures related to fair value measurements. ASU 2018-13 is effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. The Company is currently evaluating the impact of ASU 2018-13 on its consolidated financial statements.

Results of Operations

Research and Development Expense

Research and development expense consist primarily of costs of drug development work associated with our product candidates, including:

- preclinical testing,
- clinical trials,
- clinical supplies and related formulation and design costs, and
- compensation and other personnel-related expenses.

Research and development expenses decreased to $3.0 million in 2018 from $7.6 million in 2017, representing a 61% decrease. This was due primarily to decreases in REMOXY related expenses, a product candidate that we are no longer developing. We also received reimbursements of $3.0 million from research grants in 2018 from the NIH that we recorded as a reduction to our research and development expense compared to $1.4 million in 2017. Grant reimbursement increased from the prior year as additional grant awards have been received from the NIH.

Research and development expenses included non-cash stock-related compensation expenses of $1.0 million in 2018 compared to $1.2 million in reimbursements from research grants in 2017.

We expect research and development expense to fluctuate in future periods as we continue our development efforts. We expect our development efforts to result in our product candidates progressing through various stages of clinical trials. Our research and development expenses may fluctuate from period to period due to the timing and scope of our development activities and the results of clinical trials and preclinical studies.

General and Administrative Expense

General and administrative expenses consist of personnel costs, allocated expenses and other expenses for outside professional services, including legal, human resources, audit and accounting services. Personnel costs consist of salaries, bonus, benefits and stock-based compensation. Allocated expenses consist primarily of facility costs. We incur expenses associated with operating as a public company, including expenses related to compliance with the rules and regulations of the SEC and Nasdaq, additional insurance expenses, additional audit expenses, investor relations activities, SOX compliance expenses and other administrative expenses and professional services. General and administrative expense decreased to $3.7 million in 2018 from $4.3 million in 2017, representing a 15% decrease. This was due primarily to decreases in non-cash stock-based compensation expenses as well as outside professional fees.

General and administrative expenses included non-cash stock-based compensation expenses of $1.4 million in 2018 compared to $1.8 million in 2017. We expect other general and administrative expense for 2019 will be consistent with 2018.

Interest Income

Interest and other income, net, was $105,000 in 2018 compared to $38,000 in 2017. The increase was due primarily to higher cash balances from our August 2018 stock offering as well as an increase in interest rates. We expect interest income to increase in 2019 compared to 2018 due to our higher cash and cash equivalent balances as well as a higher interest rate environment.

Liquidity and Capital Resources

Since inception, we have financed our operations primarily through public and private stock offerings, payments received under collaborative agreements and interest earned on our investments. We intend to continue to use our capital resources to

fund research and development activities, capital expenditures, working capital requirements and other general corporate purposes. As of December 31, 2018, cash and cash equivalents totaled $19.8 million.

2018 Registered Direct Offering

On August 17, 2018, we completed a common stock offering pursuant to which certain investors purchased 8,860,778 shares of common stock at a price of $1.15 per share. We also issued warrants to purchase shares of common stock at a price of $0.125 per warrant share in the offering. Net proceeds of the offering were approximately $10.2 million after deducting offering expenses. The warrants are exercisable for 8,860,778 shares of common stock at $1.25 per share. Subject to certain ownership limitations described in the warrants, the warrants were immediately exercisable and will remain exercisable until the 2.5-year anniversary of their date of issuance. The warrants will be exercisable on a "cashless" basis in certain circumstances, including while there is no effective registration statement registering the shares of common stock issuable upon exercise of the warrants at any time until the expiry of the warrants. Such registration statement was declared effective by the SEC on January 30, 2019. The warrants provide that holders will have the right to participate in any rights offering or distribution of assets together with the holders of common stock on an as-exercised basis. All of the common stock warrants remained outstanding at December 31, 2018.

In conjunction with the offering, we also issued to the placement agent warrants to purchase up to 265,823 shares of common stock (the "Placement Agent Warrants"). The Placement Agent Warrants have substantially the same terms as the warrants to be issued to the purchasers of common stock, except that their exercise price is $1.59 per share. All of the common stock warrants remained outstanding at December 31, 2018.

At the Market Common Stock Issuance

At the Market Issuance Sales Agreement — On February 8, 2018, we entered into a Capital on Demand™ Sales Agreement, or the ATM Agreement, with JonesTrading. In accordance with the terms of the sales agreement, we were able to offer and sell shares of our common stock, from time to time in one or more public offerings of our common stock, with JonesTrading acting as agent, in transactions pursuant to a shelf registration statement that was declared effective by the SEC on July 31, 2017. On August 16, 2018, we suspended sales of our common stock under our ATM Agreement and limited such sales to a share value of $7,000,000.

During the year ended December 31, 2018, we sold a total of 1,763,013 shares of our common stock under the ATM Agreement in the open market for net proceeds of $3.9 million.

Net cash used in operating activities was $4.8 million for 2018, resulting primarily from a $6.6 million net loss incurred partially offset by $2.4 million of stock-based compensation expense. Net cash used in operating activities also included $0.7 million of cash used from changes in operating assets and liabilities.

Net cash used in operating activities was $8.2 million for 2017, resulting primarily from a $11.9 million net loss incurred partially offset by $3.0 million of stock-based compensation expense. Net cash used in operating activities also included $0.6 million of cash provided from changes in operating assets and liabilities.

There was no cash from investing activities in 2018. Net cash provided by investing activities was $2.1 million in 2017 primarily from sales and maturities of marketable securities.

Net cash provided by financing activities was $14.1 million in 2018 consisting of net proceeds from the sale of common stock and warrants in August 2018 as well as the sale of common stock under our At-The-Market facility, as described above. There was no cash from financing activities in 2017.

Realization of our deferred tax assets is dependent on future earnings, if any. We are uncertain about the timing and amount of any future earnings. Accordingly, we offset these net deferred tax assets with a valuation allowance.

We lease approximately 6,000 square feet of office space pursuant to a non-cancelable operating lease in Austin, TX that expires in 2020. Future minimum lease payments are $0.2 million at December 31, 2018.

We have an accumulated deficit of $164.0 million at December 31, 2018. We expect our cash requirements to be significant in the future. The amount and timing of our future cash requirements will depend on regulatory and market acceptance of our product candidates and the resources we devote to researching and developing, formulating, manufacturing, commercializing and supporting our products. We believe that our current resources should be sufficient to fund our operations for at least the next 12 months. We may seek additional future funding through public or private financing in the future, if such funding is available and on terms acceptable to us.

Off-balance Sheet Arrangements

As of December 31, 2018, we did not have any relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities, which would have been established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes. In addition, we do not engage in trading activities involving non-exchange traded contracts. Therefore, we are not materially exposed to financing, liquidity, market or credit risk that could arise if we had engaged in these relationships. We do not have relationships or transactions with persons or entities that derive benefits from their non-independent relationship with us or our related parties.

Item 7A. ***Quantitative and Qualitative Disclosures about Market Risk***

Pursuant to Item 305(e) of Regulation S-K, the information called for by Item 7A is not required.

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

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Cassava Sciences, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Cassava Sciences, Inc. (the Company) as of December 31, 2018 and 2017, the related statements of operations, stockholders' equity and cash flows for the years then ended, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2002.

Austin, Texas
March 28, 2019

CASSAVA SCIENCES, INC.

BALANCE SHEETS
(In thousands, except share and per share data)

	December 31, 2018	December 31, 2017
ASSETS		
Current assets:		
Cash and cash equivalents	$ 19,807	$ 10,479
Other current assets	233	184
Total current assets	20,040	10,663
Property and equipment, net	87	156
Other assets	12	12
Total assets	$ 20,139	$ 10,831
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 294	$ 424
Accrued development expense	156	399
Accrued compensation and benefits	61	309
Total current liabilities	511	1,132
Noncurrent liabilities	—	—
Total liabilities	511	1,132
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $.001 par value; 10,000,000 shares authorized, none issued and outstanding	—	—
Common stock, $.001 par value; 120,000,000 shares authorized; 17,219,300 and 6,595,509 shares issued and outstanding at December 31, 2018 and December 31, 2017, respectively	17	7
Additional paid-in capital	183,567	167,091
Accumulated deficit	(163,956)	(157,399)
Total stockholders' equity	19,628	9,699
Total liabilities and stockholders' equity	$ 20,139	$ 10,831

See accompanying notes to financial statements.

CASSAVA SCIENCES, INC.

STATEMENTS OF OPERATIONS
(In thousands, except per share data)

	Years ended December 31,	
	2018	**2017**
Operating expenses:		
Research and development, net of grant reimbursement	$ 2,969	$ 7,615
General and administrative	3,693	4,334
Total operating expenses	6,662	11,949
Operating loss	(6,662)	(11,949)
Interest income	105	38
Net loss	$ (6,557)	$ (11,911)
Net loss per share, basic and diluted	$ (0.61)	$ (1.82)
Shares used in computing net loss per share, basic and diluted	10,682	6,537

See accompanying notes to financial statements.

CASSAVA SCIENCES, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands)

	Common stock		Additional paid-in capital	Accumulated other comprehensive income	Accumulated deficit	Total stockholders' equity
	Shares	Par value				
Balance at December 31, 2016	6,591,705	7	164,118	—	(145,488)	18,637
Non-cash stock-related compensation for:						
Stock options for employees	—	—	2,954	—	—	2,954
Stock options for non-employees	—	—	19	—	—	19
Issuance of common stock pursuant to 7 to 1 reverse stock split	3,804	—	—	—	—	—
Net loss	—	—	—	—	(11,911)	(11,911)
Balance at December 31, 2017	6,595,509	$ 7	$ 167,091	$ —	$ (157,399)	$ 9,699
Non-cash stock-related compensation for:						
Stock options for employees	—	—	2,352	—	—	2,352
Stock options for non-employees	—	—	36	—	—	36
Sale of shares of common stock and warrants	10,623,791	10	14,088	—	—	14,098
Net loss	—	—	—	—	(6,557)	(6,557)
Balance at December 31, 2018	17,219,300	$ 17	$ 183,567	$ —	$ (163,956)	$ 19,628

See accompanying notes to financial statements.

CASSAVA SCIENCES, INC.

STATEMENTS OF CASH FLOWS
(In thousands)

	Years ended December 31,	
	2018	**2017**
Cash flows from operating activities:		
Net loss	$ (6,557)	$ (11,911)
Adjustments to reconcile net loss to net cash used in operating activities:		
Non-cash stock-based compensation	2,388	2,973
Depreciation and amortization	69	68
Non-cash net interest income	—	(2)
Changes in operating assets and liabilities:		
Other current assets	(49)	172
Other non-current assets	—	(12)
Accounts payable	(130)	129
Accrued development expense	(243)	372
Accrued compensation and benefits	(248)	(26)
Net cash used in operating activities	(4,770)	(8,237)
Cash flows from investing activities:		
Purchases of marketable securities	—	(399)
Sales of marketable securities	—	400
Maturities of marketable securities	—	2,100
Net cash provided by investing activities	—	2,101
Cash flows from financing activities:		
Proceeds from issuance of common stock and warrants, net of issuance costs	14,098	—
Net cash provided by financing activities	14,098	—
Net increase (decrease) in cash and cash equivalents	9,328	(6,136)
Cash and cash equivalents at beginning of period	10,479	16,615
Cash and cash equivalents at end of period	$ 19,807	$ 10,479

See accompanying notes to financial statements.

CASSAVA SCIENCES, INC.
NOTES TO FINANCIAL STATEMENTS

1. General and Liquidity

Cassava Sciences, Inc. (the "Company"), formerly known as Pain Therapeutics, Inc., develops proprietary drugs that offer significant improvements to patients and healthcare professionals. The Company generally focuses its drug development efforts on disorders of the nervous system.

On May 4, 2017, following stockholder approval, the Company's board of directors approved a reverse stock split at a ratio of 7-for-1. On May 4, 2017, the Company filed with the Secretary of State of the State of Delaware a Certificate of Amendment to the Company's Amended and Restated Certificate of Incorporation to effect the 7-for-1 reverse stock split of the Company's outstanding shares of common stock. The number of outstanding shares of common stock on the date of the reverse split was reduced from 46.1 million to 6.6 million shares. The Company's common stock began trading on the Nasdaq Global Market on a split-adjusted basis when the market opened for trading on May 10, 2017. As a result, all common stock share amounts included in these consolidated financial statements have been retroactively reduced by a factor of seven, and all common stock per share amounts have been increased by a factor of seven, with the exception of the Company's common stock par value.

Liquidity

The Company has incurred significant net losses and negative cash flows since inception, and as a result has an accumulated deficit of $164.0 million at December 31, 2018. The Company expects its cash requirements to be significant in the future. The amount and timing of its future cash requirements will depend on regulatory and market acceptance of the Company's product candidates and the resources it devotes to researching and developing, formulating, manufacturing, commercializing and supporting its products. The Company may seek additional future funding through public or private financing in the future, if such funding is available and on terms acceptable to the Company.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires that management make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amount of revenue earned and expenses incurred during the reporting period. Actual results could differ from those estimates.

Awards of and Proceeds from Grants

During the year ended December 31, 2018, the Company was awarded two National Institutes of Health ("NIH") grants totaling up to $6.7 million to support Phase II programs with PTI-125, the Company's drug candidate to treat Alzheimer's disease.

In January 2019, the Company was awarded an NIH grant totaling up to $1.5 million to support on-going development of new technology to detect Alzheimer's disease with a simple blood test.

In 2018, the Company received $3.0 million reimbursements from the NIH and NIDA and $1.4 million in 2017. The Company records the proceeds from these grants as reductions to its research and development expenses.

Cash and Cash Equivalents and Concentration of Credit Risk

The Company invests in cash and cash equivalents and, in the past, marketable securities. The Company considers highly-liquid financial instruments with original maturities of three months or less to be cash equivalents. Highly liquid investments that are considered cash equivalents include money market funds, certificates of deposits, treasury bills and commercial paper. The carrying value of cash equivalents approximates fair value due to the short-term maturity of these securities.

The Company's investment policy allows for investments in marketable securities with active secondary or resale markets, establishes diversification and credit quality requirements and limits investments by maturity and issuer. The Company maintains its investments at one financial institution.

Fair Value Measurements

The Company reports its cash and cash equivalents at fair value as Level 1, Level 2 or Level 3 using the following inputs:

- Level 1 includes quoted prices in active markets. The Company bases the fair value of money market funds and U.S. treasury securities on Level 1 inputs.

- Level 2 includes significant observable inputs, such as quoted prices for identical or similar investments, or other inputs that are observable and can be corroborated by observable market data for similar securities. The Company uses market pricing and other observable market inputs obtained from third-party providers. It uses the bid price to establish fair value where a bid price is available. The Company bases the fair value of its marketable securities, if any, on Level 2 inputs.

- Level 3 includes unobservable inputs that are supported by little or no market activity. The Company does not have any investments where the fair value is based on Level 3 inputs.

If a financial instrument uses inputs that fall in different levels of the hierarchy, the instrument will be categorized based upon the lowest level of input that is significant to the fair value calculation. The fair value of all cash and cash equivalents was based on Level 1 inputs at December 31, 2018 and 2017.

Business Segments

The Company reports segment information based on how it internally evaluates the operating performance of its business units, or segments. The Company's operations are confined to one business segment: the development of novel drugs.

Stock-based Compensation

The Company recognizes non-cash expense for the fair value of all stock options and other share-based awards. The Company uses the Black-Scholes option valuation model to calculate the fair value of stock options, using the single-option award approach and straight-line attribution method. This model requires the input of subjective assumptions including expected stock price volatility, expected life and estimated forfeitures of each award. These assumptions consist of estimates of future market conditions, which are inherently uncertain, and therefore, are subject to management's judgment.

For options granted to employees and directors, the Company recognizes the resulting fair value as expense on a straight-line basis over the vesting period of each respective stock option, generally four years. For options granted to non-employees, it remeasures the fair value expense using Black-Scholes each reporting period.

The Company has granted share-based awards that vest upon achievement of certain performance criteria, or performance awards. The Company multiplies the number of performance awards by the fair market value of its common stock on the date of grant to calculate the fair value of each award. It estimates an implicit service period for achieving performance criteria for each award. The Company recognizes the resulting fair value as expense over the implicit service period when it concludes that achieving the performance criteria is probable. The Company periodically reviews and updates as appropriate its estimates of implicit service periods and conclusions on achieving the performance criteria. Performance awards vest and common stock is issued upon achievement of the performance criteria.

Net Loss per Share

Basic net loss per share is computed on the basis of the weighted-average number of common shares outstanding for the reporting period. Diluted net loss per share is computed on the basis of the weighted-average number of common shares outstanding plus dilutive potential common shares outstanding using the treasury-stock method. Potential dilutive common shares consist of outstanding equity awards and warrants. There is no difference between the Company's net loss and comprehensive loss. The numerators and denominators in the calculation of basic and diluted net loss per share were as follows (in thousands):

	Years ended December 31,	
	2018	**2017**
Numerator:		
Net loss	$ (6,557)	$ (11,911)
Denominator:		
Shares used in computing net loss per share, basic and diluted	10,682	6,537
Net loss per share, basic and diluted	$ (0.61)	$ (1.82)

The Company excluded weighted equity awards and warrants outstanding to purchase common stock from the calculation of diluted net loss per share because the effect of including these shares in this calculation would be anti-dilutive.

The potential shares of common stock that have been excluded from the diluted loss per share calculation above for the years ended December 31, 2018 and 2017 were as follows:

	Year ended December 31,	
	2018	**2017**
Stock options	2,864,574	2,496,542
Stock warrants	9,126,601	-
Potential common shares	11,991,175	2,496,542

Fair Value of Financial Instruments

Financial instruments include cash and cash equivalents, accounts payable and accrued liabilities. The estimated fair value of financial instruments has been determined using available market information or other appropriate valuation methodologies. However, considerable judgment is required in interpreting market data to develop estimates of fair value; therefore, the estimates are not necessarily indicative of the amounts that could be realized or would be paid in a current market exchange. The effect of using different market assumptions and/or estimation methodologies may be material to the estimated fair value amounts. The carrying amounts of cash and cash equivalents, accounts payable and accrued liabilities are at cost, which approximates fair value due to the short maturity of those instruments.

Income Taxes

The Company makes estimates and judgments in determining the need for a provision for income taxes, including the estimation of its taxable income or loss for each full fiscal year.

The Company has accumulated significant deferred tax assets that reflect the tax effects of net operating loss and tax credit carryovers and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Realization of certain deferred tax assets is dependent upon future earnings. The Company is uncertain about the timing and amount of any future earnings. Accordingly, the Company offsets these deferred tax assets with a valuation allowance.

In the future, the Company may determine that certain deferred tax assets will likely be realized, in which case t will reduce its valuation allowance in the period in which such determination is made. If the valuation allowance is reduced, the Company may recognize a benefit from income taxes in its Statement of Operations in that period.

The Company classifies interest recognized pursuant to its deferred tax assets as interest expense, when appropriate.

Recent Accounting Pronouncements

The Company reviewed recently issued accounting pronouncements and plan to adopt those that are applicable to it, and does not expect the adoption of these pronouncements to have a material impact on its financial position, results of operations or cash flows.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*. The core principle of Topic 842 is that a lessee should recognize the assets and liabilities that arise from leases. For operating leases, a lessee is required to recognize a right-of-use asset and a lease liability, initially measured at the present value of the lease payments, in the statement of financial position. This ASU is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. The Company is evaluating the effect that the adoption of this ASU will have on its financial statements. The Company currently expects that its operating lease commitment for its office space will be subject to the new standard and recognized as right-of-use asset and operating lease liability upon adoption of ASU 2016-02, which will increase the total assets and total liabilities that it reports relative to such amounts prior to adoption.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820) - Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"), which is designed to improve the effectiveness of disclosures by removing, modifying and adding disclosures related to fair value measurements. ASU 2018-13 is effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. The Company is currently evaluating the impact of ASU 2018-13 on its consolidated financial statements.

3. Collaboration Agreements

Durect Corporation

The Company had an exclusive, worldwide Development and License Agreement with Durect Corporation to use a patented controlled-release technology that formed the basis for REMOXY. On March 20, 2019, the Company gave notice of termination of its licensing agreement for REMOXY ER with Durect Corporation. This and other actions effectively ends the Company's development of REMOXY ER. There were no payments made to Durect during the years ended December 31, 2018 and 2017.

4. Property and Equipment

The Company's property and equipment include furniture and equipment with a purchase value of $1.0 million at December 31, 2018 and 2017. Depreciation is recognized using the straight-line method over the expected life of the property and equipment. Accumulated depreciation was $0.9 million at December 31, 2018 and $0.8 million at December 31, 2017.

5. Stockholders' Equity and Stock-Based Compensation

Preferred Stock

The Company's Board of Directors has the authority to issue preferred stock in one or more series and to fix the rights, preferences, privileges, restrictions and the number of shares constituting any series or the designation of the series.

2018 Registered Direct Offering

On August 17, 2018, the Company completed a common stock offering pursuant to which certain investors purchased 8,860,778 shares of common stock at a price of $1.15 per share. The Company also issued warrants to purchase shares of

common stock at a price of $0.125 per warrant share in the offering. Net proceeds of the offering were approximately $10.2 million after deducting offering expenses. The warrants are exercisable for 8,860,778 shares of common stock at $1.25 per share. Subject to certain ownership limitations described in the warrants, the warrants were immediately exercisable and will remain exercisable until the 2.5-year anniversary of their date of issuance. The warrants will be exercisable on a "cashless" basis in certain circumstances, including while there is no effective registration statement registering the shares of common stock issuable upon exercise of the warrants until the expiry of the warrants. Such registration statement was declared effective by the SEC on January 30, 2019. The warrants provide that holders will have the right to participate in any rights offering or distribution of assets together with the holders of Common Stock on an as-exercised basis. All of the common stock warrants remained outstanding at December 31, 2018.

In conjunction with the offering, the Company also issued to the placement agent warrants to purchase up to 265,823 shares of common stock (the "Placement Agent Warrants"). The Placement Agent Warrants have substantially the same terms as the warrants to be issued to the purchasers of common stock, except that their exercise price is $1.59 per share. All of the common stock warrants remained outstanding at December 31, 2018.

The sale of common stock and issuance of warrants qualified for equity treatment under GAAP. The respective values of the warrants and common stock were calculated using their relative fair values and classified under common stock and additional paid-in capital. The value ascribed to the warrants is $7.2 million and to the common stock is approximately $3.0 million.

The fair value of these warrants was estimated using a Black-Scholes model with the following assumptions: estimated volatility 136%, risk-free interest rate of 2.65%, no dividend and an expected life of 2.5 years.

At the Market Common Stock Issuance

At the Market Issuance Sales Agreement — On February 8, 2018, the Company entered into a Capital on Demand™ Sales Agreement, or the ATM Agreement, with JonesTrading. In accordance with the terms of the sales agreement, the Company was able to offer and sell shares of its common stock, from time to time in one or more public offerings of its common stock, with JonesTrading acting as agent, in transactions pursuant to a shelf registration statement that was declared effective by the SEC on July 31, 2017. On August 16, 2018, the Company suspended sales of its common stock under the ATM Agreement and limited such sales to a share value of $7,000,000.

During the year ended December 31, 2018, the Company sold a total of 1,763,013 shares of its common stock under the ATM Agreement in the open market for net proceeds of $3.9 million.

2008 Equity Incentive Plan

Under the Company's 2008 Equity Incentive Plan, or 2008 Equity Plan, its employees, directors and consultants received share-based awards, including grants of stock options and performance awards. The 2008 Equity Plan expired in December 2017. Share-based awards generally expire ten years from the date of grant.

2018 Equity Incentive Plan

On January 31, 2018, the Company's Board of Directors approved the Company's 2018 Omnibus Incentive Plan (the "2018 Plan"). The Company's Board of Directors or a designated Committee of the Board is responsible for administration of the 2018 Plan and determined the terms and conditions of each option granted, consistent with the terms of the 2018 Plan. The Company's employees, directors, and consultants are eligible to receive awards under the 2018 Plan, including grants of stock options and performance awards. Share-based awards generally expire ten years from the date of grant. The 2018 Plan provides for issuance of up to 1,000,000 shares of common stock, par value $0.001 per share under the 2018 Plan, subject to adjustment as provided in the 2018 Plan.

When stock options or performance awards are exercised net of the exercise price and taxes, the number of shares of stock issued is reduced by the number of shares equal to the amount of taxes owed by the award recipient and that number of shares are cancelled. The Company then uses its cash to pay tax authorities the amount of statutory taxes owed by and on behalf of the award recipient.

Stock Options

The following summarizes information about stock option activity during 2018:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
			In years	In millions
Outstanding as of December 31, 2017	2,982,155	$ 16.74	6.22	$ 0.4
Options granted	297,500	1.43		
Options exercised	—	—		
Options forfeited/canceled	(314,682)	26.73		
Outstanding as of December 31, 2018	2,964,973	14.14	6.06	-
Vested and expected to vest at December 31, 2018	2,964,973	14.14	6.06	-
Exercisable at December 31, 2018	1,931,288	$ 19.63	4.56	$ -

The following summarizes information about stock options at December 31, 2018 by a range of exercise prices:

		Options outstanding			Options exercisable	
Range of exercise prices		Number of outstanding options	Weighted average remaining contractual life (in years)	Weighted average exercise price	Number of vested options	Weighted average exercise price
From	To					
$ 0.95	$ 3.24	832,500	9.0	$ 2.48	199,945	$ 3.05
$ 3.89	$ 12.04	637,568	7.8	$ 6.62	315,574	$ 8.87
$ 12.39	$ 18.06	733,616	4.2	$ 15.54	656,862	$ 15.69
$ 18.83	$ 35.00	618,413	3.4	$ 27.27	616,031	$ 27.31
$ 36.40	$ 53.55	142,876	2.5	$ 51.65	142,876	$ 51.65
		2,964,973	6.1	$ 14.14	1,931,288	$ 19.63

The Company uses Black-Scholes to estimate the fair value of options granted. Black-Scholes considers a number of factors, including the market price of the Company's common stock. For options granted to employees and directors, it used certain factors to value each stock option granted, which resulted in a weighted average fair value of options granted during 2018 and 2017, as follows:

	2018	2017
Volatility	87% to 118%	79% to 83%
Risk-free interest rates	2.7% to 2.9%	2% to 2.4%
Expected life of option	7 years	7 years
Dividend yield	zero	zero
Forfeiture rate	zero	zero
Weighted average fair value of stock options granted	$0.98	$2.74

Volatility is based on reviews of the historical volatility of the Company's common stock. Risk-free interest rates are based on yields of U.S. treasury notes in effect at the date of grant. Expected life of option is based on actual historical option exercises. Dividend yield is zero because the Company does not anticipate paying cash dividends in the foreseeable future. The Company estimates forfeitures and adjust this estimate periodically based in part on the extent to which actual forfeitures differ from its estimates.

For options granted to non-employees, the Company estimates the fair value of stock options granted using factors similar to those used for stock options granted to employees and directors and appropriate for the terms underlying the

stock options granted to non-employees. The Company re-measures the compensation expense for options granted to non-employees each reporting period.

As of December 31, 2018, the Company expects to recognize compensation expense of $2.9 million related to non-vested options held by employees and directors over the weighted average remaining recognition period of 2.8 years.

Performance Awards

The following summarizes information about performance award activity during 2018:

	Number of Performance Awards
Outstanding as of December 31, 2017	152,340
Granted	—
Vested performance awards	—
Forfeited/Canceled	(14,285)
Outstanding as of December 31, 2018	138,055

If and when outstanding performance awards vest, the Company would recognize $2.3 million in non-cash stock-based compensation expense. These performance awards expire between 2022 and 2026.

Stock-Based Compensation Expense

The following summarizes information about non-cash stock-based compensation expense, in thousands:

	Years ended December 31,	
	2018	2017
Research and development		
Vesting of stock options	$ 1,043	$ 1,205
Vesting of performance awards	—	—
	1,043	1,205
General and administrative		
Vesting of stock options	1,345	1,768
Vesting of performance awards	—	—
	1,345	1,768
Total non-cash stock-based compensation expenses		
Vesting of stock options	2,388	2,973
Vesting of performance awards	—	—
	$ 2,388	$ 2,973

6. Employee 401(k) Benefit Plan

The Company has a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code. The plan covers substantially all employees. Employees are eligible to participate in the plan the first day of the month after hire and may contribute up to the current statutory limits under Internal Revenue Service regulations. The 401(k) plan permits the Company to make additional matching contributions on behalf of all employees. Through December 31, 2018, the Company has not made any matching contributions to the 401(k) plan.

7. Income Taxes

U.S. Tax Reform

On December 22, 2017, legislation commonly known as the Tax Cuts and Jobs Act, or the Act, was signed in to law. The Tax Act, among other changes, reduces the U.S. federal corporate tax rate from 35% to 21%, requires taxpayers to pay a one-time transition tax on earnings of certain foreign subsidiaries that were previously tax deferred and creates new taxes on certain foreign sourced earnings. On December 31, 2018 and 2017, the Company did not have any foreign subsidiaries and the international aspects of the Tax Act are not applicable.

In connection with the initial analysis of the impact of the Tax Act, the Company remeasured certain deferred tax assets and liabilities based on the rates at which they are expected to reverse in the future, which is generally 21%. The remeasurement of the Company's deferred tax balance was primarily offset by application of its valuation allowance. As of December 31, 2018, the Company has completed its accounting for all of the enactment date income tax effects of the Tax Act and recognized no material adjustments.

The Company did not provide for income taxes in 2018 and 2017 because it had a net operating loss for tax purposes in those years and the tax benefit that would have resulted from the statutory rate was fully offset by the valuation allowance.

Deferred tax assets and valuation allowance

Deferred tax assets reflect the tax effects of net operating loss and tax credit carryforwards and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The Company's deferred taxes assets at December 31, 2018 and 2017 were valued at the corporate tax rate of 21% to reflect the Tax Act. The Company offsets its deferred tax assets by a valuation allowance because it is uncertain about the timing and amount of any future profits. Significant components of its deferred tax assets are as follows (in thousands):

	December 31,	
	2018	2017
Deferred tax assets:		
Net operating loss carryforwards	$ 16,500	$ 15,600
Stock-related compensation	5,700	5,300
Research & development credit carryforwards	6,500	6,400
Other	100	200
	28,800	27,500
Valuation allowance	(28,800)	(27,500)
	$ —	$ —

The valuation allowance increased by $1.3 million in 2018 and decreased by $10.3 million in 2017.

The Company's pre-tax net operating loss carryforwards of $78.7 million are federal and expire between 2029 and 2037. As of December 31, 2018, the Company had federal research and development tax credits of approximately $10.9 million, which expire in the years 2023 through 2037.

Unrecognized tax benefits

The Company has unrecognized tax benefits related to tax credits. The Company added to its unrecognized tax benefits in 2018 and 2017 as follows (in thousands):

	2018	2017
Beginning balance	$ 4,300	$ 4,200
Additions based on tax positions related to the current year	100	100
Ending balance	$ 4,400	$ 4,300

8. Leases and Commitments

The Company leases approximately 6,000 square feet of office space pursuant to a non-cancelable operating lease in Austin, TX that expires on December 31, 2020. Future minimum lease payments are (in thousands).

	2019	2020	Total
Minimum lease payments	$ 95	$ 99	$ 194

The Company believes that its facilities are adequate and suitable for its current needs. Rent expense was $0.1 million both in 2018 and 2017.

The Company conducts its product research and development programs through a combination of internal and collaborative programs that include, among others, arrangements with universities, contract research organizations and clinical research sites. It has contractual arrangements with these organizations, however these contracts are cancelable on thirty days' notice and the Company's obligations under these contracts are largely based on services performed.

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

None.

Item 9A. ***Controls and Procedures***

Evaluation of disclosure controls and procedures.

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that our disclosure controls and procedures are effective to ensure that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission, or SEC, rules and forms and that such information is accumulated and communicated to management as appropriate to allow timely decisions regarding required disclosures.

Management's annual report on internal control over financial reporting. Our management is responsible for establishing and maintaining adequate internal control over our financial reporting. Our management has assessed the effectiveness of internal control over financial reporting as of December 31, 2018. Our assessment was based on criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, in Internal Control-Integrated Framework (2013 Framework).

Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Our internal control over financial reporting includes those policies and procedures that:

(1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect our transactions and dispositions of our assets;
(2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and board of directors; and
(3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Based on the COSO criteria, we believe our internal control over financial reporting as of December 31, 2018 was effective.

Changes in internal control over financial reporting.

As previously announced, on October 31, 2018, Eric Schoen was appointed as Chief Financial Officer. Prior to Mr. Schoen's appointment, Remi Barbier, President and Chief Executive Officer, had assumed the role of Principal Financial Officer.

Item 9B. ***Other Information***

None**.**

PART III

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

The information regarding our directors, executive officers, director nomination process and the audit committee of the Board is incorporated by reference from "Directors and Executive Officers" in our Proxy Statement for our 2019 Annual Meeting of Stockholders.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Exchange Act requires our executive officers and directors and persons who own more than ten percent (10%) of a registered class of our equity securities to file reports of ownership and changes in ownership with the SEC. Executive officers, directors and greater than ten percent (10%) stockholders are required to furnish us with copies of all Section 16(a) forms they file. We believe all of our executive officers and directors complied with all applicable filing requirements during 2018.

Code of Ethics

We have adopted a Code of Ethics that applies to all of our directors, officers and employees, including our principal executive officer, principal financial officer and principal accounting officer. We publicize the Code of Ethics through posting the policy on our website, http://www.cassavasciences.com. We will disclose on our website any waivers of, or amendments to, our Code of Ethics.

Item 11. ***Executive Compensation***

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading "Executive Compensation and Other Matters."

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

The information required by this Item regarding security ownership of certain beneficial owners and management is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading "Security Ownership of Certain Beneficial Owners and Management."

The following table summarizes the securities authorized for issuance under our equity compensation plans as of December 31, 2018:

	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights	Weighted Average Exercise Price of Outstanding Options, Warrants and Rights	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans
Equity compensation plans approved by stockholders	3,103,028 (1)	$ 13.51 (2)	760,517 (3)
Equity compensation plans not approved by stockholders	—	—	—
	3,103,028	$ 13.51	760,517

(1) Includes outstanding stock options and awards for 2,805,528 shares of our common stock under the 2008 Plan and 297,500 shares of our common stock under the 2018 Plan.
(2) Includes the weighted average stock price for outstanding stock options of $15.55 under the 2008 Plan and $1.43 for the 2018 Plan.
(3) Represents 702,500 shares of our common stock for the 2018 Plan and 58,017 for the Employee Stock Purchase Plan. No future awards shall occur under the 2008 Plan.

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

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading "Certain Relationships and Related Transactions."

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

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading **"**Principal Accountant Fees and Services."

PART IV

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

(a) The following documents are filed as part of this Form 10-K:

(1) *Financial Statements (included in Part II of this report):*
Report of Independent Registered Public Accounting Firm
Balance Sheets
Statements of Operations
Statements of Stockholders' Equity
Statements of Cash Flows
Notes to Financial Statements

(2) *Financial Statement Schedules:*
All financial statement schedules are omitted because the information is inapplicable or presented in the notes to the financial statements.

(3) *Management Contracts, Compensatory Plans and Arrangements*.
Management contracts, compensatory plans and arrangements are indicated by the symbol "*" in the applicable exhibits listed in Item 15(b), below.

(b) *Exhibits*

The exhibits listed below are filed as part of this Form 10-K other than Exhibit 32.1, which shall be deemed furnished.

Exhibit No.		Description	Incorporated by Reference			Filed Herewith
			Form	Filing Date	Exhibit No.	
3.1		Amended and Restated Certificate of Incorporation.	10-Q	7/29/2005	3.1	
3.2		Certificate of Amendment of Restated Certificate of Incorporation.	8-K	5/8/2017	3.1	
3.3		Certificate of Amendment of Restated Certificate of Incorporation.				X
3.4		Amended and Restated Bylaws of Cassava Sciences, Inc.				X
4.1		Specimen Common Stock Certificate.	10-Q	7/29/2005	4.1	
10.1	*	Form of Indemnification Agreement between Registrant and each of its directors and officers.	S-1	3/14/2000	10.1	
10.2	*	Employment Agreement, dated October 23, 2001, between Registrant and Nadav Friedmann, PhD. M.D.	10-K	3/22/2002	10.5	
10.3	+	Development and License Agreement dated December 19, 2002 between Registrant and DURECT Corporation and Southern Biosystems, Inc.	10-K	2/24/2006	10.10	
10.4	+	Amendment No. 1 to the Development and License Agreement dated December 15, 2005 between Registrant and DURECT Corporation and Southern Biosystems, Inc.	10-K	2/24/2006	10.11	
10.5	*	Employment Agreement, dated July 1, 1998 and amended December 17, 2008, between Registrant and Remi Barbier.	10-K	2/13/2009	10.12	
10.6	*	2000 Employee Stock Purchase Plan, as amended and restated.	10-Q	7/29/2010	10.1	
10.7	*	Amendment Number 1 to the 2008 Equity Incentive Plan.	10-Q	8/1/2013	10.1	
10.8	*	Amendment No. 2 to Employment Agreement between Registrant and Remi Barbier.	10-Q	8/1/2013	10.2	
10.9		Lease Agreement, dated as of February 14, 2011 between Registrant and StoneCliff Office, L.P.	10-Q	4/27/2011	10.1	
10.10	*	First Amendment to Lease Agreement, dated September 21, 2011.	10-K	2/9/2012	10.20	
10.11		Second Amendment to Lease Agreement, dated as of April 3, 2014 between Registrant and StoneCliff Office, L.P.	10-Q	8/6/2014	10.1	

10.12		Third Amendment to Lease Agreement, dated as of November 3, 2017 between Registrant US REIF Eurus Austin, LLC dba StoneCliff Building as successor in interest to StoneCliff Office, L.P.	10-K	2/6/2018	10.17	
10.13		Capital on Demand™ Sales Agreement, dated February 8, 2018, between Registrant and JonesTrading Institutional Services LLC.	8-K	2/9/2018	1.1	
10.14	*	2018 Omnibus Incentive Plan.	8-K	5/11/2018	10.1	
10.15		Form of Securities Purchase Agreement, dated August 15, 2018, by and between Registrant and the purchasers named therein.	8-K	8/20/2018	10.1	
10.16		Form of Common Stock Purchase Warrant.	8-K	8/20/2018	4.1	
10.17		Form of Wainwright Warrant.	8-K	8/20/2018	4.2	
10.18		Agreement between Registrant and H.C. Wainwright & Co., dated August 15, 2018.	8-K	8/20/2018	10.2	
10.19	*	Employment Agreement, executed on October 9, 2018, by and between Registrant and Eric Schoen.	8-K	10/11/2018	10.1	
23.1		Consent of Independent Registered Public Accounting Firm.				X
24.1		Power of Attorney (included in the signature page to this report).				X
31.1		Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
31.2		Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
32.1		Certifications of the Chief Executive Officer and the Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
101.INS		XBRL Instance Document.				X
101.SCH		XBRL Taxonomy Extension Schema Document.				X
101.CAL		XBRL Taxonomy Extension Calculation Linkbase Document.				X
101.DEF		XBRL Taxonomy Extension Definition Linkbase Document.				X
101.LAB		XBRL Taxonomy Extension Labels Linkbase Document.				X
101.PRE		XBRL Taxonomy Extension Presentation Linkbase Document.				X

* Management contract, compensatory plan or arrangement.
+ Portions of this Exhibit are subject to a confidential treatment order.

(c) *Financial Statement Schedules*

All financial statement schedules are omitted because the information is inapplicable or presented in the notes to the financial statements.

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

The Company has elected not to include summary information.

SIGNATURES

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

Cassava Sciences, Inc.
(Registrant)

/s/ REMI BARBIER
Remi Barbier,
Chairman of the Board of Directors,
President and Chief Executive Officer

Dated: March 28, 2019

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Remi Barbier his true and lawful attorneys-in-fact, with full power of substitution, for him in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact or their substitute or substitutes may do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ REMI BARBIER Remi Barbier	President, Chief Executive Officer and Chairman of the Board of Directors (Principal Executive Officer)	March 28, 2019
/s/ ERIC SCHOEN Eric Schoen	Chief Financial Officer (Principal Financial Officer)	March 28, 2019
/s/ NADAV FRIEDMANN, PH.D., M.D. Nadav Friedmann, Ph.D., M.D.	Chief Operating and Medical Officer and Director	March 28, 2019
/s/ ROBERT Z. GUSSIN, PH.D. Robert Z. Gussin, Ph.D.	Director	March 28, 2019
/s/ MICHAEL J. O'DONNELL, ESQ. Michael J. O'Donnell, Esq.	Director	March 28, 2019
/s/ SAIRA RAMASASTRY Saira Ramasastry	Director	March 28, 2019
/s/ SANFORD R. ROBERTSON Sanford R. Robertson	Director	March 28, 2019
/s/ PATRICK SCANNON, M.D., PH.D. Patrick Scannon, M.D., Ph.D.	Director	March 28, 2019