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

# Form 10-K

☒ **Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

For the fiscal year ended: March 31, 2021

or

☐ **Transition Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

Commission file number: 001-37761

# VistaGen Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

| **Nevada** | **20-5093315** |
|---|---|
| (State or other jurisdiction of incorporation or organization) | (I.R.S. Employer Identification No.) |

**343 Allerton Avenue**
**South San Francisco, California 94080**
**(650) 577-3600**
(Address, including zip code, and telephone number, including area code, of registrant's principal executive office)

**Securities registered pursuant to Section 12(b) of the Act**

| **Title of each class** | **Name of each exchange on which registered** |
|---|---|
| Common Stock, par value $0.001 per share | The Nasdaq Capital Market |

**Securities registered pursuant to Section 12(g) of the Act**

**None**

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes ☒ No ☐

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

| Large accelerated filer ☐ | Accelerated filer ☐ | Non-accelerated filer ☐ | Smaller reporting company ☒ | Emerging Growth Company ☐ |
|---|---|---|---|---|

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

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

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

The aggregate market value of the common stock of the registrant held by non-affiliates of the registrant on September 30, 2020, the last business day of the registrant's second fiscal quarter, was: $51,365,745.

As of June 28, 2021, there were 191,382,350 shares of the registrant's common stock, $0.001 par value per share, outstanding.

## DOCUMENTS INCORPORATED BY REFERENCE

Items 10, 11, 12, 13 and 14 of Part III incorporate by reference certain information from VistaGen Therapeutics, Inc.'s definitive proxy statement, to be filed with the Securities and Exchange Commission on or before July 29, 2021.

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**Forward-Looking Statements**

This Annual Report on Form 10-K (*Annual Report or Report*) contains forward-looking statements that involve substantial risks and uncertainties. All statements contained in this Annual Report other than statements of historical facts, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

- the continued impact of the coronavirus (*COVID-19*) pandemic, efforts to contain the pandemic and resulting economic downturn on or affecting our operations and financial condition;
- the availability of capital to satisfy our working capital requirements and development and commercialization objectives;
- the accuracy of our estimates regarding expenses, future revenues and capital requirements;
- our plans to develop and commercialize our product candidates, including, among other things, PH94B as a potential acute treatment of anxiety in adults with social anxiety disorder (*SAD*) and other anxiety disorders, PH10 as a potential treatment for major depressive disorder (*MDD*) and other depression-related disorders, and AV-101 as a potential treatment of MDD and depression-related disorders and neurological diseases and disorders involving the Central Nervous System (*CNS*);
- our ability to initiate and complete necessary preclinical and clinical studies to advance the development of our product candidates, including the PALISADE Phase 3 program and other studies, to successfully complete any such preclinical and clinical studies, and for those studies to generate positive results;
- economic, regulatory and political developments in the U.S. and foreign countries;
- the performance of our third-party contract manufacturer(s) (*CMOs*), contract research organizations (*CROs*) and other third-party preclinical and clinical drug development collaborators and regulatory service providers on whose services we rely to support our operations;
- our ability to obtain and maintain intellectual property (*IP*) protection for our core assets, including our product candidates;
- the size of the potential markets for our product candidates and our ability to enter and serve those markets;
- the rate and degree of market acceptance of our product candidates for any indication once approved;
- the success of competing products and product candidates in development by others that are or become available for the indications that we are pursuing in the markets we seek to enter on our own or with collaborators;
- the loss of key scientific, clinical or nonclinical development, regulatory, and/or management personnel, internally or from one or more of our third-party collaborators, CMOs, CROs or other service providers; and
- other risks and uncertainties, including those listed under Part I, Item 1A of this Annual Report titled "*Risk Factors*."

These forward-looking statements are only predictions and we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, so you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in one or more of the forward-looking statements we make in this Annual Report. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and operating results. We have included important factors in the cautionary statements included in this Annual Report, particularly in Part I, Item 1A, titled "*Risk Factors*," that could cause actual future results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements in this Annual Report do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report and the documents that we have filed as exhibits to this Annual Report with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements in this Annual Report, whether as a result of new information, future events or otherwise, except as required by applicable law.

**PART I**

*All brand names or trademarks appearing in this Annual Report are the property of their respective holders. Unless the context requires otherwise, references in this report to "VistaGen," the "Company," "we," "us," and "our" refer to VistaGen Therapeutics, Inc., a Nevada corporation. All references to future quarters and years in this Annual Report refer to calendar quarters and calendar years, unless reference is made otherwise.*

**Item 1. Business**

**Overview**

We are a biopharmaceutical company committed to developing and commercializing differentiated new generation medications that go beyond the current standard of care for widespread anxiety, depression and other central nervous system (*CNS*) disorders. Our CNS pipeline includes three CNS product candidates, PH94B Nasal Spray, PH10 Nasal Spray and AV-101, each with a differentiated profile, favorable safety results observed in all clinical studies to date and therapeutic potential in multiple CNS indications. PH94B Nasal Spray (*PH94B*) is being developed for multiple anxiety disorders. We recently initiated our PH94B Phase 3 development program, which we refer to as the PALISADE program, with PALISADE-1, a U.S., multi-center, randomized, double-blind, placebo-controlled Phase 3 clinical study to evaluate the efficacy and safety of PH94B for the acute treatment of anxiety in adults with social anxiety disorder (*SAD*), as well as preparations for the additional studies required to support our potential U.S. New Drug Application (*NDA*) for that indication should the PALISADE Phase 3 program be successful. We are also preparing for exploratory Phase 2A clinical studies of PH94B in adults experiencing several other anxiety disorders. PH10 Nasal Spray (*PH10*) is being developed as a stand-alone treatment for multiple depression disorders. Exploratory Phase 2A clinical development of PH10 for major depressive disorder (*MDD*) has been completed. We are now preparing for planned Phase 2B clinical development of PH10 for this indication. We are preparing for a Phase 1B clinical study of AV-101 in combination with probenecid to assess potential future Phase 2A clinical development of the combination for MDD or certain neurological indications. Our goal is to become a biopharmaceutical company that develops and commercializes innovative CNS therapies for highly prevalent neuropsychiatry and neurology indications where current treatments options are inadequate to meet the needs of millions of patients in markets worldwide.

**Our Product Candidates**

PH94B is a synthetic investigational neurosteroid developed from proprietary compounds called pherines. With its novel mechanism of action, PH94B is an odorless nasal spray administered at microgram-level doses to achieve rapid-onset anti-anxiety, or anxiolytic, effects. The pharmacological activity of PH94B is fundamentally differentiated from that of all FDA-approved anti-anxiety drugs, including all antidepressants approved by the U.S. Food and Drug Administration (*FDA*) for treatment of SAD, as well as all benzodiazepines and beta blockers prescribed on an off-label basis. PH94B engages peripheral chemosensory receptors in nasal passages that trigger a subset of neurons in the main olfactory bulbs (*OB*) at the base of the brain. The OB neurons then stimulate inhibitory GABAergic neurons in the limbic amygdala, decreasing the activity of the sympathetic nervous system, and facilitating fear extinction activity of the limbic-hypothalamic system, the main fear and anxiety center in the brain, as well as in other parts of the brain. Importantly, PH94B does not require systemic uptake and distribution to produce its rapid-onset anti-anxiety effects. Our ongoing PALISADE Phase 3 program for PH94B is designed to further demonstrate its potential as a fast-acting, non-sedating, non-addictive acute treatment of anxiety in adults with SAD. We believe PH94B also has potential to be developed as a novel treatment for adjustment disorder with anxiety, postpartum anxiety, post-traumatic stress disorder, procedural anxiety, panic and other anxiety disorders. PH94B has been granted Fast Track designation status by the FDA for development for the acute treatment of SAD.

PH10 is a synthetic investigational neurosteroid, which also was developed from proprietary compounds called pherines. Its novel, rapid-onset mechanism of action (*MOA*) is fundamentally differentiated from the MOA of all current treatments for MDD and other depression disorders. PH10 is self-administered at microgram-level doses as an odorless nasal spray. PH10 activates nasal chemosensory cells in the nasal passages, connected to neural circuits in the brain that produce antidepressant effects. Specifically, PH10 engages peripheral chemosensory receptors in the nasal passages that trigger a subset of neurons in the main OB that stimulate neurons in the limbic amygdala. This is turn increases activity of the limbic-hypothalamic sympathetic nervous system and increases the release of catecholamines. Importantly, unlike all currently approved oral antidepressants (*ADs*), PH10 does not require systemic uptake and distribution to produce rapid-onset of antidepressant effects. In all clinical studies to date, PH10 has not caused psychological side effects (such as dissociation and hallucinations) or safety concerns that may be associated with rapid-onset ketamine-based therapy (*KBT*), including intravenous ketamine or intranasal ketamine (esketamine). We believe PH10 has potential to be a new stand-alone treatment for MDD and several other depression disorders.

AV-101 (4-Cl-KYN) targets the NMDAR (N-methyl-D-aspartate receptor), an ionotropic glutamate receptor in the brain. Abnormal NMDAR function is associated with numerous CNS diseases and disorders. AV-101 is an oral prodrug of 7-chloro-kynurenic acid (7-Cl-KYNA), which is a potent and selective full antagonist of the glycine co-agonist site of the NMDAR that inhibits the function of the NMDAR. However, unlike ketamine and many other NMDAR antagonists, 7-Cl-KYNA is not an ion channel blocker. At doses administered in all studies to date, AV-101 has been observed to be well tolerated and has not exhibited dissociative or hallucinogenic psychological side effects or safety concerns. In light of these observations and findings from preclinical studies, we believe that AV-101, in combination with FDA-approved probenecid, has potential to become a new oral treatment alternative for certain CNS indications involving the NMDAR. We are currently preparing to evaluate AV-101 in combination with probenecid in a Phase 1B clinical study. The FDA has granted Fast Track designation for development of AV-101 as a potential adjunctive treatment for MDD and as a non-opioid treatment for neuropathic pain (*NP*).

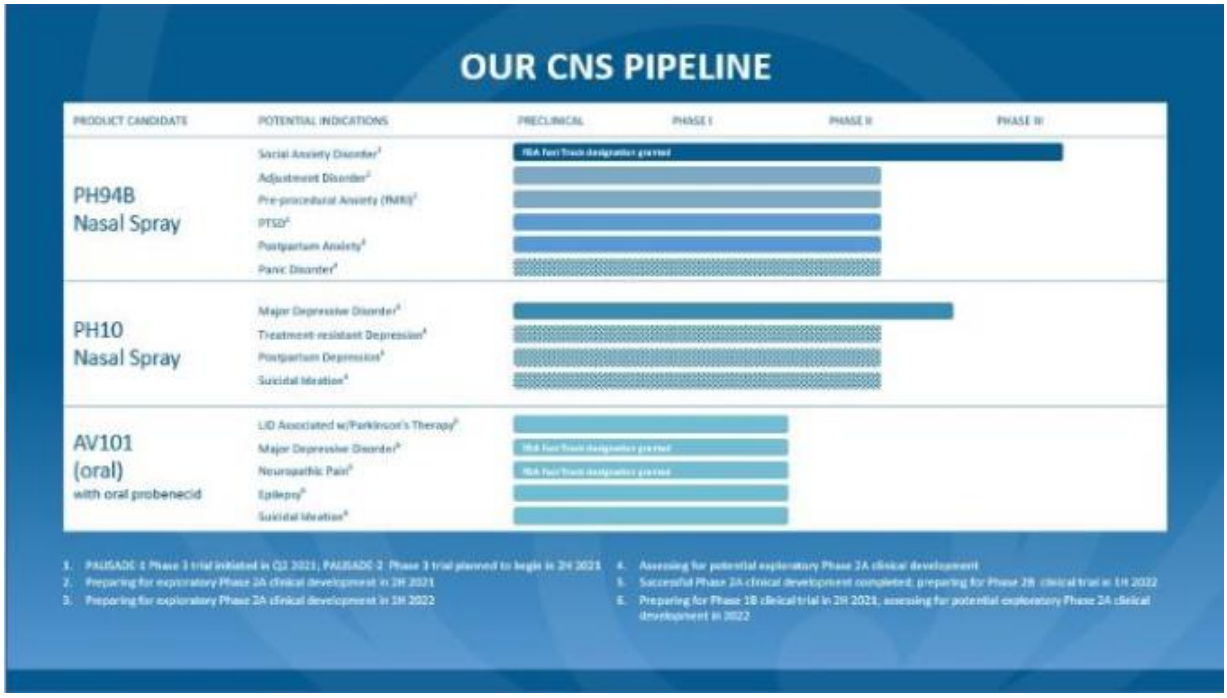
**Our Strategy**

Our goal is to be a leading biopharmaceutical company committed to development and commercialization of novel proprietary CNS therapies that go beyond the current standard of care for treatment of anxiety, depression and other CNS diseases and disorders with high unmet need. Key elements of our strategy to achieve our goal are as follows:

- Focus on highly prevalent anxiety, depression and neurological disorders affecting both adult and pediatric populations where the current standard of care is undesirable or inadequate to meet patient needs.
- Pursue global development, on our own in the U.S. and on our own or with collaborators outside the U.S., of novel proprietary CNS product candidates which are fundamentally differentiated from currently approved therapies;
- Emphasize development and commercialization of proprietary CNS product candidates with potential for (i) rapid-onset therapeutic effects, (ii) exceptional safety and tolerability, and (iii) significant commercial potential in multiple CNS indications in global markets with currently limited, undesirable or inadequate treatment options;
- Commercialize on our own, and retain all commercial rights to, our CNS product candidates in the U.S. and partner with highly-qualified third-party collaborators to commercialize our CNS product candidates in selected markets outside the U.S.; and
- Continue internal research and development efforts to (i) evaluate the expanded therapeutic and commercial potential for our existing CNS product candidates in the treatment of additional CNS indications and (ii) identify additional proprietary CNS product candidates for our CNS product pipeline.

**Our CNS Product Pipeline**

The following table summarizes the status of our CNS clinical development programs as of the filing date of this Annual Report.



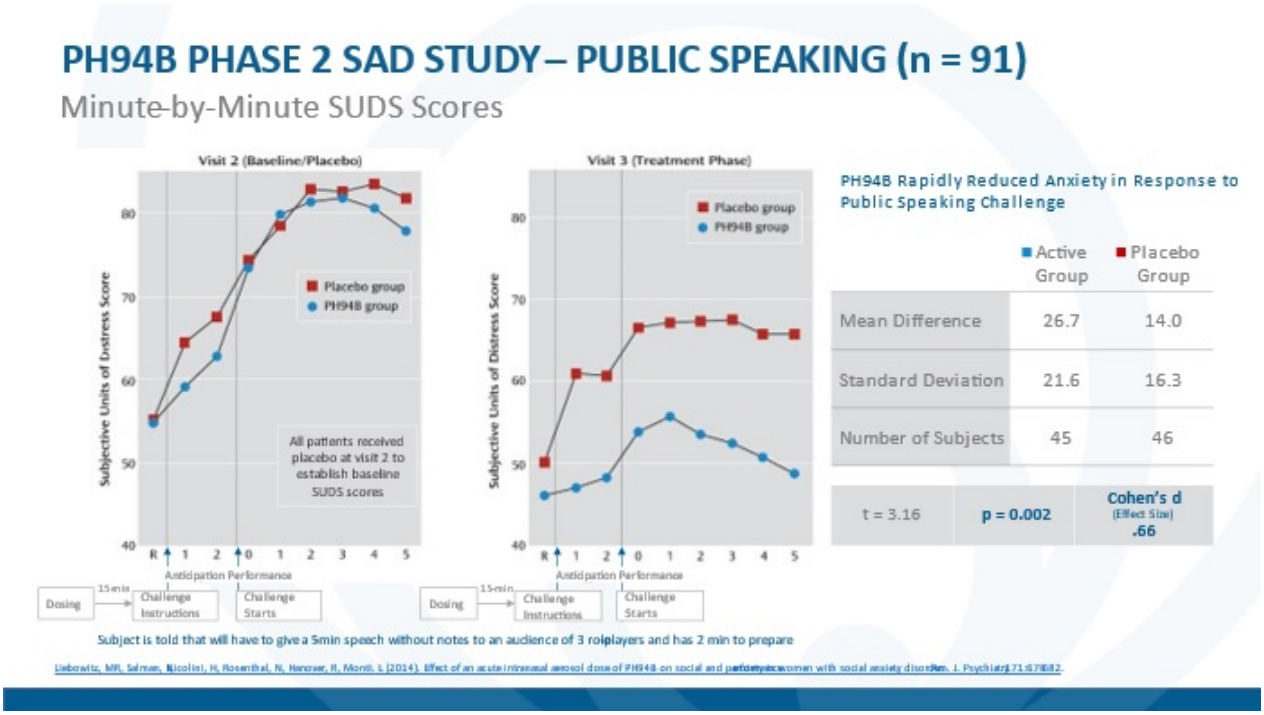

**PH94B Nasal Spray**

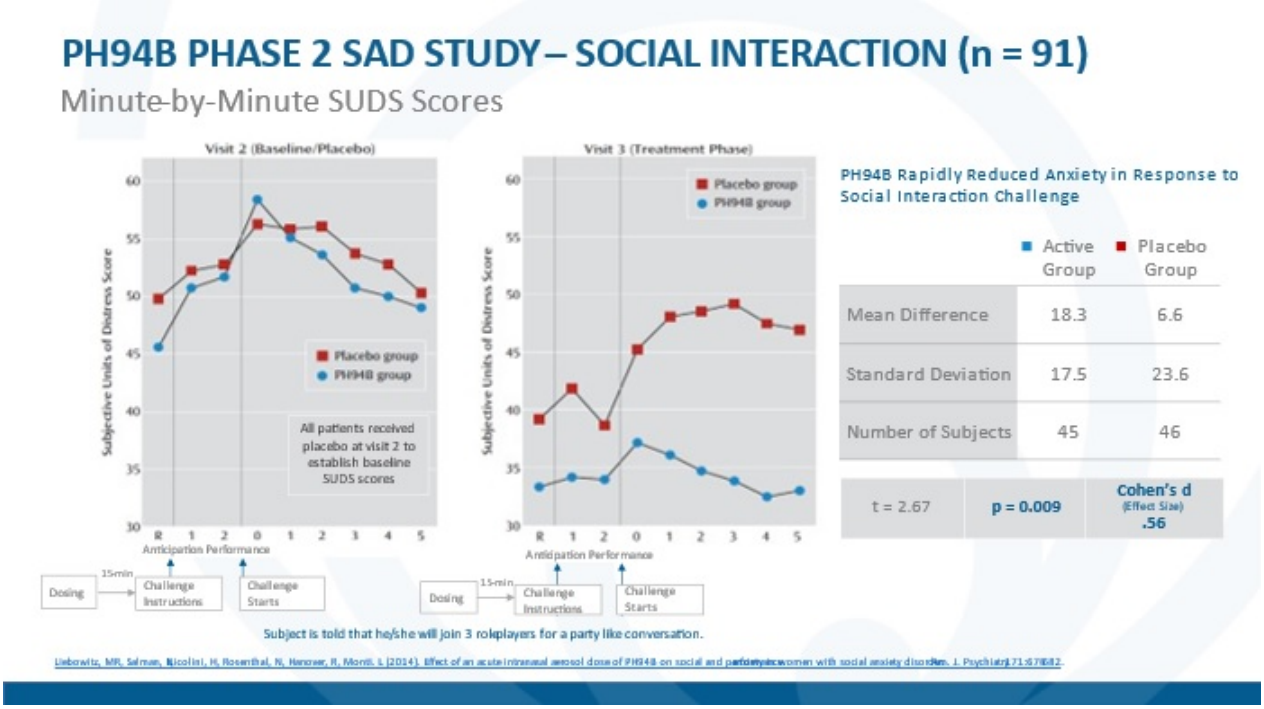
*Social Anxiety Disorder*

Social Anxiety Disorder (*SAD*) affects over 23 million Americans. According to the U.S. National Institutes of Health (*NIH*), SAD is the third most common psychiatric condition after depression and substance abuse. A person with SAD feels intense, persistent symptoms of anxiety or fear in certain social situations, such as meeting new people, dating, being on a job interview, answering a question in class, or talking to a cashier in a store. Doing common everyday things in front of people - such as eating or drinking in front of others or using a public restroom - causes profound anxiety or fear of being humiliated, evaluated, judged, or rejected. The fear that people with SAD have in social situations is so strong that they feel it is beyond their ability to control. SAD can get in the way of going to work, attending school, or doing a wide variety of things in situations that have a potential for interpersonal interaction. People with SAD may worry about these and other things for weeks before they happen. Sometimes, they end up staying away from places or events where they think they might have to do something that will embarrass them. Some people with SAD do not have anxiety in social situations, but instead have performance anxiety. They feel physical symptoms of anxiety in performance situations, such as giving a lecture, a speech or a presentation at school or work, as well as playing a sports game, or dancing or playing a musical instrument on stage. Without treatment, SAD can last for many years or a lifetime and lead to avoidance and opportunity costs that can significantly impact a person's employment, social activities and relationships, and be very disruptive to overall quality of life.

Existing treatments for SAD have not been effective acute treatment options for the large patient population suffering from SAD. Only three drugs, all chronic oral antidepressant drugs (*ADs*), are approved by the FDA specifically for treatment of SAD, and no drug is FDA-approved for acute, on-demand treatment of anxiety in adults with SAD. These FDA-approved chronic oral ADs have slow onset of effect (often many weeks or months) and significant side effects that may make them inadequate or inappropriate treatment alternatives for many individuals affected by acute SAD episodes. Benzodiazepines, often referred to as "benzos," and beta blockers, both of which have not been studied systematically in controlled studies for treatment of SAD. They are not FDA-approved to treat SAD, but are prescribed on an off-label basis by psychiatrists and other physicians for the treatment of SAD. Unlike ADs, which can take several weeks to take full effect, benzodiazepines, which act as direct positive modulators of GABA-A receptors, have a rapid-onset effect by potentiating GABA-A and slowing the nervous system to induce a calming effect that can last up to twelve hours. However, the safety concerns and side effects of benzodiazepines, many of which are similar to side effects of alcohol, also can appear rapidly. Extended use of benzodiazepines may lead to physical dependence and weaning off. Benzodiazepines can take up to many months, often resulting in severe withdrawal symptoms, including muscle pain, sweating, blurred vision, depression, seizures and delirium tremens similar to those experienced with alcohol withdrawal. Benzodiazepines users can also build up a tolerance that requires increasingly larger doses over time. When taken with opioid drugs, benzodiazepine use may be quite dangerous, so much so that in September 2020 the FDA issued an update to its 2016 Drug Safety Communication requiring that benzodiazepines display a "black box" label on bottles to warn against their potential for dangerous interactions with opioids, as well as potential risk of abuse, misuse, overuse and addiction. We believe PH94B, with its rapid-onset anti-anxiety effects, demonstrated in Phase 2 development without requiring systemic uptake and distribution, and its lack of benzodiazepine-like side effects and safety concerns in all clinical studies to date, has potential to displace both ADs and benzodiazepines in the current treatment paradigm for SAD, as well as in many other current anxiety disorder treatment paradigms.

In a peer-reviewed, published, randomized, double-blind, placebo-controlled Phase 2 clinical trial (n=91), with Dr. Michael Liebowitz, the creator of the Liebowitz Social Anxiety Scale (*LSAS*), as principal investigator, PH94B was significantly more effective than placebo in reducing both public-speaking (performance) anxiety (p=0.002) and social interaction anxiety (p=0.009) in laboratory-induced challenges of individuals with SAD, as assessed using patient-reported anxiety ratings on the Subjective Units of Distress Scale (*SUDS*) within 15 minutes of self-administration of a non-systemic 1.6 microgram dose of PH94B.






In all Phase 1 and Phase 2 studies to date, PH94B's safety profile has been exceptional, without indication of abuse potential, psychological side effects (such as dissociation, euphoria or hallucinations), sedation or other side effects and safety concerns that may be associated with ADs approved by the FDA for treatment of SAD, as well as with benzodiazepines and beta blockers prescribed off-label.

Based on its novel mechanism of pharmacological action, rapid-onset of therapeutic effects and exceptional safety and tolerability profile in all clinical studies to date, we have initiated our PH94B PALISADE Phase 3 development program with PALISADE-1, a U.S., multi-center, randomized, double-blind, placebo-controlled Phase 3 clinical study to evaluate the efficacy and safety of PH94B for the acute treatment of anxiety in adults with SAD, as well as preparations for the additional studies required to support our potential U.S. New Drug Application (*NDA*) for that indication should our PH94B PALISADE Phase 3 development program for SAD be successful. With respect to SAD, our goal is to develop and commercialize PH94B, on our own in the U.S. and with collaborators in markets outside the U.S., as the first FDA-approved, fast-acting, on-demand, acute treatment of anxiety for adults with SAD. We also plan to develop and commercialize PH94B in a similar manner for the acute treatment of anxiety in pediatric patients with SAD.

*Adjustment Disorder with Anxiety*

Almost everyone experiences significant life events, changes, or stressors and while some individuals adjust to such changes within a few months, others cannot and may struggle with adjustment disorder. Adjustment disorder with anxiety (*AjDA*) is an emotional or behavioral reaction considered excessive or disproportionate to a sudden change, stressful event or major life change, such as loss of work, divorce or health setback, occurring within three months of the stressor, and/or significantly impairing a person's social, occupational and/or other important areas of functioning. The stress-related disturbance does not represent normal bereavement or meet the criteria for another mental disorder and is not merely an exacerbation of a preexisting mental disorder.

The mental health stressors associated with the COVID-19 pandemic have directly or indirectly affected hundreds of millions of individuals around the world and have considerably increased the prevalence of AjDA. We believe the mental health impact of the COVID-19 pandemic will be long-term and varied across a wide range of anxiety disorders. PH94B has potential as a novel, treatment of anxiety for adults with AjDA, including stress and impaired functioning as a result of recent-onset of stressors brought on by the health, safety, economic and social circumstances, including, but not limited to, circumstances related to and consequences of the COVID-19 pandemic and civil unrest in 2020. With successful Phase 2 development of PH94B for acute treatment of anxiety in adults with SAD completed and Phase 3 development for that indication now underway, we are preparing to initiate exploratory Phase 2A clinical development of PH94B for treatment of anxiety in adults with AjDA. Dr. Michael Liebowitz, Professor of Clinical Psychiatry at Columbia University and director of the Medical Research Network in New York City, will serve as Principal Investigator of the exploratory Phase 2A study.

*Postpartum Anxiety*

Even before the COVID-19 pandemic, there was compelling research indicating that about approximately 17% of new mothers battle anxiety. Recent research reflects that the prevalence of postpartum anxiety (*PPA*) among new mothers increased significantly during the COVID-19 pandemic. Combined with commonly experienced hormone changes and sleep deprivation, key additional factors contributing to increasing mental health challenges among new mothers during the COVID-19 pandemic include job loss, lack of secure housing and access to healthcare, physical isolation from friends and family, increased childcare, educational and household duties, and fear and uncertainty about the state of the world for themselves and their newborn children.

With its potential to produce rapid-onset therapeutic effects at microgram-level doses, without requiring systemic uptake and distribution to achieve those therapeutic effects, and without causing sedation, we believe PH94B may be ideally suited for new mothers suffering with PPA, especially new mothers who are interested in breastfeeding and who would prefer a non-systemic, non-sedating therapeutic alternative to current therapies.

In collaboration with clinical investigators at a leading university medical center in the U.S., we are exploring opportunities to assess PH94B's potential as a novel rapid-onset treatment for PPA in a small exploratory Phase 2A clinical study.

*Post-Traumatic Stress Disorder*

Post-traumatic stress disorder (*PTSD*) is a clinically diagnosed psychiatric disorder that develops in some people who have experienced or witnessed a shocking, scary, dangerous or life-threatening event, such as military combat, natural disasters, terrorist incidents, serious accidents, or physical or sexual assault in adulthood or childhood. Symptoms of PTSD include flashbacks, nightmares, severe anxiety, uncontrollable intrusive thoughts, and emotional numbing after the event. More than 8 million people in the U.S. suffer from PTSD. Anyone can develop PTSD at any age. According to the National Center for PTSD, about seven or eight out of every 100 people will experience PTSD at some point in their lives. The prevalence of PTSD is even higher in populations at risk for exposure to trauma, such as military service members and first responders. PTSD is often accompanied by depression or one or more of the other anxiety disorders, and PTSD sufferers also have a higher rate of suicide and often struggle with simultaneous addiction, leading to an even greater social and economic burden of the disorder.

It is natural to feel afraid during and after a traumatic situation. Fear triggers many split-second changes in the body to help defend against danger or to avoid it. This "fight-or-flight" response is a typical reaction meant to protect a person from harm. Because PTSD is associated with a heightened "fight or flight" response mediated by increased sympathetic nervous response to conditioned stimuli, an agent which decreases sympathetic tone may be able to treat some symptoms of PTSD. In Phase 2 studies, at microgram doses, PH94B has been shown to have rapid-onset anti-anxiety effects in patients with both generalized anxiety disorder (*GAD*) and SAD. PH94B may therefore have utility as an as-needed, rapid-onset treatment of symptoms of PTSD. Available therapeutic options for PTSD are limited, including only two FDA-approved antidepressants, which have limited efficacy and undesirable side effects.

In collaboration with clinical investigators at leading university medical centers in the U.S., we are exploring opportunities for exploratory Phase 2A clinical development of PH94B as a potential as-needed, on-demand, fast-acting anxiolytic in the PTSD treatment paradigm.

*Generalized Anxiety Disorder*

Generalized Anxiety Disorder (*GAD*) is a common chronic neuropsychiatric disorder characterized by persistent, debilitating and excessive concern and worry about family, friends, health, money, work, or other everyday issues and situations. Individuals with GAD find it difficult to control their worry and may worry more about actual circumstances than seems appropriate. They may also expect the worst even when there is no apparent reason to do so. GAD is diagnosed when an individual is unable or finds it difficult to control worry on more days than not for at least six months and has three or more of the many symptoms of GAD, such as excessive and ongoing worrying and tension, an unrealistic view of problems, restlessness, irritability, difficulty concentrating, or being easily startled. This differentiates GAD from worry that may be specific to a set stressor or for a more limited period of time. According to the Anxiety and Depression Association, GAD affects approximately 6.8 million adults in the U.S. in any given year. GAD comes on gradually and can begin across the life cycle, though the risk is highest between childhood and middle age.

People with GAD do not know how to stop the worry cycle and feel it is beyond their control, even though they usually realize that their anxiety is more intense than the situation warrants. Many individuals with GAD may avoid situations because they have the disorder or they may not take advantage of important professional or social opportunities due to their anxiety and worry. When their anxiety is severe, it is difficult for individuals with GAD to carry out even the simplest of daily activities. Currently, the standard of care for GAD includes psychotherapy and certain medications with limited therapeutic benefits and various side effects and safety concerns, including chronic oral antidepressants (SSRIs and SNRIs) and benzodiazepines.

PH94B demonstrated efficacy in a small, exploratory, placebo-controlled Phase 2 clinical study in patients with GAD. Twenty-one patients were randomized to receive 200 picograms of PH94B or placebo in a one-second aerosol pulse to the chemosensory epithelium of the anterior nasal septum. Thirty minutes after treatment there was mean reduction of 32.0% for the PH94B group and 19.6% for the placebo group in the total Hamilton Anxiety Rating Scale (*HAM-A*) score. Electrophysiological changes (respiratory, cardiac, and electrodermal frequency), concordant with the reduction in anxiety, were significantly greater for the PH94B group. We believe these transient anti-anxiety effects of PH94B may warrant further investigation in a larger Phase 2 GAD trial.

We are also assessing PH94B's potential for exploratory Phase 2A clinical studies in pre-procedural anxiety and panic disorder.

**PH10 Nasal Spray**

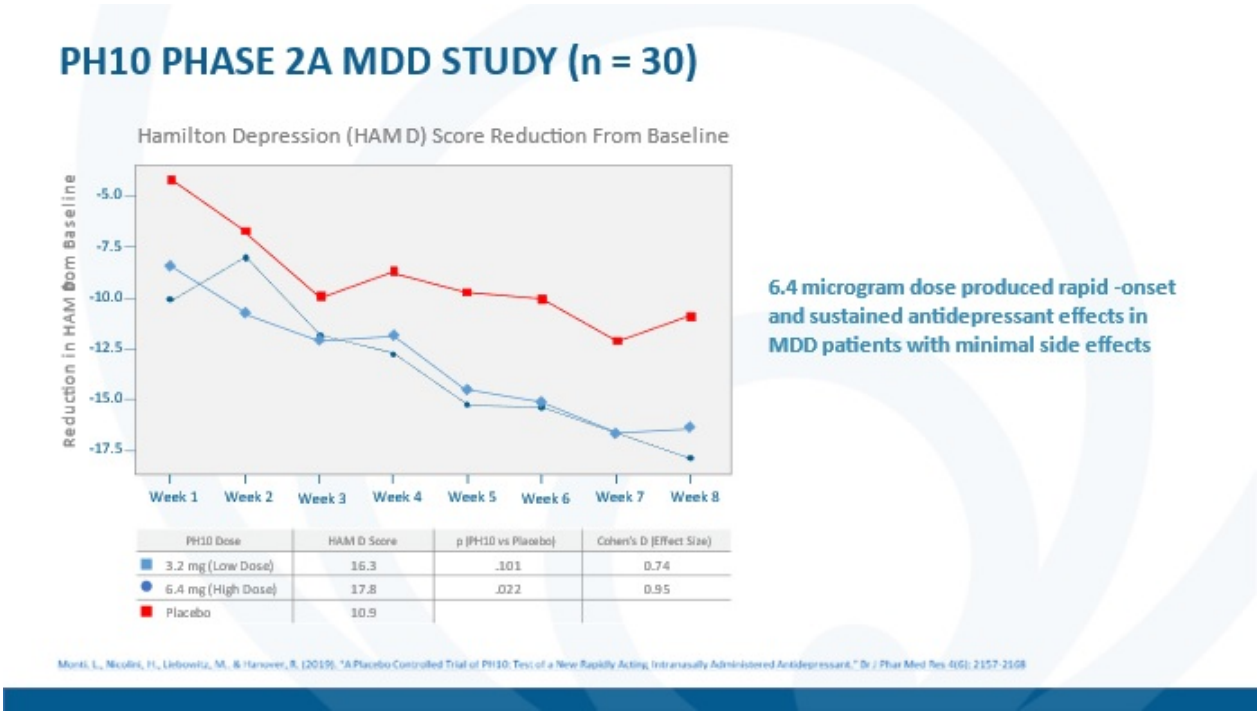
*Major Depressive Disorder*

Depression is a serious medical illness and a global public health concern that can occur at any time over a person's life. According to the World Health Organization (*WHO*), depression is the leading cause of disability worldwide, affecting over 300 million people. Statistics from the U.S. National Institute of Mental Health (*NIMH*) indicate that an estimated 17.3 million adults in the U.S., or approximately 7.1% of all adults in the U.S., had at least one major depressive episode in 2017. While most people will experience depressed mood at some point during their lifetime, MDD is different. MDD is the chronic, pervasive feeling of utter unhappiness and suffering, which impairs daily functioning. In typical depressive episodes, an individual experiences depressed mood, loss of interest and enjoyment, and reduced energy leading to diminished activity and impaired daily functioning for at least two weeks and often much longer. Symptoms of MDD also may include diminished pleasure in activities, changes in appetite that result in weight changes, insomnia or oversleeping, psychomotor agitation, loss of energy or increased fatigue, feelings of worthlessness or inappropriate guilt, difficulty thinking, concentrating or making decisions, and thoughts of death or suicide and attempts at suicide. MDD is the psychiatric diagnosis most commonly associated with suicide.

For many people, depression cannot be controlled for any length of time without treatment. Current oral ADs available in the multi-billion-dollar global depression market have modest efficacy, substantial lag of onset of action, and considerable side effects. Approximately two out of every three depression sufferers do not receive adequate therapeutic benefits from their initial treatment with a standard AD, and the likelihood of achieving remission of depressive symptoms declines with each successive AD treatment attempt. Even after multiple treatment attempts, approximately one-third of depression sufferers still fail to find an adequately effective AD. In addition, this trial and error process and the systemic effects of the various ADs involved may increase the risk of patient tolerability issues and serious side effects, including suicidal thoughts and behaviors in certain groups. New generation ADs with different mechanisms of action, faster onset activity and fewer side effects are needed.

While current FDA-approved ADs are widely used, about two-thirds of patients with MDD do not respond to their initial AD treatment. Inadequate response to current ADs is among the key reasons MDD is one of the leading public health concerns in the United States, creating a significant unmet medical need for new agents with fundamentally different mechanisms of action and safety profiles.

In a peer-reviewed, published exploratory Phase 2A clinical study (n=30), PH10, self-administered at a dose of 6.4 micrograms, was well-tolerated and demonstrated significant (p=0.022) rapid-onset antidepressant effects, which were sustained over an 8-week period, as measured by the Hamilton Depression Rating Scale-17 (*HAM-D-17*), without side effects or safety concerns that may be caused by certain oral ADs or intravenous or intranasal ketamine-based therapy (*KBT*).



With its potential for rapid-onset activity at a microgram-level dose that does not require systemic uptake and distribution to achieve sustained antidepressant effects, as well as an exceptional safety profile, we believe PH10 has transformative potential as an at-home treatment for multiple indications in global depression markets. Based on positive results from the exploratory PH10 Phase 2A program, we are conducting two nonclinical studies necessary to support submission of our Investigational New Drug (*IND*) application to the FDA for our Phase 2B clinical development program for PH10 as a stand-alone, rapid-onset treatment of MDD. Our goal is to submit our IND for a Phase 2B study of PH10 in MDD before the end of 2021, and, if authorized by the FDA, begin Phase 2B clinical development of PH10 for MDD in the first half of 2022. Although our initial plan is to develop PH94B as a new stand-alone rapid-onset therapy for MDD, we also believe PH10 has potential as a stand-alone therapy for treatment-resistant depression (*TRD*) and postpartum depression (*PPD*), and as an adjunctive therapy to augment current FDA-approved ADs for individuals with MDD, TRD and PPD who have an inadequate response to their current ADs and to prevent relapse following successful treatment with KBT.

*Treatment-Resistant Depression*

Treatment-resistant depression is a form of depression that does not get better even after an individual has tried adequate and well-controlled doses of two different oral, FDA-approved antidepressant therapies taken for a sufficient period of time, usually at least six weeks. Approximately one-third of adults with MDD battle depression symptoms that do not respond to current oral AD treatments, including persistent feelings of sadness, disturbances in their sleep patterns, low energy and thoughts of suicide. Certain populations, especially women and elderly individuals, experience TRD at higher rates than others. Individuals who endure severe or frequently recurring bouts of depression also appear to be more susceptible to TRD. Individuals with MDD who also have certain underlying medical conditions, such as thyroid disease, chronic pain, substance abuse and eating or sleep disorders, also may be at greater risk for TRD.

While certain individuals with TRD may benefit from giving their current oral antidepressant more time to work or by taking a larger dose, for others, switching to a different class of antidepressant or augmenting their current AD with an FDA-approved atypical antipsychotic may lead to remission. In recent years, KBT, which includes intravenous ketamine or intranasal esketamine given adjunctively with a new oral AD, has been effective in treating TRD. However, KBT has significant drawbacks. Certain patients receiving KBT may experience uncomfortable dissociative symptoms, hypertension, or other side effects for a few hours after administration. Additionally, because of these potential side effects and safety concerns, as well as the potential for abuse, KBT must be administered in a clinical setting.

PH10, with its potential for rapid-onset antidepressant effects at a microgram-level dose and without systemic uptake and distribution, and, as demonstrated in the PH10 Phase 2A program for MDD, an exceptional safety profile that is not expected to require administration in a clinical setting, has transformative potential in the treatment paradigm as a new stand-alone therapy for TRD and to prevent relapse following successful treatment for TRD with KBT. After we submit our IND for Phase 2B development of PH10 as a stand-alone treatment for MDD, we plan to assess its potential for exploratory Phase 2A development as a stand-alone treatment for TRD.

*Postpartum Depression*

New mothers face many challenges, both practical and emotional, when adjusting to life following the birth of a newborn child. PPD develops around the time a woman gives birth, occurring in approximately 15% of births, according to the U.S. National Institutes of Mental Health (*NIMH*). Women with PPD often struggle with anxiety, sadness, difficulty eating and sleeping, or disturbing thoughts of worthlessness, shame, guilt or suicide, all significant depressive symptoms that may commence during pregnancy or typically within the first few months following childbirth. Other symptoms of PPD may include agitation, loss of interest in daily activities, feeling overwhelmed and fatigued, and inability to concentrate. The current standard of care for PPD involves psychotherapy and, in certain mothers, off-label use of oral ADs or a recently-approved intravenous neurosteroid, all of which require systemic uptake to achieve a therapeutic effect, a potential complication for new mothers who wish to breastfeed their newborn child. The recently-approved intravenous neurosteroid requires a lengthy continuous intravenous infusion (approximately 60 hours) that must be administered in a clinical setting and may also cause sedation.

As demonstrated in an exploratory Phase 2A study of PH10 in adults, including adult women, PH10, self-administered intranasally in microgram-level doses, does not require systemic uptake and distribution to achieve antidepressant effects and, based on its safety profile in all studies to date, is not expected to require inconvenient administration in a clinical setting. PH10 is fundamentally differentiated from the FDA-approved neurosteroid for PPD, as well as all chronic oral ADs used off-label for treatment of PPD. Based on prior clinical studies of PH10, including the exploratory Phase 2A clinical study of PH10 in MDD, we believe it has potential to be a rapid-onset, non-systemic stand-alone treatment for PPD. After we submit our IND for Phase 2B development of PH10 as a stand-alone treatment for MDD, we plan to assess its potential for exploratory Phase 2A development as a treatment for PPD.

*Suicidal Ideation*

According to the WHO, every year approximately 800,000 people worldwide take their own life and many more attempt suicide. Suicidal ideation (*SI*) is characterized as suicidal thoughts and behavior. The U.S. Centers for Disease Control (*CDC*) views suicide as a major public health concern in the U.S. as rates of suicide have been increasing for both men and women and across all age groups. Suicide is the 10th leading cause of death in the U.S. and is one of just three leading causes that are on the rise. According to experts in the field of SI, the number of Americans who die by suicide is, since 2010, higher than the number of those who die in motor vehicle accidents. People of all genders, ages, and ethnicities can be at risk for suicide. SI is complex and there is no single cause. The NIMH attributes many different factors to someone making a suicide attempt, including, but not limited to, depression, other mental health disorders or substance abuse. Additionally, according to reports released by the VA, the U.S. Military Veteran population is at significantly higher risk for suicide than the general population.

We believe PH10 may play a key role in a new treatment paradigm for SI. Accordingly, based on results of various IND-enabling preclinical studies, and, after appropriate IND submissions, we will assess potential exploratory Phase 2A development of PH10 for stand-alone treatment of SI and/or adjunctive treatment of SI together with KBT or other oral AD therapies.

**AV-101 with Probenecid**

AV-101 (4-Cl-KYN) is a novel, oral prodrug that targets the NMDAR (N-methyl-D-aspartate receptor), an ionotropic glutamate receptor in the brain. Abnormal NMDAR function is associated with numerous CNS diseases and disorders. The active metabolite of AV-101, 7-chloro-kynurenic acid (7-Cl-KYNA), is a potent and selective full antagonist of the glycine coagonist site of the NMDAR that inhibits the function of the NMDAR. Unlike ketamine and many other NMDAR antagonists, 7-Cl-KYNA is not an ion channel blocker. In clinical and nonclinical testing, AV-101 has good oral bioavailability, an excellent pharmacokinetic (*PK*) profile, and is not an inhibitor or inducer of the human cytochrome P450 (*CYP*) isoforms. No binding of AV-101 or 7-Cl-KYNA to off-site targets was identified by an extensive receptor screening. Moreover, in all clinical trials to date, AV-101 has been safe and very well-tolerated with no psychological side effects or safety concerns and no treatment-related serious adverse events that are often observed with classic channel-blocking NMDAR antagonists such as ketamine and amantadine.

Recent discoveries from successful AV-101 in vivo preclinical studies suggest that there is a substantial increase in brain concentrations of AV-101 and 7-Cl-KYNA when AV-101 is given together with probenecid, a drug approved by the FDA for treatment of gout which is known to block activity of certain organic ion efflux transporters in the kidney. These surprising results in the brain were first revealed in our recent preclinical studies and are consistent with well-documented clinical studies of probenecid increasing the therapeutic levels in the blood of several unrelated classes of approved drugs, including certain antibacterial, anticancer and antivirals. Many clinical studies demonstrate that probenecid is safe and well tolerated. Probenecid administered adjunctively with AV-101 in an animal model resulted in substantial increased brain concentrations of AV-101 (7-fold) and 7-Cl-KYNA (35-fold). We also recently identified that these increases in brain levels could result from blocking of some of the same transporters in the blood brain barrier that are expressed in the kidney, which are used to regulate drug levels in the blood. This 7-Cl-KYNA efflux-blocking effect of probenecid, with the resulting increased brain levels and duration of 7-Cl-KYNA, suggests the potential impact of AV-101 with probenecid could result in far more profound therapeutic benefits for patients with MDD and other NMDAR-focused CNS diseases and disorders than was demonstrated in the Elevate Study. Nonclinical results also indicate that chronic administration of 4-Cl-KYN induces hippocampal neurogenesis, a hallmark of drugs that have antidepressive effects, and increases endogenous levels of KYNA, which also is a functional NMDAR glycine site antagonist.

In addition, a Phase 1B target engagement clinical study completed by the Baylor College of Medicine (*Baylor*), with financial support from the U.S. Department of Veterans Affairs (*VA*), involved 10 healthy volunteer U.S. military Veterans who received single doses of AV-101 (720 mg or 1440 mg) or placebo, in a double-blind, randomized, cross-over controlled trial. The primary goal of the study was to identify and define a dose-response relationship between AV-101 and multiple electrophysiological (*EEG*) biomarkers related to NMDAR function, as well as blood biomarkers associated with suicidality (the *Baylor Study*). The findings from the Baylor Study suggest that, in healthy Veterans, the higher dose of AV-101 (1440 mg) was associated with dose-related increase in the 40 Hz Auditory Steady State Response (*ASSR*), a robust measure of the integrity of inhibitory interneuron synchronization that is associated with NMDAR inhibition.

We are preparing to initiate a Phase 1B clinical study of AV-101 with adjunctive probenecid in the second half of 2021 to evaluate their safety in combination and potential for exploratory Phase 2A development in one or more of the CNS indications for which we have existing encouraging preclinical data with AV-101, including MDD, epilepsy, levodopa-induced dyskinesia, and neuropathic pain.

*Major Depressive Disorder*

In late-2019, we completed a double-blind, placebo-controlled, Phase 2 clinical trial of AV-101 as a potential adjunctive treatment, together with a standard oral AD, in MDD patients who had an inadequate response to a stable dose of a standard oral AD (the *Elevate Study*). Topline results of the Elevate Study (n=199) indicated that the AV-101 treatment arm (1440 mg) did not differentiate from placebo on the primary endpoint (change in the Montgomery-Åsberg Depression Rating Scale (*MADRS-10*) total score compared to baseline). After further analysis, we believe that this was likely due to sub-therapeutic concentrations in the brain of 7-Cl-KYNA, the active metabolite of AV-101, resulting from the activity of certain organic ion efflux transporters which reduce 7-Cl-KYNA concentrations in the brain. As in all prior clinical studies, in the Elevate Study, AV-101 was well tolerated, with no psychotomimetic side effects or drug-related serious adverse events.

The successful Baylor Study and the recent discoveries in our preclinical studies involving AV-101 and adjunctive probenecid suggest that it may be possible to increase therapeutic concentrations and duration of 7-Cl-KYNA in the brain, and thus increase NMDAR antagonism in MDD patients with an inadequate response to standard ADs when AV-101 and probenecid are combined.

*Neuropathic Pain*

Neuropathic pain (*NP*) affects approximately 33 million people in the United States (excluding patients with back pain) according to an article published in the Journal of Pain Research in 2017. NP is a complex, chronic pain state characterized by a steady burning "pins and needles" or "electric shock" sensation that results in abnormal neuronal function after nerve damage. The American Chronic Pain Association has identified various causes of NP, including tissue injury, nerve damage or disease, diabetes, infection, toxins, certain types of drugs, such as antivirals and chemotherapeutic agents, certain cancers, and even chronic alcohol intake. Current treatments for NP include antidepressants, anticonvulsants (such as gabapentin and pregabalin), and opioids, among others. However, current medications may offer inadequate efficacy, have limiting side effects, and be associated with abuse.

The effects of AV-101 as a potential new treatment for NP were assessed in published peer-reviewed preclinical studies involving four well-established models of pain. In these studies, AV-101 was observed to have robust, dose-dependent anti-nociceptive effects, as measured by dose-dependent reversal of NP in the Chung (nerve ligation), formalin and carrageenan thermal models in rats, and was well-tolerated. The publication, titled: "*Characterization of the effects of L-4-chlorokynurenine on nociception in rodents*," by lead author, Tony L. Yaksh, Ph.D., Professor in Anesthesiology at the University of California, San Diego, was published in *The Journal of Pain* in April 2017 (J Pain. 18:1184-1196, 2017)). In subsequent studies in this preclinical model, AV-101 also had positive results using pregabalin as an active control. AV-101 demonstrated robust analgesic effects, similar to pregabalin, but fewer side effects as measured in the rotarod assay. In third party literature, gabapentin and pregabalin, often prescribed for treatment of NP, have been associated with sedation and mild cognitive impairment. Other commonly prescribed medications for NP include drugs targeting opioid receptors in the brain. Unfortunately, misuse of such drugs can lead to a significantly increased risk of addiction, and, we believe, their therapeutic utility for neuropathic pain is unclear.

Based on successful preclinical studies involving AV-101, compared to gabapentin and pregabalin, as well as successful Phase 1B development of AV-101 in combination with probenecid, we may explore Phase 2A clinical development of AV-101, together with probenecid, as a potential new generation, non-opioid treatment to reduce debilitating NP. We believe AV-101 in combination with probenecid has the potential to avoid sedative side effects and cognitive impairment often associated with other NP treatments, and reduce the risk of addiction associated with pain medications targeting opioid receptors.

*Levodopa-Induced Dyskinesia associated with Therapy for Parkinson's Disease*

Parkinson's disease (*PD*) is the second most common neurodegenerative disease worldwide, affecting approximately one million people in the U.S., according to the Parkinson's Foundation. Although there is no "one-size-fits-all" description of PD, PD is a complex neurodegenerative disorder that occurs when brain cells responsible for making dopamine, a chemical that coordinates movement, stop working or die. This results in progressive deterioration of voluntary motor control. Loss of dopamine neurons is thought to be due to neurotoxicity associated with misfolding of proteins and is associated with increased signaling of glutamate, the most abundant excitatory neurotransmitter in the brain. Increased glutamate activity is involved with aberrant neuronal signaling and excitotoxic death of neurons. Classic PD motor symptoms include muscular rigidity, resting tremor, and postural and gait impairment. Typically, PD patients present with a combination of motor and non-motor symptoms. Non-motor symptoms may include cognitive impairment, sleep disorders pain and fatigue. There is currently no medication to slow, delay, stop or cure PD, and currently available treatments are symptomatic. Treatment of motor symptoms with oral levodopa, introduced about 50 years ago, remains the gold standard treatment.

Levodopa-induced dyskinesia (*LID*) is a disorder that affects people with PD who are treated with levodopa for an extended period of time. Oral levodopa remains the most effective therapy for motor symptoms of PD. However, studies published in the *New England Journal of Medicine* and *Movement Disorders* have shown LID develops in approximately 45% of levodopa-treated Parkinson's disease patients after five years and 80% after 10 years of levodopa treatment. Although clinical manifestations of LID are heterogenous, LID is commonly associated with abnormal involuntary movements, including chorea and dystonia. These motor complications tend to become more severe as PD progresses and as the duration of levodopa treatment is extended, until the impact of LID may compromise the advantage of treatment with levodopa. PD treatment with levodopa is routinely delayed due to concerns over LID. Once LID develops, levodopa-treated PD patients may be faced with a choice between immobility due to untreated and uncontrolled PD, or mobility with the associated LID. In the U.S., there are an estimated 150,000 to 200,000 people with PD who are impacted by LID.

AV-101 is not a dopamine-based drug candidate. Rather, AV-101's active metabolite, 7-Cl-KYNA, is a potent and selective NMDAR glycine site antagonist with neuroprotective properties, which receptor plays a major role in glutamatergic signaling and has been shown to be a therapeutic target for LID.

In a preclinical study in the "gold standard" MPTP monkey model of PD and LID, AV-101's efficacy against LID was measured through behavioral scores on a dyskinesia scale, and a Parkinsonian disability scale was used to measure levodopa anti-parkinsonian efficacy. This study demonstrated that AV-101 significantly (p=0.01) reduced LID. Importantly, AV-101 did not reduce the timing, extent, or duration of the therapeutic effects of levodopa, indicating that AV-101 did not impact the anti-parkinsonian efficacy of levodopa. Moreover, AV-101 did not cause adverse events often associated with amantadine therapy for LID, such as hallucinations, dizziness, and falls. These preclinical results confirmed our prior anti-dyskinesia study in this MPTP monkey model. We believe these preclinical data and AV-101's positive safety profile in all clinical studies to date support the potential of AV-101, together with probenecid, to treat LID, while both maintaining the antiparkinsonian benefits of levodopa and without causing hallucinations or other serious side effects that may be associated with amantadine therapy for LID. As a result, upon successful Phase 1B development of AV-101 in combination with probenecid, we may explore Phase 2A clinical development of AV-101, together with probenecid, as a new generation treatment for LID.

*Epilepsy*

Epilepsy is one of the most prevalent neurological disorders, affecting almost 1% of the worldwide population. According to the Epilepsy Foundation, as many as three million Americans have epilepsy, and one-third of those suffering from epilepsy are not effectively treated with currently available medications. In addition, standard anticonvulsants can cause significant side effects, which frequently interfere with compliance.

Glutamate is a neurotransmitter that is critically involved in the pathophysiology of epilepsy. Through its stimulation of the NMDAR subtype, glutamate has been implicated in the neuropathology and clinical symptoms of the disease. In support of this, NMDAR antagonists are potent anticonvulsants. However, as noted, classic ion channel-blocking NMDAR antagonists are limited by adverse effects, such as neurotoxicity, declining mental status, and the onset of psychotic symptoms following administration of the drug. The endogenous amino acid glycine modulates glutamatergic neurotransmission by stimulating the glycine coagonist site of the NMDAR. Glycine site antagonists such as AV-101's active metabolite, 7-Cl-KYNA, inhibit NMDAR function and are therefore anticonvulsant and neuroprotective. Importantly, glycine site antagonists have fewer and less severe side effects than classic ion channel-blocking NMDAR antagonists and other antiepileptic agents, making them a safer potential alternative to, and one expected to be associated with greater patient compliance than, currently available anticonvulsant medications.

In addition, another active metabolite of AV-101, 4-Cl-3-hydroxyanthranilic acid, inhibits the synthesis of quinolinic acid (*QUIN*), which is an endogenous NMDAR agonist that causes convulsions and excitotoxic neuronal damage.

AV-101 has been shown to protect against seizures and neuronal damage in preclinical animal models of epilepsy. Upon successful Phase 1B development of AV-101 in combination with probenecid, we believe exploratory preclinical data in an epilepsy model, together with human safety data in all clinical studies to date, may provide support for exploratory Phase 2A clinical development of AV-101, together with probenecid, as a potential new generation treatment for epilepsy.

## Intellectual Property

We strive to protect the proprietary know-how and technology that we believe is important to our business, including seeking and maintaining patents intended to cover our product candidates and related pharmaceutical compositions, their therapeutic methods of use, including treatment and prognostic methods, as well as processes for their manufacture, and any other aspects of our discoveries and inventions that are commercially important to the development of our business.

We may also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We also utilize know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position. We seek to obtain domestic and international patent protection in appropriate markets, and endeavor to promptly file patent applications for new commercially valuable inventions.

To protect our rights to our proprietary technology, we require all employees, as well as our external collaborators, consultants and CROs when feasible, to enter into agreements that require disclosure and assignment to us of ideas, developments, discoveries and inventions made by these employees, consultants, and CROs in the course of their service to us.

We plan to continue to expand our intellectual property estate by filing patent applications directed to compositions, methods of use, including treatment and patient selection, formulations and manufacturing processes created or identified from the ongoing development of our product candidates.

### Patents

We own and have licensed granted patents and pending patent applications in the U.S. and in certain foreign countries. These patent properties include, but are not limited to:

***PH94B (licensed by us from Pherin Pharmaceuticals, Inc. (Pherin))***

- Two granted U.S. patents and other foreign patents related to the reduction of anticipatory anxiety or social phobic response.

The U.S. patents related to PH94B will nominally expire either in 2025 or 2028, respectively, and foreign patents nominally expire in 2026, subject to extensions that may be available on a country-by-country basis, including in the U.S.

***PH94B patent application owned by VistaGen***

- Pending U.S. and Patent Cooperation Treaty (*PCT*) patent applications related to the treatment of adjustment disorder with anxiety.

Patents that may be granted on this patent application nominally will expire in 2041, including in the U.S.

***PH10 (licensed by us from Pherin)***

- One granted U.S. patent related to treatment of depressive disorders; and
- Granted foreign patents related to treatment of depressive disorders.

The U.S. and foreign patents related to PH10 nominally expire in 2033, subject to extensions that may be available on a country-by-country basis, including in the U.S.

***AV-101***

- Five granted U.S. patents related to the treatment of depression with AV-101, certain unit dose formulations of AV-101 effective to treat depression, and treatment of dyskinesia induced by the administration of L-DOPA (*LID*);
- Pending U.S. patent applications and foreign granted patents and pending foreign patent applications related to treatment of various disorders, including depression, LID, neuropathic pain (*NP*), tinnitus and obsessive-compulsive disorder;
- Pending PCT patent application related to the prognostic identification of high and low responders to treatment of various CNS disorders with AV-101; and
- Two granted U.S. patents, and foreign granted patents and pending foreign patent applications related to the manufacture of AV-10.

The U.S. and foreign patents related to AV-101 nominally expire between 2034 and 2040, depending on the particular subject matter, subject to extensions that may be available on a country-by-country basis, including in the U.S.

***Stem Cell Technology (owned by us and/or licensed by us from the University Health Network (Toronto) or Icahn School of Medicine at Mount Sinai)***

***Cardiac Cells***

- U.S. and foreign patents and patent applications relating to methods for enriching pluripotent stem cell-derived cardiomyocyte cells, methods for generating epicardium cells, methods for making and using sino-atrial node-like pacemaker and ventricular-like cardiomyocytes and methods for generation of atrial and ventricular cardiomyocyte lineages.

The U.S. and foreign patents and patent applications related to cardiac stem cells nominally expire between 2031 and 2037, subject to extensions that may be available on a country-by-country basis, including in the U.S. Additionally, therapeutic and certain other fields of use have been licensed by us to Bayer under the Bayer Agreement.

***Blood Cells***

- U.S. and foreign patents and patent applications relating mesoderm and definitive endoderm cell populations, and to populations of hematopoietic progenitors.

The U.S. and foreign patents and patent applications related to blood stem cells nominally expire between 2023 and 2032, subject to extensions that may be available on a country-by-country basis, including in the U.S.

***Cartilage and Chondrocyte Cells***

- U.S. and foreign patents and patent applications relating to methods and compositions for generating chondrocyte lineage cells and cartilage like tissue.

The U.S. and foreign patents and patent applications related to cartilage and chrondrocyte cells nominally expire in 2034, subject to extensions that may be available on a country-by-country basis, including in the U.S.

***Liver and Biliary Cells***

- U.S. and foreign patents and patent applications relating to methods for generating hepatocytes and cholangiocytes from pluripotent stem cells and to toxicity typing using liver stem cells.

The U.S. and foreign patents and patent applications related to liver and biliary cells nominally expire between 2021 and 2034, including in the U.S.

**Patent Term**

The base term of a U.S. patent is 20 years from the filing date of the earliest-filed non-provisional patent application from which the patent claims priority. The term of a U.S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the U.S. Patent and Trademark Office (*PTO*). In some cases, the term of a U.S. patent is shortened by a terminal disclaimer that reduces its term to align with that of a related patent.

Depending upon the timing, duration and specifics of the FDA approval of our drug candidates, if any, some 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, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA (*testing phase*), plus the time between the submission date of an NDA and the approval of that application (*approval phase*). This patent term restoration period may be reduced by the FDA if it finds that applicant did not act with due diligence during the testing phase or the approval phase. Only one patent related to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. PTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, if circumstances permit, we intend to apply for restoration of patent term for our applicable patents, if any, to extend patent life beyond their normal expiration dates depending on the length of the clinical trials and other factors involved in the filing of the relevant NDA.

**Data Exclusivity**

Some of our products may also be entitled to certain data exclusivity (that is not patent-related) under the Federal Food, Drug and Cosmetic Act (*FDCA*) and its related regulations. The FDCA provides a five-year period of non-patent data exclusivity within the U.S. to the first applicant to obtain approval of an NDA for a new chemical entity (*NCE*). A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule responsible for the pharmacological action of the drug substance. During the data exclusivity period, an abbreviated new drug application (*ANDA*), or a 505(b)(2) NDA submitted by another company may not be approved by the FDA for another drug containing the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data that served as the basis of granting the original NDA.

However, an ANDA or a 505(b)(2) NDA application may be submitted after four years if the innovator NDA holder does not have a patent covering the product listed with the FDA Orange Book or if the application contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA Orange Book. The FDCA also provides three years of data exclusivity for a full NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. Three-year exclusivity prevents the FDA from approving ANDAs and 505(b)(2) applications that rely on the information that served as the basis of granting the new full or supplemental NDA. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy.

Some foreign jurisdictions, including Europe and Japan, also have patent term extension provisions, which allow for extension of the term of a patent that covers a drug approved by the applicable foreign regulatory agency. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extension on patents covering those products, their methods of use, and/or methods of manufacture.

**Trade Secrets**

In addition to patents, we may rely on trade secrets to develop and maintain our competitive position. We protect trade secrets, if any, and also know-how, by establishing confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and partners. These agreements provide that all confidential information developed or made known during the course of an individual's or entity's relationship with us must be kept confidential during and after the relationship. These agreements also generally provide that all relevant inventions resulting from work performed for us or relating to our business and conceived or completed during the period of employment or assignment, as applicable, shall be our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary information by third parties.

**Trademarks**

The Company also owns a registered trademark in the U.S. for "VISTAGEN," for "biotechnology services" in international class 42, which was renewed in 2021. We have a U.S. registration application pending for VISTAGEN in international class 10 for "human and veterinary preparations for medical uses."

**Strategic Transactions and Relationships**

Strategic collaborations are an important cornerstone of our corporate development strategy. We believe that our highly selective outsourcing of certain research, development, legal, manufacturing and regulatory activities gives us flexible access to a broad range of capabilities and expertise at a lower overall cost than developing and maintaining such capabilities and expertise internally on a full-time basis. In particular, we retain third parties for certain legal manufacturing, nonclinical development, clinical development and regulatory affairs support.

We have entered into, and may seek multiple additional strategic collaborations and relationships focused on development and commercialization of our product candidates in regions outside the U.S.

**Commercial Agreements**

We have customary clinical supply agreements with multiple CMOs and customary agreements with multiple CROs to assist us with advancement and management of our nonclinical, including manufacturing, and clinical development programs. Each of our commercial agreements is non-exclusive, and we have no material contractual obligations under such agreements, except to the extent we order supplies or request services to be performed under specific work orders that we generate with such third-parties from time to time.

**Material License Agreements**

*Exclusive License and Collaboration Agreements with Pherin*

In September 2018, we acquired from Pherin Pharmaceuticals, Inc. (*Pherin*) an exclusive worldwide license to develop and commercialize PH94B. In October 2018, we acquired from Pherin an exclusive worldwide license to develop and commercialize PH10. Under the terms of the PH94B and PH10 license agreements, we are obligated to make additional cash payments, and pay royalties, to Pherin in connection with our sublicense, development and commercialization collaborations involving PH94B and/or PH10, as well as in the event that certain development milestones and commercial sales are achieved. Additionally, in connection with the license agreements, we were obligated to pay to Pherin monthly support payments of $10,000 for a term of the earlier of 18 months from the date of each license agreement or the termination of the license agreement; however, no monthly support payment was required under the 18-month period identified in the PH10 license agreement if support payments were already being made under the terms of the PH94B license agreement. In April 2020, we completed all of our obligations to pay all such monthly support payments to Pherin under the PH94B license agreement and the PH10 license agreement, and thus the contractual requirements have been fully satisfied.

*Exclusive License and Collaboration Agreement with AffaMed Therapeutics, Inc. (formerly EverInsight Therapeutics, Inc.)*

In June 2020, we entered into a license and collaboration agreement (the *EverInsight License Agreement*) with EverInsight Therapeutics Inc., a company incorporated under the laws of the British Virgin Islands (*EverInsight*), pursuant to which we granted EverInsight an exclusive license to develop, manufacture and commercialize PH94B for multiple anxiety-related disorders in Greater China (Mainland China, Hong Kong, Macau and Taiwan), South Korea and Southeast Asia (Indonesia, Malaysia, Philippines, Thailand and Vietnam) (collectively, the *Territory*). Subsequent to entering into the EverInsight License Agreement, in October 2020, EverInsight merged with AffaMed Therapeutics, Inc., which as a combined, complementary entity is focusing on developing and commercializing therapeutics to address ophthalmologic and CNS disorders in Greater China and beyond. Accordingly, we refer to EverInsight and the EverInsight License Agreement as AffaMed and the AffaMed Agreement, respectively. We retained development, manufacturing and commercialization rights for PH94B in the rest of the world.

Under the terms of the AffaMed Agreement, we received an upfront payment of $5.0 million in August 2020. We may also receive up to an additional $172 million in milestone payments upon AffaMed's achievement of certain developmental, regulatory and sales milestone events related to PH94B. In addition, we are entitled to receive certain royalties on net sales, if any, of PH94B in the Territory following receipt of any required regulatory approval. However, AffaMed's, achievement of any of such developmental, regulatory and sales milestone events, or commercial sales of PH94B in the Territory, cannot be guaranteed. AffaMed has the right to sublicense to affiliates and third parties in the Territory. AffaMed is responsible for all costs related to developing, obtaining regulatory approval of and commercializing PH94B in the Territory. A joint development committee has been established between the Company and AffaMed to coordinate and review the development, manufacturing and commercialization plans with respect to PH94B in the Territory. Unless earlier terminated due to certain material breaches of the contract, or otherwise, the AffaMed Agreement will expire on a jurisdiction-by-jurisdiction basis until the latest to occur of expiration of the last valid claim under a licensed patent of PH94B in such jurisdiction, the expiration of regulatory exclusivity in such jurisdiction or ten years after the first commercial sale of PH94B in such jurisdiction.

**Manufacturing and Supply**

Manufacturing of the drug substance and drug product for our product candidates is done by third-parties and must comply with FDA current good manufacturing practice (*cGMP*) regulations. Our product candidates are comprised of synthetic small molecules made through a series of organic chemistry steps starting with commercially available organic chemical raw materials. We do not currently own or operate, nor do we plan to own or operate, any manufacturing facilities for the production of our drug candidates for nonclinical, clinical or commercial use. We conduct manufacturing activities under individual project or work orders with independent contract manufacturing organizations (*CMOs*) to supply all of our nonclinical and clinical trial needs. We or experts from our CROs conduct periodic quality audits of their facilities. We believe that our existing suppliers of our product candidate's active pharmaceutical ingredients and drug products will be capable of providing sufficient quantities of each to meet our nonclinical and clinical development needs. Other CMOs may be used in the future for nonclinical and clinical supplies and, subject to approval, commercial manufacturing.

By design, we do not currently have any fixed contractual arrangements in place for either long-term supply or redundant supply of bulk drug substance or drug product for our product candidates. If our product candidates are approved, we intend to contract with CMOs to produce all of our future commercial supplies on our behalf. We plan to mitigate potential commercial supply risks for any products that are approved in the future through inventory management and through exploring additional back-up manufacturers, both in the U.S. and outside the U.S., to provide API and/or drug product.

**Sales and Marketing**

We intend to build a commercial infrastructure in the United States in advance of anticipated drug approval of our product candidates. We believe that we can cost effectively implement a targeted sales force required to commercialize our products, if approved, in the United States. Support for this team will include sales management, internal sales support, distribution support, and an internal marketing group. Additional requisite capabilities will include focused management of key accounts such as managed care organizations, group purchasing organizations, and government accounts. We may seek co-promotion partners for our sales efforts to achieve broader reach or call frequency with United States target physicians. We expect to focus our future sales and marketing efforts for our product candidates in the United States, if FDA-approved, on psychiatrists and select primary care physicians and, should we receive FDA approval for use in pediatric populations, on select pediatricians who are likely to see adolescents, as well as nurse practitioners, child psychiatrists and psychologists who, in some states, are permitted to prescribe medications. In order to implement this infrastructure, we will have to allocate management resources and make significant financial investments, including some prior to product approval.

We believe that there are significant market opportunities for our products outside of the United States. As a result, as we have done under the AffaMed Agreement, we plan to seek strategic partnerships with third parties, which may have greater reach and resources by virtue of their size and experience in the field, for the development and commercialization of our products in selected markets outside the United States. We may elect in the future to utilize additional strategic partners, distributors, or contract sales forces to assist in the development and commercialization of our products.

**Competition**

Our industry is highly competitive and subject to rapid and significant technological change. The large size and expanding scope of the CNS markets, especially the high unmet need in large and growing global markets for anxiety and depression disorders, make them attractive therapeutic areas for biopharmaceutical businesses. Our potential competitors include pharmaceutical, biotechnology, and specialty pharmaceutical companies. While we believe that our employees and consultants, scientific knowledge, technology, and development experience provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical, and biotechnology companies, academic institutions and governmental agencies, and public and private research institutions. Several of these entities have robust drug pipelines, readily available capital, and established research and development organizations. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. Many of our competitors may 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. Mergers and acquisitions in the pharmaceutical, biotechnology, and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Small 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 all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of branded and generic competition, and the availability of reimbursement from government and other third-party payors.

Currently there are no FDA-approved therapies for SAD with the mechanism of action of PH94B, and we are aware of no company developing a potential acute treatment of anxiety for adults with SAD that is a nasal spray and involves the same mechanism of pharmacological action as PH94B. However, although they have not been systematically developed for treatment of SAD are not FDA-approved for the acute treatment of anxiety in adults with SAD, we may face competition to PH94B for acute treatment of anxiety in adult and pediatric patients with SAD from off-label use of generic benzodiazepines and generic beta blockers. In addition, although there are three oral antidepressants approved by the FDA for treatment of SAD, such drugs do not achieve rapid-onset therapeutic effects and are associated with undesirable side effects.

Patients with MDD are typically treated with a variety of oral antidepressant medications or oral atypical antipsychotics. These treatments often include generic antidepressants such as: Fluoxetine (Prozac), previously marketed by Eli Lilly and Company; sertraline (Zoloft) and venlaxafine (Effexor), both previously marketed by Pfizer, Inc.; and paroxetine (Paxil) and bupropion (Wellbutrin), both previously marketed by GlaxoSmithKline. Treatments may also include currently marketed medications indicated for MDD such as: Trintellix, with is marketed by Takeda Pharmaceuticals America, Inc and H. Lundbeck A/S; Viibryd, which is marketed by Abbvie; and Rexulti which is marketed by Otsuka America. Although currently there are no FDA-approved oral therapies for MDD with the mechanism of pharmacological action of either PH10 or AV-101, we are aware of numerous companies that are developing therapies targeting the MDD market, including, among others, Axsome Therapeutics, Minerva Neurosciences, Relmada Therapeutics, and Sage Therapeutics. Additionally, with respect to MDD, we expect that PH10 and AV-101 will have to compete with a variety of non-pharmacological alternatives for treatment of MDD, such as psychotherapy and electroconvulsive therapy.

## Government Regulation and Product Approval

Government authorities in the U.S., at the federal, state, and local level, and in other countries and supranational regions, extensively regulate, among other things, the research, development, testing, manufacture, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, import, and export of pharmaceutical products such as those we are developing. In addition, healthcare regulatory bodies in the United States and around the world impose a range of requirements related to the payment for pharmaceutical products, including laws intended to prevent fraud, waste, and abuse of healthcare dollars. This includes, for example, requirements that manufacturers of pharmaceutical products participating in Medicaid and Medicare comply with mandatory price reporting, discount, rebate requirements, and other cost control measures, as well as anti-kickback laws and laws prohibiting false claims. Some states also have enacted fraud, waste, and abuse laws that parallel (and in some cases apply more broadly than) federal laws, and in some cases price transparency requirements. The processes for obtaining regulatory approvals in the United States and in foreign countries, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources. Further, healthcare is an active area of governmental scrutiny, and it is reasonable to expect that the requirements may become more stringent within the foreseeable future.

### *FDA Regulation*

In the U.S., the FDA regulates drugs under the FDCA and its implementing regulations. The process required by the FDA before product candidates may be marketed in the U.S. generally involves the following:

- completion of preclinical laboratory tests, animal studies, and formulation studies in compliance with the FDA's Good Laboratory Practice (*GLP*) regulations;
- submission to the FDA of an IND application which must become effective before human clinical trials may begin;
- approval by an independent Institutional Review Board (*IRB*) for each clinical site or centrally, before each trial may be initiated;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug candidates for its intended use, performed in accordance with current Good Clinical Practices (*cGCP*);
- development of manufacturing processes in compliance with current cGMPs to ensure the drug's identity, strength, quality, and purity;
- compilation of required information and submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMPs, and to assure that the facilities, methods, and controls are adequate to preserve the drug's identity, strength, quality, and purity, as well as satisfactory completion of an FDA inspection of selected clinical sites and selected clinical investigators to determine GCP compliance; and
- FDA review and approval of the NDA to permit commercial marketing for particular indications for use.

*Preclinical Studies and IND Submission*

The testing and approval process of product candidates requires substantial time, effort, and financial resources. Preclinical studies include laboratory evaluation of drug substance chemistry, pharmacology, toxicity, and drug product formulation, as well as animal studies to assess potential safety and efficacy. Such studies must generally be conducted in accordance with the FDA's GLP regulations. Prior to commencing the first clinical trial with a product candidate, an IND sponsor must submit the results of the preclinical tests and preclinical literature, together with manufacturing information, analytical data, any available clinical data or literature, and proposed clinical study protocols, among other things, to the FDA as part of an IND.

An IND becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, notifies the applicant of safety and/or product quality concerns or questions related to one or more proposed clinical trials and places the trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during trials due to safety concerns or noncompliance. As a result, submission of an IND may not result in FDA authorization to commence a clinical trial.

*Clinical Trials*

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirements that all research subjects provide their informed consent in writing for their participation in any clinical trial, as well as review and approval of the study by an IRB. Investigators must also provide certain information to the clinical trial sponsors to allow the sponsors to make certain financial disclosures to the FDA. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the trial procedures, the parameters to be used in monitoring safety, the effectiveness criteria to be evaluated, and a statistical analysis plan. A protocol for each clinical trial, and any subsequent protocol amendments, must be submitted to the FDA as part of the IND. In addition, an IRB at each study site participating in the clinical trial or a central IRB must review and approve the plan for any clinical trial, informed consent forms, and communications to study subjects before a study commences at that site. An IRB considers, among other things, whether the risks to individuals participating in the trials are minimized and are reasonable in relation to anticipated benefits and whether the planned human subject protections are adequate. The IRB must continue to oversee the clinical trial while it is being conducted.

Once an IND is in effect, each new clinical protocol and any amendments to the protocol must be submitted for FDA review, and to the IRB for approval. Progress reports detailing the results of the clinical trials must also be submitted at least annually to the FDA and the IRB and more frequently if serious adverse events or other significant safety information is found.

Information about certain clinical trials, including a description of the study and study results, must be submitted within specific timeframes to the NIH for public dissemination on their clinicaltrials.gov website.

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 regularly reviews accumulated data and advises the study sponsor regarding the continuing safety of trial subjects, enrollment of potential trial subjects, and the continuing validity and scientific merit of the clinical trial. The data safety monitoring board receives special access to unblinded data during the clinical trial and may advise the sponsor to halt the clinical trial if it determines there is an unacceptable safety risk for subjects or on other grounds, such as no demonstration of efficacy.

The manufacture of investigational drugs for the conduct of human clinical trials (and their active pharmaceutical ingredients) is subject to cGMP requirements. Investigational drugs and active pharmaceutical ingredients imported into the U.S. are also subject to regulation by the FDA relating to their labeling and distribution. Further, the export of investigational drug products outside of the United States is subject to regulatory requirements of the receiving country as well as U.S. export requirements under the FDCA.

In general, for purposes of NDA approval, human clinical trials are typically conducted in three sequential phases, which may overlap or be combined.

- *Phase 1*—Studies are initially conducted in healthy human volunteers or subjects with the target disease or condition and test the product candidate for safety, dosage tolerance, structure-activity relationships, mechanism of action, absorption, metabolism, distribution, and excretion. If possible, Phase 1 trials may also be used to gain an initial indication of product effectiveness.

- *Phase 2*—Controlled studies are conducted in limited subject populations with a specified disease or condition to evaluate preliminary efficacy, identify optimal dosages, dosage tolerance and schedule, possible adverse effects and safety risks, and expanded evidence of safety.

- *Phase 3*—These adequate and well-controlled clinical trials are undertaken in expanded subject populations, generally at geographically dispersed clinical trial sites, to generate enough data to provide statistically significant evidence of clinical efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product. Typically, two successful Phase 3 trials are required by the FDA for product approval.

The FDA may also require, or companies may conduct, additional clinical trials for the same indication after a product is approved. These so-called Phase 4 studies may be required by the FDA as a condition of approval of the NDA, to be satisfied after approval. The results of Phase 4 studies can confirm the effectiveness of a product candidate and can provide important safety information. In addition to the above traditional kinds of clinical trial data required for the approval of an NDA, the 21st Century Cures Act provides for potential FDA use of different types and sources of data in regulatory decision-making, such as patient experience data, real-world evidence for already approved products, and, for appropriate indications sought through supplemental marketing applications. Implementation of this law and related initiatives is still in progress and we do not know the extent to which we may in the future be able to utilize these types and sources of data. In the case of a 505(b)(2) NDA, which is a marketing application in which sponsors may rely on investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted, some of the above described studies and preclinical studies may not be required or may be abbreviated. Bridging studies may be needed, however, to demonstrate the applicability of the studies that were previously conducted by other sponsors to the drug that is the subject of the marketing application.

Clinical trials at any phase may not be completed successfully within any specified period, or at all. Regulatory authorities, an IRB, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk, the clinical trial is not being conducted in accordance with the FDA's or the IRB's requirements, if the drug has been associated with unexpected serious harm to the subjects, or based on evolving business objectives or competitive climate.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate 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 candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality, potency, and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

During the development of a new drug, a sponsor may be able to request a Special Protocol Assessment (*SPA*) the purpose of which is to reach agreement with the FDA on the Phase 3 clinical trial protocol design and analysis that will form the primary basis of an efficacy claim as well as preclinical carcinogenicity trials and stability studies. An SPA may only be modified with the agreement of the FDA and the trial sponsor or if the director of the FDA reviewing division determines that a substantial scientific issue essential to determining the safety or efficacy of the drug was identified after the testing began. An SPA is intended to provide assurance that, in the case of clinical trials, if the agreed-upon clinical trial protocol is followed, the clinical trial endpoints are achieved, and there is a favorable risk-benefit profile, the data may serve as the primary basis for an efficacy claim in support of an NDA. However, SPA agreements are not a guarantee of an approval of a product candidate or any permissible claims about the product candidate. In particular, SPAs are not binding on the FDA if, among other reasons, previously unrecognized public health concerns arise during the performance of the clinical trial, other new scientific concerns regarding the product candidate's safety or efficacy arise, or if the sponsoring company fails to comply with the agreed upon clinical trial protocol.

*NDA Submission, Review by the FDA, and Marketing Approval*

Assuming successful completion of the required clinical and preclinical testing, the results of product development, including chemistry, manufacturing, and control (*CMC*) information, non-clinical studies, and clinical trial results, including negative or ambiguous results as well as positive findings, are all submitted to the FDA, along with the proposed labeling, as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee, authorized every five years by Congress under the Prescription Drug User Fee Act (*PDUFA*). User fees must be paid at the time of the first submission of the application, even if the application is being submitted on a rolling basis, and if approved, program fees must be paid on an annual basis. Product candidates that are designated as orphan drugs, which are further described below, are not subject to application user fees unless the application includes an indication other than the orphan indication.

In addition, under the Pediatric Research Equity Act (*PREA*) an NDA or supplement to an NDA for a new active ingredient, indication, dosage form, dosage regimen, or route of administration must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. A sponsor who is planning to submit a marketing application for a drug product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan (*PSP*) within 60 days of an End-of-Phase 2 meeting or as may be agreed between the sponsor and the FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical studies or other clinical development programs. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. The FDA also may require submission of a risk evaluation and mitigation strategy (*REMS*) to ensure that the benefits of the drug outweigh the risks of the drug. The REMS plan could include medication guides, physician communication plans, and elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools. An assessment of the REMS must also be conducted at set intervals. Following product approval, a REMS may also be required by the FDA if new safety information is discovered and the FDA determines that a REMS is necessary to ensure that the benefits of the drug continue to outweigh the risks of the drug.

Once the FDA receives an application, it will determine within 60 days whether the NDA as filed is sufficiently complete to permit a substantive review (with this decision often referred to as the NDA being “accepted for filing.”). If the FDA determines that the NDA is not sufficiently complete to permit a substantive review, the application must be resubmitted with additional information requested by the FDA. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the NDA.

The FDA has agreed to a set of performance goals and procedures under PDUFA to review 90% of all applications within ten months from the 60-day filing date for its initial review of a standard NDA for a New Molecular Entity (*NME*). For non-NME standard applications, the FDA has set the goal of completing its review of 90% of all applications within ten months from the submission receipt date. Such deadlines are referred to as the PDUFA date. The PDUFA date is only a goal, thus, the FDA does not always meet its PDUFA goal dates. The review process and the PDUFA goal date may also be extended if the FDA requests, or the NDA sponsor otherwise provides, substantial additional information or clarification regarding the submission.

The FDA may refer an application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved, and applications for new molecular entities are generally discussed at advisory committee meetings unless the FDA determines that this type of consultation is not needed under the circumstances.

An advisory committee is typically a panel that includes clinicians and other experts, which review, evaluate, and make a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions and typically follows such recommendations.

The FDA reviews applications to determine, among other things, whether a product is safe and effective for its intended use and whether the manufacturing methods and controls are adequate to assure and preserve the product’s identity, strength, quality, safety, potency, and purity. Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured, referred to as a Pre-Approval Inspection. The FDA will not approve an application unless it determines that the manufacturing processes and facilities, including contract manufacturers and subcontractors, are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA the FDA will inspect one or more clinical trial sites to assure compliance with GCPs.

The approval process is lengthy and difficult, and involves numerous FDA personnel assigned to review different aspects of the NDA, and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional preclinical, CMC, or other data and information. Uncertainties can be presented by reviewers’ ability to exercise judgment and discretion during the review process. Even if such data and information are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than an applicant interprets the same data.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a Complete Response Letter (*CRL*). If a CRL is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter; withdraw the application; or request an opportunity for a hearing. A CRL indicates that the review cycle of the application is complete and the application is not ready for approval in its current form and describes all of the specific deficiencies that the FDA identified in the NDA. A CRL generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for the FDA to reconsider the application. The deficiencies identified may be minor, for example, requiring labeling changes; or major, for example, requiring additional clinical trials. The FDA has the goal of reviewing 90% of application and efficacy supplement resubmissions in either two or six months (from receipt) for a Class 1 or Class 2 resubmission, respectively. For non-efficacy supplements (i.e., labeling and manufacturing supplements), FDA's goal is to review the supplement within the same length of time (from receipt) as the initial review cycle (excluding an extension caused by a major amendment of the initial supplement).

Even with the submission of additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when the issues identified in a CRL have been addressed and resolved to the FDA's satisfaction, the FDA may issue an approval letter. An approval letter authorizes commercial marketing of the drug for specific indications and with specific prescribing information which was reviewed in connection with the NDA.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings, or precautions be included in the product labeling, including a boxed warning, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety and efficacy after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may also not approve label statements that are necessary for successful commercialization and marketing.

After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval. The FDA may also withdraw the product approval if compliance with the pre- and post-marketing regulatory standards are not maintained or if problems occur after the product reaches the marketplace. Further, should new safety information arise, additional testing, product labeling, or FDA notification may be required.

*505(b)(2) Approval Process*

Section 505(b)(2) of the FDCA, provides an alternate regulatory pathway to FDA approval for new or improved formulations or new uses of previously approved drug products. Specifically, Section 505(b)(2) was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act amendments, and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. The applicant may rely, in part, upon the FDA's prior findings of safety and effectiveness for an approved product that acts as the reference listed drug or on published scientific literature, in support of its application. The FDA may also require 505(b)(2) applicants to perform additional studies or measurements to support the changes from the reference listed drug as well as bridging studies to the reference listed drug. The FDA may then approve the new product candidate for all or some of the labeled indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

*Orange Book Listing*

Section 505 of the FDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A section 505(b)(2) NDA is an application in which the applicant, in part, relies on investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an Abbreviated New Drug Application (*ANDA*). An ANDA is an application for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics, and intended use, among other things, to a previously approved product. Limited changes must be pre-approved by the FDA via a suitability petition. ANDAs are termed "abbreviated" because they are generally not required to include preclinical and clinical data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through in vitro, in vivo, or other testing. The generic version must deliver the same amount of active ingredients into a subject's bloodstream in the same amount of time as the innovator drug and, under state substitution laws, may be substituted at the pharmacy for the reference listed drug.

In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, applicants are required to identify to the FDA patents that contain claims that are directed to the applicant's product and/or method(s) of use. Upon approval of an NDA, each of the identified patents is then listed in *Approved Drug Products with Therapeutic Equivalence Evaluations*, also known as the Orange Book.

An applicant who files an ANDA seeking approval of a generic version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book must make patent certifications to the FDA that (1) no patent information on the drug or method of use that is the subject of the application has been submitted to the FDA; (2) the patent has expired; (3) the date on which the patent has expired and approval will not be sought until after the patent expiration; or (4) in the applicant's opinion and to the best of its knowledge, the patent is invalid, unenforceable, or will not be infringed upon by the manufacture, use, or sale of the drug product for which the application is submitted. The last certification is known as a paragraph IV certification. Generally, the ANDA or 505(b)(2) NDA approval cannot be made effective until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through a paragraph IV certification or if the applicant is not seeking approval of a patented method of use. If the applicant does not challenge the listed patents or does not indicate that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application approval will not be made effective until all of the listed patents claimed by the referenced product have expired.

If the competitor has provided a paragraph IV certification to the FDA, the competitor must also send notice of the paragraph IV certification to the holder of the NDA for the reference listed drug and the patent owner within 20 days after the application has been accepted for filing by the FDA. The NDA holder or patent owner 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 notice prevents the FDA from making the approval of the ANDA or 505(b)(2) application effective until the earlier of 30 months from the date of the lawsuit, expiration of the patent, settlement of the lawsuit, a decision in the infringement case that is favorable to the applicant or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the automatic 30-month stay.

In practice, where an ANDA or 505(b)(2) NDA applicant files a paragraph IV certification, the NDA holder or patent owners often take action to trigger the automatic 30-month stay, resulting in patent litigation that may take many months or years to resolve. Thus, approval of an ANDA or 505(b)(2) application could be delayed for a significant period of time depending on the patent certification the applicant makes and the reference drug sponsor's decision to initiate patent litigation.

*Regulatory Exclusivity*

Regulatory exclusivity provisions under the FDCA can also delay the submission or the approval effective date of certain applications. A regulatory exclusivity can provide the holder of an approved NDA protection from new competition in the marketplace for the innovation represented by its approved drug. Five years of exclusivity are available for NCEs. An NCE is a drug that contains no active moiety that has been approved by the FDA in any other NDA. An active moiety is the molecule or ion excluding those appended portions of the molecule that cause the drug to be an ester, salt, including a salt with hydrogen or coordination bonds, or other noncovalent derivatives, such as a complex, chelate, or clathrate, of the molecule, responsible for the therapeutic activity of the drug substance. During the NCE exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA application by another company that contains the previously approved active moiety. An ANDA or 505(b)(2) application, however, may be submitted one year before NCE exclusivity expires if a paragraph IV certification is filed.

Three years of exclusivity are available to the holder of an NDA, including a 505(b)(2) NDA, for a particular condition of approval, or change to a marketed product, such as a new formulation or indication for a drug product that contains an active moiety that has been previously approved, when the application contains reports of new clinical investigations, other than bioavailability studies, conducted by the sponsor that were essential to approval of the application. Changes in an approved drug product that affect its active ingredient(s), strength, dosage form, route of administration or conditions of use may be granted this exclusivity if a new clinical investigation (*NCI*) was essential to approval of the application containing those changes. During the NCI exclusivity period, FDA may not approve an ANDA or 505(b)(2) NDA by another company for the condition of the new drug's approval. NCE and NCI exclusivities will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy.

Pediatric exclusivity is a regulatory exclusivity in the United States that provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory and statutory exclusivity, including the non-patent exclusivity periods described above as well as applicable patent terms. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the required time frames, whatever statutory or regulatory periods of exclusivity or Orange Book listed patent protection cover the drug are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot make an ANDA or 505(b)(2) application approval effective as a result of regulatory exclusivity or listed patents. Moreover, pediatric exclusivity attaches to all formulations, dosage forms, and indications for products with existing marketing exclusivity or patent life that contain the same active moiety as that which was studied.

The Orphan Drug Act provides incentives for the development of drugs intended to treat rare diseases or conditions, which generally are diseases or conditions affecting less than 200,000 individuals annually in the United States, or affecting more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making the drug available in the United States will be recovered from United States sales. If a product receives FDA approval for the indication for which it has orphan designation, the product is generally entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity. Orphan drug designation also entitles a party to financial incentives such as opportunities for grant funding towards clinical study costs, tax advantages, and application user-fee waivers.

*Special FDA Expedited Review and Approval Programs*

The FDA has various programs, including Fast Track designation, Priority Review and Breakthrough designation, that are intended to expedite or simplify the process for the development and FDA review of certain drug products that are intended for the treatment of serious or life-threatening diseases or conditions, and demonstrate the potential to address unmet medical needs or present a significant improvement over existing therapy. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a Fast Track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if the product will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy, safety, or public health factors. If Fast Track designation is obtained, drug sponsors may be eligible for more frequent development meetings and correspondence with the FDA.

In addition, if an applicant obtains "rolling review," the FDA may accept and initiate review of sections of an NDA before the application submission is complete, although it is not guaranteed that FDA will commence review before the application submission is complete, and the timing of the review depends on a number of factors including availability of review personnel at the FDA, and competing agency priorities among other things. The applicant must provide, and the FDA must agree to, a schedule for the remaining information after the initial section of the NDA.

In some cases, a Fast Track product may be eligible for Accelerated Approval or Priority Review.

The FDA may give a Priority Review designation to drugs that are intended to treat serious conditions and, if approved, would provide significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions. A Priority Review designation means that the goal for the FDA is to review an application within six months of receipt, rather than the standard review of ten months under current PDUFA guidelines, of the 60-day filing date for NMEs and within six months of the submission receipt date for non-NMEs. Products that are eligible for Fast Track designation may also be considered appropriate to receive a Priority Review.

Moreover, under the provisions of the Food and Drug Administration Safety and Innovation Act (*FDASIA*) enacted in 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are eligible for the Fast Track designation features as described above, intensive guidance on an efficient drug development program beginning as early as Phase 1 trials, and a commitment from the FDA to involve senior managers and experienced review staff in a proactive collaborative, cross-disciplinary review.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

*Post-approval Requirements*

Any product manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, as well as other federal and state agencies, including, among other things, requirements related to manufacturing, recordkeeping, and reporting, including adverse experience reporting, drug shortage reporting, and other periodic reporting; drug supply chain security surveillance and tracking requirements; product sampling and distribution; advertising; marketing; promotion; certain electronic records and signatures; licensure in certain states for the manufacturing and distribution of drug products; and post-approval obligations imposed as a condition of approval, such as Phase 4 clinical trials, REMS, and surveillance to assess safety and effectiveness after commercialization.

After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There are also continuing annual prescription drug program user fee requirements for any approved products. In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies and list their drug products, and are subject to periodic announced and unannounced inspections by the FDA and these state agencies for compliance with cGMP and other requirements, which impose certain procedural and documentation requirements upon the company and third-party manufacturers.

Changes to the manufacturing process are strictly regulated and often require prior FDA approval or notification before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and product specifications and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

The FDA also strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. A company can make only those claims relating to safety and efficacy, purity, and potency that are approved by the FDA. Physicians, in their independent professional medical judgment, may prescribe legally available products for unapproved indications that are not described in the product's labeling and that differ from those tested and approved by the FDA. Pharmaceutical companies, however, are required to promote their drug products only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including, but not limited to, criminal and civil penalties under the FDCA and False Claims Act, exclusion from participation in federal healthcare programs, mandatory compliance programs under corporate integrity agreements, debarment, and refusal of government contracts. Recent court decisions have impacted the FDA's enforcement activity regarding off-label promotion in light of First Amendment considerations; however, there are still significant risks in this area in part due to the potential False Claims Act exposure. Further, the FDA has not materially changed its position on off-label promotion following legal setbacks on First Amendment grounds and the Department of Justice has consistently asserted in FCA briefings that "speech that serves as a conduit for violations of the law is not constitutionally protected."

The Drug Supply Chain Security Act (*DSCSA*) imposes obligations on manufacturers of prescription biopharmaceutical products for commercial distribution, regulating the distribution of the products at the federal level, and sets certain standards for federal or state registration and compliance of entities in the supply chain (manufacturers and repackagers, wholesale distributors, third-party logistics providers, and dispensers). The DSCSA preempts certain previously enacted state pedigree laws and the pedigree requirements of the Prescription Drug Marketing Act (*PDMA*). Trading partners within the drug supply chain must now ensure certain product tracing requirements are met that they are doing business with other authorized trading partners; and they are required to exchange transaction information, transaction history, and transaction statements. Further, the DSCSA limits the distribution of prescription pharmaceutical products and imposes requirements to ensure overall accountability and security in the drug supply chain. Product identifier information (an aspect of the product tracing scheme) is also now required. The DSCSA requirements, development of standards, and the system for product tracing have been and will continue to be phased in over a period of years through 2023, and subject companies will need to continue their implementation efforts. Many states still have in place licensure and other requirements for manufacturers and distributors of drug products. The distribution of product samples continues to be regulated under the PDMA, and some states also impose regulations on drug sample distribution.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in significant regulatory actions. Such actions may include refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, imposition of a clinical hold or termination of clinical trials, warning letters, untitled letters, modification of promotional materials or labeling, provision of corrective information, imposition of post-market requirements including the need for additional testing, imposition of distribution or other restrictions under a REMS, product recalls, product seizures or detentions, refusal to allow imports or exports, total or partial suspension of production or distribution, FDA debarment, injunctions, fines, consent decrees, corporate integrity agreements, debarment from receiving government contracts and new orders under existing contracts, exclusion from participation in federal and state healthcare programs, restitution, disgorgement, or civil or criminal penalties including fines and imprisonment, and may result in adverse publicity, among other adverse consequences.

*Fraud and Abuse, and Transparency Laws and Regulations*

Following product approval, our business activities, including but not limited to research, sales, promotion, marketing, distribution, medical education, sponsorships, relationships with prescribers and other referral sources, and other activities will be subject to regulation by numerous federal and state regulatory and law enforcement authorities in the United States in addition to the FDA, including potentially the Department of Justice, the Department of Health and Human Services and its various divisions, including the Centers for Medicare & Medicaid Services (*CMS*), the Office of Inspector General (*OIG*), and the Health Resources and Services Administration (*HRSA*), the Department of Veterans Affairs, the Department of Defense, and certain state and local governments. Our business activities must comply with numerous healthcare laws, including but not limited to, anti-kickback and false claims laws and regulations as well as data privacy and security laws and regulations, which are described below.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting, or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, furnishing, or order of any item or service reimbursable under Medicare, Medicaid, or other federal healthcare programs, in whole or in part. The term "remuneration" has been interpreted broadly to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, formulary managers, and beneficiaries on the other. There are certain statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly, and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor, however, does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case by case basis based on a cumulative review of all of its facts and circumstances to determine whether one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business. The Patient Protection and Affordable Care Act (*ACA*) of 2010, as amended, modified the intent requirement under the Anti-Kickback Statute to a stricter standard, such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. The ACA further amended the federal civil False Claims Act to provide that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim under the False Claims Act. Therefore, either the federal government or private citizens under the False Claims Act's qui tam provisions (discussed further below) can bring an action under the False Claims Act for violations of the Anti-Kickback Statute, potentially exposing an alleged violator to substantial monetary damages and penalties. Certain Anti-Kickback safe harbor provisions that protect the rebates paid by drug manufacturers to third parties may also be repealed or materially revised, as contemplated in a recent regulatory proposal.

The government has asserted False Claims Act liability against manufacturers by alleging that improper arrangements with ordering physicians caused them or another provider to file false claims in violation of the False Claims Act or that manufacturers' support of patient assistance programs improperly induced beneficiaries to choose their products in violation of the Anti-Kickback Statute. Sales, marketing and business arrangements in the healthcare industry are also subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, patient assistance programs, and other business arrangements. Medicare Advantage and Medicaid managed care plan regulations prohibit certain forms of marketing to enrollees that are designed to discriminate against beneficiaries on the basis of their health conditions or history. These regulations may require regulatory review of marketing materials, and coordination with health plan or governmental regulators. Additionally, the federal government has pursued electronic health record (*EHR*) vendors and pharmaceutical manufacturers for remunerative relationships involving the EHR platform's recommendation of particular drugs and "prompting" technology to increase prescribing of particular drugs.

The ACA further created new federal requirements for reporting under the Physician Payments Sunshine Act (the *Sunshine Act*) by applicable manufacturers of covered drugs, payments and other transfers of value to physicians and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members. 2018 legislation extended the Sunshine Act to cover payments and transfers of value to physician assistants, nurse practitioners, and other mid-level practitioners (with reporting requirements going into effect in 2022 for payments and transfers of value made in 2021).

The federal civil False Claims Act (*FCA*) prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal government, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or avoiding, decreasing, or concealing an obligation to pay money to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. The civil FCA has been used to assert liability on the basis of kickbacks and other improper referrals, improperly reported government pricing metrics such as Best Price or Average Manufacturer Price, or submission of inaccurate information required by government contracts, improper use of Medicare provider or supplier numbers when detailing a provider of services, improper promotion of off-label uses not expressly approved by the FDA in a drug's label, and allegations as to misrepresentations with respect to the products supplied or services rendered. Several pharmaceutical and other healthcare companies have further been sued under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Intent to deceive is not required to establish liability under the civil FCA; however, a November 2017 Department of Justice memorandum now prohibits the use of subregulatory guidance documents to impose new or more stringent requirements on entities outside the Executive Branch of the federal government. Because the Department has experienced recent administration changes, it is unclear whether the new Attorney General will continue this policy. Civil FCA actions may be brought by the government or may be brought by private individuals on behalf of the government, called "qui tam" actions. If the government decides to intervene in a qui tam action and prevails in the lawsuit, the individual will share in the proceeds from any fines or settlement funds. If the government declines to intervene, the individual may pursue the case alone, subject to governmental review and certain approvals. Qui tam complaints are filed under seal, and the cases may progress for a number of years before a complaint is unsealed and a manufacturer becomes aware of its existence. Since 2004, these FCA lawsuits against pharmaceutical companies have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements, as much as $3.0 billion, regarding certain sales practices and promoting off-label drug uses. For example, civil FCA liability may be imposed for Medicare or Medicaid overpayments arising out of claims that were filed by providers but alleged to have been caused by manufacturers' incentives, impermissible discounts, or overpayments caused by understated rebate amounts. FCA enforcement may also arise from claims filed as the result of manufacturing marketing materials that contained inaccurate statements or provided certain reimbursement guidance.

The government may further prosecute conduct constituting a false claim under the criminal FCA. The criminal FCA prohibits the making or presenting of a claim to the government knowing such claim to be false, fictitious, or fraudulent and, unlike the civil FCA, requires proof of intent to submit a false claim.

Similarly, the criminal healthcare fraud statutes impose criminal liability for, among other things, knowingly and willfully attempting or executing a scheme to defraud any healthcare benefit program, including private third-party payors, obtaining money or property of a benefit program by false or fraudulent means, or falsifying, concealing, or covering up a material fact or submitting a materially false statement in connection with the delivery of, or payment from healthcare benefits, items, or services. These statutes are not limited to items and services reimbursed by a governmental health care program and have been used to prosecute commercial insurance fraud as well.

The civil monetary penalties statute is another potential statute under which biopharmaceutical companies may be subject to enforcement. Among other things, the civil monetary penalties statue imposes fines against any person who is determined to have presented, or caused to be presented, claims to a federal healthcare program that the person knows, or should know, is for an item or service that was not provided as claimed or is false or fraudulent.

The exclusion statute requires the exclusion of entities and individuals who have been convicted of federal- program related crimes or health care felony fraud or controlled substance charges. The statute also permits the exclusion of those that have been convicted of any form of fraud, the anti-kickback statute, for obstructing an investigation or audit, misdemeanor controlled substance charges, those whose health care license has been revoked or suspended, and those who have filed claims for excessive charges or unnecessary services. If a company were to be excluded, its products would be ineligible for reimbursement from any federal programs, including Medicare and Medicaid, and no other entity participating in those programs would be permitted to enter into contracts with the company. Further, employment or contracting with an individual or entity that has been excluded from participation in federal healthcare programs could serve as a basis to invalidate claims for items or services submitted by that entity and to exclude that entity from participation in such programs as well. In order to preserve access to beneficial drugs, the government may elect to exclude officers and key employees of manufacturers, rather than excluding the organization. Such enforcement actions would prohibit the Company from engaging those individuals, which could adversely affect operations, and could result in significant reputational harm.

Payment or reimbursement of prescription drugs by Medicaid or Medicare requires manufacturers of the drugs to submit pricing information to CMS. The Medicaid Drug Rebate statute requires manufacturers to calculate and report price points, which are used to determine Medicaid rebate payments shared between the states and the federal government and Medicaid payment rates for certain drugs. For drugs paid under Medicare Part B, manufacturers must also calculate and report their Average Sales Price, which is used to determine the Medicare Part B payment rate for the drug. Drugs that are approved under a Biologic License Application (*BLA*) or an NDA, including 505(b)(2) drugs, are subject to an additional inflation penalty which can substantially increase rebate payments. In addition, for BLA and NDA drugs, the Veterans Health Care Act (*VHCA*) requires manufacturers to calculate and report to the VA a different price called the Non-Federal Average Manufacturing Price, which is used to determine the maximum price that can be charged to certain federal agencies, referred to as the Federal Ceiling Price, or FCP. Like the Medicaid rebate amount, the FCP includes an inflation penalty. A Department of Defense regulation requires manufacturers to provide this discount through prescription rebates on drugs dispensed by retail pharmacies when paid by the TRICARE Program. All of these price reporting requirements create a risk of submitting false information to the government resulting in potential FCA liability.

The VHCA also requires manufacturers of covered drugs participating in the Medicaid program to enter into Federal Supply Schedule contracts with the VA through which their covered drugs must be sold to certain federal agencies at FCP and to report pricing information. This necessitates compliance with applicable federal procurement laws and regulations and subjects us to contractual remedies as well as administrative, civil, and criminal sanctions. In addition, the VHCA requires manufacturers participating in Medicaid to agree to provide different mandatory discounts to certain Public Health Service grantees and other safety net hospitals and clinics under the 340B Drug Pricing Program and report the ceiling price to the HRSA within Department of Health and Human Services. Manufacturers can be audited by the HRSA and be subjected to civil monetary penalties for knowingly and intentionally overcharging covered entities for drugs.

The federal Health Insurance Portability and Accountability Act of 1996 (*HIPAA*) also created federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, a healthcare benefit program, regardless of whether the payor is public or private, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense, and knowingly and willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items, or services relating to healthcare matters. The ACA, as amended, modified the intent requirement under the certain portions of these federal criminal statutes such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it.

Further, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (*HITECH*) and its respective implementing regulations, extended certain requirements relating to the privacy, security, and transmission of individually identifiable health information directly to business associates of HIPAA-covered entities. A business associate is defined as a person or organization, other than a member of a covered entity's workforce, that performs certain functions or activities that involve the use or disclosure of protected health information on behalf of, or provides services to, a covered entity. We are not a covered entity under HIPAA but in certain limited situations, we may be considered a business associate. HITECH also strengthened the civil and criminal penalties that may be imposed against covered entities, business associates, and individuals, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, other federal and state laws may govern the privacy and security of health and other information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Even for entities that are not deemed “covered entities” or “business associates” under HIPAA, according to the United States Federal Trade Commission (*FTC*) failing to take appropriate steps to keep consumers' personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act (*FTCA*) 15 USC § 45(a). The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Medical data is considered sensitive data that merits stronger safeguards. The FTC's guidance for appropriately securing consumers' personal information is similar to what is required by the HIPAA Security Rule. The FTC’s authority under Section 5 is concurrent with HIPAA’s jurisdiction and with any action taken under state law.

In addition, other federal and state laws may govern the privacy and security of health and other information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. For example, California recently enacted legislation – the California Consumer Privacy Act *(CCPA*) was made effective January 1, 2020. The CCPA, among other things, created new data privacy obligations for covered companies and provided new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also created a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. The California Attorney General will issue clarifying regulations. Although the law includes limited exceptions, including for certain information collected as part of clinical trials as specified in the law, it may regulate or impact our processing of personal information depending on the context, and it remains unclear what language the final Attorney General regulations will contain or how the statute and the regulations will be interpreted.

Many states have also adopted laws similar to each of the above federal laws, which may be broader in scope and apply to items or services reimbursed by any third-party payor, including commercial insurers, and some have transparency laws that require reporting price increases and related information. Certain state laws also regulate manufacturers’ use of prescriber-identifiable data. Certain states also require implementation of commercial compliance programs and compliance with the pharmaceutical industry’s voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict payments or the provision of other items of value that may be made to healthcare providers and other potential referral sources; impose restrictions on marketing practices; or require drug manufacturers to track and report information related to payments, gifts, and other items of value to physicians and other healthcare providers. These laws may affect our future sales, marketing, and other promotional activities by imposing administrative and compliance burdens.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that certain business activities could be subject to challenge under one or more of such laws. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between pharmaceutical companies and providers and patients, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring that business arrangements with third parties comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert management’s attention from the business, even if investigators ultimately find that no violation has occurred.

If our operations are found to be in violation of any of the laws or regulations described above or any other laws that apply to us, we may be subject penalties or other enforcement actions, including criminal and significant civil monetary penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, corporate integrity agreements, debarment from receiving government contracts or refusal of new orders under existing contracts, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

***Coverage and Reimbursement Generally***

The commercial success of our product candidates and our ability to commercialize any approved product candidates successfully will depend in part on the extent to which governmental payor programs at the federal and state levels, including Medicare and Medicaid, private health insurers, and other third-party payors provide coverage for and establish adequate reimbursement levels for our product candidates. Government authorities, private health insurers, and other organizations generally decide which drugs they will pay for and establish reimbursement levels and potential access restrictions. Medicare is a federally funded program managed by the Centers for Medicare and Medicaid Services (*CMS*) through local contractors that administer coverage and reimbursement for certain healthcare items and services furnished to the elderly and disabled. Medicaid is an insurance program for certain categories of patients whose income and assets fall below state-defined levels and who are otherwise uninsured that is both federally and state funded and managed by each state. The federal government sets general guidelines for Medicaid and each state creates specific regulations that govern its individual program, including supplemental rebate programs that prioritize coverage for drugs on the state Preferred Drug List. Similarly, government laws and regulations establish the parameters for coverage of prescription drugs by Tricare, the health care program for military personnel, retirees, and related beneficiaries. Many states have also created pharmacy assistance programs for individuals who do not qualify for federal programs. In the United States, private health insurers and other third-party payors often provide reimbursement for products and services based on the level at which the government provides reimbursement through the Medicare or Medicaid programs for such products and services.

In the U.S. and other potentially significant markets for our product candidates, government authorities and third-party payors are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which often has resulted in average selling prices lower than they would otherwise be. For example, in the U.S., federal and state governments reimburse covered prescription drugs at varying rates generally below average wholesale price. Governmental and private payors may also establish certain access restrictions, such as prior approvals or evidence of failure on existing medications or therapies.

These restrictions and limitations influence the purchase of healthcare services and products. Third-party payors are developing increasingly sophisticated methods of controlling healthcare costs. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drug products for a particular indication. Third-party payors also control costs by requiring prior authorization or imposing other dispensing restrictions before covering certain products and by broadening therapeutic classes to increase competition. Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. Absent clinical differentiators, third-party payors may treat products as therapeutically equivalent and base formulary decisions on net cost. To lower the prescription cost, manufacturers frequently rebate a portion of the prescription price to the third-party payors.

Federal programs also impose price controls through mandatory ceiling prices on purchases by federal agencies and federally funded hospitals and clinics and mandatory rebates on retail pharmacy prescriptions paid by Medicaid and Tricare. These restrictions and limitations influence the purchase of healthcare services and products. Legislative proposals to reform healthcare or reduce costs under government programs may result in lower reimbursement for our product candidates or exclusion of our product candidates from coverage. In addition, government programs like Medicaid include substantial penalties for increasing commercial prices over the rate of inflation which can affect realization and return on investment.

Private payors often rely on the lead of the governmental payors in rendering coverage and reimbursement determinations. Therefore, achieving favorable CMS coverage and reimbursement is usually a significant gating issue for successful introduction of a new product. In addition, many government programs as a condition of participation mandate fixed discounts or rebates from manufacturers regardless of formulary position or utilization, and then rely on competition in the market to attain further price reductions, which can greatly reduce realization on the sale.

Further, the increased emphasis on managed healthcare in the U.S. and on country and regional pricing and reimbursement controls in the European Union will put additional pressure on product pricing, reimbursement, and utilization, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups and health technology assessment bodies, competition within therapeutic classes, availability of generic equivalents, judicial decisions and governmental laws and regulations related to Medicare, Medicaid, and healthcare reform, pharmaceutical coverage and reimbursement policies, and pricing in general. Patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Sales of our product candidates will therefore depend substantially, both domestically and abroad, on the extent to which the costs of our products will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, such as Medicare and Medicaid, private health insurers, and other third-party payors.

As a result of the above, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA and other comparable foreign regulatory authority approvals. Our product candidates may not be considered medically necessary or cost-effective, or the rebate percentages required to secure coverage may not yield an adequate margin over cost.

There is often pressure to renegotiate pricing and reimbursement levels, including, in particular, in connection with changes to Medicare. Third-party payors continue to demand discounted fee structures, and the trend toward consolidation among third-party payors tends to increase their bargaining power over price structures. If third-party payors reduce their rates for our products, then our revenue and profitability may decline and our operating margins will be reduced. Because some third-party payors rely on all or portions of Medicare payment systems to determine payment rates, changes to government healthcare programs that reduce payments under these programs may negatively impact payments from third-party payors. Our inability to maintain suitable financial arrangements with third-party payors could have a material adverse impact on our business. Additionally, the reimbursement process is complex and can involve lengthy delays. Third party payors may disallow, in whole or in part, providers' requests for reimbursement based on determinations that certain amounts are not reimbursable under plan coverage, that the drugs provided were not medically necessary, or that additional supporting documentation is necessary. Retroactive adjustments may change amounts realized from third party payors. Delays and uncertainties in the reimbursement process may adversely affect market acceptance and utilization of our products, resulting in reduced revenues. The unavailability or inadequacy of third-party coverage and reimbursement could negatively affect the market acceptance of our products and the future revenues we may expect to receive from those products. In addition, we are unable to predict what additional legislation or regulation relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future, or what effect such legislation or regulation would have on our business. Many hospitals implement a controlled and defined process for developing and approving formularies. Any marketing efforts that are determined to have violated such policies could result in the denial or removal of our products from that hospital's formulary.

Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in drug development. Legislative proposals to reform healthcare or reduce costs under government insurance programs may result in lower reimbursement for our products and product candidates or exclusion of our products and product candidates from coverage. The cost containment measures that healthcare payors and providers are instituting and any healthcare reform could significantly reduce our revenues from the sale of any approved product candidates. We cannot provide any assurances that we will be able to obtain and maintain third-party coverage or adequate reimbursement for our product candidates in whole or in part.

Pharmacy benefit managers (*PBM*) rebates and pricing transparency are key areas of legislative and regulatory focus and there may be changes in the regulatory landscape that could have a significant impact on the pharmaceutical supply chain and drug pricing more generally, which could affect our business operations and prospects in unknown and material ways.

***Healthcare Reform Measures***

The U.S. and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals designed to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality, and expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (*MMA*) established a prescription drug benefit program for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Part D plans include both standalone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, which do not utilize formularies to restrict coverage, Part D coverage varies by plan. With some exceptions, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for any products for which we receive marketing approval. However, Part D plans use competition for coverage to leverage manufacturer rebates. Further, the law requires manufacturers to absorb a significant percentage of the prescription price paid for NDA drugs, including 504(b)(2) drugs, during a beneficiary's coverage gap. The Bipartisan Budget Act of 2018 permanently increased manufacturer liability for the prescription price in the coverage gap from 50% to 70% beginning in 2019, while simultaneously accelerating closure of the gap. These cost reduction initiatives and other provisions of the legislation, as well as any negotiated price discounts for our future products covered by a Part D prescription drug plan, may decrease the coverage and reimbursement rate that we receive, lower the net price realized on our sales to pharmacies, or both. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from Medicare Part D may result in a similar reduction in payments from non-governmental payors.

The ACA established the Patient-Centered Outcome Research Institute to organize and coordinate federally funded research to compare the effectiveness of different treatments for the same illness. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of any product, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidates. If third-party payors do not consider our product candidates to be cost-effective compared to other available therapies, they may not cover our product candidates, once approved, as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The ACA made other changes intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health care industry, and impose additional health policy reforms. The law expanded the eligibility criteria for Medicaid programs, thereby potentially increasing both the volume of sales and manufacturers' Medicaid rebate liability. The law also expanded the entities eligible for discounts under the 340B Drug Discount Program, which mandates discounts to certain hospitals, community centers, and other qualifying providers, although, with the exception of children's hospitals, these newly eligible entities are not eligible to receive discounted 340B pricing on orphan drugs and the Health Resources and Services Administration has narrowed its interpretation of which beneficiaries may fill prescriptions through 340B inventories. The law additionally extended manufacturer's Medicaid rebate liability to covered drugs dispensed to patients enrolled in Medicaid managed care organizations, increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate program, and created an alternative rebate formula for certain new formulations of certain existing products, which is intended to increase the amount of rebates due on those drugs. The revisions to the Medicaid rebate formula can have the further effect of increasing the required 340B discounts. Finally, the ACA imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted through the ACA and otherwise, including the reporting of drug sample distribution, which may require us to modify our business practices with healthcare practitioners. Moreover, in the coming years, additional changes could be made to governmental healthcare programs that could significantly impact the success of our product candidates.

The ACA also imposed an affirmative obligation to report and repay any overpayments, including those payments that resulted from violations of the Anti-Kickback Statute, false claims act, or civil monetary penalties statute, within sixty (60) days after such overpayment has been identified. Corresponding case law imposes an obligation on entities to exercise reasonable diligence in identifying such overpayments. The failure to timely report and repay is, itself, considered to constitute a violation of the False Claims Act.

The cost of pharmaceuticals continues to generate substantial governmental and third-party payor interest, and pharmaceutical pricing and marketing currently received a great deal of Congressional and administrative attention. There have been numerous initiatives on the federal and state levels in the United States for comprehensive reforms affecting the payment for, the availability of, and reimbursement for, healthcare services. In particular, there have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States. Congressional inquiries and proposed and enacted federal and state legislation have also been released and are designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. Recent federal budget proposals have included measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Current and future U.S. legislative healthcare reforms may result in price controls and other restrictions for any approved products, if covered, and could seriously harm our business. Drug pricing is and will remain a key bipartisan issue in the coming year. Drug pricing reform policies may be pursued in the future and may be more aggressive, regardless of which party controls the White House. Given that drug pricing controls is a key legislative and administration priority, it is likely that additional pricing controls will be enacted and could harm our business, financial condition and results of operations. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Some states, such as California, have enacted transparency laws that require manufacturers to report drug price increases and related information. The boom in state laws targeting drug pricing is unprecedented and the requirements are not uniform from state to state, creating additional compliance and commercialization challenges for manufacturers. We further expect that the pharmaceutical industry will experience pricing pressures due to the trend toward managed healthcare, the increasing influence of managed care organizations, judicial interpretation of health care reform efforts, and additional legislative and regulatory proposals resulting in ongoing, relatively rapid changes to applicable laws and regulations. Our results of operations could be adversely affected by current and future healthcare reforms.

Government and private payors also increasingly require pre-approval of coverage for new or innovative devices or drug therapies or condition coverage on unsuccessful alternative treatment before they will reimburse healthcare providers that use such therapies. For some specialty drugs, payors are conditioning payment on successful treatment measured by objective metrics. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, the announcement or adoption of these proposals could have a material adverse effect on our ability to obtain adequate prices for our product candidates and operate profitably.

Congress and the former Trump Administration, from 2017 – 2020, engaged in various efforts to repeal or materially modify various aspects of ACA. The results and effects of such ongoing efforts were varied after facing judicial and Congressional challenges, but could affect our business operations and prospects in unknown ways, and it is unclear how ACA and other laws ultimately will be implemented. For example, in the case of Texas v. Azar, a federal district court in Texas struck down the ACA in its entirety, finding that the Tax Cuts and Jobs Act of 2017 rendered the individual mandate unconstitutional. The December 15, 2019 opinion concluded that since the individual mandate is "essential" to the ACA, it could not be severed from the rest of the ACA and therefore, the entire ACA was unconstitutional. Despite its decision, however, the court did not issue an injunction and therefore, immediate compliance was not required. Following appeal of the Fifth Circuit's decision upholding the ruling of the federal district court, on June 17, 2021, the Supreme Court reversed the decision of the Fifth Circuit and remanded the case back to the lower court with instructions to dismiss the case.

Despite the Supreme Court's recent ruling in California v. Texas (formerly Texas v. Azar), it remains unclear how future decisions from the Supreme Court and the various other courts across the country, if any, to repeal and replace the ACA will impact the ACA and our business. It is also unclear how regulations and sub-regulatory policy, which fluctuate continually, may affect interpretation and implementation of the ACA and its practical effects on our business.

In the future, there may continue to be additional proposals relating to the reform of the U.S. healthcare system, some of which could further limit the prices we will be able to charge for our product candidates, or the amounts of reimbursement available for our product candidates. If future legislation were to impose direct governmental price controls or access restrictions, it could have a significant adverse impact on our business. Additionally, with the change in administration it is possible that President Biden may issue Executive Orders with the potential to change a number of prior executive branch actions on drug pricing. We continue to monitor the potential impact of proposals to lower prescription drug costs at the federal and state level. Managed care organizations, as well as Medicaid and other government agencies, continue to seek price discounts. Some states have implemented, and other states are considering, measures to reduce costs of the Medicaid program, and some states are considering implementing measures that would apply to broader segments of their populations that are not Medicaid-eligible. Due to the volatility in the current economic and market dynamics, we are unable to predict the impact of any unforeseen or unknown legislative, regulatory, payor or policy actions, which may include cost containment and healthcare reform measures. Such policy actions could have a material adverse impact on our profitability.

These and other healthcare reform initiatives may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our financial operations. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

***The Foreign Corrupt Practices Act***

The Foreign Corrupt Practices Act (*FCPA*) prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party, or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA has been applied to the marketing of drugs and the conduct of clinical trials outside the United States. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. Activities that violate the FCPA, even if they occur wholly outside the United States, can result in criminal and civil fines, imprisonment, disgorgement, oversight, and debarment from government contracts.

***Foreign Regulation***

To the extent we choose to develop or sell any products outside of the U.S., we will be subject to a variety of foreign regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales, and distribution of our products. For example, in the European Union (*EU*) we must obtain authorization of a clinical trial application in each member state in which we intend to conduct a clinical trial prior to the pending introduction of a EU portal for EU-wide approvals. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary greatly from country to country. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others. As in the U.S., post-approval regulatory requirements, such as those regarding product manufacture, marketing, or distribution, would apply to any product that is approved outside the U.S.

**Subsidiaries and Inter-Corporate Relationships**

VistaGen Therapeutics. Inc., a California corporation, dba VistaStem Therapeutics (*VistaStem*), is our wholly-owned subsidiary and has a wholly-owned subsidiary, Artemis Neuroscience, Inc., a corporation incorporated pursuant to the laws of the State of Maryland. The operations of VistaStem, and its wholly owned subsidiary are managed by our senior management team based in South San Francisco, California.

## Corporate History

VistaGen Therapeutics, Inc., a California corporation incorporated on May 26, 1998, dba VistaStem, is our wholly-owned subsidiary. Excaliber Enterprises, Ltd. (*Excaliber*), a publicly-held company (formerly OTCBB: EXCA) was incorporated under the laws of the State of Nevada on October 6, 2005. Pursuant to a strategic merger transaction on May 11, 2011, Excaliber acquired all outstanding shares of VistaStem in exchange for 341,823 shares of our common stock and assumed all of VistaStem's pre-Merger obligations (the *Merger*). Shortly after the Merger, Excaliber's name was changed to "VistaGen Therapeutics, Inc." (a Nevada corporation).

VistaStem, as the accounting acquirer in the Merger, recorded the Merger as the issuance of common stock for the net monetary assets of Excaliber, accompanied by a recapitalization. The accounting treatment for the Merger was identical to that resulting from a reverse acquisition, except that we recorded no goodwill or other intangible assets. A total of 78,450 shares of our common stock, representing the shares held by stockholders of Excaliber immediately prior to the Merger are reflected as outstanding for all periods presented in the Consolidated Financial Statements of the Company included in Item 8 of this Annual Report. Additionally, the Consolidated Balance Sheets reflect the $0.001 par value of Excaliber's common stock.

The Consolidated Financial Statements included in Item 8 of this Annual Report represent the activity of VistaStem from May 26, 1998, and the consolidated activity of VistaStem and Excaliber (now VistaGen Therapeutics, Inc., a Nevada corporation), from May 11, 2011 (the date of the Merger) through March 31, 2021. The Consolidated Financial Statements also include the accounts of VistaStem's two inactive wholly-owned subsidiaries, Artemis Neuroscience, Inc., a Maryland corporation (*Artemis*), and VistaStem Canada, Inc., a corporation organized under the laws of Ontario, Canada (*VistaStem Canada*).

## Research and Development

Conducting research and development is central to our business model. We have invested and expect to continue to invest significant time and capital in our research and development operations. Our research and development expenses were $12.5 million and $13.4 million for the fiscal years ended March 31, 2021 and 2020, respectively. We plan to increase our research and development expenses for the foreseeable future as we seek to complete the development of PH94B, PH10 and AV-101.

## Employees

As of June 29, 2021, we employed 21 full-time employees, nine females and 12 males. Ten of our employees have doctorate degrees. Thirteen full-time employees work in research and development and laboratory support services and eight full-time employees work in business development, commercialization and general and administrative roles. Staffing for other functional areas is achieved through our diverse network of strategic relationships with multiple CROs, CDMOs, and other third-party service providers and consultants. These service providers and consultants provide us with support services on a flexible, real-time, as-needed basis, including services related to, among others, payroll, information technology, legal, investor and public relations, manufacturing, product development, regulatory affairs and FDA program management to complement our internal resources in these areas.

We have never had a work stoppage, and none of our employees is represented by a labor organization or under any collective bargaining agreement. We consider our employee relations to be good.

## Facilities

We lease our office and laboratory space, which consists of approximately 10,900 square feet located in South San Francisco, California, under a lease expiring on July 31, 2022 which also provides a five-year option to renew.

## Legal Proceedings

None.

## Environmental Regulation

Our business does not require us to comply with any extraordinary environmental regulations.

## Available Information

We file reports and other information with the SEC, as required by the Exchange Act. We make available free of charge through our website (http://www.vistagen.com) our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investors," as a source of information about us. The foregoing references to our website are not intended to, nor shall they be deemed to, incorporate information on our website into this Annual Report on Form 10-K by reference.

**Item 1A. Risk Factors**

**Risk Factor Summary**

*Our business is subject to substantial risk and an investment in our securities involves various risks. Some of the material risks include those set forth below. You should consider carefully these risks, and those discussed under "Risk Factors" below, before investing in our securities. These risks include, among others:*

- the COVID-19 pandemic has, and continues to have, an impact on our business, including delays in manufacturing of certain drug substance and drug products and potential delays in recruitment and enrollment in the PALISADE Phase 3 clinical program and other planned clinical studies of PH94B;
- we are a development stage biopharmaceutical company with no recurring revenues from product sales or approved products, and limited experience developing or commercializing new drug candidates, which makes it difficult to assess our future viability;
- we depend heavily on the success of our three CNS product candidates PH94B, PH10 and AV-101, and we cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, any of our current or future product candidates;
- failures or delays in the commencement or completion of our planned clinical trials, including, among others, clinical studies in our PALISADE Phase 3 program, could delay, prevent or limit our ability to generate revenue and continue our business;
- we face significant competition, and if we are unable to compete effectively, we may not be able to achieve or maintain significant market penetration or improve our results of operations;
- if we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents that are sufficient to protect our product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects;
- we have incurred significant net losses since inception and we will continue to incur substantial operating losses for the foreseeable future;
- although we are taking steps to mitigate them, we have identified material weaknesses in our internal control over financial reporting, and our business and stock price may be adversely affected if we do not adequately address those weaknesses or if we have other material weaknesses or significant deficiencies in our internal control over financial reporting;
- we require additional financing to execute our long-term business plan, including further development and commercialization of our CNS pipeline, and to continue to operate as a going concern;
- raising additional capital will cause substantial dilution to our existing stockholders, may restrict our operations or require us to relinquish rights, and may require us to seek stockholder approval to authorize additional shares of our common stock; and
- other risks and uncertainties, including those described under "*Risk Factors*" below.

If we are unable to effectively manage the impact of these and other risks, our ability to operate and execute our business plan would be substantially impaired. In turn, the value of our securities would be materially reduced.

## Risk Factors

*You should consider carefully the risks and uncertainties described below, together with all of the other information in this Annual Report before investing in our securities. The risks described below are not the only risks facing our Company. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial may also materially adversely affect our business, financial condition and/or operating results. If any of the following risks are realized, our business, financial condition and results of operations could be materially and adversely affected.*

***The COVID-19 pandemic has adversely impacted, and may continue to adversely impact our business.***

Beginning in late 2019, a new strain of coronavirus (*COVID-19*) spread across the world, and the outbreak has since been declared a pandemic by the World Health Organization. The U.S. Secretary of Health and Human Services has also declared a public health emergency in the United States in response to the outbreak. Considerable uncertainty still surrounds COVID-19 and its potential effects, and the extent of and effectiveness of responses taken on international, national and local levels. Measures taken to limit the impact of COVID-19, including shelter-in-place orders, social distancing measures, travel bans and restrictions, and business and government shutdowns resulted in significant negative economic impacts on a global basis.

Although the negative effects of the COVID-19 pandemic appear to be lessening, we cannot at this time accurately predict the effects of these conditions on our operations. Uncertainties remain as to the duration of the pandemic, the success of treatments and vaccines designed to combat the pandemic, and the length and scope of the travel restrictions and business closures imposed by the governments of impacted countries and localities. The continued COVID-19 pandemic, the spread of variants of the COVID-19 virus or another highly transmissible and pathogenic infectious disease may lead to the implementation of further responses, including additional travel restrictions, government-imposed quarantines or stay-at-home orders, and other public health safety measures, which may result in further disruptions to our business and operations. The COVID-19 pandemic has impacted our business and may continue to do so as the pandemic persists. Additionally, future outbreaks may have several adverse effects on our business, results of operations and financial condition.

- ***Delayed product development:*** We have faced, and may continue to face, delays and other disruptions to our ongoing development programs for PH94B, PH10 and AV-101 due to the ongoing COVID-19 pandemic. In addition, regulatory oversight and actions regarding our products may be disrupted or delayed in regions impacted by COVID-19, including the United States and elsewhere, which may impact review and approval timelines for products in development. Although we remain invested in continuing our development programs for our current product candidates, our research and development efforts may be impacted if our employees, our contract research organizations (*CROs*) and our third-party contract manufacturer(s) (*CMOs*) are advised to continue to work remotely as part of social distancing measures. Additionally, social distancing measures, stay-at-home orders and other governmental restrictions designed to combat the COVID-19 pandemic may impair our ability to conduct studies in our PALISADE Phase 3 program for PH94B in a timely manner.

- ***Negative impacts on our suppliers and employees***: COVID-19 has impacted, and COVID-19, variants of COVID-19 or another highly transmissible and pathogenic infectious disease, may impact or continue to impact the health of our employees, contractors or suppliers, reduce the availability of our workforce or those of companies with which we do business, divert our attention toward succession planning, or create disruptions in our supply or distribution networks. Since the beginning of the COVID-19 pandemic, we have experienced delays of the delivery of supplies of active pharmaceutical product (*API*) required to continue development of PH94B and PH10. Although our supply of raw materials and API remains sufficiently operational, we may experience adverse effects of such events, which may result in a significant, material disruption to clinical development programs and our operations. Additionally, having substantially shifted to remote working arrangements, we also face a heightened risk of cybersecurity attacks or data security incidents and are more dependent on internet and telecommunications access and capabilities.

COVID-19 has also created significant disruption and volatility in national, regional and local economies and markets. Uncertainties related to, and perceived or experienced negative effects from COVID-19, may cause significant volatility or decline in the trading price of our securities, capital markets conditions and general economic conditions. Our future results of operations and liquidity could be adversely impacted by supply chain disruptions and operational challenges faced by our CROs, CMOs and other contractors. The ongoing COVID-19 pandemic, or another highly transmissible and pathogenic infectious disease, could result in a widespread health crisis that could adversely affect the economies and financial markets of many countries, resulting in a further economic downturn or a global recession. Such events may limit or restrict our ability to access capital on favorable terms, or at all, lead to consolidation that negatively impacts our business, weaken demand, increase competition, cause us to reduce our capital spend further, or otherwise disrupt our business or make it more difficult to implement our strategic plans.

**Risks Related to Product Development, Regulatory Approval and Commercialization**

***We depend heavily on the success of one or more of our current CNS drug candidates and we cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize any of our product candidates.***

We currently have no drug products for sale and may never be able to develop and commercialize marketable drug products. Our business currently depends heavily on the successful development, manufacturing, regulatory approval and commercialization of one or more of our current CNS drug candidates, as well as, but to a more limited extent, our ability to acquire, license or produce, develop and commercialize additional product candidates. Each of our current CNS drug candidates will require substantial additional nonclinical and clinical development, manufacturing and regulatory approval before any of them may be commercialized, and there can be no assurance that any of them will ever achieve regulatory approval. Any new chemical entity (*NCE*) we may produce through drug rescue activities will require substantial nonclinical development, all phases of clinical development, manufacturing and regulatory approval before it may be commercialized. The nonclinical and clinical development of our product candidates are, and the manufacturing and marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the U.S. and in other countries where we or our collaborators intend to test and, if approved, market any product candidate. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through numerous nonclinical and clinical studies that the product candidate is safe and effective for use in each target indication. Research and development of product candidates in the pharmaceutical industry is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of nonclinical or clinical studies. This process takes many years and may also include post-marketing studies, surveillance obligations and drug safety programs, which would require the expenditure of substantial resources beyond the proceeds we have raised to date. Of the large number of drug candidates in development in the U.S., only a small percentage will successfully complete the required FDA regulatory approval process and will be commercialized. Accordingly, we cannot assure you that any of our current drug candidates or any future product candidates will be successfully developed or commercialized in the U.S. or any market outside the U.S.

We are not permitted to market our product candidates in the U.S. until we receive approval of a New Drug Application (*NDA*) from the FDA, or in any foreign countries until we receive the requisite approval from such countries. Obtaining FDA approval of a NDA is a complex, lengthy, expensive and uncertain process. The FDA may refuse to permit the filing of our NDA, delay, limit or deny approval of a NDA for many reasons, including, among others:

- if we submit a NDA and it is reviewed by a FDA advisory committee, the FDA may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional nonclinical or clinical studies, limitations on approved labeling or distribution and use restrictions;

- a FDA advisory committee may recommend, or the FDA may require, a Risk Evaluation and Mitigation Strategies (*REMS*) safety program as a condition of approval or post-approval;

- a FDA advisory committee or the FDA or applicable regulatory agency may determine that there is insufficient evidence of overall effectiveness or safety in a NDA and require additional clinical studies;

- the FDA or the applicable foreign regulatory agency may determine that the manufacturing processes or facilities of third-party contract manufacturers with which we contract do not conform to applicable requirements, including current Good Manufacturing Practices (*cGMPs*); or

- the FDA or applicable foreign regulatory agency may change its approval policies or adopt new regulations.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain regulatory approval for and successfully commercialize any current or future drug product candidate we may develop. Any such setback in our pursuit of regulatory approval for any product candidate would have a material adverse effect on our business and prospects.

In addition, we anticipate that certain of our product candidates, including PH94B and PH10, will be subject to regulation as combination products, which means that they are composed of both a drug product and device product. Although we do not contemplate doing so, if marketed individually, each component would be subject to different regulatory pathways and reviewed by different centers within the FDA. Our product candidates that are considered to be drug-device combination products will require review and coordination by FDA's drug and device centers prior to approval, which may delay approval. In the U.S., a combination product with a drug primary mode of action generally would be reviewed and approved pursuant to the drug approval processes under the Federal Food, Drug and Cosmetic Act of 1938. In reviewing the NDA application for such a product, however, FDA reviewers in the drug center could consult with their counterparts in the device center to ensure that the device component of the combination product met applicable requirements regarding safety, effectiveness, durability and performance. Under FDA regulations, combination products are subject to cGMP requirements applicable to both drugs and devices, including the Quality System (*QS*) regulations applicable to medical devices. Problems associated with the device component of the combination product candidate may delay or prevent approval.

***We have been granted Fast Track designation from the FDA for development of PH94B for the treatment of social anxiety disorder (SAD) and AV-101 for the adjunctive treatment of major depressive disorder (MDD) and for the treatment of neuropathic pain (NP). However, these designations may not actually lead to faster development or regulatory review or approval processes for PH94B or AV-101. Further, there is no guarantee the FDA will grant Fast Track designation for PH94B or AV-101 as a treatment option for other CNS indications or for any of our other product candidates in the future.***

The Fast Track designation is a program offered by the FDA, pursuant to certain mandates under the FDA Modernization Act of 1997, designed to facilitate drug development and to expedite the review of new drugs that are intended to treat serious or life-threatening conditions. Compounds selected must demonstrate the potential to address unmet medical needs. The FDA's Fast Track designation allows for close and frequent interaction with the FDA. A designated Fast Track drug may also be considered for priority review with a shortened review time, rolling submission, and accelerated approval if applicable. The designation does not, however, guarantee FDA approval or expedited approval of any application for the product candidate.

In December 2017, the FDA granted Fast Track designation for development of AV-101 for the adjunctive (add-on) treatment of MDD in patients with an inadequate response to current antidepressants. In September 2018, the FDA granted Fast Track designation for development of AV-101 for the treatment of NP. In December 2019, the FDA granted Fast Track designation for development of PH94B for the treatment of SAD. However, these FDA Fast Track designations may not lead to a faster development or regulatory review or approval process for PH94B or AV-101 and the FDA may withdraw Fast Track designation of PH94B or AV-101 if it believes that the respective designation is no longer supported by data from our clinical development programs.

In addition, we may apply for Fast Track designation for PH94B, PH10 and AV-101 as a treatment option for other CNS indications. The FDA has broad discretion whether or not to grant a Fast Track designation, and even if we believe PH94B, PH10, AV-101 or other product candidates may be eligible for this designation, we cannot be sure that the FDA will grant it.

***Results of earlier clinical trials may not be predictive of the results of later-stage clinical trials.***

The results of preclinical studies and early clinical trials of PH94B, PH10, AV-101 and/or our other future product candidates, if any, including positive results, may not be predictive of the results of later-stage clinical trials. PH94B, PH10, AV-101 or any other future product candidates in later stages of clinical development may fail to show the desired safety and efficacy results despite having progressed through nonclinical studies and initial clinical trials. Many companies in the biopharmaceutical industry have suffered significant setbacks in later-stage clinical trials due to adverse safety profiles or lack of efficacy, notwithstanding promising results in earlier studies. Similarly, our future clinical trial results may not be successful for these or other reasons.

Moreover, nonclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in nonclinical studies and clinical trials nonetheless failed to obtain FDA approval or approval from a similar regulatory authority in another country. With respect to our current product candidates, if our PALISADE Phase 3 program, including the PALISADE-1 Phase 3 clinical study of PH94B for acute treatment of anxiety in adults with SAD, any future nonclinical or clinical study of PH94B, PH10 or AV-101 fail(s) to produce positive results, the development timeline and regulatory approval and commercialization prospects for PH94B, PH10 or AV-101 and, correspondingly, our business and financial prospects, could be materially adversely affected.

This drug candidate development risk is heightened by any changes in planned timing or nature of clinical trials compared to completed clinical trials. As product candidates are developed through preclinical to early- and late-stage clinical trials towards regulatory approval and commercialization, it is customary that various aspects of the development program, such as manufacturing and methods of administration, are altered along the way in an effort to optimize processes and results. While these types of changes are common and are intended to optimize the product candidates for later stage clinical trials, approval and commercialization, such changes do carry the risk that they will not achieve these intended objectives.

For example, the results of planned clinical trials have been affected by supply chain disruptions experienced by certain of our CMOs as a result of the ongoing COVID-19 pandemic. In addition, clinical development of our products may be further affected if we or any of our collaborators seek to optimize and scale-up production of a product candidate. In such case, we will need to demonstrate comparability between the newly manufactured drug substance and/or drug product relative to the previously manufactured drug substance and/or drug product. Demonstrating comparability may cause us to incur additional costs or delay initiation or completion of our clinical trials, including the need to initiate a dose escalation study and, if unsuccessful, could require us to complete additional nonclinical or clinical studies of our product candidates. In addition, health and safety precautions at clinical sites related to the COVID-19 pandemic could cause us to incur additional costs or delay initiation or completion of planned nonclinical and clinical trials.

***If serious adverse events or other undesirable side effects or safety concerns attributable to our product candidates occur, including PH94B in the PALISADE Phase 3 program, they may adversely affect or delay our clinical development and commercialization of PH94B, PH10 or AV-101.***

Undesirable side effects or safety concerns caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt our clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval. Although no treatment-related serious adverse events (*SAEs*) were observed in any clinical trials of any of our product candidates to date, if treatment-related SAEs or other undesirable side effects or safety concerns, or unexpected characteristics attributable to PH94B, PH10 and/or AV-101, are observed in any future clinical trials, including clinical studies in the PALISADE Phase 3 program, and/or other clinical trials involving our drug candidates, they may adversely affect or delay our clinical development and commercialization of the effected product candidate, and the occurrence of these events could have a material adverse effect on our business and financial prospects. Results of our future clinical trials could reveal a high and unacceptable severity and prevalence of adverse side effects. In such an event, our trials could be suspended or terminated and the FDA or other regulatory agency could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims.

Additionally, if any of our product candidates receives marketing approval and we or others later identify undesirable or unacceptable side effects or safety concerns caused by these product candidates, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw, suspend, or limit approvals of such product and require us to take them off the market;
- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;
- regulatory authorities may require a medication guide outlining the risks of such side effects for distribution to patients, or that we implement a REMS or REMS-like plan to ensure that the benefits of the product outweigh its risks;
- we may be required to change the way a product is distributed or administered, conduct additional clinical trials or change the labeling of a product;
- we may be required to conduct additional post-marketing studies or surveillance;
- we may be subject to limitations on how we may promote the product;
- sales of the product may decrease significantly;
- we may be subject to regulatory investigations, government enforcement actions, litigation or product liability claims; and
- our products may become less competitive or our reputation may suffer.

Any of these events could prevent us or any collaborators from achieving or maintaining market acceptance of our product candidates or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenue from the sale of our product candidates.

***Failures or delays in the commencement or completion of our planned nonclinical and clinical studies of PH94B, PH10, AV-101 or other our product candidates could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business.***

In addition to the PALISADE-1 Phase 3 clinical study, we will need to complete at least one additional Phase 3 clinical study of PH94B, additional toxicology and other standard nonclinical and clinical safety studies, as well as certain other clinical studies prior to our submission of an NDA for regulatory approval of PH94B as an acute treatment of anxiety in adults with SAD, or for any other anxiety disorder or phobia. For PH10, at present, we believe we will need to complete at least one additional Phase 2 clinical study, two pivotal Phase 3 clinical trials, additional toxicology and other standard nonclinical and clinical safety studies, as well as certain standard smaller clinical studies prior to the submission of an NDA for regulatory approval of PH10 as a stand-alone rapid-onset treatment for MDD, or any other depression disorder. For AV-101 in combination with probenecid, at present, for treatment of any CNS indication, we believe we will need to complete at least one Phase 1B clinical study, two Phase 2 clinical studies, two pivotal Phase 3 clinical trials, additional toxicology and other standard nonclinical and clinical safety studies, as well as certain standard smaller clinical studies prior to the submission of an NDA for regulatory approval. Successful completion of our nonclinical and clinical trials is a prerequisite to submitting an NDA and, consequently, the ultimate approval required before commercial marketing of any product candidate we may develop. We do not know whether any of our future-planned nonclinical and clinical trials of PH94B, PH10, AV-101 or any other product candidate will be completed on schedule, if at all, as the commencement and completion of nonclinical and clinical trials can be delayed or prevented for a number of reasons, including, among others:

- delays due to events resulting from the ongoing COVID-19 pandemic;
- the regulatory authority may deny permission to proceed with planned clinical trials or any other clinical trials we may initiate, or may place a planned or ongoing clinical trial on hold;
- delays in filing or receiving approvals from regulatory authorities of additional INDs that may be required;
- negative or ambiguous results from nonclinical or clinical studies;
- delays in reaching or failing to reach agreement on acceptable terms with prospective CROs, investigators and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs, investigators and clinical trial sites;
- delays in the manufacturing of, or insufficient supply of product candidates necessary to conduct nonclinical or clinical trials, including delays in the manufacturing of sufficient supply of drug substance or finished drug product;
- inability to manufacture or obtain clinical supplies of a product candidate meeting required quality standards;

- difficulties obtaining Institutional Review Board (*IRB*) approval to conduct a clinical trial at a prospective clinical site or sites;
- challenges in recruiting and enrolling patients to participate in clinical trials, including the proximity of patients to clinical trial sites;
- eligibility criteria for a clinical trial, the nature of a clinical trial protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications;
- severe or unexpected adverse drug-related side effects experienced by patients in a clinical trial;
- delays in validating any endpoints utilized in a clinical trial;
- the regulatory authority may disagree with our clinical trial design and our interpretation of data from prior nonclinical studies or clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials;
- reports from nonclinical or clinical testing of other CNS indications or therapies that raise safety or efficacy concerns; and
- difficulties retaining patients who have enrolled in a clinical trial but may be prone to withdraw due to rigors of the clinical trial, lack of efficacy, side effects, personal issues or loss of interest.

Clinical trials may also be delayed or terminated prior to completion as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the regulatory authority, the IRBs at the sites where the IRBs are overseeing a clinical trial, a data and safety monitoring board (*DSMB*), overseeing the clinical trial at issue or other regulatory authorities due to a number of factors, including, among others:

- failure to conduct the clinical trial in accordance with regulatory requirements or approved clinical protocols;
- inspection of the clinical trial operations or trial sites by the regulatory authority that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a clinical hold;
- unforeseen safety issues, including any that could be identified in nonclinical carcinogenicity studies, adverse side effects or lack of effectiveness;
- changes in government regulations or administrative actions;
- problems with clinical supply materials that may lead to regulatory actions; and
- lack of adequate funding to continue nonclinical or clinical studies.

***Changes in regulatory requirements, regulatory guidance or unanticipated events during our nonclinical studies and clinical trials of PH94B, PH10, AV-101 or other CNS product candidates may occur, which may result in changes to nonclinical studies and clinical trial protocols or additional nonclinical studies and clinical trial requirements, which could result in increased costs to us and could delay our development timeline.***

Changes in regulatory requirements, guidance or unanticipated events during our nonclinical studies and clinical trials of PH94B, PH10, AV-101 or other CNS product candidates may force us to amend nonclinical studies and clinical trial protocols or the regulatory authority may impose additional nonclinical studies and clinical trial requirements. Amendments or changes to our clinical trial protocols would require resubmission to the regulatory authority and IRBs for review and approval, which may adversely impact the cost, timing or successful completion of clinical trials. Similarly, amendments to our nonclinical studies may adversely impact the cost, timing, or successful completion of those nonclinical studies. If we experience delays completing, or if we terminate, any of our nonclinical studies or clinical trials, or if we are required to conduct additional nonclinical studies or clinical trials, the commercial prospects for PH94B, PH10, AV-101 or other CNS product candidates may be harmed and our ability to generate product revenue will be delayed.

***We rely, and expect that we will continue to rely, on third parties to conduct our nonclinical and clinical trials of our current CNS product candidates and will continue to do so for any other future CNS product candidates. If these third parties do not successfully carry out their contractual duties and/or meet expected deadlines, completion of our nonclinical or clinical trials and development of PH94B, PH10, AV-101 or other CNS future product candidates may be delayed and we may not be able to obtain regulatory approval for or commercialize PH94B, PH10, AV-101 or other future CNS product candidates and our business could be substantially harmed.***

By strategic design, we do not have the extensive internal staff resources to independently conduct nonclinical and clinical trials of our product candidates completely on our own. We rely on our network of strategic relationships with various academic research centers, medical institutions, nonclinical and clinical investigators, contract laboratories, CROs and other third parties to assist us to conduct and complete nonclinical and clinical trials of our product candidates. We enter into agreements with third-party CROs to provide monitors for and to manage data for our clinical trials, as well as provide other services necessary to prepare for, conduct and complete clinical trials. We rely heavily on these and other third-parties for execution of nonclinical and clinical trials for our product candidates and we control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing and completion of these nonclinical and clinical trials and the management of data developed through nonclinical and clinical trials than would be the case if we were relying entirely upon our own internal staff resources. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. CROs and other outside parties may:

- experience disruptions to their operations, such as reduced staffing and supply chain disruptions, as a result of the ongoing COVID-19 pandemic;
- have staffing difficulties and/or undertake obligations beyond their anticipated capabilities and resources;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our nonclinical and clinical trials and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that each of our nonclinical studies and clinical trials is conducted and completed in accordance with the applicable protocol, legal, regulatory and scientific requirements and standards, and our reliance on CROs, or independent investigators does not relieve us of our regulatory responsibilities. We and our CROs, and any investigator in an investigator-sponsored study are required to comply with regulations and guidelines, including current Good Clinical Practice regulations (*cGCPs*) for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any products in clinical development. The FDA enforces cGCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we, any of our CROs or any of our third-party collaborators fail to comply with applicable cGCPs, the clinical data generated in clinical trials involving our product candidates may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. In addition, our clinical trials must be conducted with product candidates produced under cGMPs and will require a large number of test patients. Our failure or the failure of our CROs or other third-party collaborators to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action up to and including civil and criminal penalties.

Although we design our clinical trials for our product candidates, our clinical development strategy involves having CROs and other third-party investigators and medical institutions conduct clinical trials of our product candidates. As a result, many important aspects of our drug development programs are outside of our direct control. In addition, although CROs, or independent investigators or medical institutions, as the case may be, may not perform all of their obligations under arrangements with us or in compliance with applicable regulatory requirements, under certain circumstances, we may be responsible and subject to enforcement action that may include civil penalties up to and including criminal prosecution for any violations of FDA laws and regulations during the conduct of clinical trials of our product candidates. If such third parties do not perform clinical trials of our product candidates in a satisfactory manner, breach their obligations to us or fail to comply with applicable regulatory requirements, the development and commercialization of our product candidates may be delayed or our development program materially and irreversibly harmed. In certain cases, including the Baylor Study and other investigator-sponsored clinical studies, we cannot control the amount and timing of resources these third-parties devote to clinical trials involving our product candidates. If we are unable to rely on nonclinical and clinical data collected by our third-party collaborators, we could be required to repeat, extend the duration of, or increase the size of our clinical trials and this could significantly delay commercialization and require significantly greater expenditures.

If our relationships with one or more of our third-party collaborators terminates, we may not be able to enter into arrangements with alternative third-party collaborators. If such third-party collaborators, including our CROs, do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to their failure to adhere to applicable clinical protocols, regulatory requirements or for other reasons, any clinical trials that such third-parties are associated with may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully develop and commercialize our product candidates. As a result, we believe that our financial results and the commercial prospects for our product candidates in the subject indication would be harmed, our costs would increase and our ability to generate revenue would be delayed.

***We rely completely on third-parties to manufacture, formulate, analyze, hold and distribute supplies of our CNS product candidates for all nonclinical and clinical studies, and we intend to continue to rely on third parties to produce all nonclinical, clinical and commercial supplies of our CNS product candidates in the future.***

By strategic design, we do not currently have, nor do we plan to acquire or develop, extensive internal infrastructure or technical capabilities to manufacture, formulate, analyze, hold or distribute supplies of our product candidates, for use in nonclinical and clinical studies or commercial scale. As a result, with respect to all of our product candidates, we rely, and will continue to rely, completely on CMOs to manufacture API and formulate, hold and distribute final drug product. The facilities used by our CMOs to manufacture PH94B, PH10 and AV-101 API and formulate PH94B, PH10 and AV-101 final drug product are subject to a pre-approval inspection by the FDA and other comparable foreign regulatory agencies to assess compliance with applicable regulatory guidelines and requirements, including cGMPs, and may be required to undergo similar inspections by the FDA or other comparable foreign regulatory agencies, after we submit INDs, NDAs or relevant foreign regulatory submission equivalent to the applicable regulatory agency.

We do not directly control the manufacturing process or the supply or quality of materials used in the manufacturing, analysis and formulation of our product candidates, and, with respect to all of our product candidates, we are completely dependent on our CMOs to comply with all applicable cGMPs for the manufacturing of both API and finished drug product. If our CMOs cannot secure adequate supplies of suitable raw materials or successfully manufacture our product candidates, including PH94B, PH10 and AV-101 API and finished drug product, that conforms to our specifications and the strict regulatory requirements of the FDA or applicable foreign regulatory agencies, production of sufficient supplies of our product candidates, including PH94B, PH10 and AV-101 API and finished drug product, may be delayed and our CMOs may not be able to secure and/or maintain regulatory approval for their manufacturing facilities, or the FDA may take other actions, including the imposition of a clinical hold. In addition, we have no direct control over our CMOs' ability to maintain adequate quality control, quality assurance and qualified personnel. All of our CMOs are engaged with other companies to supply and/or manufacture materials or products for such other companies, which exposes our CMOs to regulatory risks for the production of such materials and products. As a result, failure to satisfy the regulatory requirements for the production of those materials and products may affect the regulatory clearance of our CMO's facilities generally or affect the timing of manufacture of PH94B, PH10 and AV-101 for required or planned nonclinical and/or clinical studies. If the FDA or an applicable foreign regulatory agency determines now or in the future that our CMOs' facilities are noncompliant, we may need to find alternative manufacturing facilities, which would adversely impact our ability to develop, obtain regulatory approval for or market our product candidates. Our reliance on CMOs also exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information.

With respect to PH94B, PH10 and AV-101, we do not yet have long-term supply agreements in place with our CMOs and each batch of PH94B, PH10 and AV-101 is or will be individually contracted under a separate supply agreement. If we engage new CMOs, such contractors must complete an inspection by the FDA and other applicable foreign regulatory agencies. We plan to continue to rely upon CMOs and, potentially, collaboration partners, to manufacture research and development scale, and, if approved, commercial quantities of our product candidates. Although we believe our current scale of API manufacturing for AV-101, and our contemplated scale of API manufacturing for PH94B and PH10, and the current and projected supply of PH94B, PH10 and AV-101 API and finished drug product will be adequate to support our planned nonclinical and clinical studies of PH94B, PH10 and AV-101, no assurance can be given that unanticipated supply shortages or CMO-related delays in the manufacture and formulation of PH94B, PH10 or AV-101 API and/or finished drug product will not occur in the future.

Additionally, we anticipate that PH94B and PH10 will be considered drug-device combination products. Third-party manufacturers may not be able to comply with cGMP requirements applicable to drug/device combination products, including applicable provisions of the FDA's or a comparable foreign regulatory authority's drug cGMP regulations, device cGMP requirements embodied in the Quality System Regulation (*QSR*) or similar regulatory requirements outside the U.S. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates, operating restrictions and criminal prosecutions, any of which could significantly affect supplies of our product candidates. The facilities used by our CMOs to manufacture our product candidates must be approved by the FDA and comparable foreign regulatory authorities pursuant to inspections that will or may be conducted after we submit our NDA. We do not control the manufacturing process of, and are completely dependent on, our CMO partners for compliance with cGMPs and QSRs. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other comparable foreign regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. CMOs may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP and QSR requirements. Any failure to comply with cGMP or QSR requirements or other FDA, EMA and comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop our product candidates and market our products following approval.

***Even if we receive marketing approval for PH94B, PH10, AV-101 or any other CNS product candidate in the U.S., we may never receive regulatory approval to market PH94B, PH10, AV-101 or any other CNS product candidate outside of the U.S.***

In order to market PH94B, PH10, AV-101 or any other CNS product candidate outside of the U.S., we must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other countries. Approval procedures vary among countries and can involve additional product candidate testing and additional administrative review periods. The time required to obtain approvals in other countries might differ from that required to obtain FDA approval. The marketing approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the U.S. as well as other risks. In particular, in many countries outside of the U.S., products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in others. Failure to obtain marketing approval in other countries or any delay or other setback in obtaining such approval would impair our ability to market our product candidates in such foreign markets. Any such impairment would reduce the size of our potential market, which could have a material adverse impact on our business, results of operations and prospects.

***If any of our CNS product candidates are ultimately regulated as controlled substances, we, our CMOs, as well as future distributors, prescribers, and dispensers will be required to comply with additional regulatory requirements which could delay the marketing of our product candidates, and increase the cost and burden of manufacturing, distributing, dispensing, and prescribing our product candidates.***

Before we can commercialize our product candidates in the U.S. or any market outside the U.S., the U.S. Drug Enforcement Administration (*DEA*) or its foreign counterpart may need to determine whether such product candidates will be considered to be a controlled substance, taking into account the recommendation of the FDA or its foreign counterpart, as the case may be. This may be a lengthy process that could delay our marketing of a product candidate and could potentially diminish any regulatory exclusivity periods for which we may be eligible, which would increase the cost associated with commercializing such products and, in turn, may have an adverse impact on our results of operations. Although we currently do not know whether the DEA or any foreign counterpart will consider any of our current or future product candidate to be controlled substances, we cannot yet give any assurance that such product candidates, including PH94B, PH10 and AV-101 will not be regulated as controlled substances.

If any of our product candidates are regulated as controlled substances, depending on the DEA controlled substance schedule in which the product candidates are placed or that of its foreign counterpart, we, our CMOs, and any future distributers, prescribers, and dispensers of the scheduled product candidates may be subject to significant regulatory requirements, such as registration, security, recordkeeping, reporting, storage, distribution, importation, exportation, inventory, quota and other requirements administered by the DEA or a foreign counterpart of the DEA as the case may be. Moreover, if any of our product candidates are regulated as controlled substances, we and our CMOs would be subject to initial and periodic DEA inspection. If we or our CMOs are not able to obtain or maintain any necessary DEA registrations or comparable foreign registrations, we may not be able to commercialize any product candidates that are deemed to be controlled substances or we may need to find alternative CMOs, which would take time and cause us to incur additional costs, delaying or limit our commercialization efforts.

Because of their restrictive nature, these laws and regulations could limit commercialization of our product candidates, should they be deemed to contain controlled substances. Failure to comply with the applicable controlled substance laws and regulations can also result in administrative, civil or criminal enforcement. The DEA or its foreign counterparts may seek civil penalties, refuse to renew necessary registrations, or initiate administrative proceedings to revoke those registrations. In some circumstances, violations could result in criminal proceedings or consent decrees. Individual states also independently regulate controlled substances.

***If we are unable to establish broad sales and marketing capabilities on our own or enter into agreements with third parties to market and sell our CNS product candidates, we may not be able to generate any revenue.***

We currently have limited internal resources for the sale, marketing and distribution of pharmaceutical products, and we may not be able to create broad internal capabilities in the foreseeable future. Therefore, to market our CNS product candidates, if approved by the FDA or any other regulatory body, we must establish broad internal capabilities related to sales, marketing, managerial and other non-technical capabilities relating to the commercialization of our product candidates, or make contractual arrangements with third parties to perform services, prior to market approval. If we are unable to establish adequate internal sales, marketing and distribution capabilities, or if we are unable to do so contractually on commercially reasonable terms, our business, results of operations, financial condition and prospects will be materially adversely affected.

***Even if we receive marketing approval for our CNS product candidates, our product candidates may not achieve broad market acceptance, which would limit the revenue that we generate from their sales.***

The commercial success of our CNS product candidates, if approved by the FDA or other regulatory authorities, will depend upon the awareness and acceptance of our product candidates among the medical community, including physicians, patients and healthcare payors. Market acceptance of our product candidates, if approved, will depend on a number of factors, including, among others:

- the efficacy and safety of our product candidates as demonstrated in clinical trials, and, if required by any applicable regulatory authority in connection with the approval for the applicable indications, to provide patients with incremental health benefits, as compared with other available therapies;
- limitations or warnings contained in the labeling approved for our product candidates by the FDA or other applicable regulatory authorities;
- the clinical indications for which our product candidates are approved;
- availability of alternative treatments already approved or expected to be commercially launched in the near future;
- the potential and perceived advantages of our product candidates over current treatment options or alternative treatments, including future alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies;
- our ability to increase awareness of our product candidates through marketing efforts;
- our ability to obtain sufficient third-party coverage or reimbursement; or
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage.

If our CNS product candidates are approved but do not achieve an adequate level of acceptance by patients, physicians and payors, we may not generate sufficient revenue from our product candidates to become or remain profitable. Before granting reimbursement approval, healthcare payors may require us to demonstrate that our product candidates, in addition to treating these target indications, also provide incremental health benefits to patients. Our efforts to educate the medical community and third-party payors about the benefits of our product candidates may require significant resources and may never be successful.

***Our CNS product candidates may cause undesirable safety concerns and side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.***

If our product candidates are determined to cause undesirable side effects and safety concerns, we or regulatory authorities may interrupt, delay or halt nonclinical studies and clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by regulatory authorities.

Further, clinical trials by their nature utilize a sample of potential patient populations. With a limited number of patients and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. If our product candidates receive marketing approval and we or others identify undesirable safety concerns or side effects caused by such product candidates (or any other similar products) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such product candidates;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we may be required to change the way such product candidates are distributed or administered, conduct additional clinical trials or change the labeling of the product candidates;
- we may be subject to regulatory investigations and government enforcement actions;
- we may decide to remove such product candidates from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our product candidates; and
- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidates and would substantially increase the costs of commercializing our product candidates and significantly impact our ability to successfully commercialize our product candidates and generate revenues.

***Even if we receive marketing approval for our CNS product candidates, we may still face future development and regulatory difficulties.***

Even if we receive marketing approval for our CNS product candidates, regulatory authorities may still impose significant restrictions on our product candidates, indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies. Our product candidates will also be subject to ongoing regulatory requirements governing the labeling, packaging, storage and promotion of the product and record keeping and submission of safety and other post-market information. The FDA and other regulatory authorities have significant post-marketing authority, including, for example, the authority to require labeling changes based on new safety information and to require post-marketing studies or clinical trials to evaluate serious safety risks related to the use of a drug. The FDA and other regulatory authorities also have the authority to require, as part of an NDA or post-approval, the submission of a REMS or comparable safety program. Any REMS or comparable safety program required by the FDA or other regulatory authority may lead to increased costs to assure compliance with new post-approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue.

Manufacturers of drug and device products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMPs and other regulations. If we or a regulatory agency discover problems with our product candidates, such as adverse events of unanticipated severity or frequency, or problems with the facility where our product candidates are manufactured, a regulatory agency may impose restrictions on our product candidates, the manufacturer or us, including requiring withdrawal of our product candidates from the market or suspension of manufacturing. If we, our product candidates, or the manufacturing facilities for our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may, among other things:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw marketing approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications submitted by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products, or require that we initiate a product recall.

***Competing therapies could emerge adversely affecting our opportunity to generate revenue from the sale of our CNS product candidates.***

The pharmaceutical industry is highly competitive. There are many public and private pharmaceutical companies, universities, governmental agencies and other research organizations actively engaged in the research and development of product candidates that may be similar to and compete with our product candidates or address similar markets. It is probable that the number of companies seeking to develop product candidates similar to and competitive with our product candidates will increase in the future.

Currently, management is unaware of any FDA-approved rapid-onset, acute treatment of anxiety in adults with SAD having the same mechanism of pharmacological action and safety profile as our PH94B. Also, management is currently unaware of any FDA-approved oral treatment for MDD having the same mechanism of pharmacological action and safety profile as our intranasally-administered PH10 or our orally-administered AV-101 in combination with probenecid. However, new antidepressant products with other mechanisms of pharmacological action or products approved for other indications, including the FDA-approved anesthetic ketamine hydrochloride administered intravenously, are being or may be used for treatment of MDD, as well as other CNS indications for which PH10 or AV-101 in combination with probenecid may have therapeutic potential. Additionally, other non-pharmaceutical treatment options, such psychotherapy and electroconvulsive therapy (*ECT*) are used before or instead of standard antidepressant medications to treat patients with MDD.

With respect to PH94B and current treatment options for SAD in the U.S., our competition may include, but is not limited to, current generic oral antidepressants approved by the FDA for treatment of SAD, as well as certain classes of drugs prescribed on an off-label basis for treatment of SAD, including benzodiazepines such as alprazolam, and beta blockers such as propranolol. In the field of new generation, oral treatments for adult patients with MDD, we believe our principal competitors may be Axsome, Alkermes, Relmada and Sage. Additional potential competitors may include, but not be limited to, academic and private commercial clinics providing intravenous ketamine therapy on an off-label basis and Janssen's intranasally-administered esketamine.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery, and development of product candidates, obtaining FDA and other regulatory approvals of treatments and the commercialization of those treatments. With respect to PH94B, in addition to potential competition from certain current FDA-approved antidepressants and off-label use of benzodiazepines and beta blockers, we believe additional drug candidates in development for SAD may include, but potentially not be limited to, an oral fatty acid amide hydrolase inhibitor in development by Janssen. With respect to PH10 and AV-101 in combination with probenecid for treatment of depression disorders, including MDD, and AV-101 in combination with probenecid for treatment of certain neurological disorders, including levodopa-induced dyskinesia associated with therapy for Parkinson's disease, neuropathic pain, and epilepsy, we believe a range of pharmaceutical and biotechnology companies have programs to develop drug candidates and/or medical device technologies for such indications, including, but not limited to, Abbott Laboratories, Acadia, Allergan, Alkermes, Aptynix, AstraZeneca, Axsome, Eli Lilly, GlaxoSmithKline, IntraCellular, Janssen, Lundbeck, Merck, Neurocrine, Novartis, Ono, Otsuka, Pfizer, Relmada, Roche, Sage, Sumitomo Dainippon, and Takeda, as well as any affiliates of the foregoing companies. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. 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. Our competitors also may obtain FDA 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.

***We may seek to establish collaborations, and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.***

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates, such as the License and Collaboration Agreement we entered into with AffaMed Therapeutics (formerly EverInsight Therapeutics) in June 2020 for the development and commercialization of PH94B in Greater China, South Korea and Southeast Asia.

We may derive revenue from research and development fees, license fees, milestone payments and royalties under any collaborative arrangement into which we enter, including the AffaMed Agreement. However, our ability to generate revenue from such arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, our collaborators have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms. As a result, we can expect to relinquish some or all of the control over the future success of a product candidate that we license to a third party in the territories included in the licenses.

We face significant competition in seeking appropriate collaborators. Whether we reach additional definitive agreements for collaborations will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of nonclinical and clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential markets for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidate. The terms of any collaboration or other arrangements that we may establish may not be favorable to us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

In addition, any future collaboration that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

***We may not be successful in our efforts to identify or discover additional CNS product candidates, or we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

The success of our business depends primarily upon our ability to identify, develop and commercialize CNS product candidates with commercial and therapeutic potential. We may fail to pursue additional development opportunities for PH94B, PH10 or AV-101, or identify additional CNS product candidates for development and commercialization for a number of reasons. Our research methodology may be unsuccessful in identifying new product candidates or our product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

We strategically focus on a limited number of research and development programs and product candidates and are currently focused primarily on development of PH94B, PH10 and AV-101. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other potential CNS-related indications for PH94B, PH10 and/or AV-101 that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable drugs. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through future collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

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

***We are subject to healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.***

Although we do not currently have any products on the market, once we begin commercializing our CNS product candidates, we may be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of our product candidates, if approved. Our future arrangements with third-party payors will 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 our product candidates, if we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- The federal anti-kickback statute prohibits, among other things, persons from 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 healthcare programs such as Medicare and Medicaid.

- The federal False Claims Act imposes criminal and civil penalties, including those from 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.

- The federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

- The federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.

- The federal transparency requirements, sometimes referred to as the "Sunshine Act," under the Patient Protection and Affordable Care Act, require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests.

- Analogous state laws and regulations, such as state anti-kickback and false claims laws and transparency laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance.

- Guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and drug pricing.

- Foreign Corrupt Practices Act and its application to marketing and selling practices as well as to clinical trials.

Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could be costly. It is possible that governmental authorities will conclude that our business practices do 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 were 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 and exclusion from government funded healthcare programs, such as Medicare and Medicaid, any of which could substantially disrupt our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be out of compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

***The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have improperly promoted off-label uses, we may become subject to significant liability.***

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, such as PH94B, PH10 and AV-101, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. For example, if we receive FDA marketing approval for PH94B as an acute treatment of anxiety in adults with SAD, physicians may prescribe PH94B to their patients in a manner that is inconsistent with the FDA-approved label. However, if we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper off-label promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or imposed permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

***Even if approved, reimbursement policies could limit our ability to sell our CNS product candidates.***

Market acceptance and sales of our product candidates will depend heavily on reimbursement policies and may be affected by healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels for those medications. Cost containment is a primary concern in the United States healthcare industry and elsewhere. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that reimbursement will be available for our product candidates and, if reimbursement is available, the level of such reimbursement. Reimbursement may impact the demand for, or the price of, our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates.

In some foreign countries, particularly in Canada and European countries, the pricing of prescription pharmaceuticals is subject to strict governmental control. In these countries, pricing negotiations with governmental authorities can take six months or longer after the receipt of regulatory approval and product launch. To obtain favorable reimbursement for the indications sought or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates with other available therapies. If reimbursement for our product candidates is unavailable in any country in which we seek reimbursement, if it is limited in scope or amount, if it is conditioned upon our completion of additional clinical trials, or if pricing is set at unsatisfactory levels, our operating results could be materially adversely affected.

***We may seek FDA Orphan Drug designation for one or more of our CNS product candidates. Even if we have obtained FDA Orphan Drug designation for a product candidate, there may be limits to the regulatory exclusivity afforded by such designation.***

We may, in the future, choose to seek FDA Orphan Drug designation for one or more of our current or future CNS product candidates. Even if we obtain Orphan Drug designation from the FDA for a product candidate, there are limitations to the exclusivity afforded by such designation. In the U.S., the company that first obtains FDA approval for a designated orphan drug for the specified rare disease or condition receives orphan drug marketing exclusivity for that drug for a period of seven years. This orphan drug exclusivity prevents the FDA from approving another application, including a full NDA to market the same drug for the same orphan indication, except in very limited circumstances, including when the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. For purposes of small molecule drugs, the FDA defines "same drug" as a drug that contains the same active moiety and is intended for the same use as the drug in question. To obtain Orphan Drug status for a drug that shares the same active moiety as an already approved drug, it must be demonstrated to the FDA that the drug is safer or more effective than the approved orphan designated drug, or that it makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the U.S. may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition or if another drug with the same active moiety is determined to be safer, more effective, or represents a major contribution to patient care.

***Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.***

Our future profitability may depend, in part, on our ability to commercialize our product candidates in foreign markets for which we may rely on collaboration with third parties such as our collaboration with AffaMed to develop and commercialize PH94B in key Asian markets. If we commercialize our product candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for our product candidates in foreign markets;
- our inability to directly control commercial activities because we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights, different standards of patentability and different availability of prior art in some foreign countries as compared with the U.S.;
- the existence of additional potentially relevant third party intellectual property rights;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of our product candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

***We are a development stage biopharmaceutical company with no recurring revenues from product sales or approved products, and limited experience developing new therapeutic product candidates, including conducting clinical trials and other areas required for the successful development and commercialization of therapeutic products, which makes it difficult to assess our future viability.***

We are a development stage biopharmaceutical company. We currently have no approved products and no recurring revenues from product sales, and we have not yet fully demonstrated an ability to overcome many of the fundamental risks and uncertainties frequently encountered by development stage companies in new and rapidly evolving fields of technology, particularly biotechnology. To execute our business plan successfully, we will need to accomplish or continue to accomplish the following fundamental objectives, either on our own or with collaborators:

- develop and obtain required regulatory approvals for commercialization of PH94B, PH10, AV-101 and/or other CNS product candidates;
- maintain, leverage and expand our intellectual property portfolio;
- establish and maintain sales, distribution and marketing capabilities, and/or enter into strategic partnering arrangements to access such capabilities;
- gain market acceptance for our product candidates; and
- obtain adequate capital resources and manage our spending as costs and expenses increase due to research, production, development, regulatory approval and commercialization of product candidates.

***Our future success is highly dependent upon our ability to successfully develop and commercialize any of our current CNS product candidates, acquire or license additional CNS product candidates, and we cannot provide any assurance that we will successfully develop and commercialize PH94B, PH10, AV-101 or acquire or license additional CNS product candidates, or that, if produced, PH94B, PH10, AV-101 or any other CNS product candidate will be successfully commercialized.***

Business development and research and development programs designed to identify, acquire or license additional product candidates require substantial technical, financial and human resources, whether or not any additional CNS product candidate is acquired or licensed. We are in the beginning stages of building a sales and marketing infrastructure, including hiring certain executive officers and other employees that have pharmaceutical sales, marketing or distribution experience. In addition, if beneficial, we may seek to collaborate with others to develop and commercialize PH94B, PH10, AV-101, and/or other CNS product candidates if and when they are acquired and developed, or we may seek to establish those commercial capabilities ourselves. If we enter into arrangements with third parties to perform sales, marketing and distribution services for our products, the resulting revenues or the profitability from these revenues to us are likely to be lower than if we had sold, marketed and distributed our products ourselves. In addition, we may not be successful entering into arrangements with third parties to sell, market and distribute PH94B, PH10, AV-101, or other CNS product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of these third parties may fail to devote the necessary resources and attention to sell, market and distribute our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

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

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

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development, or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties, or other sanctions, which could have a material adverse effect on our operations.

**Risks Related to Our Financial Position**

***We have incurred significant net losses since inception and we will continue to incur substantial operating losses for the foreseeable future. We may never achieve or sustain profitability, which would depress the market price of our common stock and could cause you to lose all or a part of your investment.***

We have incurred significant net losses in each fiscal year since our inception in 1998, including net losses of approximately $17.9 million and $20.8 million during our fiscal years ended March 31, 2021 and 2020, respectively. At March 31, 2021, we had an accumulated deficit of approximately $242.8 million. We do not know whether or when we will become profitable. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to incur increasing levels of operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect our research and development expenses to significantly increase in connection with nonclinical studies and clinical trials of our product candidates. In addition, if we obtain marketing approval for our product candidates, we may incur significant sales, marketing and outsourced-manufacturing expenses should we elect not to collaborate with one or more third parties for such services and capabilities. As a public company, we incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Our ability to become profitable depends upon our ability to generate recurring revenues. Through March 31, 2021, we have generated approximately $22.7 million in revenues, consisting of receipts of non-dilutive cash payments from collaborators, sublicense revenue, including the $5.0 million cash payment received under the AffaMed Agreement during the quarter ended September 30, 2020, the majority of which has been recorded as deferred revenue at March 31, 2021, and research and development grant awards from the NIH. We have not yet commercialized any product or generated any revenues from product sales, and we do not know when, or if, we will generate any revenue from product sales. We do not expect to generate significant revenue unless and until we obtain marketing approval of, and begin to experience sales of, PH94B, PH10, AV-101 or another future CNS product candidate, or we enter into one or more development and commercialization agreements with respect to PH94B, PH10, AV-101 or one or more other future CNS product candidates. Our ability to generate recurring revenue depends on a number of factors, including, but not limited to, our ability to:

- initiate and successfully complete nonclinical and clinical trials that meet their prescribed endpoints;
- initiate and successfully complete all safety studies required to obtain U.S. and foreign marketing approval for our CNS product candidates;
- timely complete and compose successful regulatory submissions such as NDAs or comparable documents for both the U.S. and foreign jurisdictions;
- commercialize our CNS product candidates, if approved, by developing a sales force or entering into collaborations with third parties for sales and marketing capabilities; and
- achieve market acceptance of our CNS product candidates in the medical community and with third-party payors.

If our Phase 3 studies of PH94B for the acute treatment of anxiety in adults with SAD are successful, unless we enter into a contractual arrangement for the commercialization of PH94B in the U.S., we expect to incur significant sales and marketing costs as we prepare to commercialize PH94B on our own in the U.S. Even if we initiate and successfully complete Phase 3 clinical trials of PH94B and our other CNS product candidates, and all of our CNS product candidates are approved for commercial sale, and despite expending substantial capital for sales and marketing costs, PH94B and our other product candidates may not be commercially successful. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate product revenue, we will not become profitable and may be unable to continue operations without continued funding.

***We require additional financing to execute our long-term business plan.***

Since our inception, a substantial portion of our resources have been dedicated to research and development of AV-101 and VistaStem's stem cell technology platform. In particular, (i) for AV-101, we have expended substantial resources on research and development of methods and processes relating to the production of API and drug product, IND-enabling preclinical studies, Phase 1 clinical safety studies, and a Phase 2 clinical study completed in 2019 and (ii) for VistaStem, development of cardiac stem cell technology. In addition, beginning in 2018, we have expended a considerable portion of our resources for research, development, manufacturing and regulatory expenses related to the development and production of PH94B, including costs related to the PALISADE Phase 3 program, and PH10. We expect to continue to expend substantial resources for the foreseeable future developing and commercializing our CNS product candidates on our own or in collaborations. These expenditures will include costs associated with general and administrative costs, facilities costs, research and development, acquiring new technologies, manufacturing product candidates, conducting nonclinical experiments and clinical trials and obtaining regulatory approvals, as well as commercializing any products approved for sale.

At March 31, 2021, we had cash and cash equivalents of approximately $103.1 million. We believe this amount is sufficient to enable us to fund our planned operations for at least the twelve months following the issuance of the financial statements included elsewhere in this Report.

Although we received the $5 million non-dilutive cash upfront payment under the AffaMed Agreement in August 2020 and expect to recognize that amount as revenue in future periods, we have no other recurring source of revenue or recurring cash flows from product sales to sustain our present activities, and we do not expect to generate sustainable positive operating cash flows until, and unless, we (i) out-license or sell a product candidate to a third-party that is subsequently successfully developed and commercialized, (ii) enter into additional license arrangements involving our stem cell technology, or (iii) obtain approval from the FDA or other regulatory authorities and successfully commercialize PH94B, on our own or through a future collaboration, or one of our other product candidates.

As the outcome of our ongoing research and development activities, including the outcome of future anticipated nonclinical studies and clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our current CNS product candidates, on our own or in collaboration with others. As in prior periods, we will continue to incur substantial costs associated with other development programs for PH94B, PH10 and AV-101. In addition, other unanticipated costs may arise. As a result of these and other factors, we will need to seek additional capital to meet our future operating plans and requirements, including capital necessary to develop, obtain regulatory approval for, and to commercialize our CNS product candidates, and may seek additional capital in the event there exists favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans and requirements. We have completed in the past a range of potential financing transactions, including public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches, and we may pursue and complete additional financing arrangements in the future. Even if we believe we have sufficient funds for our current or future operating plans and requirements, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

Our future capital requirements may depend on many factors, including:

- the number and characteristics of the product candidates we pursue;
- the scope, progress, results and costs of researching and developing our product candidates, and conducting preclinical and clinical studies;
- the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates;
- the cost of commercialization activities if any of our product candidates are approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing and formulating our product candidates and any products we successfully commercialize;
- our ability to establish and maintain strategic partnerships, licensing or other collaborative arrangements and the financial terms of such agreements;
- market acceptance of our product candidates;
- the effect of competing technological and market developments;
- our ability to obtain government funding for our research and development programs;
- the costs involved in obtaining, maintaining and enforcing patents to preserve our intellectual property;
- the costs involved in defending against such claims that we infringe third-party patents or violate other intellectual property rights and the outcome of such litigation;
- the timing, receipt and amount of potential future licensee fees, milestone payments, and sales of, or royalties on, our future products, if any; and
- the extent to which we may acquire or invest in additional businesses, product candidates and technologies.

Any additional fundraising efforts will divert certain members of our management team from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. We cannot guarantee that future financing will be available in sufficient amounts, in a timely manner, or on terms acceptable to us, if at all. The terms of any future financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity securities and the conversion, exchange or exercise of certain of our outstanding securities will dilute all of our stockholders. The incurrence of debt could result in increased fixed payment obligations and we could be required to agree to certain 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. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

When necessary, if we are unable to obtain additional funding on a timely basis and on acceptable terms, we may be required to significantly curtail, delay or discontinue one or more of our research or product development programs or the commercialization of any product candidate 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 and results of operations.

***Current volatile and/or recessionary economic conditions in the U.S. or abroad could adversely affect our business or our access to capital markets in a material manner.***

To date, our principal sources of capital used to fund our development programs and other operations have been the net proceeds we received from sales of equity securities. We have and will continue to use significant capital for the development and commercialization of our product candidates, and, as such, we expect to seek additional capital from future issuance(s) of our securities, which may consist of issuances of equity and/or debt securities, to fund our planned operations.

Accordingly, our results of operations and the implementation of both our short-term and long-term business plan could be adversely affected by general conditions in the global economy, including conditions that are outside of our control, such as the impact of health and safety concerns from the current COVID-19 pandemic. The ongoing COVID-19 pandemic has resulted in extreme volatility and disruptions in the capital and credit markets. A prolonged economic downturn could result in a variety of risks to our business and may have a material adverse effect on us, including limiting or restricting our ability to access capital on favorable terms, or at all, which would limit our ability to obtain adequate financing to maintain our operations.

***We have identified material weaknesses in our internal control over financial reporting, and our business and stock price may be adversely affected if we do not adequately address those weaknesses or if we have other material weaknesses or significant deficiencies in our internal control over financial reporting.***

We have identified and are now taking steps to correct material weaknesses in our internal control over financial reporting. In particular, we concluded that (i) the size of our staff has not allowed appropriate segregation of duties to (a) permit appropriate review of accounting transactions and/or accounting treatment by multiple qualified individuals, and (b) prevent one individual from overriding the internal control system by initiating, authorizing and completing all transactions, and (ii) we have utilized accounting software that did not prevent erroneous or unauthorized changes to previous reporting periods and/or could be adjusted so as to not provide an adequate auditing trail of entries made in the accounting software.

The existence of one or more material weaknesses or significant deficiencies could result in errors in our financial statements, and substantial costs and resources may be required to rectify any internal control deficiencies. If we cannot produce reliable financial reports, investors could lose confidence in our reported financial information, we may be unable to obtain additional financing to operate and expand our business and our business and financial condition could be harmed.

***Raising additional capital will cause substantial dilution to our existing stockholders, may restrict our operations or require us to relinquish rights, and may require us to seek stockholder approval to authorize additional shares of our common stock.***

We may pursue private and public equity offerings, debt financings, strategic collaborations and licensing arrangements in the future. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, or to the extent, for strategic purposes, we convert or exchange certain of our outstanding securities into common stock, our current stockholders' ownership interest in our company will be substantially diluted. In addition, the terms of any such securities may include liquidation or other preferences that materially adversely affect rights of our stockholders. Debt financing, if available, would increase our fixed payment obligations and 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 collaboration, strategic partnerships and licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, our intellectual property, future revenue streams or grant licenses on terms that are not favorable to us.

***We may be required to raise additional financing by issuing new securities with terms or rights superior to those of our existing securityholders, which could adversely affect the market price of shares of our common stock and our business.***

We will require additional financing to fund future operations, including our research and development activities for our CNS product candidates and our anticipated pre-launch commercialization activities, assuming our clinical development programs are successful and we receive necessary approvals from the FDA. We may not be able to obtain financing on favorable terms, if at all. If we raise additional funds by issuing equity securities, the percentage ownership of our current stockholders will be reduced, and the holders of the new equity securities may have rights superior to those of our existing security holders, which could adversely affect the market price of our common stock and the voting power of shares of our common stock. If we raise additional funds by issuing debt securities, the holders of these debt securities would similarly have some rights senior to those of our existing securityholders, and the terms of these debt securities could impose restrictions on operations and create a significant interest expense for us, which could have a materially adverse effect on our business.

***Our ability to use net operating losses to offset future taxable income is subject to certain limitations.***

As of March 31, 2021, we had federal and state net operating loss carryforwards of approximately $139.2 million and $64.6 million, respectively, which have begun to expire in fiscal 2022 and will continue to expire in future periods. Under Section 382 of the Internal Revenue Code of 1986, as amended (the *Code*), changes in our ownership may limit the amount of our net operating loss carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50% within a three-year period. Any such limitation may significantly reduce our ability to utilize our net operating loss carryforwards and tax credit carryforwards before they expire. Any such limitation, whether as the result of future offerings, prior private placements, sales of our common stock by our existing stockholders or additional sales of our common stock by us in the future, could have a material adverse effect on our results of operations in future years. We have not completed a study to assess whether an ownership change for purposes of Section 382 has occurred, or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such study.

**General Company-Related Risks**

***If we fail to attract and retain senior management and key scientific personnel, we may be unable to successfully produce, develop and commercialize our product candidates.***

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management and scientific and technical personnel. We are highly dependent upon our Chief Executive Officer, President and Chief Scientific Officer, Chief Medical Officer, Chief Financial Officer, Chief Commercial Officer and Senior Vice President – Head of CMC, as well as our other employees, advisors, consultants and scientific and clinical collaborators. As of the date of this Report, we have 21 full-time employees, which may make us more reliant on our individual employees than companies with a greater number of employees. The loss of services of any of these individuals could delay or prevent the successful development of our product candidates or disrupt our administrative functions.

Although we have not historically experienced unique difficulties attracting and retaining qualified employees, we could experience such problems in the future. For example, competition for qualified personnel in the pharmaceuticals field is intense. We will need to hire additional personnel to expand our administrative, research and development and commercial activities. We may not be able to attract and retain quality personnel on acceptable terms.

In addition, we rely on a broad and diverse range of strategic consultants and advisors, including manufacturing, nonclinical and clinical development and regulatory advisors and CMOs and CROs, to assist us in designing and implementing our research and development and regulatory strategies and plans for our product candidates. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

As we seek to advance development of our product candidates, we may need to expand our research and development capabilities and/or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners and other third parties. Future growth will impose significant added responsibilities on members of management. Our future financial performance and our ability to develop and commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our research and development efforts effectively and hire, train and integrate additional management, administrative, commercial and technical personnel. The hiring, training and integration of new employees may be more difficult, costly and/or time-consuming for us because we have fewer resources than a larger organization. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing the company.

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

As we develop our product candidates. either on our own or in collaboration with others, we will face inherent risks of product liability as a result of the required clinical testing of such product candidates, and will face an even greater risk if we or our collaborators commercialize any such product candidates. For example, we may be sued if PH94B, PH10, AV-101, or any other product candidate we or our collaborators develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for product candidates that we may develop;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients; or
- product recalls, withdrawals or labeling, marketing or promotional restrictions.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. Although we maintain general and product liability insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

***Unfavorable global economic or political conditions could adversely affect our business, financial condition or results of operations.***

Our results of operations could be adversely affected by global political conditions, as well as general conditions in the global economy and in the global financial and stock markets. Global financial and political crises cause extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the recent economic downturn triggered by the ongoing COVID-19 pandemic, could result in a variety of risks to our business, including, weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

***We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.***

Natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party CMOs, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

***Our business and operations would suffer in the event of cybersecurity or other system failures. Our business depends on complex information systems, and any failure to successfully maintain these systems or implement new systems to handle our changing needs could result in a material disruption of our product candidates' development programs or otherwise materially harm our operations.***

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, our proprietary business information and that of our suppliers, as well as personally identifiable information of employees. Similarly, our third-party CROs, CMOs and other contractors and consultants possess certain of our sensitive data. The secure maintenance of this information is material to our operations and business strategy. Despite the implementation of security measures, our internal computer systems and those of our third-party CROs, CMOs and other contractors and consultants are vulnerable to attacks by hackers, damage from computer viruses, unauthorized access, breach due to employee error, malfeasance or other disruptions, natural disasters, terrorism and telecommunication and electrical failures. Additionally, having shifted substantially to remote working arrangements, we also face a heightened risk of cybersecurity attacks or data security incidents and are more dependent on internet and telecommunications access and capabilities. Any such attack or breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including recently enacted laws in a majority of states requiring security breach notification. Thus, any access, disclosure or other loss of information, including our data being breached at our partners or third-party providers, could result in legal claims or proceedings and liability under laws that protect the privacy of personal information, disruption of our operations, and damage to our reputation, which could adversely affect our business.

While we have not experienced any such system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for PH94B, PH10, AV-101 or other product candidates could result in substantial delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed.

***We may acquire businesses or product candidates, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions.***

We may acquire additional businesses or CNS product candidates, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new product candidates resulting from a strategic alliance, licensing transaction or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition or licensing transaction, we will achieve the expected synergies to justify the transaction.

***Current politics in the U.S. could diminish the value of the pharmaceutical industry, thereby diminishing the value of our securities.***

The current political environment in the U.S. has led many incumbents and political candidates to propose various measures to reduce the prices for pharmaceuticals. As a result of the U.S. presidential 2020 elections, it is likely that these proposals will receive increasing publicity which, in turn, may cause the investing public to reduce the perceived value of pharmaceutical companies. Any decrease in the overall perception of the pharmaceutical industry may have an adverse impact on our share price and may limit our ability to raise capital needed to continue our drug development programs.

**Risks Related to Our Intellectual Property Rights**

***If we are unable to adequately protect our proprietary technology or obtain and maintain issued patents that are sufficient to protect our product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.***

We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking patents intended to cover our product candidates, their compositions and formulations, their methods of use and methods of manufacturing and any other inventions we consider important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, to defend and enforce our patents, to preserve the confidentiality of our trade secrets and to operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain the proprietary position of our product candidates. We own and have licensed patents and patent applications related to product candidates PH94B, PH10, AV-101 and also to certain stem cell technology.

Although we own and have licensed issued and allowed patents and patent applications relating to PH94B, PH10 and AV-101 in the U.S., selected countries in the EU and other jurisdictions, we cannot yet provide any assurances that any of our pending U.S. and additional foreign patent applications will mature into issued patents and, if they do, that any of our patents will include claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage.

Moreover, other parties may have developed technologies that may be related or competitive to our approach and may have filed or may file patent applications and may have received or may receive patents that may overlap or conflict with our patent properties, for example, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent position. Such third-party patent positions may limit or even eliminate our ability to obtain or maintain patent protection.

The uncertainty about adequate protection includes changes to the patent laws through either legislative action to change statutory patent law or court action that may reinterpret existing law in ways affecting the scope or validity of issued patents. Moreover, relevant laws differ from country-to-country.

***The patent positions of biotechnology and pharmaceutical companies, including our patent portfolio with respect to our product candidates, involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any patent claims that we may be granted cannot be predicted with certainty.***

Our ability to obtain valid and enforceable patents depends, among other factors, on whether the differences between our technology and the prior art allow our inventions to be patentable over relevant prior art. Such prior art includes, for example, scientific publications, investment blogs, granted patents and published patent applications. Patent uncertainty cannot be eliminated because of the potential existence of other prior art, about which we are currently unaware, that may be relevant to our patent applications and patents and that may prevent a pending patent application from being granted or result in an issued patent being held invalid or unenforceable. Moreover, the relevant standards for granting and reviewing patents varies among countries in which we pursue patents.

In addition, some patent-related uncertainty exists because of the challenge in finding and addressing all of the relevant and material prior art in the biotechnology and pharmaceutical fields. For example, there are numerous reports in the scientific literature of compounds that target similar cellular receptors as do certain of our product candidates or that were evaluated in early (often pre-clinical) studies that did not progress to regulatory approval. In addition, even some reports in the trade press and public announcements made by us before the filing date of our AV-101 patent applications mentioned that AV-101 was in development for certain therapeutic purposes. For example, we published a web post on the NIH clinical trials website prior to the filing of our initial AV-101 patent application, which describes unit doses for a then future study, but does not mention treatment of depression and does not provide any preclinical or clinical study data relating to depression or any other medical condition, disease or disorder. This post was not submitted to the United States Patent and Trademark Office (*USPTO*) in our two granted U.S. patents related to (i) unit dose formulations of AV-101 effective to treat depression and (ii) methods of treating depression with AV-101, respectively. However, it was submitted in two continuation depression-related AV-101 patent applications that have similar claims and the USPTO did not make further rejection based on that post. Another source of uncertainty pertains to patent properties that were in-licensed by us for which prior art submissions were under the control of the licensor. We rely on these licensors to have satisfied the relevant disclosure obligations.

In the event any previously published prior art is deemed to be invalidating prior art, it may cause certain of our issued patents to be invalid and/or unenforceable, which would cause us to lose at least part, and perhaps all, of the patent protection on relevant product candidates. Such a loss of patent protection would have a material adverse impact on our business.

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

The USPTO, the European Patent Office (*EPO*) and various other foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

***Even if patents do successfully issue, third parties may challenge the validity, enforceability or scope of such issued patents or any other issued patents we own or license, which may result in such patents being narrowed, invalidated or held unenforceable.***

United States and foreign patents and patent applications may be subject to various types of infringement and validity proceedings, including interference proceedings, *ex parte* reexamination, *inter partes* review proceedings, supplemental examination and challenges in district court. Patents may be subjected to opposition, post-grant review, invalidity actions, or comparable proceedings lodged in various foreign, both national and regional, patent offices or courts. These proceedings could result in loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent in such a way that they no longer cover our product candidates or competitive products.

Furthermore, though an issued patent is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Even if a patent issues and is held to be valid and enforceable, competitors may be able to design around our patents, for example, by using pre-existing or newly developed technology. Other parties may develop and obtain patent protection for more effective technologies, designs or methods.

If we or one of our licensing partners initiated legal proceedings against a third-party to enforce a patent covering one of our product candidates, including patents related to PH94B, PH10 or AV-101, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection would have a material adverse impact on our business.

In addition, such patent-related proceedings may be costly. Thus, any patent properties that we may own or exclusively license ultimately may not provide commercially meaningful protection against competitors. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize our product candidates.

We may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, vendors, or former or current employees. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the United States, and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales.

Our ability to enforce our patent rights also depends on our ability to detect infringement. It is difficult to detect infringers who do not advertise the components or manufacturing processes that are used in their products. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product. Any litigation to enforce or defend our patent rights, even if we were to prevail, could be costly and time-consuming and would divert the attention of our management and key personnel from our business operations. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any patents covering our product candidates are invalidated or found unenforceable, our financial position and results of operations would be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered our product candidates, our financial position and results of operations would also be materially and adversely impacted.

Overall, the degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any issued patents related to PH94B, PH10, AV-101 or any pending patent applications, if issued and challenged by others, will include or maintain claims having a scope sufficient to protect PH94B, PH10, AV-101 or any other products or product candidates against generic or other competition, particularly considering that any patent rights to these compounds *per se* have expired;
- any of our pending patent applications will issue as patents at all;
- we will be able to successfully commercialize our product candidates, if approved, before our relevant patents expire;
- we were the first to make the inventions covered by each of our patents and pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe our patents;
- others will not use pre-existing technology to effectively compete against us;
- any of our patents, if issued, will ultimately be found to be valid and enforceable, including on the basis of prior art relating to our patent applications and patents;
- any patents currently held or issued to us in the future will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- our commercial activities or products will not infringe upon the patents or proprietary rights of others.

We also rely upon unpatented trade secrets, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our collaborators and consultants. It is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees, collaborators and consultants who are parties to these agreements breach or violate the terms of these agreements, we may not discover or have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors.

***Third parties may initiate legal proceedings against us alleging that we infringe their intellectual property rights, which may prevent or delay our product development efforts and stop us from commercializing candidate products or increase the costs of commercializing them, if approved. Also, we may file counterclaims or initiate other legal proceedings against third parties to challenge the validity or scope of their intellectual property rights, the outcomes of which also would be uncertain and could have a material adverse effect on the success of our business.***

We cannot assure that our business, product candidates and methods do not or will not infringe the patents or other intellectual property rights of third parties. Third parties may initiate legal proceedings against us or our licensors or collaborators alleging that we or our licensors or collaborators infringe their intellectual property rights. In addition, we or our licensors or collaborators may file counterclaims in such proceedings or initiate separate legal proceedings against third parties to challenge the validity or scope of their intellectual property rights, including in oppositions, interferences, reexaminations, *inter partes* reviews or derivation proceedings before the United States or other jurisdictions.

Our success will depend in part on our ability to operate without infringing the intellectual property and proprietary rights of third parties. Success also will depend on our ability to prevail in litigation if we are sued for infringement or to resolve litigation matters with rights and at costs favorable to us.

The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that our product candidates or the use of our technologies infringes patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. As we continue to develop and, if approved, commercialize our current product candidates and future product candidates, competitors may claim that our technology infringes their intellectual property rights as part of their business strategies designed to impede our successful commercialization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, third parties may have currently pending patent applications that later result in issued patents that our product candidates may infringe, or that such third parties assert are infringed by our technologies.

The foregoing types of proceedings can be expensive and time-consuming and many of our own or our licensors' or collaborators' adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our licensors or collaborators can. Our defense of litigation or other proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States or European Union.

The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient financial resources to bring these actions to a successful conclusion.

An unfavorable outcome in the foregoing kinds of proceedings could require us or our licensors or collaborators to cease using the related technology or developing or commercializing our product candidates, or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us or our licensors or collaborators a license on commercially reasonable terms or at all. Even if we or our licensors or collaborators obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our licensors or collaborators.

In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business.

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

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcomes are uncertain. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorney's fees if we are found to have willfully infringed a third party's patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced to take a license. In addition, if any such claim is successfully asserted against us and we could not obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing our product candidates.

Patent litigation is costly and time-consuming. We may not have sufficient resources to bring these actions to a successful conclusion. Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our products.

In addition, intellectual property litigation or claims could force us to do one or more of the following:

- cease developing, selling or otherwise commercializing our product candidates;
- pay substantial damages for past use of the asserted intellectual property;
- obtain a license from the holder of the asserted intellectual property, which license may not be available on reasonable terms, if at all; and
- in the case of trademark claims, redesign, or rename, some or all of our product candidates to avoid infringing the intellectual property rights of third parties, which may not be possible and, even if possible, could be costly and time-consuming.

Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects.

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

We enter into confidentiality and intellectual property assignment agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. For example, even if we have a consulting agreement in place with an academic advisor pursuant to which such academic advisor is required to assign any inventions developed in connection with providing services to us, such academic advisor may not have the right to assign such inventions to us, as it may conflict with his or her obligations to assign their intellectual property to his or her employing institution.

Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

***We do not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.***

Filing, prosecuting and defending patents on product candidates in all countries and jurisdictions throughout the world is prohibitively expensive, and our intellectual property rights in some countries outside the U.S. could be less extensive than those in the United States, assuming that rights are obtained in the U.S. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in 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 United States or other jurisdictions. The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications. For the pending patent applications relating to AV-101, as well as for other of the patent families that we own or license, the relevant statutory deadlines have not yet expired. Thus, for each of the patent families that we believe provide coverage for our lead product candidates or technologies, we will need to decide whether and where to pursue protection outside the U.S.

Competitors may use our technologies in jurisdictions where we do not pursue and obtain 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. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the U.S. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology and pharmaceuticals. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties under certain circumstances. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

An unfavorable outcome could require us or our licensors or collaborators to cease using the related technology or developing or commercializing our product candidates, or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us or our licensors or collaborators a license on commercially reasonable terms or at all. Even if we or our licensors or collaborators obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our licensors or collaborators. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business.

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

Furthermore, proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, 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 rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

***We are dependent, in part, on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing our product candidates, if approved. If we breach any of the agreements under which we license the use, development and commercialization rights to our product candidates or technology from third parties or, in certain cases, we fail to meet certain development or payment deadlines, we could lose license rights that are important to our business.***

For PH94B, PH10 and certain stem cell technologies, we are a party to a number of license agreements under which we are granted rights to intellectual properties that are or could become important to our business. Our existing license agreements impose, and we expect that any future license agreements will impose on us, various development, regulatory and/or commercial diligence obligations, payment of fees, milestones and/or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to develop or market products, which could be covered by the license. Our business could suffer, for example, if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms.

As we have done previously, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we cannot provide any assurances that third-party patents do not exist that might be enforced against our current product candidates or future products in the absence of such a license. We may fail to obtain any of these licenses on commercially reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We have entered into several licenses, both in-license agreements and out-license agreements, to support and leverage our various stem cell technology-related programs. We may enter into additional license(s) to third-party intellectual property that are necessary or useful to our business. Our current licenses, and any future licenses that we may enter into, impose various royalty payments, milestone, and other obligations on us. For example, the licensor may retain control over patent prosecution and maintenance under a license agreement, in which case, we may not be able to adequately influence patent prosecution or prevent inadvertent lapses of coverage due to failure to pay maintenance fees. If we fail to comply with any of our obligations under a current or future license agreement, our licensor(s) may allege that we have breached our license agreement and may accordingly seek to terminate our license with them. In addition, future licensor(s) may decide to terminate our license at will. Termination of any of our current or future licenses could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop and commercialize a product candidate or product, if approved, as well as harm our competitive business position and our business prospects.

In addition, if our licensors fail to abide by the terms of the license, if the licensors fail to prevent infringement by third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms our business could suffer.

***Some intellectual property which we have licensed may have been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements, and a preference for U.S. industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements, and limit our ability to contract with non-U.S. manufacturers.***

Some of the intellectual property rights we have licensed or will license in the future may have been generated through the use of U.S. government funding and may therefore be subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980 (*Bayh-Dole Act*). These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose.

In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if we fail, or the applicable licensor fails, to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Also, the U.S. government may acquire title to these inventions in any country in which a patent application is not filed within specified time limits.

Intellectual property generated under a government funded program is further subject to certain reporting requirements, compliance with which may require us, or the applicable licensor, to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the U.S. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the U.S. or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property.

In the event we apply for additional U.S. government funding, and we discover compounds or drug candidates as a result of such funding, intellectual property rights to such discoveries may be subject to the applicable provisions of the Bayh-Dole Act.

***If we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent terms and obtaining data exclusivity for our product candidates, our business may be materially harmed.***

In the U.S., depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of the U.S. patents we own or license may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. For example, we may not be granted an extension if the active ingredient of PH94B, PH10 or AV-101 is used in another drug company's product candidate and that product candidate is the first to obtain FDA approval.

Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected.

Similar kinds of patent term and regulatory and data protection periods are available outside of the U.S. We will pursue such opportunities to extend the exclusivity of our products, but we cannot predict the availability of such exclusivity pathways or that we will be successful in pursuing them.

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

As is the case with other pharmaceutical and biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the U.S. in recent years enacted and is currently implementing wide-ranging patent reform legislation: the Leahy-Smith America Invents Act, referred to as the America Invents Act. The America Invents Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. It is not yet clear what, if any, impact the America Invents Act will have on the operation of our business. However, 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 any patents that may issue from our patent applications, all of which could have a material adverse effect on our business and financial condition.

In addition, 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. The full impact of these decisions is not yet known. For example, on March 20, 2012 in *Mayo Collaborative Services, DBA Mayo Medical Laboratories, et al. v. Prometheus Laboratories, Inc.*, the Court held that several claims drawn to measuring drug metabolite levels from patient samples and correlating them to drug doses were not patentable subject matter. The decision appears to impact diagnostics patents that merely apply a law of nature via a series of routine steps and it has created uncertainty around the ability to obtain patent protection for certain inventions. Additionally, on June 13, 2013 in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the Court held that claims to isolated genomic DNA are not patentable, but claims to complementary DNA molecules are patent eligible because they are not a natural product. The effect of the decision on patents for other isolated natural products is uncertain.

Additionally, on March 4, 2014, the USPTO issued a memorandum to patent examiners providing guidance for examining claims that recite laws of nature, natural phenomena or natural products under the Myriad and Prometheus decisions. This guidance did not limit the application of Myriad to DNA but, rather, applied the decision to other natural products. Further, in 2015, in *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, the Court of Appeals for the Federal Circuit held that methods for detecting fetal genetic defects were not patent eligible subject matter. Other more recent court decisions and related USPTO examination guidelines must be taken into account, particularly as they relate to changes in what types of inventions are eligible for patent protection. Foreign patent and intellectual property laws also are evolving and are not predictable as to their impact on the Company and other biopharmaceutical companies.

In addition to increasing uncertainty regarding our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on these and other decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce any patents that may issue in the future.

***We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of their former employers.***

Certain of our current employees have been, and certain of our future employees may have been, previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We also engage advisors and consultants who are concurrently employed at universities or who perform services for other entities.

Although we are not aware of any claims currently pending or threatened against us, we may be subject to claims that we or our employees, advisors or consultants have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third party. We have and may in the future also be subject to claims that an employee, advisor or consultant performed work for us that conflicts with that person’s obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying monetary claims, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our product candidates, which would materially adversely affect our commercial development efforts.

***Numerous factors may limit any potential competitive advantage provided by our intellectual property rights.***

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, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative:

- others may be able to develop and/or practice technology that is similar to our technology or aspects of our technology but that is not covered by the claims of patents, should such patents issue from our patent applications;
- we might not have been the first to make the inventions covered by a pending patent application that we own;
- we might not have been the first to file patent applications covering an invention;
- others may independently develop similar or alternative technologies without infringing our intellectual property rights;
- pending patent applications that we own or license may not lead to issued patents;
- patents, if issued, that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable or be narrowed, as a result of legal challenges by our competitors;
- third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection;
- we may not be able to obtain and/or maintain necessary or useful licenses on reasonable terms or at all; and
- the patents of others may have an adverse effect on our business.

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

With regard to our stem cell technology, if, instead of identifying a potential NCE candidate based on information available to us in the public domain, we seek to in-license a NCE candidate from biotechnology, medicinal chemistry and pharmaceutical companies, academic, governmental and nonprofit research institutions, including the NIH, or other third parties, there can be no assurances that we will obtain material ownership or economic participation rights over intellectual property we may derive from such licenses or similar rights to the NCEs that we may produce and develop. If we are unable to obtain ownership or substantial economic participation rights over intellectual property related to NCEs we produce and develop, our business may be adversely affected.

**Risks Related to our Securities**

***Market volatility may affect our stock price and the value of your investment.***

The market price for our common stock, similar to that of other biopharmaceutical companies, is likely to remain highly volatile. The market price of our common stock may fluctuate significantly in response to a number of factors, most of which we cannot control, including, among others:

- volatility resulting from uncertainty and general economic conditions caused by the ongoing COVID-19 pandemic;
- plans for, progress of or results from nonclinical and clinical development activities related to our product candidates;
- the failure of the FDA or other regulatory authority to approve our product candidates;
- announcements of new products, technologies, commercial relationships, acquisitions or other events by us or our competitors;
- the success or failure of other CNS therapies;
- regulatory or legal developments in the U.S. and other countries;
- announcements regarding our intellectual property portfolio;
- failure of our product candidates, if approved, to achieve commercial success;
- fluctuations in stock market prices and trading volumes of similar companies;
- general market conditions and overall fluctuations in U.S. equity markets;
- variations in our quarterly operating results;
- changes in our financial guidance or securities analysts' estimates of our financial performance;
- changes in accounting principles;

- our ability to raise additional capital and the terms on which we can raise it;
- sales or purchases of large blocks of our common stock, including sales or purchases by our executive officers, directors and significant stockholders;
- establishment of short positions by holders or non-holders of our stock or warrants;
- additions or departures of key personnel;
- discussion of us or our stock price by the press and by online investor communities; and
- other risks and uncertainties described in these risk factors.

***Future sales and issuances of our common stock may cause our stock price to decline.***

Sales or issuances of a substantial number of shares of our common stock in the public market, or the perception that such sales or issuances are occurring or might occur, could significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities.

The stock market in general, and small biopharmaceutical companies like ours in particular, have frequently experienced significant volatility in the market prices for securities that often has been unrelated to the operating performance of the underlying companies. These broad market and industry fluctuations may adversely affect the market price of our common stock, regardless of our actual operating performance. In certain situations in which the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit against us, the defense and disposition of the lawsuit could be costly and divert the time and attention of our management and harm our operating results. Additionally, if the trading volume of our common stock remains low and limited there will be an increased level of volatility and you may not be able to generate a return on your investment.

***A portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future. Future sales of shares by existing stockholders could cause our stock price to decline, even if our business is doing well.***

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Future sales and issuances of a substantial number of shares of our common stock in the public market, including shares issued upon the conversion of our Series A Preferred, Series B Preferred or Series C Preferred, and the exercise of outstanding options and warrants for common stock which are issuable upon exercise, in the public market, or the perception that these sales and issuances are occurring or might occur, could significantly reduce the market price for our common stock and impair our ability to raise adequate capital through the sale of equity securities.

***If equity research analysts do not publish research or reports about our business or if they issue unfavorable commentary or downgrade our common stock, the price of our common stock could decline.***

The trading market for our common stock relies in part on the research and reports that equity research analysts publish about us and our business. We do not control these analysts. The price of our common stock could decline if one or more equity research analysts downgrade our common stock or if such analysts issue other unfavorable commentary or cease publishing reports about us or our business.

***There may be additional issuances of shares of preferred stock in the future.***

Our Restated Articles of Incorporation, as amended (the *Articles*), permit us to issue up to 10.0 million shares of preferred stock. Our Board has authorized the issuance of (i) 500,000 shares of Series A Preferred, all of which shares are issued and outstanding as of the date of this Report; (ii) 4.0 million shares of Series B 10% Convertible Preferred stock, of which approximately 1.1 million shares remain issued and outstanding as of the date of this Report; (iii) 3.0 million shares of Series C Convertible Preferred Stock, of which approximately 2.3 million shares are issued and outstanding as of the date of this Report; and (iv) 2.0 million shares of Series D Convertible Preferred stock, of which no shares were issued or outstanding as of the date of this Report. Our Board could authorize the issuance of additional series of preferred stock in the future and such preferred stock could grant holders preferred rights to our assets upon liquidation, the right to receive dividends before dividends would be declared to holders of our common stock, and the right to the redemption of such shares, possibly together with a premium, prior to the redemption of the common stock. In the event and to the extent that we do issue additional preferred stock in the future, the rights of holders of our common stock could be impaired thereby, including without limitation, with respect to liquidation.

***We do not intend to pay dividends on our common stock and, consequently, our stockholders' ability to achieve a return on their investment will depend on appreciation in the price of our common stock.***

We have never declared or paid any cash dividend on our common stock and do not currently intend to do so in the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends in the foreseeable future. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which our stockholders purchased them.

***We incur significant costs to ensure compliance with corporate governance, federal securities law and accounting requirements.***

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended (*Exchange Act*), which requires that we file annual, quarterly and current reports with respect to our business and financial condition, and the rules and regulations implemented by the SEC, the Sarbanes-Oxley Act of 2002, the Dodd-Frank Act, and the Public Company Accounting Oversight Board, each of which imposes additional reporting and other obligations on public companies. We have incurred and will continue to incur significant costs to comply with these public company reporting requirements, including accounting and related audit costs, legal costs to comply with corporate governance requirements and other costs of operating as a public company. These legal and financial compliance costs will continue to require us to divert a significant amount of resources that we could otherwise use to achieve our research and development and other strategic objectives.

The filing and internal control reporting requirements imposed by federal securities laws, rules and regulations on companies that are not "smaller reporting companies" under federal securities laws are rigorous and, once we are no longer a smaller reporting company, we may not be able to meet them, resulting in a possible decline in the price of our common stock and our inability to obtain future financing. Certain of these requirements may require us to carry out activities we have not done previously and complying with such requirements may divert management's attention from other business concerns, which could have a material adverse effect on our business, results of operations, financial condition and cash flows. Any failure to adequately comply with applicable federal securities laws, rules or regulations could subject us to fines or regulatory actions, which may materially adversely affect our business, results of operations and financial condition.

In addition, changing laws, regulations and standards relating to corporate governance and public disclosure are creating uncertainty for public companies, increasing legal and financial compliance costs and making some activities more time consuming. These laws, regulations and standards are subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We will continue to invest resources to comply with evolving laws, regulations and standards, however this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to their application and practice, regulatory authorities may initiate legal proceedings against us and our business may be adversely affected.

**Item 1B. Unresolved Staff Comments**

The disclosures in this section are not required since we qualify as a smaller reporting company.

**Item 2. Properties**

Our corporate headquarters and laboratories are located at 343 Allerton Avenue, South San Francisco, California 94080, where we occupy approximately 10,900 square feet of office and lab space under a lease expiring on July 31, 2022, which contains a 5-year option to renew. We believe that our facilities are suitable and adequate for our current and foreseeable 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 Information**

Our common stock was approved for listing and has traded since May 11, 2016 on The Nasdaq Capital Market under the symbol "VTGN".

Below is the range of high and low sales prices for our common stock for the periods indicated as reported by the Nasdaq Capital Market. The market quotations reflect inter-dealer prices, without retail mark-up, mark-down or commissions and may not necessarily represent actual transactions.

| | High | Low |
|---|---|---|
| **Year Ended March 31, 2021** | | |
| First quarter ended June 30, 2020 | $ 0.68 | $ 0.35 |
| Second quarter ended September 30, 2020 | $ 1.06 | $ 0.46 |
| Third quarter ended December 31, 2020 | $ 1.96 | $ 0.6088 |
| Fourth quarter ended March 31, 2021 | $ 3.18 | $ 1.83 |
| | | |
| **Year Ended March 31, 2020** | | |
| First quarter ended June 30, 2019 | $ 1.35 | $ 0.52 |
| Second quarter ended September 30, 2019 | $ 1.32 | $ 0.38 |
| Third quarter ended December 31, 2019 | $ 1.49 | $ 0.29 |
| Fourth quarter ended March 31, 2020 | $ 0.90 | $ 0.30 |

On June 28, 2021 the closing price of our common stock on the Nasdaq Capital Market was $2.84 per share.

As of June 28, 2021, we had 191,382,350 shares of common stock outstanding and approximately 20,000 stockholders of record. On the same date, two stockholders held all 500,000 outstanding restricted shares of our Series A Preferred Stock (*Series A Preferred*), which shares are convertible into 750,000 shares of common stock; one stockholder held 1,131,669 outstanding shares of our Series B 10% Convertible Preferred Stock (*Series B Preferred*), which shares are convertible into 1,131,669 shares of common stock, excluding shares of our common stock which may be issued in payment of accrued dividends upon conversion of the Series B Preferred; and one stockholder held all 2,318,012 outstanding shares of our Series C Convertible Preferred Stock (*Series C Preferred*), which shares are convertible into 2,318,012 shares of common stock.

**Dividend Policy**

We have never paid or declared any cash dividends on our common stock, and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. Our Series B Preferred accrues dividends at a rate of 10% per annum, which dividends are payable solely in unregistered shares of our common stock at the time the Series B Preferred is converted into common stock.

**Recent Sales of Unregistered Securities**

None.

### Item 6. Selected Financial Data

The disclosures in this section are not required because we qualify as a smaller reporting company under federal securities laws.

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

**Cautionary Note Regarding Forward-Looking Statements**

*This Annual Report on Form 10-K (Annual Report or Report) includes forward-looking statements. All statements contained in this Annual Report other than statements of historical fact, including statements regarding our future results of operations and financial position, our business strategy and plans, and our objectives for future operations, are forward- looking statements. The words "believe," "may," "estimate," "continue," "anticipate," "intend," "expect" and similar expressions are intended to identify forward-looking statements. We have based these forward- looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy, short-term and long-term business operations and objectives, and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions. Our business is subject to significant risks including, but not limited to, our ability to obtain additional financing, the results of our research and development efforts, the results of nonclinical and clinical testing, the effect of regulation by the United States Food and Drug Administration (FDA) and other agencies, the impact of competitive products, product development, commercialization and technological difficulties, the effect of our accounting policies, and other risks as detailed in the section entitled "Risk Factors" in this Annual Report. Further, even if our product candidates appear promising at various stages of development, our share price may decrease such that we are unable to raise additional capital without significant dilution or other terms that may be unacceptable to our management, Board of Directors (our Board) and stockholders.*

*Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management or Board to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the future events and trends discussed in this Annual Report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.*

*You should not rely upon forward-looking statements as predictions of future events. The events and circumstances reflected in the forward-looking statements may not be achieved or occur. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. We are under no duty to update any of these forward-looking statements after the date of this Annual Report or to conform these statements to actual results or revised expectations. If we do update one or more forward-looking statements, no inference should be drawn that we will make additional updates with respect to those or other forward-looking statements.*

**Business Overview**

We are a biopharmaceutical company committed to developing and commercializing differentiated new generation medications that go beyond the current standard of care for widespread anxiety, depression and other central nervous system (*CNS*) disorders. Our CNS pipeline includes three CNS product candidates, PH94B Nasal Spray, PH10 Nasal Spray and AV-101, each with a differentiated profile, favorable safety results observed in all clinical studies to date and therapeutic potential in multiple CNS indications. PH94B Nasal Spray (*PH94B*) is being developed for multiple anxiety disorders. We recently initiated our PH94B Phase 3 development program, which we refer to as the PALISADE program, with PALISADE-1, a U.S., multi-center, randomized, double-blind, placebo-controlled Phase 3 clinical study to evaluate the efficacy and safety of PH94B for the acute treatment of anxiety in adults with social anxiety disorder (*SAD*), as well as preparations for the additional studies required to support our potential U.S. New Drug Application (*NDA*) for that indication should the PALISADE Phase 3 program be successful. We are also preparing for exploratory Phase 2A clinical studies of PH94B in adults experiencing several other anxiety disorders. PH10 Nasal Spray (*PH10*) is being developed as a stand-alone treatment for multiple depression disorders. Exploratory Phase 2A clinical development of PH10 for major depressive disorder (*MDD*) has been completed. We are now preparing for planned Phase 2B clinical development of PH10 for this indication. We are preparing for a Phase 1B clinical study of AV-101 in combination with probenecid to assess potential future Phase 2A clinical development of the combination for MDD or certain neurological indications. Our goal is to become a biopharmaceutical company that develops and commercializes innovative CNS therapies for highly prevalent neuropsychiatry and neurology indications where current treatments options are inadequate to meet the needs of millions of patients in markets worldwide.

**Our Product Candidates**

PH94B is a synthetic investigational neurosteroid developed from proprietary compounds called pherines. With its novel mechanism of action, PH94B is an odorless nasal spray administered at microgram-level doses to achieve rapid-onset anti-anxiety, or anxiolytic, effects. The pharmacological activity of PH94B is fundamentally differentiated from that of all FDA-approved anti-anxiety drugs, including all antidepressants approved by the U.S. Food and Drug Administration (*FDA*) for treatment of SAD, as well as all benzodiazepines and beta blockers prescribed on an off-label basis. PH94B engages peripheral chemosensory receptors in nasal passages that trigger a subset of neurons in the main olfactory bulbs (*OB*) at the base of the brain. The OB neurons then stimulate inhibitory GABAergic neurons in the limbic amygdala, decreasing the activity of the sympathetic nervous system, and facilitating fear extinction activity of the limbic-hypothalamic system, the main fear and anxiety center in the brain, as well as in other parts of the brain. Importantly, PH94B does not require systemic uptake and distribution to produce its rapid-onset anti-anxiety effects. Our ongoing PALISADE Phase 3 program for PH94B is designed to further demonstrate its potential as a fast-acting, non-sedating, non-addictive acute treatment of anxiety in adults with SAD. We believe PH94B also has potential to be developed as a novel treatment for adjustment disorder with anxiety, postpartum anxiety, post-traumatic stress disorder, procedural anxiety, panic and other anxiety disorders. PH94B has been granted Fast Track designation status by the FDA for development for the acute treatment of SAD.

PH10 is a synthetic investigational neurosteroid, which also was developed from proprietary compounds called pherines. Its novel, rapid-onset mechanism of action (*MOA*) is fundamentally differentiated from the MOA of all current treatments for MDD and other depression disorders. PH10 is self-administered at microgram-level doses as an odorless nasal spray. PH10 activates nasal chemosensory cells in the nasal passages, connected to neural circuits in the brain that produce antidepressant effects. Specifically, PH10 engages peripheral chemosensory receptors in the nasal passages that trigger a subset of neurons in the main OB that stimulate neurons in the limbic amygdala. This is turn increases activity of the limbic-hypothalamic sympathetic nervous system and increases the release of catecholamines. Importantly, unlike all currently approved oral antidepressants (*ADs*), PH10 does not require systemic uptake and distribution to produce rapid-onset of antidepressant effects. In all clinical studies to date, PH10 has not caused psychological side effects (such as dissociation and hallucinations) or safety concerns that may be associated with rapid-onset ketamine-based therapy (*KBT*), including intravenous ketamine or intranasal ketamine (esketamine). We believe PH10 has potential to be a new stand-alone treatment for MDD and several other depression disorders.

AV-101 (4-Cl-KYN) targets the NMDAR (N-methyl-D-aspartate receptor), an ionotropic glutamate receptor in the brain. Abnormal NMDAR function is associated with numerous CNS diseases and disorders. AV-101 is an oral prodrug of 7-chloro-kynurenic acid (7-Cl-KYNA), which is a potent and selective full antagonist of the glycine co-agonist site of the NMDAR that inhibits the function of the NMDAR. However, unlike ketamine and many other NMDAR antagonists, 7-Cl-KYNA is not an ion channel blocker. At doses administered in all studies to date, AV-101 has been observed to be well tolerated and has not exhibited dissociative or hallucinogenic psychological side effects or safety concerns. In light of these observations and findings from preclinical studies, we believe that AV-101, in combination with FDA-approved probenecid, has potential to become a new oral treatment alternative for certain CNS indications involving the NMDAR. We are currently preparing to evaluate AV-101 in combination with probenecid in a Phase 1B clinical study. The FDA has granted Fast Track designation for development of AV-101 as a potential adjunctive treatment for MDD and as a non-opioid treatment for neuropathic pain (*NP*).

**Critical Accounting Policies and Estimates**

We consider certain accounting policies related to revenue recognition, determination of right of use assets under lease transactions and related lease obligations, impairment of long-lived assets, research and development, stock-based compensation, warrant liability and income taxes to be critical accounting policies that require the use of significant judgments and estimates relating to matters that are inherently uncertain and may result in materially different results under different assumptions and conditions. The preparation of financial statements in conformity with United States generally accepted accounting principles (*GAAP*) requires us to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes to the consolidated financial statements. These estimates include, but are not limited to, those relating to stock-based compensation, revenue recognition, research and development expenses, determination of right of use assets under lease transactions and related lease obligations, and the assumptions used to value warrants, warrant modifications, and useful lives for property and equipment and related depreciation calculations. Our actual results could differ from these estimates.

*Revenue Recognition*

We have historically generated revenue principally from collaborative research and development arrangements, licensing and technology access fees and government grants. We adopted Accounting Standards Update (*ASU*) No. 2014-09, *Revenue from Contracts with Customers (Topic 606)* and its related amendments, collectively referred to as ASC (*Accounting Standards Codification*) Topic 606, as of April 1, 2018, using the modified retrospective transition method.

Under ASC Topic 606, we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration that we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of Topic 606, we perform the following five steps: (i) identify the contract with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration to which we are entitled in exchange for the goods or services we transfer to a customer.

Once a contract is determined to be within the scope of Topic 606, we assess the goods or services promised within each contract and determine those that are performance obligations. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. We assess whether these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right may be accounted for as a contract modification or as a continuation of the contract for accounting purposes.

We assess whether each promised good or service is distinct for the purpose of identifying the performance obligations in the contract. This assessment involves subjective determinations and requires judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (that is, the good or service is capable of being distinct) and (ii) our promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract). In assessing whether a promised good or service is distinct in the evaluation of a collaboration arrangement subject to Topic 606, we consider factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. We also consider the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, we are required to combine that good or service with other promised goods or services until we identify a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices (*SSP*) on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and satisfaction of the performance obligations. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, we consider applicable market conditions and relevant Company-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. In certain circumstances, we may apply the residual method to determine the SSP of a good or service if the standalone selling price is considered highly variable or uncertain. We validate the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, we estimate the amount of consideration to which we will be entitled in exchange for transferring the promised goods or services to a customer. We determine the amount of variable consideration by using the expected value method or the most likely amount method. We include the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, we re-evaluate the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development and regulatory milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received.

In determining the transaction price, we adjust consideration for the effects of the time value of money if the timing of payments provides us with a significant benefit of financing. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensee and the transfer of the promised goods or services to the licensee will be one year or less. For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time, based on the use of an output or input method.

*Right of use assets and lease obligations*

We adopted Accounting Standards Update No. 2016-02, *"Leases (Topic 842)"* (*ASU 2016-02*) effective April 1, 2019. ASU 2016-02 requires that we determine, at the inception of an arrangement, whether the arrangement is or contains a lease, based on the unique facts and circumstances present. Operating lease assets represent our right to use an underlying asset for the lease term (*Right of use assets*) and operating lease liabilities represent our obligation to make lease payments arising from the lease. Right of use assets and operating lease liabilities are recognized at the commencement date of the lease based upon the present value of lease payments over the lease term. When determining the lease term, we include options to extend or terminate the lease when it is reasonably certain, at inception, that we will exercise that option. The interest rate implicit in lease contracts is typically not readily determinable; accordingly, we use our incremental borrowing rate, which is the rate that would be incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment, based upon the information available at the commencement date. The lease payments used to determine our operating lease assets may include lease incentives, stated rent increases and escalation clauses linked to rates of inflation, when determinable, and are recognized in determining our Right of use assets. Our operating lease is reflected in the right-of-use asset – operating lease; operating lease obligation - current portion; and operating lease obligation - non-current portion in our consolidated balance sheets.

Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term. As a result of our adoption of ASU 2016-02, we no longer recognize deferred rent on the consolidated balance sheet. Short-term leases, defined as leases that have a lease term of 12 months or less at the commencement date, are excluded from this treatment and are recognized on a straight-line basis over the term of the lease. Variable lease payments are amounts owed by us to a lessor that are not fixed, such as reimbursement for common area maintenance costs for our facility lease; and are expensed when incurred.

Financing leases, formerly referred to as capitalized leases, are treated similarly to operating leases except that the asset subject to the lease is included in the appropriate fixed asset category, rather than recorded as a Right of use asset, and depreciated over its estimated useful life, or lease term, if shorter.

*Impairment of Long-Lived Assets*

In accordance with ASC 360-10, *Property, Plant & Equipment—Overall*, we review long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of property and equipment may not be recoverable. Determination of recoverability is based on an estimate of undiscounted future cash flows resulting from the use of the asset and its eventual disposition. In the event that such cash flows are not expected to be sufficient to recover the carrying amount of the assets, we write down the assets to their estimated fair values and recognize the loss in the Consolidated Statements of Operations and Comprehensive Loss.

*Research and Development Expenses*

Research and development expenses are composed of both internal and external costs. Internal costs include salaries and employment-related expenses, including stock-based compensation expense, of scientific personnel and direct project costs. External research and development expenses consist primarily of costs associated with clinical and nonclinical development of PH94B, PH10, and AV-101, stem cell research and development costs, and costs related to the application and prosecution of patents related to AV-101, PH94B, PH10 and our stem cell technology platform. All such costs are charged to expense as incurred.

We also record accruals for estimated ongoing clinical trial costs. Clinical trial costs represent costs incurred by contract research organizations (*CRO*s) and clinical trial sites. Progress payments are generally made to CROs, clinical sites, investigators and other professional service providers. We analyze the progress of the clinical trial, including levels of subject enrollment, invoices received and contracted costs when evaluating the adequacy of accrued liabilities. Significant judgments and estimates must be made in determining the clinical trial accrual in any reporting period. Actual results could differ from those estimates under different assumptions. Revisions are charged to research and development expense in the period in which the facts that give rise to the revision become known.

Costs incurred in obtaining product or technology licenses are charged immediately to research and development expense if the product or technology licensed has not achieved regulatory approval or reached technical feasibility and has no alternative future uses. In September 2018, we acquired an exclusive license to develop and commercialize PH94B and an option to acquire a license to develop and commercialize PH10 by issuing an aggregate of 1,630,435 unregistered shares of our common stock having a fair market value of $2,250,000. In October 2018, we exercised our option to acquire an exclusive license to develop and commercialize PH10 by issuing 925,926 shares of our unregistered common stock having a fair market value of $2,000,000. Since, at the date of each acquisition, neither product candidate had achieved regulatory approval and each requires significant additional development and expense, we recorded the costs related to acquiring the licenses and the option as research and development expense.

*Stock-Based Compensation*

We recognize compensation cost for all stock-based awards to employees and non-employee consultants based on the grant date fair value of the award. We record stock-based compensation expense over the period during which the employee or other grantee is required to perform services in exchange for the award, which generally represents the scheduled vesting period. We have not granted restricted stock awards to employees or consultants nor do we have any awards with market or performance conditions. Prior to our April 1, 2019 adoption of ASU 2018-07, *Compensation-Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting* (*ASU 2018-07*), we historically re-measured the fair value of option grants to non-employees as they vested and any resulting increase in value was recognized as an expense during the period over which the services were performed. Under ASU 2018-17, expense recognition for grants to non-employees follows the same methodology as for employees. Noncash expense attributable to compensatory grants of our common stock to non-employees is determined by the quoted market price of the stock on the date of grant and is either recognized as fully-earned at the time of the grant or expensed ratably over the term of the related service agreement, depending on the terms of the specific agreement.

We use the Black-Scholes option pricing model to estimate the fair value of stock-based awards as of the grant date. The Black-Scholes model is complex and dependent upon key data input estimates. The primary data inputs with the greatest degree of judgment are the expected term of the stock options and the estimated volatility of our stock price. The Black-Scholes model is highly sensitive to changes in these two inputs. The expected term of the options represents the period of time that options granted are expected to be outstanding. We use the simplified method in accordance with guidance provided by the Securities and Exchange Commission (*SEC*) to estimate the expected term as an input into the Black-Scholes option pricing model. We determine expected volatility using the historical method, which, because of the relatively limited period during which our stock has been publicly traded on a major exchange and its historically limited trading volume, is based on the historical daily trading data of the common stock of a peer group of public companies over the expected term of the option.

*Warrants Issued in Connection with Equity Financing*

We generally account for warrants issued in connection with equity financings as a component of equity, unless there is a deemed possibility that we may have to settle the warrants in cash or the warrants contain other features requiring them to be treated as liabilities. For warrants issued with the possibility of cash settlement or otherwise requiring liability treatment, we record the fair value of the issued warrants as a liability at each reporting period and record changes in the estimated fair value as noncash gain or loss in the Consolidated Statements of Operations and Comprehensive Loss.

*Income Taxes*

We account for income taxes using the asset and liability approach for financial reporting purposes. We recognize deferred tax assets and liabilities for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. Valuation allowances are established, when necessary, to reduce the deferred tax assets to an amount expected to be realized.

*Recent Accounting Pronouncements*

See Note 3 to the Consolidated Financial Statements included in Item 8 in this Annual Report on Form 10-K for information on recent accounting pronouncements.

**Financial Operations Overview and Results of Operations**

*Net Loss*

Although we entered into the AffaMed Agreement in June 2020 and the Bayer Agreement in December 2016, we have not yet achieved recurring revenue-generating status in amounts sufficient to sustain our operations and enable our strategic business plans from any of our product candidates or technologies. Since inception, we have devoted substantial time and effort to developing AV-101 for multiple CNS indications, including manufacturing research, process development and production of AV-101 drug substance and finished drug product, preclinical efficacy and safety studies, and clinical efficacy and safety studies in CNS indications. Since acquiring our exclusive worldwide licenses to PH94B and PH10 in 2018, we have devoted substantial resources focused on research, development and commercialization of PH94B and PH10, including initiatives to advance manufacturing research, process development and production programs for drug substance and finished drug product, additional preclinical safety studies, and clinical efficacy and safety studies in multiple neuropsychiatry indications. Also, from-time-to-time, we have devoted resources to VistaStem's stem cell technology research and development, bioassay development and small molecule drug rescue initiatives, as well as creating, protecting and patenting intellectual property (*IP*) related to our product candidates and stem cell technologies, with the corollary initiatives of recruiting and retaining personnel and raising working capital. As of March 31, 2021, we had an accumulated deficit of approximately $242.8 million. Our net loss for the fiscal years ended March 31, 2021 and 2020 was approximately $17.9 million and $20.8 million, respectively. We expect losses to continue for the foreseeable future, primarily as we engage in further research, development and commercialization activities related to PH94B, PH10 and AV-101, and pursue VistaStem's potential drug rescue, drug development and CT and RM opportunities.

*Summary of the Fiscal Year Ended March 31, 2021*

On December 22, 2020, we completed a transformative $100 million underwritten public offering (the *December 2020 Public Offering*) of our securities, consisting of shares of our common stock and shares of our newly created Series D Convertible Preferred Stock (*Series D Preferred*). After deducting underwriting discounts and commissions and offering expenses payable by us, we received net proceeds of approximately $93.6 million from the sale of our securities in the December 2020 Public Offering. Combined with financing and development and commercialization partnering transactions completed earlier in our fiscal year, aggregating approximately an additional $25 million, the proceeds from the December 2020 Public Offering have provided us with working capital to advance an important stream of potential catalysts across our CNS pipeline, including, among others, our Phase 3 development program for PH94B for the acute treatment of anxiety in adults with social anxiety disorder (*SAD*) and, upon successful Phase 3 development, submission of our New Drug Application to the U.S. Food and Drug Administration and potential U.S. market approval of PH94B.

From an operational perspective, during our fiscal year ended March 31, 2021 (*Fiscal 2021*), we continued to advance our manufacturing, preclinical and clinical development, and regulatory initiatives necessary for our Phase 3 clinical development of PH94B as a potential acute treatment of anxiety in adults with SAD, PH10 as a potential stand-alone treatment of MDD and AV-101 in combination with probenecid as a potential treatment for NMDAR-focused indications. During the quarter ended March 31, 2021, and thereafter, following the completion of the December 2020 Public Offering, we increased our headcount with the addition of twelve additional employees with significant expertise in various disciplines including manufacturing, regulatory affairs, clinical development, commercial affairs and administrative functions. Further, we accelerated our planning for clinical trials for both PH94B and PH10, culminating in the start of the PALISADE-1 Phase 3 clinical study in late-May 2021. The PALISADE-1 Phase 3 clinical study is part of our PH94B PALISADE Phase 3 program for the acute treatment of anxiety in adult patients with SAD. Throughout Fiscal 2021, we continued to expand our regulatory and intellectual property foundation to support broad clinical development and, ultimately, commercialization of our CNS product candidates in the U.S. and foreign markets.

Throughout Fiscal 2021 and through the date of this Report, a strain of SARS-CoV-2, commonly referred to as COVID-19, has spread to many countries in the world and the outbreak was declared a pandemic by the World Health Organization. The U.S. Secretary of Health and Human Services also declared a public health emergency in the U.S. in response to the outbreak. From time to time during the COVID-19 pandemic, our operations and those of our CROs and CMOs have been and still may be impacted by shelter-in-place orders, social distancing measures, travel bans and restrictions, and certain business and government closures or reductions in service. Our headquarters operations have been significantly curtailed and our employees have worked remotely since the beginning of the COVID-19 pandemic. From time to time since the beginning of the COVID-19 pandemic, we have experienced delays in the delivery of supplies of active pharmaceutical product (*API*) or other key materials required to continue development of PH94B and PH10. Future unexpected delays may result in a significant, material delay or disruption to our current clinical development plans, programs, and operations.

During our fiscal quarter ended June 30, 2020, we completed a successful and positive meeting with the FDA regarding Phase 3 clinical development of PH94B for the acute treatment of anxiety in adult patients with SAD, reaching consensus with the FDA on key aspects of the design of our Phase 3 clinical trials of PH94B, which studies will be randomized, double-blind, placebo-controlled, studies involving a single-event, laboratory-simulated public speaking challenge in adult subjects with SAD. As noted earlier, the initial Phase 3 clinical trial of PH94B, PALISADE-1, commenced in late-May 2021. Dr. Michael Liebowitz, Professor of Clinical Psychiatry at Columbia University, director of the Medical Research Network in New York City, and creator of the Liebowitz Social Anxiety Scale (*LSAS*), is the Principal Investigator of PALISADE-1. Target enrollment for PALISADE-1 (completed patients) is approximately 208 adult patients with SAD. As in the statistically significant (p=0.002) public speaking component of the Phase 2 study, the patient-reported Subjective Units of Distress Scale (*SUDS*) will be used to assess the primary efficacy endpoint in PALISADE-1. Throughout Fiscal 2021, we have been actively engaged in formalizing processes and procedures for the manufacture of PH94B for the PALISADE Phase 3 program and Phase 2 programs in other anxiety indications, and of PH10 for our planned Phase 2B clinical study of PH10 in MDD and other Phase 2 and nonclinical studies of PH10.

In June 2020, we entered into a strategic licensing and collaboration agreement for the clinical development and commercialization of PH94B (the *EverInsight Agreement*) with EverInsight Therapeutics Inc. (*EverInsight*), a biopharmaceutical company focused on developing and commercializing transformative pharmaceutical products for patients in Greater China and other parts of Asia. Subsequent to entering into the EverInsight Agreement, in October 2020, EverInsight merged with AffaMed Therapeutics, Inc., which as a combined, complementary entity is focusing on developing and commercializing therapeutics to address ophthalmologic and CNS disorders in Greater China and beyond. Accordingly, we are now referring to EverInsight and the EverInsight Agreement as AffaMed and the AffaMed Agreement, respectively. Under the terms of the AffaMed Agreement, AffaMed is responsible for clinical development, regulatory submissions and commercialization of PH94B for the treatment of SAD, and potentially other anxiety-related indications, in key markets in Asia, including markets in Greater China, South Korea and Southeast Asia (collectively, the *Territory*). Under the terms of the AffaMed Agreement, in August 2020, we received a non-dilutive upfront license fee payment of $5.0 million from AffaMed. Upon successful development and commercialization of PH94B in the Territory, we are eligible to receive up to $172 million in additional development and commercial milestone payments, plus royalties on commercial sales of PH94B in the Territory. After payment of sublicense fees to Pherin Pharmaceuticals, Inc. (*Pherin*) pursuant to our PH94B license from Pherin, and payment of consulting fees related to consummation of the AffaMed Agreement, we received net cash proceeds of approximately $4.655 million.

In December 2020, we sold 63,000,000 shares of our common stock in at a public offering price of $0.92 per share and 2,000,000 shares of our Series D Preferred at a public offering price of $21.16 per share, resulting in gross proceeds to us of $100 million (the *December 2020 Public Offering*). Net proceeds to us from the securities sold in the December 2020 Public Offering, after deducting underwriting discounts and commissions and offering expenses payable by us, was approximately $93.6 million. Earlier in Fiscal 2021, in August 2020, we sold, in an underwritten public offering (the *August 2020 Public Offering*), an aggregate of 15,625,000 shares of our common stock for a public offering price of $0.80 per share, resulting in gross proceeds to us of $12,500,000. We also granted to the underwriter an over-allotment option to purchase up to an additional 2,343,750 shares at a public offering price of $0.80 per share, which option was exercised with respect to 2,243,250 shares (the *Exercised Option Shares*). The sale of the Exercised Option Shares resulted in additional gross proceeds to us of $1,794,600. Aggregate net proceeds to us from the August 2020 Public Offering, after deducting underwriting discounts and commissions and offering expenses payable by us, was approximately $12.9 million.

To satisfy our obligations under the common stock purchase and registration rights agreements that we entered into with Lincoln Park Capital Fund (*Lincoln Park*) in March 2020, we filed a Registration Statement on Form S-1 (the *LPC Registration Statement*) with the SEC on March 31, 2020 (Registration No. 333-237514), which the SEC declared effective on April 14, 2020 (the *Commencement Date*). Subsequent to the Commencement Date and through July 2020, we sold 6,301,995 registered shares of our common stock to Lincoln Park and received aggregate cash proceeds of $2,891,200. We have not sold any additional shares to Lincoln Park under these agreements since July 2020. We terminated the stock purchase agreement with Lincoln Park effective on June 25, 2021.

As a matter of course, we continue to minimize, to the greatest extent possible, cash commitments and expenditures for both internal and external research and development and general and administrative services. To further advance the nonclinical and clinical development of PH94B, PH10 and AV-101, as well as support our operating activities, we continue to carefully manage our routine operating costs, including our internal employee related expenses, as well as external costs relating to regulatory consulting, contract research and development, investor relations and corporate development, legal, acquisition and protection of intellectual property, public company compliance and other professional services and internal costs.

***Comparison of Fiscal Years Ended March 31, 2021 and 2020***

The following table summarizes the results of our operations for the fiscal years ended March 31, 2021 and 2020 (amounts in thousands).

| | Fiscal Years Ended March 31, | |
|---|---|---|
| | **2021** | **2020** |
| Sublicense revenue | $ 1,089 | $ - |
| Operating expenses: | | |
| Research and development | 12,476 | 13,374 |
| General and administrative | 6,547 | 7,427 |
| Total operating expenses | 19,023 | 20,801 |
| Loss from operations | (17,934) | (20,801) |
| Interest income, net | 2 | 30 |
| Other income | 1 | - |
| Loss before income taxes | (17,931) | (20,771) |
| Income taxes | (3) | (3) |
| Net loss | (17,934) | (20,774) |
| Accrued dividend on Series B Preferred Stock | (1,386) | (1,264) |
| Beneficial conversion feature on Series D Preferred Stock | (23,000) | - |
| Net loss attributable to common stockholders | $ (42,320) | $ (22,038) |

*Revenue*

We recognized $1,089,500 in sublicense revenue pursuant to the AffaMed Agreement in Fiscal 2021 compared to none in the fiscal year ended March 31, 2020 (*Fiscal 2020*). As noted earlier, in June 2020, we entered into the AffaMed Agreement, pursuant to which we received a non-dilutive upfront license fee payment of $5.0 million in August 2020. We initially recorded this payment as deferred revenue and we are recognizing it as revenue on a straight-line basis over the period in which we expect to perform the services required under the AffaMed Agreement. We currently estimate that we will complete our performance obligations at the end of calendar 2023. While we may potentially receive additional cash payments and royalties in the future under the AffaMed Agreement in the event certain performance-based milestones and commercial sales are achieved, there can be no assurance that the AffaMed Agreement will provide additional revenue beyond that noted or cash payments to us in the near term, or at all.

*Research and Development Expense*

Research and development (*R&D*) expense decreased from $13.4 million in Fiscal 2020 to $12.5 million in Fiscal 2021, primarily due to the completion of the Elevate Study of AV-101 in Fiscal 2020, noticeably offset by increased developmental expenses in Fiscal 2021 for PH94B and PH10. Expenses related to the Elevate Study and other AV-101 related nonclinical activities decreased by approximately $5.9 million in Fiscal 2021 compared to Fiscal 2020, while expenses for PH94B and PH10 preclinical and clinical readiness initiatives increased by $5.2 million in Fiscal 2021 compared to Fiscal 2020. Salaries and benefits expense increased in Fiscal 2021 as a result of the addition of six new senior-level employees during the third and fourth quarters of Fiscal 2021 and bonus payments made in the third quarter of Fiscal 2021. Noncash research and development expenses, primarily stock-based compensation and equipment depreciation in both periods, accounted for approximately $841,000 and $1,380,000 in Fiscal 2021 and Fiscal 2020, respectively.

The following table indicates the primary components of R&D expense for each of the periods (amounts in thousands):

| | Fiscal Years Ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| Salaries and benefits | $ 1,986 | $ 1,381 |
| Stock-based compensation | 747 | 1,287 |
| Consulting and other professional services | 327 | 533 |
| Technology licenses and royalties | 551 | 546 |
| Project-related research, licenses and supplies: | | |
| Elevate study and other AV-101 expenses | 611 | 6,483 |
| PH94B and PH10 development expenses | 7,620 | 2,448 |
| Stem cell and all other | 24 | 110 |
| | 8,255 | 9,041 |
| Rent | 545 | 535 |
| Depreciation | 64 | 49 |
| All other | 1 | 2 |
| | | |
| Total Research and Development Expense | $ 12,476 | $ 13,374 |

The increase in salaries and benefits expense in Fiscal 2021 reflects (i) the impact of bonus payments made to our Chief Medical Officer (*CMO*), Chief Scientific Officer (*CSO*), and members of our scientific staff in December 2020, (ii) modest salary increases to those officers and employees effective in the fourth quarter of Fiscal 2021; and (iii) the addition of six officer-level employees between December 2020 and March 2021. There were no changes in base compensation levels for our CMO, CSO, or other members of our scientific staff between April 2019 and December 2020 and no bonus expense or payments during that same period.

Current year stock-based compensation expense reflects the amortization of option grants made to our CMO, CSO, members of our scientific staff, our new senior-level employees and certain clinical and scientific consultants since June 2016, all earlier outstanding grants having become fully vested and amortized during Fiscal 2021 or earlier. Grants awarded after March 31, 2020, including those granted during Fiscal 2021, account for approximately $348,700 of expense in Fiscal 2021, offset by an expense reduction of approximately $814,400 attributable to certain options granted between June 2016 and January 2019 that became fully vested and amortized during Fiscal 2021 or earlier. Fiscal 2021 stock compensation expense is further reduced by approximately $79,500 due to the absence of the impact of immediate vesting attributable to certain options granted in May 2019 or fully vesting prior to March 31, 2020. Except for grants to new employees, expense attributable to recent option grants is generally being amortized over two-year to three-year vesting periods, with essentially all of the grants made since May 2019, including those made in Fiscal 2021, being 25% vested and expensed upon grant, in accordance with the terms of the respective grants. Grants to new employees generally vest 25% on the first anniversary of the grant date and ratably monthly over the next three years.

Consulting and other professional services reflects fees incurred, generally on an as-needed basis, for project-based scientific, nonclinical and clinical development and regulatory advisory and analytical services rendered to us by third parties, including by members of our Scientific Advisory Board and CNS Clinical and Regulatory Advisory Board, especially in support of our PH94B and PH10 development initiatives. Fiscal 2021 expense reflects a reduction of $110,000 in development support payments to Pherin which terminated in April 2020 under the terms of our PH94B and PH10 license agreements and a $95,000 reduction in analytical and other services in support of PH94B and PH10 development compared to Fiscal 2020, a portion of which is attributable to the conversion of a consultant to an employee in Fiscal 2021.

Technology license and royalties expense primarily reflects legal counsel and other costs related to patent prosecution and protection pursuant to our stem cell technology license agreements, our AV-101 patents, or patents that we have elected to pursue for commercial purposes, as well as recurring annual license fees. These costs do not occur ratably throughout the year or between years. In both periods, this expense includes legal counsel and other costs we have incurred to advance various patent applications in the U.S. and numerous foreign countries, primarily with respect to AV-101 and our stem cell technology platform, but also nominally with respect to our PH94B and PH10 intellectual property portfolios during Fiscal 2021.

AV-101 project expense for Fiscal 2020 reflects the costs of actively conducting the Elevate Study in MDD, including various CROs, investigator and clinical site costs, and determination of topline study results, as well as CRO support services for AV-101 projects for indications other than MDD, and, to lesser extent, expense incurred to manufacture additional quantities of AV-101 for use in potential future clinical development of AV-101 in a number of potential CNS indications. AV-101 project expense for Fiscal 2021 primarily reflects the cost of certain preclinical studies related to the use of AV-101 with probenecid and certain AV-101 manufacturing stability studies, and costs incurred to finalize the results of the Elevate Study for regulatory submission.

PH94B and PH10 project expenses for both Fiscal 2021 and Fiscal 2020 reflect research and development and manufacturing and regulatory initiatives necessary to facilitate Phase 3 clinical development and readiness of PH94B for acute treatment of anxiety in adults with SAD and Phase 2B development of PH10 for MDD. Manufacturing, formulation and analysis of sufficient quantities of drug substance and drug product have been the key initiatives during Fiscal 2021 for advancing the further clinical development of both PH94B and PH10, with costs for PH94B significantly exceeding those for PH10 in Fiscal 2021 and in comparison to those of Fiscal 2020. From time to time during Fiscal 2021, production, logistics and analytical processes for both of these product candidates were delayed due to the ongoing COVID-19 pandemic.

Stem cell and other project related expenses reflects costs associated with drug rescue applications of our stem cell technology in both years. These expenses are typically incurred by our in-house scientific personnel. As a result of shelter-in-place and remote working requirements related to the ongoing COVID-19 pandemic, such expenses were reduced to an insignificant level during Fiscal 2021.

Rent expense for both Fiscal 2020 and Fiscal 2021 reflects our implementation of ASC 842 effective April 1, 2019 and the requirement to recognize, as an operating lease related to our South San Francisco office and laboratory facility, a right-of-use asset and a lease liability, both of which must be amortized over the expected lease term. The underlying lease reflects commercial property rents prevalent in the South San Francisco real estate market at the time of our November 2016 lease amendment extending the lease of our headquarters facilities in South San Francisco by five years from July 31, 2017 to July 31, 2022. We allocate total rent expense for our South San Francisco facility between research and development expense and general and administrative expense based generally on square footage dedicated to each function. Following our implementation of ASC 842, the modest increase in rent expense between periods is primarily related to Fiscal 2021 increases in such items as common area maintenance fees, taxes and insurance which are generally assessed to us by our landlord.

*General and Administrative Expense*

General and administrative (*G&A*) expense decreased to approximately $6.5 million in Fiscal 2021 from approximately $7.4 million in Fiscal 2020. Cash compensation in Fiscal 2021 increased by approximately $0.7 million while noncash stock-based compensation decreased by approximately $1.0 million in Fiscal 2021. Further, during Fiscal 2020 we modified certain outstanding warrants and recognized non-cash warrant modification expense of $826,900. Noncash G&A expense, approximately $1,731,000 for Fiscal 2021, decreased from approximately $3,543,000 for Fiscal 2020, primarily due to the decreases in stock-based compensation and warrant modifications noted above and the noncash components of investor and public relations expense in Fiscal 2020 attributable to the amortization of the fair value of common stock or warrants granted to service providers.

The following table indicates the primary components of G&A expense for each of the periods (amounts in thousands):

| | Fiscal Years Ended March 31, | |
|---|---|---|
| | **2021** | **2020** |
| Salaries and benefits | $ 2,052 | $ 1,382 |
| Stock-based compensation | 1,559 | 2,533 |
| Board fees and other consulting services | 428 | 185 |
| Legal, accounting and other professional fees | 564 | 575 |
| Investor and public relations | 695 | 933 |
| Insurance | 449 | 348 |
| Travel expenses | 4 | 81 |
| Rent and utilities | 354 | 354 |
| Sublicense contract amortized acquisition expense | 102 | - |
| Warrant modification expense | - | 827 |
| All other expenses | 340 | 209 |
| | $ 6,547 | $ 7,427 |

The increase in salaries and benefits expense for Fiscal 2021 primarily reflects the impact of (i) bonus payments made to our Chief Executive Officer (*CEO*), Chief Financial Officer (*CFO*), Vice President-Corporate Development (*VP-Corporate Development*) and a non-officer member of our administrative staff in December 2020; (ii) modest salary increases to those officers and employee effective in the fourth quarter of Fiscal 2021; and (iii) the addition of three senior-level employees during February 2021 and March 2021. There were no changes in base compensation levels for our CEO, CFO, or VP-Corporate Development between April 2019 and December 2020 and no bonus expense or payments to them during that same period.

Current year stock-based compensation expense reflects the amortization of option grants made to our CEO, CFO, VP Corporate Development, administrative staff, independent members of our Board and certain consultants since June 2016, all earlier outstanding grants having become fully vested and amortized during Fiscal 2021 or earlier. Grants awarded after March 31, 2020 account for approximately $677,000 of expense in Fiscal 2021, offset by an expense reduction of approximately $1,515,000 attributable to certain options granted between June 2016 and January 2019 that became fully vested and amortized during Fiscal 2021 or earlier. Fiscal 2021 stock compensation expense is further reduced by approximately $141,700 due to the absence of the impact of immediate vesting attributable to certain options granted in May 2019 or fully vesting prior to March 31, 2020. Except for grants to new employees, expense attributable to recent option grants is generally being amortized over two-year to three-year vesting periods, with essentially all of the grants made since May 2019, including those made in Fiscal 2021, being 25% vested and expensed upon grant, in accordance with the terms of the respective grants. Grants to new employees generally vest 25% on the first anniversary of the grant date and ratably monthly over the next three years.

Board fees and other consulting services represent, in both periods, fees paid as consideration for Board and Board Committee services to the independent members of our Board of Directors and, additionally in the current year, other consulting service fees related to commercial analyses of both PH94B and PH10.

Legal, accounting and other professional fees for Fiscal 2021 and Fiscal 2020 includes expense related to routine corporate legal fees as well as the accounting expense related to the annual audit of our prior year financial statements and the three quarterly reviews of our current year financial statements. In Fiscal 2021, we incurred additional consulting fees related to revenue recognition accounting for the AffaMed Agreement and, in Fiscal 2020, we incurred fees attributable to services provided by an international business development consultant.

Investor and public relations expense includes the fees of our various external service providers for a broad spectrum of investor relations, public relations and social media services, and well as market awareness and strategic advisory and support functions and initiatives that, in Fiscal 2020, included numerous in-person meetings in multiple U.S. and certain foreign markets and other communication activities focused on expanding global market awareness of the Company, our CNS product candidate pipeline and technologies and our research and development programs, including among registered investment professionals and investment advisors, individual and institutional investors, and prospective strategic collaborators for development and commercialization of our product candidates in major pharmaceutical markets worldwide. During Fiscal 2021, we curtailed the number and scope of external service providers engaged in these activities compared to the prior year. Further, in Fiscal 2020, in addition to cash fees and expenses we incurred for such activities, we recognized approximately $105,900 of noncash expense attributable to the amortization of the fair value of stock and warrants granted in previous periods to various corporate development, investor relations, and market awareness service providers. No such noncash expense was incurred in Fiscal 2021.

The increase in insurance expense for Fiscal 2021 is primarily attributable to the market-rate increase in the premium for our directors and officers liability insurance upon renewal of our policy in May 2020.

In Fiscal 2020, travel expense reflects costs associated with in-person management presentations and meetings held in multiple U.S. markets and certain international markets with existing and potential individual and institutional investors, investment professionals and advisors, media, and securities analysts, as well as various investor relations, market awareness and corporate development and partnering initiatives and in monitoring the progress of our Elevate Study. As a result of periodic shelter-in-place restrictions and travel and workplace precautions and restrictions associated with the ongoing COVID-19 pandemic, during Fiscal 2021, such meetings have occurred remotely without requiring in-person business travel by our executives.

Rent expense for both periods presented reflects our implementation of ASC 842 effective April 1, 2019 and the requirement to recognize, as an operating lease related to our South San Francisco office and laboratory facility, a right-of-use asset and a lease liability, both of which must be amortized over the expected lease term. The underlying lease reflects commercial property rents prevalent in the South San Francisco real estate market at the time of our November 2016 lease amendment extending the lease of our headquarters facilities in South San Francisco by five years from July 31, 2017 to July 31, 2022. We allocate total rent expense for our South San Francisco facility between research and development expense and general and administrative expense based generally on square footage dedicated to each function. Following our implementation of ASC 842, increases or decreases in rent expense between periods are primarily related to changes in such items as common area maintenance fees, taxes and insurance which are generally assessed to us by our landlord.

Beginning in the second quarter of Fiscal 2021, we began to amortize the deferred contract acquisition costs related to our acquisition of the AffaMed Agreement, composed of the cash payments of $220,000 for sublicense fees which we were obligated to make pursuant to our PH94B license from Pherin, and $125,000 of cash fees and $125,000 fair value of common stock issued for consulting services, in each case exclusively related to our acquisition of the AffaMed Agreement. The contract acquisition costs are amortized over the expected term of the services to be provided under the AffaMed Agreement. During Fiscal 2021, we amortized $102,400 of contract acquisition costs.

During Fiscal 2020, we completed three warrant modifications resulting in an aggregate of $826,900 of noncash warrant modification expense as described below.

- On December 4, 2019, we modified outstanding warrants previously issued as a part of completed private placements to purchase an aggregate of approximately 6.6 million unregistered shares of our common stock to temporarily reduce, for a period of two years or until the expiration of the warrant, if sooner, the exercise price of such warrants to $0.50 per share, in order to more closely align the exercise price of the warrants with the then-current trading price of our common stock. Following the two-year period during which the exercise price is reduced, the exercise price will revert to its pre-modification price. We determined that this modification increased the fair value of the modified warrants by $702,500, which we recorded as warrant modification expense.

- Also, on December 4, 2019, we issued additional warrants (the *Additional Warrants*) to purchase an aggregate of 325,000 additional shares of our common stock to the participants in our fall 2019 private placement of shares of common stock and warrants to increase the number of unregistered shares of common stock issuable upon exercise of the warrants from 50% to 100% of the number of shares issued in the private placement. The Additional Warrants are exercisable through March 31, 2024 at an exercise price of $0.50 per share. We determined that the fair value of the Additional Warrants was $88,800, which we also recognized as noncash warrant modification expense.

- Further, on December 19, 2019, we modified additional outstanding warrants previously issued as a part of a completed private placement to purchase a total of 80,431 shares of our unregistered common stock to permanently reduce the exercise price of such warrants to $0.805 per share and to extend the term of such warrants through December 31, 2022, in order to more closely align the exercise price of the warrants with the then-current trading price of our common stock and to provide additional time for the holders to exercise the warrants. We determined that these modifications increased the fair value of the subject warrants by $35,600, which we also recognized as noncash warrant modification expense.

The shares underlying the modified warrants and the Additional Warrants were included in a Registration Statement on Form S-3 (File No. 333-237968) that was declared effective by the Commission on May 13, 2020.

*Interest and Other Income, Net*

Interest income, net totaled $1,600 for Fiscal 2021 compared to interest income, net of $30,100 for Fiscal 2020. The following table indicates the primary components of interest income and expense for each of the periods (amounts in thousands):

| | Fiscal Years Ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| Interest income | $ 15 | $ 45 |
| Interest expense on financing lease, insurance premium financing notes and Payroll Protection Program loan (2021) | (13) | (15) |
| Interest income, net | $ 2 | $ 30 |

In both periods, interest income relates to cash deposits in interest-bearing cash equivalent accounts. Although cash balances were generally higher during Fiscal 2021, the decline in market interest rates during Fiscal 2021 compared to Fiscal 2020 resulted in reduced interest income. Interest expense in both periods relates to interest paid on insurance premium financing notes and on our financing lease of office equipment subject to ASC 842, and in Fiscal 2021, to interest accrued on our Payroll Protection Program loan prior to its voluntary repayment, including interest, in December 2020.

We recognized $1,385,600 and $1,263,600 in Fiscal 2021 and Fiscal 2020, respectively, representing the 10% cumulative dividend accrued on outstanding shares of our Series B 10% Convertible Preferred Stock (*Series B Preferred*) as an additional deduction in arriving at net loss attributable to common stockholders in the Consolidated Statement of Operations and Comprehensive Loss included in Item 8, Part II of this Annual Report. In December 2020, one holder of Series B Preferred converted 28,571 shares of Series B Preferred into an equal number of unregistered shares of our common stock and we issued an additional 160,062 unregistered shares of our common stock in payment of $124,600 of accrued dividends.

The Series D Preferred that we issued in the December 2020 Public Offering contained a beneficial conversion feature (a *BCF*), which arises when a debt or equity security is issued with an embedded conversion option that is deemed beneficial to the investor, that is, in-the-money, at inception because the conversion option has an effective conversion price that is less than the market price of the underlying stock at the commitment date (with respect to the Series D Preferred, the date the security was actually issued rather than the date the agreement to do so was entered into, referred to as the *Commitment Date*). In accordance with Accounting Standards Codification 470-20, *Debt- Debt with Conversion and Other Options* (*ASC 470-20*), an embedded BCF is required to be recognized separately by allocating a portion of the proceeds equal to the intrinsic value of the feature to additional paid-in capital. ASC 470-20 also provides that the intrinsic value is to be calculated as of the Commitment Date. The Series D Certificate of Designation provides that the Series D Preferred has a conversion price of $0.92 per share on an as-converted basis the (*Conversion Price*). The Conversion Price compared to the closing price of $1.42 per share of our common stock on the Commitment Date results in a difference of $0.50 per share. That difference multiplied by the 46 million shares of our common stock issuable upon conversion of the Series D Preferred resulted in an aggregate BCF of $23.0 million. We did not recognize the impact of the BCF at December 31, 2020 because the Series D Preferred was not convertible into common stock prior to the Approval Date (the date of our Special Meeting of Stockholders held on March 5, 2021). Following approval by our stockholders of the Charter Amendment at the Special Meeting in March 2021, the contingency of the BCF was eliminated and we recognized the BCF as a noncash charge in arriving at net loss attributable to common stockholders in our Consolidated Statement of Operations and Comprehensive Loss for the fiscal year ended March 31, 2021 and as a corresponding increase in additional paid-in capital in our Consolidated Statement of Stockholders' Equity (Deficit). The recognition of the BCF on the Series D Preferred had no impact in aggregate on our stockholders' equity or on our cash position.

**Liquidity and Capital Resources**

Since our inception in May 1998 through March 31, 2021, we have financed our operations and technology acquisitions primarily through the issuance and sale of our equity and debt securities for cash proceeds of approximately $197.8 million, as well as from an aggregate of approximately $22.7 million of government research grant awards (excluding the fair market value of government sponsored and funded clinical trials), strategic collaboration payments, intellectual property licensing and other revenues. Additionally, we have issued equity securities with an approximate value at issuance of $38.2 million in noncash acquisitions of product licenses and in settlements of certain liabilities, including liabilities for professional services rendered to us or as compensation for such services.

*Recent Developments*

*Jefferies ATM*. On May 14, 2021, we entered into an Open Market Sale AgreementSM (the *Sales Agreement*) with Jefferies LLC, as sales agent (*Jefferies*), with respect to an at-the-market offering program under which we may offer and sell, from time to time, shares of our common stock with an aggregate offering price of up to $75.0 million through Jefferies as our sales agent. As of the date of this Report, we have not completed any sales under the Sale Agreement.

*December 2020 Public Offering*. In December 2020, we entered into an underwriting agreement (the *December 2020 Underwriting Agreement*) pursuant to which we sold 63,000,000 shares of our common stock in the December 2020 Public Offering at a public offering price of $0.92 per share and 2,000,000 shares of Series D Preferred at a public offering price of $21.16 per share, resulting in gross proceeds to us of $100 million. Net proceeds to us from the securities sold in the December 2020 Public Offering, after deducting underwriting discounts and commissions and offering expenses payable by us, was approximately $93.6 million. Following approval by our stockholders of the Charter Amendment at the Special Meeting in March 2021 and through the date of this Annual Report, we issued 46 million shares of our common stock upon conversion of all outstanding shares of Series D Preferred issued in the December 2020 Public Offering.

*August 2020 Public Offering*. In August 2020, we entered into an underwriting agreement pursuant to which we sold, in the August 2020 Public Offering an underwritten public offering (the *August 2020 Public Offering*), an aggregate of 15,625,000 shares of our common stock at a public offering price of $0.80 per share, resulting in gross proceeds to us of $12,500,000. Under the terms of the August 2020 Underwriting Agreement, we granted to the underwriter an over-allotment option (the *Over-Allotment Option*) to purchase up to an additional 2,343,750 shares of common stock at a public offering price of $0.80 per share. The underwriter exercised the Over-Allotment Option with respect to 2,243,250 shares (the *Exercised Option Shares*), resulting in additional gross proceeds to us of $1,794,600. Aggregate net proceeds to us from the August 2020 Public Offering, after deducting underwriting discounts and commissions and offering expenses payable by us, was approximately $12.9 million.

*AffaMed Agreement*. In June 2020, we entered into the AffaMed Agreement, a strategic licensing and collaboration agreement for the clinical development and commercialization of PH94B for acute treatment of anxiety in adults with SAD and other potential anxiety-related disorders, with EverInsight, now operating as AffaMed Therapeutics. Under the terms of the AffaMed Agreement, AffaMed agreed to make a non-dilutive upfront license payment of $5.0 million to us, which we received in August 2020. The $5.0 million upfront license payment resulted in net cash proceeds to us of approximately $4.655 million after the sublicense payment we agreed to make to Pherin pursuant to our PH94B license from Pherin, and payment for consulting services related to the AffaMed Agreement.

*LPC Agreement*. Additionally, on March 24, 2020, we entered into the LPC Agreement with Lincoln Park, pursuant to which Lincoln Park committed to purchase up to $10,250,000 of our common stock at market-based prices over a period of 24 months. To satisfy our obligations under the registration rights agreement, we filed the LPC Registration Statement, which the SEC declared effective on April 14, 2020 (Registration No. 333-237514). Subsequent to the effectiveness of the LPC Registration Statement and through July 2020, we sold 6,301,995 registered shares of our common stock to Lincoln Park and received gross cash proceeds of $2,891,200. We have not sold any shares of our common stock pursuant to the Lincoln Park Agreement since July 2020.

*Warrant Exercises*. Further, between December 2020 and March 31, 2021, certain holders of outstanding warrants exercised such warrants to purchase an aggregate of 6,396,302 shares of our common stock and we received cash proceeds of $4,924,800 from such exercises. Since March 31, 2021 and through the date of this Annual Report, holders of outstanding warrants have exercised warrants to purchase an additional 1,508,768 shares of our common stock and we have received cash proceeds of approximately $1,105,700, resulting in aggregate cash proceeds of $6,030,500 received from warrant exercises between December 2020 and the date of this Annual Report.

*Liquidity and Capital Resources*

During Fiscal 2021, we received approximately $119 million in net cash proceeds from the transactions described above. At March 31, 2021, we had cash and cash equivalents of approximately $103.1 million, which we believe is sufficient to fund our planned operations for well beyond the twelve months following the issuance of the financial statements included in Part II, Item 8 of this Annual Report, and indicating our ability to continue as a going concern. Nevertheless, we have not yet developed products that generate recurring revenue and, assuming successful completion of our planned clinical and nonclinical programs, we will need to invest substantial additional capital resources to commercialize any of them.

During the next twelve months, we plan to (i) continue PALISADE-1 and prepare for and initiate multiple studies in our PALISADE Phase 3 program for development and commercialization of PH94B as an acute treatment of anxiety in adult patients with SAD, (ii) prepare for and initiate multiple small exploratory Phase 2A studies of PH94B in additional anxiety disorders, (iii) prepare for and initiate a Phase 2B clinical study of PH10 as a potential stand-alone treatment for MDD, (iv) prepare for and initiate a Phase 1B clinical study of AV-101 in combination with probenecid to enable assessment of potential exploratory Phase 2A development of the combination in MDD and certain neurological disorders, and (v) conduct nonclinical studies involving PH94B, PH10 and AV-101.

Although we believe our current cash position is sufficient to fund our planned operations for well beyond the next twelve months, when necessary and advantageous, we may raise additional capital through the sale of our equity securities in one or more (i) public offerings (ii) private placements to accredited investors, and/or (iii) in strategic licensing and development collaborations involving one or more of our drug candidates in markets outside the United States, similar to the AffaMed Agreement. Subject to certain restrictions, our Registration Statement on Form S-3 (Registration No. 333-254299) (the *S-3 Registration Statement*), which became effective on March 26, 2021 remains available for future sales of our equity securities under the Sales Agreement with Jefferies, or in one or more public offerings from time to time. While we may make additional sales of our equity securities under the S-3 Registration Statement, we do not have an obligation to do so.

In addition to the potential sale of our equity securities, we may also seek to enter research, development and/or commercialization collaborations similar to the AffaMed Agreement and the Bayer Agreement to provide funding, including non-dilutive funding, for development of one or more of our CNS product candidate programs. We may also seek additional government grant awards or agreements similar to our prior agreement with the U.S. National Institutes of Health (*NIH*), Baylor University and the U.S. Department of Veterans Affairs in connection with certain government-sponsored studies of AV-101. Such strategic collaborations may provide non-dilutive resources to advance our strategic initiatives while reducing a portion of our future cash outlays and working capital requirements. We may also pursue intellectual property arrangements similar to the AffaMed Agreement and the Bayer Agreement with other parties. Although we may seek additional collaborations that could generate revenue and/or provide non-dilutive funding for development of our product candidates, as well as new government grant awards and/or agreements, no assurance can be provided that any such collaborations, awards or agreements will occur in the future.

Our future working capital requirements will depend on many factors, including, without limitation, potential impacts related to the continuing COVID-19 pandemic, the scope and nature of opportunities related to our success and the success of certain other companies in nonclinical and clinical trials, including our development and commercialization of our current product candidates and various applications of our stem cell technology platform, the availability of, and our ability to obtain, government grant awards and agreements, and our ability to enter into collaborations on terms acceptable to us. To further advance the clinical development of PH94B, PH10, and AV-101 and, to a lesser extent, our stem cell technology platform, as well as support our operating activities, we plan to continue to carefully manage our routine operating costs, including our employee headcount and related expenses, as well as costs relating to regulatory consulting, contract manufacturing, research and development, investor and public relations, business development, legal, intellectual property acquisition and protection, public company compliance and other professional services and operating costs.

Notwithstanding the foregoing, there can be no assurance that our current strategic collaborations under the AffaMed Agreement and/or the Bayer Agreement will generate revenue from future potential milestone payments, or that future financings or government or other strategic collaborations will be available to us in sufficient amounts, in a timely manner, or on terms acceptable to us, if at all. If we are unable to obtain additional financing on a timely basis when needed, our business, financial condition, and results of operations may be harmed, the price of our stock may decline, we may be required to reduce, defer, or discontinue certain of our research and development activities and we may not be able to continue as a going concern. As noted above, the Consolidated Financial Statements included in part II, Item 8 of this Annual Report do not include any adjustments that might result from the negative outcome of this uncertainty.

*Cash and Cash Equivalents*

The following table summarizes changes in cash and cash equivalents for the fiscal years stated (in thousands):

| | Fiscal Years Ended March 31, | |
|---|---|---|
| | **2021** | **2020** |
| Net cash used in operating activities | $ (12,074) | $ (15,757) |
| Net cash used in investing activities | (275) | - |
| Net cash provided by financing activities | 114,102 | 4,012 |
| Net increase (decrease) in cash and cash equivalents | 101,753 | (11,745) |
| Cash and cash equivalents at beginning of period | 1,355 | 13,100 |
| Cash and cash equivalents at end of period | $ 103,108 | $ 1,355 |

The decrease in cash used in operations results primarily from increased spending on PH94B and PH10 nonclinical development, manufacturing advancements, and, for PH94B in particular, Phase 3-enabling initiatives as a part of our preparations for the PALISADE Phase 3 program, combined with expansion of our infrastructure by the addition of experienced senior-level executives in manufacturing, clinical and regulatory disciplines in the fourth quarter of Fiscal 2021, offset by the impact of the completion of the Elevate Study, which commenced at the end of the first calendar quarter of 2018 and was operationally completed during the third fiscal quarter of Fiscal 2020. Additionally, cash used in operations during Fiscal 2021 was reduced by the August 2020 receipt of the $5.0 million nondilutive upfront payment from EverInsight under the AffaMed Agreement. Cash used in investing activities in Fiscal 2021 primarily reflects the purchase of certain manufacturing equipment acquired for use by our contract development and manufacturing organization in connection with the production of PH94B drug product. Cash provided by financing activities in Fiscal 2021 primarily reflects net cash proceeds to us from sales of our common stock and Series D Preferred stock pursuant to the December 2020 Public Offering and from sales of our common stock pursuant to the August 2020 Public Offering, the LPC Agreement and the Spring 2020 Private Placement, as well as from the exercise of outstanding warrants, net of routine insurance premium financing note and financing lease payments. We received a Payroll Protection Program loan in April 2020 and voluntarily repaid all principal and accrued interest on the loan in December 2020, following the completion of the December 2020 Public Offering. Cash provided by financing activities in Fiscal 2020 reflects the cash proceeds from our Fall 2019 Private Placement, our Fall 2019 Warrant Offering, the exercise of certain warrants following the modification of their exercise prices, proceeds from our January 2020 Registered Direct Offering and initial transactions under the LPC Agreement, net of routine payments on our insurance premium financing notes and lease.

**Off-Balance Sheet Arrangements**

Other than contractual obligations incurred in the normal course of business, we do not have any off-balance sheet financing arrangements or liabilities, guarantee contracts, retained or contingent interests in transferred assets or any obligation arising out of a material variable interest in an unconsolidated entity. VistaStem has two inactive, wholly owned subsidiaries, Artemis Neuroscience, Inc., a Maryland corporation, and VistaStem Canada, Inc., an Ontario corporation.

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

The disclosures in this section are not required because we qualify as a smaller reporting company under federal securities laws.

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

**INDEX TO CONSOLIDATED FINANCIAL STATEMENTS**

## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

**Opinion on the Financial Statements**

We have audited the accompanying consolidated balance sheets of VistaGen Therapeutics, Inc. (the "Company") as of March 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, cash flows, and stockholders' equity (deficit) for each of the two fiscal years in the period ended March 31, 2021, 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 March 31, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended March 31, 2021**,** in conformity with accounting principles generally accepted in the United States of America.

**Basis for Opinion**

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated 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 consolidated 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 consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

**Critical Audit Matter**

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

*Revenues from Contracts with Customers*

Description of the Matter – License Agreement with AffaMed

As discussed in Note 12 to the consolidated financial statements, the Company recognized approximately $1.1 million in revenue under the license agreement with AffaMed Therapeutics. Inc. ("AffaMed") during the fiscal year ended March 31, 2021. The Company evaluated each of the deliverables identified in the license agreement and determined the license is not distinct within the context of the contract and is combined with development and regulatory approval services; as such, the Company combined the license and promised services into one combined performance obligation.

Auditing management's identification of performance obligations was challenging as the license agreement includes implicit and explicit obligations. Significant judgment was required in the evaluation of the identification of performance obligations and in the determination of whether the identified license and promised services meet the criteria of being distinct and capable of being distinct within the context of the contract. The Company's revenue from its licensing agreement is recognized over time, as the combined performance obligation is satisfied.

We identified license revenue recognition as a critical audit matter because of the judgments necessary for management to: identify performance obligations, determine variable consideration, and determine the timing of recognition for such revenue. Because of the complexity associated with applying the recognition criteria of ASC 606, notably related to identification of performance obligations, determination of variable consideration, and determination of timing of revenue recognition, this required extensive audit effort and a high degree of auditor judgment when performing audit procedures and evaluating the results of those procedures.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to the recognition of license revenue, included the following, among others:

- We evaluated the Company's revenue recognition for the license agreement through an inspection of the agreement and an evaluation of management's revenue recognition analysis corresponding to the license agreement. Our objective was to validate that revenue from the license agreement was recognized in a manner commensurate with the terms of the established agreement and the relevant accounting guidance. Evaluating the reasonableness of management's accounting conclusions involved:
    - Evaluating the accuracy and completeness of the performance obligations identified by management in the license agreement. Management identified one combined performance obligation. We analyzed the license agreement to determine if the arrangement terms that may have an impact on revenue recognition were identified and properly considered in the evaluation of the accounting for the contract. We also inquired of management, and reviewed source documentation, to assess whether the one combined performance obligation identified by management was complete and whether the license and promised services within it were both capable of being distinct and distinct within the context of the contract.
    - Determining the reasonableness of the amounts of variable consideration included within the total transaction price. We analyzed the nature of the combined performance obligation and the contingencies related to the variable consideration in assessing management's methods in estimating the amount of variable consideration to be included in the total transaction price.
    - Testing the measurement of efforts toward satisfaction of the combined performance obligation which included, among other procedures:
        - Reviewing management's revenue schedules for accuracy and completeness by agreeing data to the underlying agreement.
        - Evaluating the manner in which the combined performance obligation was satisfied, and corroborating management estimates and judgments through a review of press releases and third-party data as a potential source of corroborating or contradictory evidence.
        - Discussing management's judgments with the Company's research and development personnel that oversee aspects of the license agreement.

/s/ OUM & CO. LLP

San Francisco, California
June 29, 2021
We have served as the Company's auditor since 2006.

**VISTAGEN THERAPEUTICS, INC.**

**CONSOLIDATED BALANCE SHEETS**
**(Amounts in dollars, except share amounts)**

| | March 31, 2021 | March 31, 2020 |
|---|---|---|
| **ASSETS** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 103,108,300 | $ 1,355,100 |
| Receivable from collaboration partner | 40,600 | - |
| Prepaid expenses and other current assets | 835,100 | 225,100 |
| Deferred contract acquisition costs - current portion | 133,500 | - |
| Total current assets | 104,117,500 | 1,580,200 |
| Property and equipment, net | 367,400 | 209,600 |
| Right of use asset - operating lease | 3,219,600 | 3,579,600 |
| Deferred offering costs | 294,900 | 355,100 |
| Deferred contract acquisition costs - non-current portion | 234,100 | - |
| Security deposits and other assets | 47,800 | 47,800 |
| Total assets | $ 108,281,300 | $ 5,772,300 |
| **LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)** | | |
| Current liabilities: | | |
| Accounts payable | $ 838,300 | $ 1,836,600 |
| Accrued expenses | 1,562,700 | 561,500 |
| Current notes payable | - | 56,500 |
| Deferred revenue - current portion | 1,420,200 | - |
| Operating lease obligation - current portion | 364,800 | 313,400 |
| Financing lease obligation - current portion | 3,000 | 3,300 |
| Total current liabilities | 4,189,000 | 2,771,300 |
| Non-current liabilities: | | |
| Accrued dividends on Series B Preferred Stock | 6,272,700 | 5,011,800 |
| Deferred revenue - non-current portion | 2,490,300 | - |
| Operating lease obligation - non-current portion | 3,350,800 | 3,715,600 |
| Financing lease obligation - non-current portion | - | 3,000 |
| Total non-current liabilities | 12,113,800 | 8,730,400 |
| Total liabilities | 16,302,800 | 11,501,700 |
| Commitments and contingencies (Note 15) | | |
| Stockholders' equity (deficit): | | |
| Preferred stock, $0.001 par value; 10,000,000 shares authorized at March 31, 2021 and 2020: | | |
| Series A Preferred, 500,000 shares authorized, issued and outstanding at March 31, 2021 and 2020 | 500 | 500 |
| Series B Preferred; 4,000,000 shares authorized at March 31, 2021 and 2020; 1,131,669 shares and 1,160,240 shares issued and outstanding at March 31, 2021 and 2020, respectively | 1,100 | 1,200 |
| Series C Preferred; 3,000,000 shares authorized at March 31, 2021 and 2020; 2,318,012 shares issued and outstanding at March 31, 2021 and 2020 | 2,300 | 2,300 |
| Series D Preferred; 2,000,000 shares and no shares authorized at March 31, 2021 and 2020, respectively; 402,149 shares and no shares issued and outstanding at March 31, 2021 and March 31, 2020, respectively | 400 | - |
| Common stock, $0.001 par value; 325,000,000 shares and 175,000,000 shares authorized at March 31, 2021 and 2020, respectively; 180,751,234 and 49,348,707 shares issued at March 31, 2021 and 2020, respectively | 180,800 | 49,300 |
| Additional paid-in capital | 315,603,100 | 200,092,800 |
| Treasury stock, at cost, 135,665 shares of common stock held at March 31, 2021 and 2020 | (3,968,100) | (3,968,100) |
| Accumulated deficit | (219,841,600) | (201,907,400) |
| Total stockholders' equity (deficit) | 91,978,500 | (5,729,400) |
| Total liabilities and stockholders' equity (deficit) | $ 108,281,300 | $ 5,772,300 |

See accompanying notes to consolidated financial statements.

**VISTAGEN THERAPEUTICS, INC.**

**CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS**
**(Amounts in dollars, except share amounts)**

| | Fiscal Years Ended March 31, | |
|---|---|---|
| | **2021** | **2020** |
| Sublicense revenue | $ 1,089,500 | $ - |
| Total revenues | 1,089,500 | - |
| Operating expenses: | | |
| Research and development | 12,476,400 | 13,374,200 |
| General and administrative | 6,546,900 | 7,427,300 |
| Total operating expenses | 19,023,300 | 20,801,500 |
| Loss from operations | (17,933,800) | (20,801,500) |
| Other income and expenses, net: | | |
| Interest income, net | 1,600 | 30,100 |
| Other income | 600 | - |
| Loss before income taxes | (17,931,600) | (20,771,400) |
| Income taxes | (2,600) | (2,600) |
| Net loss and comprehensive loss | $ (17,934,200) | $ (20,774,000) |
| | | |
| Accrued dividends on Series B Preferred stock | (1,385,600) | (1,263,600) |
| Beneficial conversion feature on Series D Preferred stock | (23,000,000) | - |
| Net loss attributable to common stockholders | $ (42,319,800) | $ (22,037,600) |
| | | |
| Basic and diluted net loss attributable to common stockholders per common share | $ (0.49) | $ (0.50) |
| | | |
| Weighted average shares used in computing basic and diluted net loss attributable to common stockholders per common share | 86,133,644 | 43,869,523 |

See accompanying notes to consolidated financial statements.

**VISTAGEN THERAPEUTICS, INC.**

**CONSOLIDATED STATEMENTS OF CASH FLOWS**
**(Amounts in dollars)**

| | Fiscal Years Ended March 31, | |
|---|---|---|
| | **2021** | **2020** |
| Cash flows from operating activities: | | |
| Net loss | $ (17,934,200) | $ (20,774,000) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Depreciation and amortization | 117,600 | 103,100 |
| Stock-based compensation | 2,306,100 | 3,820,800 |
| Expense related to modification of warrants | - | 826,900 |
| Amortization of fair value of common stock issued for services | - | 92,100 |
| Amortization of fair value of warrants issued for services | - | 13,800 |
| Changes in operating assets and liabilities: | | |
| Receivable from collaboration partner or supplier | (40,600) | 300,000 |
| Prepaid expenses and other current assets | (287,800) | 182,600 |
| Right of use asset - operating lease | 360,000 | 335,400 |
| Operating lease liability | (313,500) | (267,000) |
| Deferred sublicense revenue, net of deferred contract acquisition costs | 3,667,900 | - |
| Accounts payable and accrued expenses | 51,000 | (390,700) |
| Net cash used in operating activities | (12,073,500) | (15,757,000) |
| Cash flows from property and investing activities: | | |
| Purchases of manufacturing and other equipment | (275,400) | - |
| Net cash used in investing activities | (275,400) | - |
| Cash flows from financing activities: | | |
| Net proceeds from issuance of common stock and Series D Preferred stock | 93,675,200 | - |
| Net proceeds from issuance of common stock and warrants, including Units | 12,957,800 | 3,349,000 |
| Net proceeds from exercise of warrants | 5,009,500 | 410,000 |
| Proceeds from sale of warrants | - | 300,000 |
| Net proceeds from sale of common stock under equity line | 2,841,600 | 249,400 |
| Proceeds from issuance of note under Payroll Protection Plan | 224,400 | - |
| Repayment of capital lease obligations | (3,300) | (3,000) |
| Repayment of notes payable, including Payroll Protection Plan note | (603,100) | (293,600) |
| Net cash provided by financing activities | 114,102,100 | 4,011,800 |
| Net increase (decrease) in cash and cash equivalents | 101,753,200 | (11,745,200) |
| Cash and cash equivalents at beginning of period | 1,355,100 | 13,100,300 |
| Cash and cash equivalents at end of period | $ 103,108,300 | $ 1,355,100 |
| Supplemental disclosure of cash flow activities: | | |
| Cash paid for interest | $ 13,300 | $ 14,800 |
| Cash paid for income taxes | $ 2,600 | $ 2,600 |
| Supplemental disclosure of noncash activities: | | |
| Insurance premiums settled by issuing note payable | $ 322,200 | $ 292,800 |
| Accrued dividends on Series B Preferred | $ 1,385,600 | $ 1,263,600 |
| Accrued dividends on Series B Preferred settled upon conversion by issuance of common stock | $ 124,600 | $ - |

See accompanying notes to consolidated financial statements.

**VISTAGEN THERAPEUTICS, INC.**

**CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)**

**Fiscal Years Ended March 31, 2020 and 2021**
**(Amounts in dollars, except share amounts)**

| | Series A Preferred Stock | | Series B Preferred Stock | | Series C Preferred Stock | | Series D Preferred Stock | | Common Stock | | Additional Paid-in | Treasury | Accumulated | Total Stockholders' Equity |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | Shares | Amount | Shares | Amount | Shares | Amount | Capital | Stock | Deficit | (Deficit) |
| **Balances at March 31, 2019** | **500,000** | **$ 500** | **1,160,240** | **$ 1,200** | **2,318,012** | **$ 2,300** | **-** | **$ -** | **42,758,630** | **$ 42,800** | **$192,129,900** | **$(3,968,100)** | **$(181,133,400)** | **$ 7,075,200** |
| Proceeds from sale of units of common stock and warrants for cash in private placements | - | - | - | - | - | - | - | - | 650,000 | 600 | 649,400 | - | - | 650,000 |
| Proceeds from sale of warrants in private placement | - | - | - | - | - | - | - | - | | | 300,000 | - | - | 300,000 |
| Proceeds from sale of units of common stock and warrants for cash in public offering and concurrent private placement | - | - | - | - | - | - | - | - | 3,870,077 | 3,900 | 2,695,100 | - | - | 2,699,000 |
| Issuance of commitment shares and net proceeds of initial sale of common stock under equity line | - | - | - | - | - | - | - | - | 1,250,000 | 1,200 | 525,100 | - | - | 526,300 |
| Proceeds from exercise of warrants | - | - | - | - | - | - | - | - | 820,000 | 800 | 409,200 | - | - | 410,000 |
| Accrued dividends on Series B Preferred stock | - | - | - | - | - | - | - | - | - | - | (1,263,600) | - | - | (1,263,600) |
| Stock-based compensation expense | - | - | - | - | - | - | - | - | - | - | 3,820,800 | - | - | 3,820,800 |
| Increase in fair value attributed to warrant modifications and additional warrants issued | - | - | - | - | - | - | - | - | - | - | 826,900 | - | - | 826,900 |
| | | | | | | | | | | | | | | - |
| Net loss for the fiscal year ended March 31, 2020 | - | - | - | - | - | - | - | - | - | - | - | - | (20,774,000) | (20,774,000) |
| **Balances at March 31, 2020** | **500,000** | **$ 500** | **1,160,240** | **$ 1,200** | **2,318,012** | **$ 2,300** | **-** | **$ -** | **49,348,707** | **$ 49,300** | **$200,092,800** | **$(3,968,100)** | **$(201,907,400)** | **$ (5,729,400)** |
| Net proceeds from sale of common stock under equity line | - | - | - | - | - | - | - | - | 6,301,995 | 6,300 | 2,790,500 | - | - | 2,796,800 |
| Net proceeds from sale of common stock in public offering | - | - | - | - | - | - | - | - | 17,868,250 | 17,900 | 12,887,200 | - | - | 12,905,100 |
| Net proceeds from sale of common stock and Series D Preferred stock in public offering | - | - | - | - | - | - | 2,000,000 | 2,000 | 63,000,000 | 63,000 | 93,582,900 | - | - | 93,647,900 |
| Net proceeds from exercise of warrants | - | - | - | - | - | - | - | - | 6,624,302 | 6,600 | 5,002,900 | - | - | 5,009,500 |
| Comversion of Series D Preferred stock to common stock | - | - | - | - | - | - | (1,597,851) | (1,600) | 36,750,573 | 36,800 | (35,200) | - | - | - |
| Comversion of Series B Preferred stock to common stock and payment of accrued dividends in common stock | - | - | (28,571) | (100) | - | - | - | - | 188,633 | 200 | 124,500 | - | - | 124,600 |
| Accrued dividends on Series B Preferred stock | - | - | - | - | - | - | - | - | - | - | (1,385,600) | - | - | (1,385,600) |
| Stock-based compensation expense | - | - | - | - | - | - | - | - | - | - | 2,306,100 | - | - | 2,306,100 |
| Sale of common stock pursuant to 2019 Employee Stock Purchase Plan | - | - | - | - | - | - | - | - | 58,125 | 100 | 26,100 | - | - | 26,200 |
| Issuance of common stock upon cashless exercise of stock options | - | - | - | - | - | - | - | - | 222,004 | 200 | (200) | - | - | - |
| Net proceeds from exercise of stock options for cash | - | - | - | - | - | - | - | - | 30,000 | - | 36,500 | | | 36,500 |
| Issuance of common stock at fair value for professional services | - | - | - | - | - | - | - | - | 233,645 | 200 | 124,800 | - | - | 125,000 |
| Beneficial conversion feature on Series D Preferred stock | - | - | - | - | - | - | - | - | - | - | 23,000,000 | - | - | 23,000,000 |
| Deemed dividend from beneficial conversion feature of Series D Preferred Stock | - | - | - | - | - | - | - | - | - | - | (23,000,000) | - | - | (23,000,000) |
| Net loss for the fiscal year ended March 31, 2021 | - | - | - | - | - | - | - | - | - | - | | - | (17,934,200) | (17,934,200) |
| **Balances at March 31, 2021** | **500,000** | **$ 500** | **1,131,669** | **$ 1,100** | **2,318,012** | **$ 2,300** | **402,149** | **$ 400** | **180,751,234** | **$ 180,800** | **$315,603,100** | **$(3,968,100)** | **$(219,841,600)** | **$91,978,500** |

See accompanying notes to consolidated financial statements.

## 1. Description of Business

### Overview

VistaGen Therapeutics, Inc., a Nevada corporation (which may be referred to as *VistaGen*, the *Company*, *we*, *our*, or *us*), is a biopharmaceutical company committed to developing and commercializing differentiated new generation medications that go beyond the current standard of care for widespread anxiety, depression and other central nervous system (*CNS*) disorders. Our CNS pipeline includes three CNS product candidates, PH94B Nasal Spray, PH10 Nasal Spray and AV-101, each with a differentiated profile, favorable safety results observed in all clinical studies to date and therapeutic potential in multiple CNS indications. PH94B Nasal Spray (*PH94B*) is being developed for multiple anxiety disorders. We recently initiated our PH94B Phase 3 development program, which we refer to as the PALISADE program, with PALISADE-1, a U.S., multi-center, randomized, double-blind, placebo-controlled Phase 3 clinical study to evaluate the efficacy and safety of PH94B for the acute treatment of anxiety in adults with social anxiety disorder (*SAD*), as well as preparations for the additional studies required to support our potential U.S. New Drug Application (*NDA*) for that indication should the PALISADE Phase 3 program be successful. We are also preparing for exploratory Phase 2A clinical studies of PH94B in adults experiencing several other anxiety disorders. PH10 Nasal Spray (*PH10*) is being developed as a stand-alone treatment for multiple depression disorders. Exploratory Phase 2A clinical development of PH10 for major depressive disorder (*MDD*) has been completed. We are now preparing for planned Phase 2B clinical development of PH10 for this indication. We are preparing for a Phase 1B clinical study of AV-101 in combination with probenecid to assess potential future Phase 2A clinical development of the combination for MDD or certain neurological indications. Our goal is to become a biopharmaceutical company that develops and commercializes innovative CNS therapies for highly prevalent neuropsychiatry and neurology indications where current treatments options are inadequate to meet the needs of millions of patients in markets worldwide.

### Our Product Candidates

PH94B is a synthetic investigational neurosteroid developed from proprietary compounds called pherines. With its novel mechanism of action, PH94B is an odorless nasal spray administered at microgram-level doses to achieve rapid-onset anti-anxiety, or anxiolytic, effects. The pharmacological activity of PH94B is fundamentally differentiated from that of all FDA-approved anti-anxiety drugs, including all antidepressants approved by the U.S. Food and Drug Administration (*FDA*) for treatment of SAD, as well as all benzodiazepines and beta blockers prescribed on an off-label basis. PH94B engages peripheral chemosensory receptors in nasal passages that trigger a subset of neurons in the main olfactory bulbs (*OB*) at the base of the brain. The OB neurons then stimulate inhibitory GABAergic neurons in the limbic amygdala, decreasing the activity of the sympathetic nervous system, and facilitating fear extinction activity of the limbic-hypothalamic system, the main fear and anxiety center in the brain, as well as in other parts of the brain. Importantly, PH94B does not require systemic uptake and distribution to produce its rapid-onset anti-anxiety effects. Our ongoing PALISADE Phase 3 program for PH94B is designed to further demonstrate its potential as a fast-acting, non-sedating, non-addictive acute treatment of anxiety in adults with SAD. We believe PH94B also has potential to be developed as a novel treatment for adjustment disorder with anxiety, postpartum anxiety, post-traumatic stress disorder, procedural anxiety, panic and other anxiety disorders. PH94B has been granted Fast Track designation status by the FDA for development for the acute treatment of SAD.

PH10 is a synthetic investigational neurosteroid, which also was developed from proprietary compounds called pherines. Its novel, rapid-onset mechanism of action (*MOA*) is fundamentally differentiated from the MOA of all current treatments for MDD and other depression disorders. PH10 is self-administered at microgram-level doses as an odorless nasal spray. PH10 activates nasal chemosensory cells in the nasal passages, connected to neural circuits in the brain that produce antidepressant effects. Specifically, PH10 engages peripheral chemosensory receptors in the nasal passages that trigger a subset of neurons in the main OB that stimulate neurons in the limbic amygdala. This is turn increases activity of the limbic-hypothalamic sympathetic nervous system and increases the release of catecholamines. Importantly, unlike all currently approved oral antidepressants (*ADs*), PH10 does not require systemic uptake and distribution to produce rapid-onset of antidepressant effects. In all clinical studies to date, PH10 has not caused psychological side effects (such as dissociation and hallucinations) or safety concerns that may be associated with rapid-onset ketamine-based therapy (*KBT*), including intravenous ketamine or intranasal ketamine (esketamine). We believe PH10 has potential to be a new stand-alone treatment for MDD and several other depression disorders.

AV-101 (4-Cl-KYN) targets the NMDAR (N-methyl-D-aspartate receptor), an ionotropic glutamate receptor in the brain. Abnormal NMDAR function is associated with numerous CNS diseases and disorders. AV-101 is an oral prodrug of 7-chloro-kynurenic acid (7-Cl-KYNA), which is a potent and selective full antagonist of the glycine co-agonist site of the NMDAR that inhibits the function of the NMDAR. However, unlike ketamine and many other NMDAR antagonists, 7-Cl-KYNA is not an ion channel blocker. At doses administered in all studies to date, AV-101 has been observed to be well tolerated and has not exhibited dissociative or hallucinogenic psychological side effects or safety concerns. In light of these observations and findings from preclinical studies, we believe that AV-101, in combination with FDA-approved probenecid, has potential to become a new oral treatment alternative for certain CNS indications involving the NMDAR. We are currently preparing to evaluate AV-101 in combination with probenecid in a Phase 1B clinical study. The FDA has granted Fast Track designation for development of AV-101 as a potential adjunctive treatment for MDD and as a non-opioid treatment for neuropathic pain (*NP*).

**Subsidiaries**

VistaGen Therapeutics, Inc., a California corporation d/b/a VistaStem (*VistaStem*),is our wholly-owned subsidiary. Our Consolidated Financial Statements in this Annual Report on Form 10-K (*Annual Report*) also include the accounts of VistaStem's two wholly-owned inactive subsidiaries, Artemis Neuroscience, Inc., a Maryland corporation, and VistaStem Canada, Inc., a corporation organized under the laws of Ontario, Canada.

**2. Basis of Presentation and Going Concern**

The accompanying Consolidated Financial Statements have been prepared assuming that we will continue as a going concern. As a clinical-stage biopharmaceutical company having not yet developed commercial products or achieved sustainable revenues, we have experienced negative cash flows from operations and recurring losses resulting in a deficit of $242.8 million accumulated from inception (May 1998) through March 31, 2021. We expect losses and negative cash flows from operations to continue for the foreseeable future as we engage in further development of PH94B, PH10 and AV-101.

Since our inception in May 1998 through March 31, 2021, we have financed our operations and technology acquisitions primarily through the issuance and sale of our equity and debt securities for cash proceeds of approximately $197.8 million, as well as from an aggregate of approximately $22.7 million of government research grant awards (excluding the fair market value of government sponsored and funded clinical trials), strategic collaboration payments, intellectual property licensing and other revenues. Additionally, we have issued equity securities with an approximate value at issuance of $38.2 million in noncash acquisitions of product licenses and in settlements of certain liabilities, including liabilities for professional services rendered to us or as compensation for such services.

*Recent Developments*

As described more completely in Note 9, *Capital Stock*, in December 2020, we entered into an underwriting agreement (the *December 2020 Underwriting Agreement*) pursuant to which we sold, in an underwritten public offering (the *December 2020 Public Offering*), 63,000,000 shares of our common stock at a public offering price of $0.92 per share and 2,000,000 shares of a newly issued series of convertible preferred stock (*Series D Preferred)* and, together with the common stock, the *Securities*) at a public offering price of $21.16 per share, resulting in gross proceeds to us of $100 million. Net proceeds to us from the securities sold in the December 2020 Public Offering, after deducting underwriting discounts and commissions and offering expenses payable by us, was approximately $93.6 million.

As also described more completely in Note 9, *Capital Stock*, in August 2020, we entered into an underwriting agreement (the August 2020 *Underwriting Agreement*) pursuant to which we sold, in an underwritten public offering (the *August 2020 Public Offering*), an aggregate of 15,625,000 shares of our common stock at a public offering price of $0.80 per share, resulting in gross proceeds to us of $12,500,000. Under the terms of the August 2020 Underwriting Agreement, we granted to the underwriter an over-allotment option (the *Over-Allotment Option*) to purchase up to an additional 2,343,750 shares of common stock at a public offering price of $0.80 per share. The underwriter exercised the Over-Allotment Option with respect to 2,243,250 shares (the *Exercised Option Shares*), resulting in additional gross proceeds to us of $1,794,600. Aggregate net proceeds to us from the August 2020 Public Offering, after deducting underwriting discounts and commissions and offering expenses payable by us, were approximately $12.9 million.

As more completely described in Note 12, *Licensing, Sublicensing and Collaboration Agreements*, in June 2020, we entered into a strategic licensing and collaboration agreement for the clinical development and commercialization of PH94B for acute treatment of anxiety in adults with SAD and other potential anxiety-related disorders (the *EverInsight Agreement*), with EverInsight Therapeutics Inc., (*EverInsight*), a biopharmaceutical company focused on developing and commercializing transformative pharmaceutical products for patients in Greater China and other parts of Asia, and funded by CBC Group, a global healthcare-focused venture capital firm. Subsequent to entering into the EverInsight Agreement, in October 2020, EverInsight merged with AffaMed Therapeutics, also funded by CBC Group, which as a combined, complementary entity is focusing on developing and commercializing therapeutics to address ophthalmologic and CNS disorders in Greater China and beyond. Accordingly, we are now referring to EverInsight and the EverInsight Agreement as AffaMed and the AffaMed Agreement, respectively. Under the terms of the AffaMed Agreement, AffaMed agreed to make a non-dilutive upfront license payment of $5.0 million to us, which we received in August 2020. The $5.0 million upfront license payment resulted in net cash proceeds to us of approximately $4.655 million after the sublicense payment we agreed to make to Pherin Pharmaceuticals, Inc. (*Pherin*) pursuant to our PH94B license from Pherin, and payment for consulting services related to the AffaMed Agreement.

Additionally, as described in Note 9, *Capital Stock*, on March 24, 2020, we entered into a purchase agreement and a registration rights agreement with Lincoln Park Capital Fund (*Lincoln Park*) pursuant to which Lincoln Park committed to purchase up to $10,250,000 of our common stock at market-based prices over a period of 24 months (the *LPC Agreement*). To satisfy our obligations under the registration rights agreement, we filed a Registration Statement on Form S-1 (the *LPC Registration Statement*) with the Securities and Exchange Commission (the *SEC*) on March 31, 2020, which the SEC declared effective on April 14, 2020 (Registration No. 333-237514). Subsequent to the effectiveness of the LPC Registration Statement and through July 2020, we sold 6,301,995 registered shares of our common stock to Lincoln Park and received gross cash proceeds of $2,891,200. We have not sold any shares of our common stock pursuant to the Lincoln Park Agreement since July 2020.

As also described in Note 9, *Capital Stock*, between December 2020 and March 31, 2021, certain holders of outstanding warrants exercised such warrants to purchase an aggregate of 6,396,302 shares of our common stock and we received cash proceeds of $4,924,800 from such exercises. As disclosed in Note 16, *Subsequent Events*, since March 31, 2021, holders of outstanding warrants have exercised warrants to purchase an additional 1,508,768 shares of our common stock and we have received cash proceeds of approximately $1,105,700.

*Liquidity and Capital Resources*

During the fiscal year ended March 31, 2021, we received approximately $119 million in net cash proceeds from the transactions described above. At March 31, 2021, we had cash and cash equivalents of approximately $103.1 million, which we believe is sufficient to fund our planned operations for well beyond the twelve months following the issuance of these financial statements, and indicating our ability to continue as a going concern. Nevertheless, we have not yet developed products that generate recurring revenue and, assuming successful completion of our planned clinical and nonclinical programs, we will need to invest substantial additional capital resources to commercialize any of them.

During the next twelve months, we plan to (i) continue PALISADE-1 and prepare for and initiate multiple studies in our PALISADE Phase 3 program for development and commercialization of PH94B as an acute treatment of anxiety in adult patients with SAD, (ii) prepare for and initiate multiple small exploratory Phase 2A studies of PH94B in additional anxiety disorders, (iii) prepare for and initiate a Phase 2B clinical study of PH10 as a potential stand-alone treatment for MDD, (iv) prepare for and initiate a Phase 1B clinical study of AV-101 in combination with probenecid to enable assessment of potential exploratory Phase 2A development of the combination in MDD and certain neurological disorders, and (v) conduct nonclinical studies involving PH94B, PH10 and AV-101.

Although we believe our current cash position is sufficient to fund our planned operations for more than the next twelve months following the issuance of this Annual Report, when necessary and advantageous, we may raise additional capital through the sale of our equity securities in one or more (i) public offerings (ii) private placements to accredited investors, and/or (iii) in strategic licensing and development collaborations involving one or more of our drug candidates in markets outside the United States, similar to the AffaMed Agreement. Subject to certain restrictions, our Registration Statement on Form S-3 (Registration No. 333-254299) (the *S-3 Registration Statement*), which became effective on March 26, 2021, remains available for future sales of our equity securities in one or more public offerings from time to time. While we may make additional sales of our equity securities under the S-3 Registration Statement, we do not have an obligation to do so.

In addition to the potential sale of our equity securities, we may also seek to enter research, development and/or commercialization collaborations similar to the AffaMed Agreement and the Bayer Agreement (defined in Note 12, below) to provide funding, including non-dilutive funding, for development of one or more of our CNS product candidate programs. We may also seek additional government grant awards or agreements similar to our prior agreement with the U.S. National Institutes of Health (*NIH*), Baylor University and the U.S. Department of Veterans Affairs in connection with certain government-sponsored studies of AV-101. Such strategic collaborations may provide non-dilutive resources to advance our strategic initiatives while reducing a portion of our future cash outlays and working capital requirements. We may also pursue intellectual property arrangements similar to the AffaMed Agreement and the Bayer Agreement with other parties. Although we may seek additional collaborations that could generate revenue and/or provide non-dilutive funding for development of our product candidates, as well as new government grant awards and/or agreements, no assurance can be provided that any such collaborations, awards or agreements will occur in the future.

Our future working capital requirements will depend on many factors, including, without limitation, potential impacts related to the current COVID-19 pandemic, the scope and nature of opportunities related to our success and the success of certain other companies in nonclinical and clinical trials, including our development and commercialization of our current product candidates and various applications of our stem cell technology platform, the availability of, and our ability to obtain, government grant awards and agreements, and our ability to enter into collaborations on terms acceptable to us. To further advance the clinical development of PH94B, PH10, and AV-101 and, to a lesser extent, our stem cell technology platform, as well as support our operating activities, we plan to continue to carefully manage our routine operating costs, including our employee headcount and related expenses, as well as costs relating to regulatory consulting, contract manufacturing, research and development, investor and public relations, business development, legal, intellectual property acquisition and protection, public company compliance and other professional services and operating costs.

Notwithstanding the foregoing, there can be no assurance that our current strategic collaborations under the AffaMed Agreement and/or the Bayer Agreement will generate revenue from future potential milestone payments, or that future financings or government or other strategic collaborations will be available to us in sufficient amounts, in a timely manner, or on terms acceptable to us, if at all. If we are unable to obtain additional financing on a timely basis when needed, our business, financial condition, and results of operations may be harmed, the price of our stock may decline, we may be required to reduce, defer, or discontinue certain of our research and development activities and we may not be able to continue as a going concern.

**3. Summary of Significant Accounting Policies**

***Use of Estimates***

The preparation of financial statements in conformity with U.S. generally accepted accounting principles (*U.S. GAAP*) requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates. Significant estimates include, but are not limited to, those relating to stock-based compensation, revenue recognition, research and development expenses, determination of right of use assets under lease transactions and related lease obligations, and the assumptions used to value warrants, warrant modifications and useful lives for property and equipment and related depreciation calculations.

***Principles of Consolidation***

The accompanying consolidated financial statements include the Company's accounts, VistaStem's accounts and the accounts of VistaStem's two wholly-owned inactive subsidiaries, Artemis Neurosciences and VistaStem Canada. All material intercompany accounts and transactions have been eliminated in consolidation.

***Cash and Cash Equivalents***

Cash and cash equivalents are considered to be highly liquid investments with maturities of three months or less at the date of purchase.

***Property and Equipment***

Property and equipment is stated at cost. Repairs and maintenance costs are expensed in the period incurred. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets. The estimated useful lives of laboratory, information technology and office equipment range from three to seven years; the estimated useful lives of manufacturing equipment ranges from five to ten years. Leasehold improvements are amortized over the shorter of the lease term or the useful life of the improvements.

***Impairment of Long-Lived Assets***

Our long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that we consider in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in our use of the assets. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows. To date, we have not recorded any impairment losses on long-lived assets.

***Deferred Offering Costs***

Deferred offering costs are expenses directly related to our current S-3 Registration Statement (the *Shelf Registration*), which became effective on March 26, 2021, and expenses transferred from our predecessor registration statement on Form S-3, and the LPC Registration Statement which became effective on April 14, 2020. These costs consist of legal, accounting, printing, SEC filing fees, and, as appropriate, Nasdaq filing fees, and, in the case of the LPC Registration Statement, the issuance-date fair value of certain shares of our common stock issued to Lincoln Park under the terms of the LPC Agreement. Deferred costs associated with the Shelf Registration are reclassified to additional paid-in capital on a pro-rata basis as we complete offerings under the S-3 Registration Statement, with any remaining deferred costs to be charged to results of operations at the end of the three-year life of the S-3 Registration Statement. During the fiscal years ended March 31, 2021 and 2020, we charged deferred offering costs of $15,800 and $300, respectively, to additional paid-in capital as a result of offerings under the Shelf Registration. Deferred costs associated with the LPC Registration Statement are reclassified to additional paid-in capital on a pro-rata basis as we complete sales of our common stock pursuant to the LPC Agreement, with any remaining deferred costs to be charged to results of operations at the end of the two-year life of the LPC Agreement. We charged deferred offering costs of $94,400 and $8,100 to additional paid-in capital during the fiscal years ended March 31, 2021 and 2020, respectively, as a result of sales of our common stock under the LPC Agreement.

***Revenue Recognition***

Our primary source of revenue for the fiscal year ended March 31, 2021 is from the AffaMed Agreement involving clinical development and commercialization of PH94B for acute treatment of anxiety in adults with SAD, and potentially other anxiety-related disorders, in Greater China, South Korea, and Southeast Asia. The terms of the AffaMed Agreement include a $5.0 million non-refundable upfront license fee which we received in August 2020, potential payments based upon achievement of certain development and commercial milestones, and royalties on product sales. We have historically generated revenue principally from collaborative research and development arrangements, licensing and technology transfer agreements, including strategic licenses or sublicenses, and government grants. We adopted Accounting Standards Update (*ASU*) No. 2014-09, *Revenue from Contracts with Customers (Topic 606)* and its related amendments, collectively referred to as ASC (*Accounting Standards Codification*) Topic 606, as of April 1, 2018, using the modified retrospective transition method. We did not recognize any revenue under the Bayer Agreement (defined in Note 12) which we entered in our fiscal year ended March 31, 2017, in the fiscal years ended March 31, 2021 or 2020. Upon adoption of ASC Topic 606, there was no change to the units of accounting previously identified with respect to the Bayer Agreement under legacy GAAP, which are now considered performance obligations under ASC Topic 606, and there was no change to the revenue recognition pattern for the performance obligation. Accordingly, there was no cumulative effect change to our opening accumulated deficit upon the adoption of ASC Topic 606.

Under ASC Topic 606, we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration that we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of Topic 606, we perform the following five steps: (i) identify the contract with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration to which we are entitled in exchange for the goods or services we transfer to a customer.

Once a contract is determined to be within the scope of Topic 606, we assess the goods or services promised within each contract and determine those that are performance obligations. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. We assess whether these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right may be accounted for as a contract modification or as a continuation of the contract for accounting purposes.

We assess whether each promised good or service is distinct for the purpose of identifying the performance obligations in the contract. This assessment involves subjective determinations and requires judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (that is, the good or service is capable of being distinct) and (ii) our promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract). In assessing whether a promised good or service is distinct in the evaluation of a collaboration arrangement subject to Topic 606, we consider factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. We also consider the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, we are required to combine that good or service with other promised goods or services until we identify a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices (*SSP*) on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and satisfaction of the performance obligations. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, we consider applicable market conditions and relevant Company-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. In certain circumstances, we may apply the residual method to determine the SSP of a good or service if the standalone selling price is considered highly variable or uncertain. We validate the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, we estimate the amount of consideration to which we will be entitled in exchange for transferring the promised goods or services to a customer. We determine the amount of variable consideration by using the expected value method or the most likely amount method. We include the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, we re-evaluate the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development and regulatory milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received.

In determining the transaction price, we adjust consideration for the effects of the time value of money if the timing of payments provides us with a significant benefit of financing. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensee and the transfer of the promised goods or services to the licensee will be one year or less. For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time, based on the use of an output or input method.

***Research and Development Expenses***

Research and development expenses are composed of both internal and external costs. Internal costs include salaries and employment-related expenses, including stock-based compensation expense, of scientific personnel and direct project costs. External research and development expenses consist primarily of costs associated with clinical and nonclinical development of PH94B, PH10 and AV-101, stem cell research and development costs, and costs related to the application and prosecution of patents related to AV-101 and our stem cell technology platform. All such costs are charged to expense as incurred.

We also record accruals for estimated ongoing clinical trial costs. Clinical trial costs represent costs incurred by contract research organizations (*CRO*s) and clinical trial sites. Progress payments are generally made to CROs, clinical sites, investigators and other professional service providers. We analyze the progress of the clinical trial, including levels of subject enrollment, invoices received and contracted costs when evaluating the adequacy of accrued liabilities. Significant judgments and estimates must be made in determining the clinical trial accrual in any reporting period. Actual results could differ from those estimates under different assumptions. Revisions are charged to research and development expense in the period in which the facts that give rise to the revision become known.

Costs incurred in obtaining product or technology licenses are charged immediately to research and development expense if the product or technology licensed has not achieved regulatory approval or reached technical feasibility and has no alternative future uses. In September 2018, we acquired an exclusive license to develop and commercialize PH94B and an option to acquire a license to develop and commercialize PH10 by issuing an aggregate of 1,630,435 unregistered shares of our common stock having a fair market value of $2,250,000. In October 2018, we exercised our option to acquire an exclusive license to develop and commercialize PH10 by issuing 925,926 shares of our unregistered common stock having a fair market value of $2,000,000. Since, at the date of each acquisition, neither product candidate had achieved regulatory approval and each required significant additional development and expense, we recorded the costs related to acquiring the licenses and the option as research and development expense.

***Stock-Based Compensation***

We recognize compensation cost for all stock-based awards to employees and non-employee consultants based on the grant date fair value of the award. We record stock-based compensation expense over the period during which the employee or other grantee is required to perform services in exchange for the award, which generally represents the scheduled vesting period. We have not granted restricted stock awards to employees or consultants nor do we have any awards with market or performance conditions. Prior to our April 1, 2019 adoption of ASU 2018-07, *Compensation-Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting* (*ASU 2018-07*), we historically re-measured the fair value of option grants to non-employees as they vested and any resulting increase in value was recognized as an expense during the period over which the services were performed. Under ASU 2018-17, expense recognition for grants to non-employees now follows the same methodology as for employees. Noncash expense attributable to compensatory grants of our common stock to non-employees is determined by the quoted market price of the stock on the date of grant and is either recognized as fully-earned at the time of the grant or expensed ratably over the term of the related service agreement, depending on the terms of the specific agreement.

***Income Taxes***

We account for income taxes using the asset and liability approach for financial reporting purposes. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. Valuation allowances are established, when necessary, to reduce the deferred tax assets to an amount expected to be realized.

***Right of Use Assets and Operating Lease Obligations***

We adopted Accounting Standards Update No. 2016-02, *"Leases (Topic 842)"* (*ASU 2016-02*) effective April 1, 2019. ASU 2016-02 requires that we determine, at the inception of an arrangement, whether the arrangement is or contains a lease, based on the unique facts and circumstances present. Operating lease assets represent our right to use an underlying asset for the lease term (*Right of use assets*) and operating lease liabilities represent our obligation to make lease payments arising from the lease. Right of use assets and operating lease liabilities are recognized at the commencement date of the lease based upon the present value of lease payments over the lease term. When determining the lease term, we include options to extend or terminate the lease when it is reasonably certain, at inception, that we will exercise that option. The interest rate implicit in lease contracts is typically not readily determinable; accordingly, we use our incremental borrowing rate, which is the rate that would be incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment, based upon the information available at the commencement date. The lease payments used to determine our operating lease assets may include lease incentives, stated rent increases and escalation clauses linked to rates of inflation, when determinable, and are recognized in determining our Right of use assets. Our operating lease is reflected in the Right-of-use asset – operating lease; Operating lease obligation - current portion; and Operating lease obligation - non-current portion in our consolidated balance sheets.

Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term. As a result of our adoption of ASU 2016-02, we no longer recognize deferred rent on the consolidated balance sheet. Short-term leases, defined as leases that have a lease term of 12 months or less at the commencement date, are excluded from this treatment and are recognized on a straight-line basis over the term of the lease. Variable lease payments are amounts owed by us to a lessor that are not fixed, such as reimbursement for common area maintenance costs for our facility lease; and are expensed when incurred.

Financing leases, formerly referred to as capitalized leases, are treated similarly to operating leases except that the asset subject to the lease is included in the appropriate fixed asset category, rather than recorded as a Right of use asset, and depreciated over its estimated useful life, or lease term, if shorter.

***Concentrations of Credit Risk***

Financial instruments, which potentially subject us to concentrations of credit risk, consist of cash and cash equivalents. Our investment policies limit any such investments to short-term, low-risk instruments. We deposit cash and cash equivalents with quality financial institutions which are insured to the maximum of federal limitations. Balances in these accounts may exceed federally insured limits at times.

***Fair Value Measurements***

We do not use derivative instruments for hedging of market risks or for trading or speculative purposes. When applicable, we follow the principles of fair value accounting as they relate to our financial assets and financial liabilities. Fair value is defined as the estimated exit price received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date, rather than an entry price that represents the purchase price of an asset or liability. Where available, fair value is based on observable market prices or parameters or derived from such prices or parameters. Where observable prices or inputs are not available, valuation models are applied. These valuation techniques involve some level of management estimation and judgment, the degree of which is dependent on several factors, including the instrument's complexity. The required fair value hierarchy that prioritizes observable and unobservable inputs used to measure fair value into three broad levels is described as follows:

- *Level 1* — Quoted prices (unadjusted) in active markets that are accessible at the measurement date for assets or liabilities. The fair value hierarchy gives the highest priority to Level 1 inputs.

- *Level 2* — Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

- *Level 3* — Unobservable inputs (*i.e.*, inputs that reflect the reporting entity's own assumptions about the assumptions that market participants would use in estimating the fair value of an asset or liability) are used when little or no market data is available. The fair value hierarchy gives the lowest priority to Level 3 inputs.

A financial instrument's categorization within the valuation hierarchy is based upon the lowest level of input that is significant to the fair value measurement. Where quoted prices are available in an active market, securities are classified as Level 1 of the valuation hierarchy. If quoted market prices are not available for the specific financial instrument, then we estimate fair value by using pricing models, quoted prices of financial instruments with similar characteristics or discounted cash flows. In certain cases where there is limited activity or less transparency around inputs to valuation, financial assets or liabilities are classified as Level 3 within the valuation hierarchy.

We carried no assets or liabilities that are measured on a recurring basis at fair value at March 31, 2021 or 2020.

***Warrants Issued in Connection with Equity Financing***

We generally account for warrants issued in connection with equity financings as a component of equity, unless there is a deemed possibility that we may have to settle the warrants in cash or the warrants contain other features requiring them to be treated as liabilities. For warrants issued with the possibility of cash settlement, or otherwise requiring liability treatment, we record the fair value of the issued warrants as a liability at each reporting period and record changes in the estimated fair value as noncash gain or loss in the Consolidated Statements of Operations and Comprehensive Loss.

***Comprehensive Loss***

We have no components of other comprehensive loss other than net loss, and accordingly our comprehensive loss is equivalent to our net loss for the periods presented.

***Loss per Common Share Attributable to Common Stockholders***

Basic net loss attributable to common stockholders per share of common stock excludes the effect of dilution and is computed by dividing net loss increased by the accrual of dividends on outstanding shares of our Series B 10% Convertible Preferred Stock (*Series B Preferred*) for the fiscal years ended March 30, 2021 and 2020, respectively, and, in the fiscal year ended March 31, 2021, by the beneficial conversion feature related to our Series D Convertible Stock (*Series D Preferred*), as described in Note 9, *Capital Stock*, by the weighted-average number of shares of common stock outstanding for the period. Diluted net loss attributable to common stockholders per share of common stock reflects the potential dilution that could occur if securities or other contracts to issue shares of common stock were exercised or converted into shares of common stock. In calculating diluted net loss attributable to common stockholders per share, we have generally not increased the denominator to include the number of potentially dilutive common shares assumed to be outstanding during the period using the treasury stock method because the result is antidilutive.

As a result of our net loss for both years presented, potentially dilutive securities were excluded from the computation of diluted loss per share, as their effect would be antidilutive.

Basic and diluted net loss attributable to common stockholders per share was computed as follows:

| | Fiscal Years Ended March 31, | |
|---|---|---|
| | **2021** | **2020** |
| Numerator: | | |
| Net loss attributable to common stockholders for basic and diluted earnings pershare | $ (42,319,800) | $ (22,037,600) |
| Denominator: | | |
| Weighted average basic and diluted common shares outstanding | 86,133,644 | 43,869,523 |
| Basic and diluted net loss attributable to common stockholders per common share | $ (0.49) | $ (0.50) |

Potentially dilutive securities excluded in determining diluted net loss per common share for the fiscal years ended March 31, 2021 and 2020 are as follows:

| | At March 31, 2021 | At March 31, 2020 |
|---|---|---|
| Series A Preferred stock issued and outstanding [1] | 750,000 | 750,000 |
| Series B Preferred stock issued and outstanding [2] | 1,131,669 | 1,160,240 |
| Series C Preferred stock issued and outstanding [3] | 2,318,012 | 2,318,012 |
| Series D Preferred stock issued and outstanding [4] | 402,149 | - |
| Outstanding options under the Company's Amended and Restated 2016 (formerly 2008) Stock Incentive Plan and 2019 Omnibus Equity Incentive Plan | 14,638,088 | 10,003,088 |
| Outstanding warrants to purchase common stock | 19,362,532 | 26,555,281 |
| Total | 38,602,450 | 40,786,621 |

[1] Assumes exchange under the terms of the October 11, 2012 Note Exchange and Purchase Agreement, as amended.
[2] Assumes exchange under the terms of the Certificate of Designation of the Relative Rights and Preferences of the Series B 10% Convertible Preferred Stock, effective May 5, 2015; excludes shares of unregistered common stock issuable in payment of dividends on Series B Preferred upon conversion.
[3] Assumes exchange under the terms of the Certificate of Designation of the Relative Rights and Preferences of the Series C Convertible Preferred Stock, effective January 25, 2016.
[4] Assumes exchange under the terms of the Certificate of Designation of the Relative Rights and Preferences of the Series D Convertible Preferred Stock, effective December 21, 2020.

***Recent Accounting Pronouncements***

We believe the following recent accounting pronouncements or changes in accounting pronouncements are of significance or potential significance to the Company.

In August 2020, the Financial Accounting Standards Board (*FASB*) issued ASU 2020-06, Debt – Debt with Conversion and Other Options (Subtopic 470- 20) and Derivatives and Hedging – Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity (*ASU 2020-06*), to reduce complexity in applying GAAP to certain financial instruments with characteristics of liabilities and equity.

The guidance in ASU 2020-06 simplifies the accounting for convertible debt instruments and convertible preferred stock by removing the existing guidance in ASC 470-20, Debt: Debt with Conversion and Other Options, that requires entities to account for beneficial conversion features and cash conversion features in equity, separately from the host convertible debt or preferred stock. The guidance in ASC 470-20 applies to convertible instruments for which the embedded conversion features are not required to be bifurcated from the host contract and accounted for as derivatives.

In addition, the amendments revise the scope exception from derivative accounting in ASC 815-40 for freestanding financial instruments and embedded features that are both indexed to the issuer's own stock and classified in stockholders' equity, by removing certain criteria required for equity classification. These amendments are expected to result in more freestanding financial instruments qualifying for equity classification (and, therefore, not accounted for as derivatives), as well as fewer embedded features requiring separate accounting from the host contract.

The amendments in ASU 2020-06 further revise the guidance in ASC 260, Earnings Per Share, to require entities to calculate diluted earnings per share (EPS) for convertible instruments by using the if-converted method. In addition, entities must presume share settlement for purposes of calculating diluted EPS when an instrument may be settled in cash or shares.

The amendments in ASU 2020-06 are effective for our fiscal year beginning April 1, 2024. We are evaluating the impact of this new guidance, but do not believe that our adoption of ASU 2020-06 will have a material impact on our consolidated financial statements.

Other accounting standards that have been issued or proposed by the FASB or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on our consolidated financial statements upon adoption.

**4. Receivable from Collaboration Partner**

This amount reflects a payment we made to a contract manufacturing organization for certain drug substance manufacturing services on behalf of our collaboration partner. Our collaboration partner reimbursed us for the payment in May 2021.

**5. Prepaid Expenses and Other Current Assets**

Prepaid expenses and other current assets consists of the following:

| | March 31, 2021 | March 31, 2020 |
|---|---|---|
| Clinical and nonclinical materials and contract services | $ 686,900 | $ 115,200 |
| Insurance | 121,800 | 107,200 |
| All other | 26,400 | 2,700 |
| | $ 835,100 | $ 225,100 |

**6. Property and Equipment**

Property and equipment consists of the following:

| | March 31, 2021 | March 31, 2020 |
|---|---|---|
| Laboratory equipment | $ 937,400 | $ 892,500 |
| Tenant improvements | 214,400 | 214,400 |
| Information technology equipment | 73,900 | 54,600 |
| Office furniture and equipment | 84,600 | 84,600 |
| Manufacturing equipment | 211,200 | - |
| | 1,521,500 | 1,246,100 |
| | | |
| Accumulated depreciation and amortization | (1,154,100) | (1,036,500) |
| Property and equipment, net | $ 367,400 | $ 209,600 |

The following table summarizes depreciation and amortization expense attributable to owned and leased property and equipment for the fiscal years ended March 31, 2021 and 2020:

| | Fiscal Years Ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| Owned assets | $ 114,600 | $ 100,200 |
| Leased assets | 3,000 | 2,900 |
| Total depreciation and amortization | $ 117,600 | $ 103,100 |

The amount reported above for manufacturing equipment at March 31, 2021 reflects the cost of certain process equipment acquired in connection with the manufacture of PH94B drug product and placed in service in the fourth quarter of the fiscal year ended March 31, 2021. Included in amounts reported above for office furniture and equipment is the right-of-use asset related to a financing lease of certain office equipment. Amounts associated with assets subject to the financing lease at March 31, 2021 and 2020 are as follows:

| | March 31, 2021 | March 31, 2020 |
|---|---|---|
| Office equipment subject to financing lease | $ 14,700 | $ 14,700 |
| Accumulated depreciation | (12,400) | (9,400) |
| | | |
| Net book value of office equipment subject to financing lease | $ 2,300 | $ 5,300 |

Other than certain leased office equipment, none of our assets were subject to third party security interests at March 31, 2021 or 2020.

**7. Accrued Expenses**

Accrued expenses consist of:

| | March 31, 2021 | March 31, 2020 |
|---|---|---|
| Accrued expenses for clinical and nonclinical materials, development and contract services | $ 1,449,400 | $ 462,300 |
| Accrued professional services | 85,500 | 76,500 |
| All other | 27,800 | 22,700 |
| | $ 1,562,700 | $ 561,500 |

**8. Notes Payable**

The following table summarizes our notes payable:

| | March 31, 2021 | | | March 31, 2020 | | |
|---|---|---|---|---|---|---|
| | Principal Balance | Accrued Interest | Total | Principal Balance | Accrued Interest | Total |
| 7.30% Note payable to insurance premium financing company (current) | $ - | $ - | $ - | $ 56,500 | $ - | $ 56,500 |

In February 2020, we executed a 7.30% promissory note in the principal amount of $62,600 in connection with certain insurance policy premiums. That note was payable in monthly installments of $6,500, including principal and interest, through December 2020 and was fully paid at March 31, 2021. In May 2020, we executed a 6.30% promissory note in the principal amount of $322,200 in connection with other insurance policy premiums. The note was payable in monthly installments of $33,200, including principal and interest, through March 2021, and was fully paid at March 31, 2021.

In April 2020, we entered into a note payable agreement (the *PPP Loan Agreement*) with Silicon Valley Bank as lender (the *Lender*), pursuant to which we received net proceeds of $224,400 from a potentially forgivable loan from the U.S. Small Business Administration (*SBA*) pursuant to the Paycheck Protection Program (*PPP*) enacted by Congress under the Coronavirus Aid, Relief, and Economic Security Act (the *CARES Act*) administered by the SBA (the *PPP Loan*). In accordance with its terms, the PPP Loan was to mature on April 22, 2022. The PPP Loan accrued interest at a rate of 1.00% per annum throughout the period it was outstanding. The CARES Act provided that all or a portion of the PPP Loan might be forgiven upon our request to the Lender, subject to requirements in the PPP Loan Agreement and the CARES Act. While we believe our use of the PPP Loan proceeds met all of the conditions for forgiveness under the PPP, following the completion of the December 2020 Public Offering, on December 23, 2020, we voluntarily repaid in full the outstanding principal balance of the PPP Loan, $224,400, plus accrued interest of approximately $1,500.

**9. Capital Stock**

***Common Stock***

At our Special Meeting of Stockholders on March 5, 2021, as approved by and recommended to our stockholders by our Board, our stockholders approved an amendment to our Restated Articles of Incorporation to increase the authorized number of shares of common stock that we may issue from 175.0 million shares to 325.0 million shares. The amendment became effective on March 5, 2021, upon our filing of a certificate of amendment with the Nevada Secretary of State. Previously, at our Annual Meeting of Stockholders on September 5, 2019, as approved by and recommended to our stockholders by our Board, our stockholders approved an amendment to our Restated Articles of Incorporation to increase the authorized number of shares of common stock that we may issue from 100.0 million shares to 175.0 million shares. The amendment became effective on September 6, 2019, upon our filing of a certificate of amendment with the Nevada Secretary of State. In connection with an underwritten public offering of our common stock and warrants in May 2016, our common stock was approved for listing on the Nasdaq Capital Market. Our common stock has traded on the Nasdaq Capital Market under the symbol “VTGN” since May 11, 2016.

***Series A Preferred Stock***

In December 2011, our Board authorized the creation of a series of up to 500,000 shares of Series A Preferred, par value $0.001 (*Series A Preferred*). Each restricted share of Series A Preferred is currently convertible at the option of the holder into one and one-half restricted shares of our common stock. The Series A Preferred ranks prior to the common stock for purposes of liquidation preference.

The Series A Preferred has no separate dividend rights, however, whenever the Board declares a dividend on the common stock, each holder of record of a share of Series A Preferred shall be entitled to receive an amount equal to such dividend declared on one share of common stock multiplied by the number of shares of common stock into which such share of Series A Preferred could be converted on the applicable record date.

Except with respect to transactions upon which the Series A Preferred shall be entitled to vote separately as a class, the Series A Preferred has no voting rights. The restricted common stock into which the Series A Preferred is convertible shall, upon issuance, have all of the same voting rights as other issued and outstanding shares of our common stock.

In the event of the liquidation, dissolution or winding up of our affairs, after payment or provision for payment of our debts and other liabilities, the holders of Series A Preferred then outstanding shall be entitled to receive distributions out of our assets, if any, an amount per share of Series A Preferred calculated by taking the total amount available for distribution to holders of all of our outstanding common stock before deduction of any preference payments for the Series A Preferred, divided by the total of (x), all of the then outstanding shares of our common stock, plus (y) all of the shares of our common stock into which all of the outstanding shares of the Series A Preferred can be converted before any payment shall be made or any assets distributed to the holders of the common stock or any other junior stock.

At March 31, 2021 and 2020, there were 500,000 restricted shares of Series A Preferred outstanding, convertible into 750,000 shares of our common stock at the option of the holders.

***Series B Preferred Stock***

In July 2014, our Board authorized the creation of a class of Series B Preferred Stock, par value $0.001 (*Series B Preferred*). In May 2015, we filed a Certificate of Designation of the Relative Rights and Preferences of the Series B 10% Preferred Stock of VistaGen Therapeutics, Inc. (*Series B Certificate of Designation*) with the Nevada Secretary of State to designate 4.0 million shares of our authorized preferred stock as Series B Preferred.

Except with respect to transactions upon which the Series B Preferred shall be entitled to vote separately as a class, the Series B Preferred has no voting rights. The common stock into which the Series B Preferred is convertible shall, upon issuance, have all of the same voting rights as other issued and outstanding shares of our common stock.

Each share of Series B Preferred is convertible, at the option of the holder (*Voluntary Conversion*), into one (1) share of our common stock, subject to adjustment only for customary stock dividends, reclassifications, splits and similar transactions set forth in the Certificate of Designation. As permitted by the Series B Certificate of Designation, approximately 2.4 million shares of Series B Preferred were converted automatically into approximately 2.4 million shares of our common stock following the completion of our underwritten public offering in May 2016, which occurred concurrently with and facilitated the listing of our common stock on the Nasdaq Capital Market (*Automatic Conversion*). Both Automatic Conversion and Voluntary Conversion (collectively, *Conversion*) are subject to certain beneficial ownership blockers as set forth in the Certificate of Designation and/or securities purchase agreements.

Prior to Conversion, shares of Series B Preferred accrue in-kind dividends (payable only in unregistered shares of our common stock) at a rate of 10% per annum (*Accrued Dividends*). The Accrued Dividends are payable on the date of either a Voluntary Conversion or Automatic Conversion in that number of shares of common stock equal to the Accrued Dividends. We have recognized a liability in the amount of $6,272,700 for Accrued Dividends in the accompanying Consolidated Balance Sheet at March 31, 2021, based on the Series B Preferred issued and outstanding through that date. We have recognized a deduction from net loss of $1,385,600 and $1,263,600 related to dividends on Series B Preferred in arriving at net loss attributable to common stockholders in the accompanying Consolidated Statement of Operations and Comprehensive Loss for the fiscal years ended March 31, 2021 and 2020, respectively.

In the event of the liquidation, dissolution or winding-up of our affairs, after payment or provision for payment of our debts and other liabilities, the holders of the Series B Preferred then outstanding shall be entitled to receive distributions out of our assets, if any, of an amount equal to the Stated Value of the Series B Preferred ($7.00 per share), plus any accrued and unpaid dividends thereon, before any distribution or payment shall be made to the holders of any junior securities, including holders of our common stock. If our assets are insufficient to pay, in full, such amounts, then the entire assets to be distributed to the holders of the Series B Preferred shall be ratably distributed among the holders in accordance with the respective amounts that would be payable on such shares if all amounts payable thereon were paid in full. Upon liquidation, each share of Series B Preferred ranks pari-passu with our Series A Preferred, our Series C Preferred and Series D Preferred stock (the latter two defined below). The liquidation value of the Series B Preferred at March 31, 2021 is approximately $14,194,400.

In December 2020, an institutional holder of 28,571 shares of our Series B Preferred converted such shares into an equal number of unregistered shares of our common stock. In accordance with the conversion terms of the Series B Preferred, we also issued 160,062 shares of our unregistered common stock in payment of $124,600 of dividends that had accrued on the holder’s Series B Preferred since issuance. Following the conversion, at March 31, 2021 there were 1,131,669 shares of Series B Preferred outstanding, which are exchangeable at the option of the holder by Voluntary Conversion into 1,131,669 shares of our common stock, excluding shares of our common stock which may be issued in payment of Accrued Dividends upon conversion.

***Series C Preferred Stock***

In January 2016, our Board authorized the creation of and we filed a Certificate of Designation of the Relative Rights and Preferences of the Series C Convertible Preferred Stock of VistaGen Therapeutics, Inc. (the *Series C Preferred Certificate of Designation*) with the Nevada Secretary of State to designate 3.0 million shares of our preferred stock, par value $0.001 per share, as Series C Convertible Preferred Stock (*Series C Preferred*).

In the event of the liquidation, dissolution or winding up of our affairs, after payment or provision for payment of our debts and other liabilities, the holders of Series C Preferred then outstanding shall be entitled to receive, out of our assets, if any, an amount per share of Series C Preferred calculated by taking the total amount available for distribution to holders of all of our outstanding common stock before deduction of any preference payments for the Series C Preferred, divided by the total of (x), all of the then outstanding shares of our common stock, plus (y) all of the shares of our common stock into which all of the outstanding shares of the Series C Preferred can be exchanged before any payment shall be made or any assets distributed to the holders of the common stock or any other junior stock. Upon liquidation, each share of Series C Preferred ranks pari-passu with our Series A Preferred, our Series B Preferred and our Series D Preferred (defined below).

Each share of Series C Preferred is convertible, at the option of the holder into one share of our common stock, subject to certain beneficial ownership limitations as set forth in the Series C Preferred Certificate of Designation. Shares of the Series C Preferred do not accrue dividends, and holders of the Series C Preferred have no voting rights. At March 31, 2021 and 2020, one holder and its affiliates held all 2,318,012 outstanding shares of Series C Preferred.

***Series D Preferred Stock***

On December 17, 2020, in connection with the December 2020 Public Offering (defined below), our Board authorized the creation of a series of up to 2,000,000 shares of Series D Preferred Stock, par value $0.001 (*Series D Preferred*), which became effective with the filing of a Certificate of Designation of the Relative Rights and Preferences of the Series D Convertible Preferred Stock (*Series D Certificate of Designation*) with the State of Nevada on December 21, 2020.

Each share of our Series D Preferred is initially convertible into 23 shares of our common stock at any time at the option of the holder, provided that, the Series D Preferred is not convertible prior to the date on which we have received approval from our stockholders to increase the total authorized shares of our common stock by at least an amount necessary to reserve shares sufficient to satisfy our conversion obligations in respect of the Series D Preferred and an amendment to our Restated and Amended Articles of Incorporation reflecting such increase becomes effective (the *Approval Date*). Additionally, a holder of shares of Series D Preferred will be prohibited, subject to certain exceptions, from converting such shares into shares of our common stock if, as a result of such conversion, the holder, together with its affiliates and other attribution parties, would own more than 9.99% of the total number of shares of our common stock then issued and outstanding, which percentage may be changed at the holder's election to a lower percentage at any time or to a higher percentage not to exceed 19.99% upon 61 days' prior notice to us.

Prior to the Approval Date, in the event of our liquidation, dissolution, or winding up of the Company's affairs, holders of Series D Preferred will receive a payment equal to $0.001 per share before any proceeds are distributed to the holders of our common stock. On and after the Approval Date, the Series D Preferred will have no liquidation preference.

Prior to the Approval Date, holders of shares of our Series D Preferred will have one vote per share of Series D Preferred and will vote as a single class with our shares of common stock. On and after the Approval Date, shares of Series D Preferred will generally have no voting rights, except to the extent expressly provided in our Restated and Amended Articles of Incorporation or as otherwise required by law.

For as long as shares of Series D Preferred are outstanding, the affirmative consent of holders of a majority of the outstanding shares of Series D Preferred will be required before we can:

- amend, alter, modify or repeal (whether by merger, consolidation or otherwise) the Series D Preferred Certificate of Designation, our articles of incorporation or our bylaws in any manner that adversely affects the rights, preferences, privileges or the restrictions provided for the benefit of, the Series D Preferred;
- issue further shares of Series D Preferred or increase or decrease (other than by conversion) the number of authorized shares of Series D Preferred; or
- enter into any agreement to do any of the foregoing that is not expressly made conditional on obtaining the affirmative vote or written consent of the requisite holders.

In the event of the liquidation, dissolution or winding up of our affairs, the Series D Preferred ranks senior to any class or series of our capital stock hereafter created specifically ranking by its terms junior to the preferred stock; until the Approval Date, senior to our common stock; on parity with any class or series of capital stock hereafter created specifically ranking by its terms on parity with the preferred stock; and junior to any class or series of capital stock hereafter created specifically ranking by its terms senior to the preferred stock.

At the time of its issuance in connection with the December 2020 Public Offering (described below), we did not have a sufficient number of authorized shares of our common stock to permit the conversion in full of our Series D Preferred and the issuance upon exercise or conversion of all other outstanding series of preferred stock, warrants to purchase common stock or outstanding stock options or shares reserved for issuance of the same. Accordingly, on March 5, 2021, we held a Special Meeting of Stockholders (the *Special Meeting*) at which our stockholders approved an amendment to our Restated and Amended Articles of Incorporation to increase the number of authorized shares of our common stock from 175 million shares to 325 million shares (the *Charter Amendment*), an amount sufficient to permit the conversion of all outstanding shares of Series D Preferred. The affirmative vote by a majority of our common stockholders and Series D Preferred holders, voting as a single class, at the Special Meeting constituted the Approval Date noted above.

Following the Special Meeting, between March 12, 2021 and March 31, 2021, holders of an aggregate of 1,597,851 shares of Series D Preferred converted such shares into 36,750,573 registered shares of our common stock. At March 31, 2021, there were 402,149 shares of Series D Preferred outstanding which were convertible into 9,249,427 shares of our common stock. See Note 16, *Subsequent Events*, for information regarding additional conversions after March 31, 2021.

During our fiscal years ended March 31, 2021 and 2020, we completed private placement and public offerings as described below.

***Common Stock and Warrants Issued in Fall 2019 Private Placement***

Between October 30, 2019 and November 7, 2019, in a self-placed private placement and pursuant to subscription agreements received from certain accredited investors, we sold to such investors units, at a purchase price of $1.00 per unit, consisting of an aggregate of 650,000 unregistered shares of our common stock and warrants, exercisable beginning six months and one day following issuance and through November 1, 2023, to purchase 325,000 unregistered shares of our common stock at an exercise price of $2.00 per share (the *Fall 2019 Private Placement*). We received cash proceeds of $650,000 from the Fall 2019 Private Placement.

As further described below under “Winter 2019 Warrant Modification,” in December 2019, we modified the warrants issued in connection with the Fall 2019 Private Placement to (i) reduce the exercise price from $2.00 per share to $0.50 per share and (ii) to allow for the warrants to become immediately exercisable. Further, we issued warrants to purchase an aggregate of 325,000 additional shares of our common stock to the participants in the Fall 2019 Private Placement (the *Additional Warrants*) to increase the number of unregistered shares of common stock issuable upon exercise of the warrants from 50% to 100%. The Additional Warrants are immediately exercisable through March 31, 2024 at an exercise price of $0.50 per share.

We calculated the fair value of the Additional Warrants using the Black Scholes Option Pricing Model and the weighted average assumptions indicated in the table below, recognizing $88,800 as the fair value of the new warrants and as warrant modification expense, included as a component of general and administrative expenses, in our Consolidated Statement of Operations and Comprehensive Loss for the fiscal year ended March 31, 2020.

| **Assumption:** | **Additional Warrants** |
|---|---|
| Market price per share | $ 0.44 |
| Exercise price per share | $ 0.50 |
| Risk-free interest rate | 1.59% |
| Contractual term in years | 4.32 |
| Volatility | 86.64% |
| Dividend rate | 0.0% |
| | |
| Number of warrant shares | 325,000 |
| **Weighted average fair value per share** | **$ 0.27** |

***Winter 2019 Warrant Modification***

On December 4, 2019, we modified outstanding warrants previously issued as a part of completed private placements to temporarily reduce, for a period of two years or, if sooner, until the expiration of the warrant, the exercise price of such warrants to $0.50 per share, in order to more closely align the exercise price of the warrants with the trading price of our common stock at such time (the *Winter 2019 Warrant Modification*). Following the two-year period during which the exercise price is reduced, the exercise price of each then-outstanding modified warrant will revert to its pre-modification price. As a result of the Winter 2019 Warrant Modification, outstanding warrants to purchase a total of approximately 6.6 million unregistered shares of our common stock were modified.

We calculated the fair value of the modified warrants, including those issued in the Fall 2019 Private Placement, immediately before and after the modification using the Black Scholes Option Pricing Model for pre-modification valuations and for post-modification valuations for warrants expiring in less than two years. For the warrants expiring after the December 4, 2021 exercise price reversion date, we ran a binomial model using 24 steps, one for each month, and lognormal distribution to estimate our stock price at December 4, 2021, the termination date for the exercise price reduction. We then compared the exercise value of each warrant at each estimated stock price to the remaining option value if the warrant was not exercised on December 4, 2021 and allowed to revert to its original exercise price. For any estimated stock price above $0.50 per share (an in-the-money warrant), we determined that the holders would convert their warrants. For any estimated stock price below $0.50 per share, we determined that the holders would continue to hold their warrants. Given the significant reductions in exercise price (the pre-modification exercise prices ranged from $1.50 to $2.24 per share), if the warrants are not exercised prior to December 4, 2021, the Black-Scholes values upon the reversion of the exercise prices are very low, such that there is nominal additional value for continuing to hold the warrants. Accordingly, our estimated post-modification fair value for warrants having an expiration date later than the two-year exercise price reversion date, December 4, 2021, is equal to the value of an option determined using the Black Scholes Option Pricing Model having an exercise price of $0.50 per share and a two-year term and related assumptions. The table below indicates the pre- and post-modification weighted average assumptions used in our valuations. We recognized the incremental fair value, $702,500, as warrant modification expense, included as a component of general and administrative expenses, in our Consolidated Statement of Operations and Comprehensive Loss for the fiscal year ended March 31, 2020.

| **Assumption:** | **Pre-modification** | **Post-modification** |
|---|---|---|
| Market price per share | $ 0.44 | $ 0.44 |
| Exercise price per share | $ 1.85 | $ 0.50 |
| Risk-free interest rate | 1.58% | 1.58% |
| Remaining contractual term in years | 2.25 | 1.91 |
| Volatility | 87.5% | 88.1% |
| Dividend rate | 0.0% | 0.0% |
| | | |
| Number of warrant shares | 6,611,759 | 6,611,759 |
| **Weighted average fair value per share** | **$ 0.08** | **$ 0.19** |

Following the Winter 2019 Warrant Modification, investors holding a total of 820,000 warrants exercised their warrants at the reduced price of $0.50 per share, resulting in cash proceeds to us of $410,000 during the quarter ended December 31, 2019.

***December 19, 2019 Warrant Modification***

On December 19, 2019, we modified additional outstanding warrants previously issued as a part of a completed private placement to permanently reduce the exercise price of such warrants to $0.805 per share and to extend the term of such warrants through December 31, 2022, in order to more closely align the exercise price of the warrants with the current trading price of our common stock and to provide additional time for the holders to exercise the warrants (the *December 19, 2019 Warrant Modification*). As a result of the December 19, 2019 Warrant Modification, we modified outstanding warrants to purchase a total of 80,431 shares of our common stock.

We calculated the fair value of the modified warrants immediately before and after the modification using the Black Scholes Option Pricing Model and the weighted average assumptions indicated in the table below. We recognized the incremental fair value, $35,600, as warrant modification expense, included as a component of general and administrative expenses, in our Consolidated Statement of Operations and Comprehensive Loss for the fiscal year ended March 31, 2020.

| **Assumption:** | **Pre-modification** | **Post-modification** |
|---|---|---|
| Market price per share | $ 0.805 | $ 0.805 |
| Exercise price per share | $ 7.00 | $ 0.805 |
| Risk-free interest rate | 1.57% | 1.65% |
| Remaining contractual term in years | 0.58 | 3.034 |
| Volatility | 98.7% | 84.9% |
| Dividend rate | 0.0% | 0.0% |
| | | |
| Number of warrant shares | 80,431 | 80.431 |
| **Weighted average fair value per share** | **$ 0.00** | **$ .044** |

***Warrants issued in Winter 2019 Warrant Offering***

In December 2019, we commenced a self-placed private placement of warrants to purchase unregistered shares of our common stock at an offering price of $0.15 per warrant (the *Winter 2019 Warrant Offering*). Warrants offered and sold in the Winter 2019 Warrant Offering have an exercise price of $0.50 per share and term of three years from the issuance date. Over the course of the Winter 2019 Warrant Offering, we sold warrants to purchase a total of 2.0 million unregistered shares of common stock for cash proceeds to us of $300,000, which we accounted for with a corresponding credit to additional paid-in capital, an equity account.

***Registered Direct Offering of Common Stock and Concurrent Warrant Offering***

In January 2020, we entered into a self-placed securities purchase agreement with certain accredited investors pursuant to which we received gross cash proceeds of $2.75 million upon the sale of an aggregate of 3,870,077 shares of our common stock at a purchase price of $0.71058 per share (the *January 2020 Offering*). Concurrently with the January 2020 Offering, we also commenced a private placement in which we issued and sold warrants (the *January 2020 Warrants*) exercisable for an aggregate of 3,870,077 unregistered shares of our common stock (the *Warrant Shares*), having an exercise price of $0.73 per Warrant Share. The 3,870,077 shares of common stock sold in the January 2020 Offering (but not the January 2020 Warrants or the Warrant Shares) were offered and sold pursuant to a prospectus, dated September 30, 2019, and a prospectus supplement dated January 24, 2020, in connection with a takedown from our shelf registration statement on Form S-3 (File No. 333-234025).

The January 2020 Warrants contain customary provisions allowing for adjustment to the exercise price and number of Warrant Shares issuable only in the event of any stock dividend and split, reverse stock split, recapitalization, reorganization or similar transaction, as described in the January 2020 Warrants. In addition, subject to limited exceptions, holders of the January 2020 Warrants will not have the right to exercise any portion of their respective January 2020 Warrants if the holder, together with any affiliates, would beneficially own in excess of 4.99% of the number of shares of our common stock outstanding immediately after giving effect to such exercise. The January 2020 Warrants are exercisable from any time after the six-month anniversary of issuance (the *Initial Exercise Date*) and will expire on the fifth year anniversary of the Initial Exercise Date. Refer to Note 16, *Subsequent Events*, for disclosure regarding filing of a registration statement including the shares of common stock underlying the January 2020 Warrants.

***Common Stock Purchase Agreement with Lincoln Park***

On March 24, 2020, we entered into a purchase agreement and a registration rights agreement with Lincoln Park Capital Fund (*LPC*) pursuant to which LPC committed to purchase up to $10,250,000 of our common stock at market-based prices over a period of 24 months (the *LPC Agreement*). On March 24, 2020, we sold 500,000 unregistered shares of our common stock (the *Initial Purchase Shares*) to LPC under the purchase agreement at a price of $0.50 per share for gross cash proceeds of $250,000 (the *Initial Purchase*) and we also issued 750,000 unregistered shares of our common stock to LPC under the terms of the LPC Agreement (the *Commitment Shares*). To satisfy our obligations under the registration rights agreement, we filed a Registration Statement on Form S-1 (the *LPC Registration Statement*) with the SEC on March 31, 2020 (Registration No. 333-237514), which the SEC declared effective on April 14, 2020 (the *Commencement Date*). The LPC Registration Statement included registration of the Initial Purchase Shares and the Commitment Shares. The fair value of the Commitment Shares, $284,400, determined based on the quoted closing market price of our common stock on March 24, 2020, is a component of deferred offering costs attributable to this offering, which costs are amortized ratably to additional paid-in capital as we sell shares of our common stock to LPC under the LPC Agreement.

Following the Commencement Date, on any business day over the term of the LPC Agreement, we have the right, in our sole discretion, to direct LPC to purchase up to 100,000 shares on such business day (the "*Regular Purchase*") (subject to adjustment under certain circumstances as provided in the LPC Agreement). The purchase price per share for each such Regular Purchase will be based on prevailing market prices of our common stock immediately preceding the time of sale as computed under the LPC Agreement. In each case, LPC's maximum commitment in any single Regular Purchase may not exceed $1,000,000. In addition to Regular Purchases, provided that we present LPC with a purchase notice for the full amount allowed for a Regular Purchase, we may also direct LPC to make accelerated purchases and additional accelerated purchases as described in the LPC Agreement. Although LPC has no right to require us to sell any shares of our common stock to LPC, LPC is obligated to make purchases as we direct, subject to certain conditions. In all instances, we may not sell shares of our common stock to LPC under the LPC Agreement if such sales would result in LPC beneficially owning more than 9.99% of our common stock. There are no upper limits on the price per share that LPC must pay for shares of our common stock.

Subsequent to the Commencement Date and through July 2020, we sold an additional 6,301,995 registered shares of our common stock to Lincoln Park and received aggregate gross cash proceeds of $2,891,200. We have sold no shares of our common stock under the LPC Agreement since July 2020. At March 31, 2021, there were approximately 2.04 million registered shares of our common stock remaining available for sale under the LPC Agreement; however, we have no obligation to sell any additional shares under the LPC Agreement in the future.

***Sale of Common Stock and Warrants in the Spring 2020 Private Placement***

In April 2020, in a self-directed private placement, we sold units of common stock and warrants to an accredited investor to purchase an aggregate of 125,000 unregistered shares of our common stock and four-year warrants to purchase 125,000 shares of our common stock at an exercise price of $0.50 per share and we received cash proceeds of $50,000 (the *Spring 2020 Private Placement*).

***Registration Statement for shares underlying warrants issued in Private Placements and warrant exercises***

On May 1, 2020, we filed a registration statement on Form S-3 (Registration No. 333-237968) to register approximately 12.1 million shares of common stock underlying outstanding warrants that we had issued in earlier private placement offerings, including the Spring 2020 Private Placement, as well as common stock underlying warrants that had been previously issued to various consultants as full or partial compensation for their services. Included in the registration statement were shares of our common stock underlying approximately 5.8 million outstanding warrants to purchase shares of our common stock that had been modified in December 2019 to temporarily reduce, for a period of two years or, if sooner, until the expiration of the warrant, the exercise price of such warrants to $0.50 per share, in order to more closely align the exercise price of the warrants with the trading price of our common stock at that time (the *Winter 2019 Warrant Modification*). We also registered approximately 0.8 million shares of unregistered outstanding common stock held by former holders of warrants who had exercised such warrants subsequent to the Winter 2019 Warrant Modification. Further, we registered the 125,000 shares of common stock issued in the Spring 2020 Private Placement. The SEC declared the registration statement effective on May 13, 2020 (the *Warrant Registration Statement*). As a result of the effectiveness of this registration statement, the shares of common stock underlying essentially all of our outstanding warrants have been registered.

During July 2020, holders of warrants to purchase an aggregate of 228,000 shares of our common stock exercised such warrants, and we received aggregate cash proceeds of $114,000. We issued 228,000 registered shares of our common stock upon these exercises pursuant to the effectiveness of the Warrant Registration Statement. Between December 2020 and March 31, 2021, holders of outstanding warrants to purchase an aggregate of 6,396,302 registered shares of our common stock exercised such warrants and we received $4,200,900 in cash proceeds.

***August 2020 Registered Public Offering of Common Stock***

On August 2, 2020, we entered into an underwriting agreement (the *Underwriting Agreement*) with Maxim Group, LLC as representative of the underwriters named therein (*Maxim*), pursuant to which we sold, in an underwritten public offering (the *August 2020 Public Offering*), an aggregate of 15,625,000 shares (the *Shares*) of our common stock for a public offering price of $0.80 per share, resulting in gross proceeds to us of $12,500,000. The August 2020 Public Offering closed on August 5, 2020. Under the terms of the Underwriting Agreement, we granted to Maxim a 45-day over-allotment option to purchase up to an additional 2,343,750 shares at a public offering price of $0.80 per share, which Maxim elected to exercise on August 5, 2020 with respect to an aggregate of 2,243,250 shares (the *Exercised Option Shares*). We completed the sale of the Exercised Option Shares on August 7, 2020 and received additional gross proceeds of $1,794,600. After deducting underwriting discounts and commissions and offering expenses payable by us, we received net proceeds of approximately $12.9 million from the August 2020 Public Offering.

***December 2020 Registered Public Offering of Common Stock and Series D Preferred Stock***

On December 18, 2020, we entered into an underwriting agreement (the *December 2020 Underwriting Agreement*) with Jefferies LLC (*Jefferies*) and William Blair & Company, L.L.C. (*Willian Blair)*, as representatives of the underwriters named therein (collectively, the *Underwriters*), pursuant to which we agreed to issue and sell to the Underwriters, in an underwritten public offering (the *December 2020 Public Offering*), 63,000,000 shares of our common stock, at a public offering price of $0.92 per share and 2,000,000 shares of the newly created Series D Preferred (together with the common stock, the *Securities*) at a public offering price of $21.16 per share, resulting in gross proceeds to us of $100.28 million. The December 2020 Public Offering closed on December 22, 2020 at which time the shares of common stock and Series D Preferred were sold to the Underwriters. After deducting underwriting discounts and commissions and offering expenses payable by us, we received net proceeds of approximately $93.6 million from the December 2020 Public Offering.

The Series D Preferred that we issued in the December 2020 Public Offering contained a beneficial conversion feature (a *BCF*), which arises when a debt or equity security is issued with an embedded conversion option that is deemed beneficial to the investor, that is, in-the-money, at inception because the conversion option has an effective conversion price that is less than the market price of the underlying stock at the commitment date (with respect to the Series D Preferred, the date the security was actually issued rather than the date the agreement to do so was entered into, herein referred to as the *Commitment Date*). In accordance with Accounting Standards Codification 470-20, *Debt- Debt with Conversion and Other Options* (*ASC 470-20*), an embedded BCF is required to be recognized separately by allocating a portion of the proceeds equal to the intrinsic value of the feature to additional paid-in capital. ASC 470-20 also provides that the intrinsic value is to be calculated as of the Commitment Date. The Series D Certificate of Designation provides that the Series D Preferred has a conversion price of $0.92 per share on an as-converted basis (the *Conversion Price*). The Conversion Price compared to the closing price of $1.42 per share of our common stock on the Commitment Date results in a difference of $0.50 per share. That difference multiplied by the 46 million shares of our common stock issuable upon conversion of the Series D Preferred resulted in an aggregate BCF of $23.0 million. We did not recognize the impact of the BCF at December 31, 2020 because the Series D Preferred was not convertible into common stock prior to the Approval Date. Following approval by our stockholders of the Charter Amendment at the Special Meeting in March 2021, the contingency of the BCF was eliminated and we recognized the BCF as a noncash charge in arriving at net loss attributable to common stockholders in our Consolidated Statement of Operations and Comprehensive Loss for the quarter and fiscal year ended March 31, 2021 and as a corresponding increase in additional paid-in capital in our Consolidated Statement of Stockholders' Equity (Deficit). The BCF was also treated as a deemed dividend in our Consolidated Statement of Stockholders' Equity (Deficit). Since we have an accumulated deficit, we recorded the deemed dividend as a reduction in additional paid-in capital, resulting in a net impact of $0 to additional paid-in capital. The recognition of the BCF on the Series D Preferred had no impact in aggregate on our stockholders' equity or on our cash position.

***Stock Option Exercises***

During the fiscal year ended March 31, 2021, holders of outstanding stock options, including two members of our Board, exercised options to purchase an aggregate of 252,004 shares of our common stock and we received cash proceeds of $36,500. There were no stock option exercises during the fiscal year ended March 31, 2020.

**Warrants Outstanding**

Following the Winter 2019 Warrant Modifications, the December 19, 2019 Warrant Modification, the Winter 2019 Warrant Offering, the issuance of the January 2020 Warrants and the warrants included in the Spring 2020 Private Placement and the warrant exercises noted above, the following table summarizes outstanding and exercisable warrants to purchase shares of our common stock as of March 31, 2021. The weighted average exercise price of outstanding and exercisable warrants at March 31, 2021 was $1.78 per share.

| Exercise Price per Share | Expiration Date | Warrants Exercisable and Outstanding at March 31, 2021 |
|---|---|---|
| $ 0.50 | 4/30/2021 to 3/31/2024 | 4,944,680 |
| $ 0.73 | 7/25/2025 | 1,670,077 |
| $ 0.805 | 12/31/2022 | 80,431 |
| $ 1.50 | 12/13/2022 | 8,375,530 |
| $ 1.82 | 3/7/2023 | 1,388,931 |
| $ 3.51 | 12/31/2021 | 50,000 |
| $ 5.30 | 5/16/2021 | 2,705,883 |
| $ 7.00 | 3/3/2023 | 147,000 |
| | | 19,362,532 |

At March 31, 2021, with the effectiveness of the Warrant Registration Statement in May 2020, the shares of common stock underlying essentially all of the outstanding warrants except those having an exercise price of $7.00 per share have been registered for resale by the warrant holders. Additionally, no outstanding warrant is subject to any down round anti-dilution protection features and all of the outstanding warrants are exercisable by the holders only by payment in cash of the stated exercise price per share.

**Reserved Shares**

At March 31, 2021, we have reserved shares of our common stock for future issuance as follows:

**COMMON STOCK RESERVED FOR FUTURE ISSUANCE AT 3/31/21**

| | |
|---|---|
| Upon exchange of all shares of Series A Preferred currently issued and outstanding [(1)] | 750,000 |
| Upon exchange of all shares of Series B Preferred currently issued and outstanding [(2)] | 4,000,000 |
| Upon exchange of all shares of Series C Preferred currently issued and outstanding [(3)] | 2,318,012 |
| Upon exchange of all shares of Series D Preferred currently issued and outstanding [(4)] | 9,249,427 |
| Pursuant to warrants to purchase common stock: | |
| Subject to outstanding warrants | 19,365,532 |
| Pursuant to stock incentive plans: | |
| Subject to outstanding options under the Amended and Restated 2016 Stock Incentive Plan and the 2019 Omnibus Equity Incentive Plan | 14,638,088 |
| Available for future grants under the 2019 Omnibus Equity Incentive Plan | 1,843,158 |
| Available for future issuance under the 2019 Employee Stock Purchase Plan | 941,875 |
| | 17,423,121 |
| Reserved for issuance under Lincoln Park Purchase Agreement | 320,272 |
| Total reserves | 53,426,364 |

(1) Assumes exchange under the terms of the October 11, 2012 Note Exchange and Purchase Agreement.

(2) Assumes exchange under the terms of the Certificate of Designation of the Relative Rights and Preferences of the Series B 10% Convertible Preferred Stock, effective May 5, 2015; includes 2,868,331 shares of common stock reserved for payment of dividends on Series B Preferred upon conversion. Refer to *Series B Preferred Stock*, above, for additional information regarding payment of dividends in common stock.

(3) Assumes exchange under the terms of the Certificate of Designation of the Relative Rights and Preferences of the Series C Convertible Preferred Stock, effective January 25, 2016.

(4) Assumes exchange under the terms of the Certificate of Designation of the Relative Rights and Preferences of the Series D Convertible Preferred Stock, effective December 21, 2020.

At March 31, 2021, we have 90,958,067 authorized shares of our common stock not subject to reserves and available for future issuance.

**10. Research and Development Expenses**

We recorded research and development expenses of approximately $12.5 million and $13.4 million in the fiscal years ended March 31, 2021 and 2020, respectively, including approximately $0.8 million and $1.4 million of noncash expense in the fiscal years ended March 31, 2021 and 2020, respectively. Research and development expense is composed of employee compensation expenses, including stock–based compensation, direct project expenses, notably including preclinical and nonclinical projects for PH94B, PH10 and AV-101 in both years and costs attributable to our AV-101 clinical trial in MDD in the fiscal year ended March 31, 2020, as well as costs to maintain and prosecute our intellectual property suite, including patent applications for AV-101 in combination with probenecid for various indications in the fiscal year ended March 31, 2021.

**11. Income Taxes**

The provision for income taxes for the periods presented in the Consolidated Statements of Operations and Comprehensive Loss represents minimum California franchise tax, Maryland and North Carolina income tax.

Income tax expense (benefit) differed from the amounts computed by applying the statutory federal income tax rate of 21% to pretax income (loss) as a result of the following:

| | Fiscal Years Ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| Computed expected tax benefit | (21.00)% | (21.00)% |
| State income taxes, net of federal benefit | 0.01% | 0.01% |
| Tax effect of warrant modifications | -% | 0.84% |
| Tax effect of research and development credits | (1.45)% | (1.60)% |
| Tax effect of stock compensation | 4.71% | 2.39% |
| Tax effect of other non-deductible items | 0.00% | 0.00% |
| Expired net operating loss carryforwards | 1.99% | 0.36% |
| Change in valuation allowance (federal only) | 15.74% | 19.02% |
| Income tax expense | 0.00% | 0.02% |

Deferred income taxes reflect the net tax effect of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of our deferred tax assets are as follows:

| | March 31, | |
|---|---|---|
| | 2021 | 2020 |
| Deferred tax assets: | | |
| Net operating loss carryovers | $ 33,587,300 | $ 30,607,500 |
| Basis differences in property and equipment | 12,500 | 9,100 |
| Research and development credit carryforwards | 2,589,000 | 2,256,400 |
| Stock based compensation | 3,515,500 | 3,919,900 |
| Operating lease Right of Use asset | 105,300 | 95,400 |
| Accruals and reserves | 67,000 | 66,500 |
| Total deferred tax assets | 39,876,600 | 36,954,800 |
| Valuation allowance | (39,876,600) | (36,954,800) |
| Net deferred tax assets | $ - | $ - |

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by $2,921,800 and $4,202,500 during the fiscal years ended March 31, 2021 and 2020, respectively.

As of March 31, 2021, we had U.S. federal net operating loss carryforwards of approximately $139,175,200. Federal net operating loss carryforwards of approximately $86,276,400 generated through our fiscal year ended March 31, 2018 will expire in our fiscal years ending March 31, 2022 through March 31, 2038. Federal net operating loss carryforwards of approximately $52,898,800 generated in fiscal years ending after March 31, 2018 will carry forward indefinitely, but are subject to an 80% taxable income limitation. As of March 31, 2021, we had state net operating loss carryforwards of approximately $64,556,500, which will expire in fiscal years ending in 2029 through 2041. We also have federal and state research and development tax credit carryforwards of approximately $2,415,500 and $1,311,900, respectively. The federal tax credits will expire at various dates beginning with our fiscal year ending March 31, 2029, unless previously utilized. The state tax credits do not expire and will carry forward indefinitely until utilized.

On March 27, 2020 the U.S. enacted the Coronavirus Aid, Relief, and Economic Security Act (the *CARES Act*) to provide economic relief in response to the coronavirus pandemic. The CARES Act, among other things, includes provisions to allow certain net operating losses to be carried-back up to five years, to increase interest deduction limitations, and to make technical corrections to tax depreciation methods for qualified improvement property. The CARES Act may affect the corporate income taxes imposed by state governments and may result in future responses by state legislatures, some of which could have retroactive effect. The Company evaluated the provisions of the CARES Act and determined that it did not have a material impact on the Company's income tax accounts at March 31, 2021 or 2020.

On June 29, 2020, California Assembly Bill 85 (*AB 85*) was signed into law, suspending the use of California net operating losses and limiting the use of California research tax credits for tax years beginning in 2020 and before 2023. The suspension of net operating losses and the restriction of research tax credits did not result in a significant impact on the value of our deferred tax assets.

U.S. federal and state tax laws include substantial restrictions on the utilization of net operating loss carryforwards in the event of an ownership change of a corporation. We have not performed a change in ownership analysis since our inception in 1998 and accordingly some or all of our net operating loss carryforwards may not be available to offset future taxable income, if any.

We file income tax returns in the U.S. federal, Canada and various U.S. state jurisdictions. We are subject to U.S. federal and state income tax examinations by tax authorities for tax years 2002 through 2021 due to net operating losses that are being carried forward for tax purposes, but we are not currently under examination by tax authorities in any jurisdiction.

*Uncertain Tax Positions*

Our unrecognized tax benefits at March 31, 2021 and 2020 relate entirely to research and development tax credits. The total amount of unrecognized tax benefits at March 31, 2021 and 2020 is $931,900 and $814,600, respectively. If recognized, none of the unrecognized tax benefits would impact our effective tax rate. The following table summarizes the activity related to our unrecognized tax benefits.

| | Fiscal Years Ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| Unrecognized benefit - beginning of period | $ 814,600 | $ 668,700 |
| Current period tax position increases | 117,300 | 146,000 |
| Prior period tax position increases (decreases) | - | (100) |
| Unrecognized benefit - end of period | $ 931,900 | $ 814,600 |

Our policy is to recognize interest and penalties related to income taxes as components of interest expense and other expense, respectively. We incurred no interest or penalties related to unrecognized tax benefits in the years ended March 31, 2021 or 2020. We do not anticipate any significant changes of our uncertain tax positions within twelve months of this reporting date.

**12. Licensing, Sublicensing and Collaborative Agreements**

***PH94B Sublicense Agreement with EverInsight***

On June 24, 2020, we entered into a license and collaboration agreement (the *EverInsight Agreement*) with EverInsight Therapeutics Inc., a company incorporated under the laws of the British Virgin Islands and funded by CBC Group, a global healthcare-focused venture capital firm (*EverInsight*). Subsequent to entering into the EverInsight Agreement, in October 2020, EverInsight merged with AffaMed Therapeutics, Inc., also funded by CBC Group, which as a combined, complementary entity is focusing on developing and commercializing therapeutics to address ophthalmologic and CNS disorders in Greater China and beyond. Accordingly, we are now referring to EverInsight and the EverInsight Agreement as AffaMed and the AffaMed Agreement, respectively. Under the AffaMed Agreement, we granted AffaMed an exclusive license to develop and commercialize PH94B, our neuroactive pherin drug candidate for SAD and other anxiety-related disorders, in Greater China (which includes Mainland China, Hong Kong, Macau and Taiwan), South Korea and Southeast Asia (which includes Indonesia, Malaysia, Philippines, Thailand and Vietnam) (collectively, the *Territory*). We retain exclusive development and commercialization rights for PH94B in the rest of the world.

Under the terms of the AffaMed Agreement, AffaMed is responsible for all costs related to developing, obtaining regulatory approval of, and commercializing PH94B for treatment of SAD, and potentially other anxiety-related indications, in the Territory. A joint development committee has been established between AffaMed and us to coordinate and review the development and commercialization plans with respect to PH94B in the Territory.

We are responsible for pursuing clinical development and regulatory submissions of PH94B for acute treatment of anxiety in adults with SAD, and potentially other anxiety-related indications, in the United States on a ‘‘best efforts’’ basis, with no guarantee of success. EverInsight has the option to participate in the Phase 3 global clinical trial of PH94B and will assume all direct costs and expenses of conducting such clinical trial in the Territory and a portion of the indirect costs of the global trial. We will transfer all development data (nonclinical and clinical data) and our regulatory documentation related to PH94B throughout the term as it is developed or generated or otherwise comes into our control. We will grant to AffaMed a Right of Reference to our regulatory documentation and our development data.

Under the terms of the AffaMed Agreement, AffaMed agreed to pay us a non-refundable upfront license payment of $5.0 million within 30 business days of the effective date of the AffaMed Agreement, and AffaMed paid the $5 million in August 2020. Additionally, upon successful development and commercialization of PH94B in the Territory, we are eligible to receive milestone payments of up to $172.0 million. Further, we are eligible to receive royalty payments on a country-by-country basis on net sales for the later of ten years or the expiration of market or regulatory exclusivity in the jurisdiction, except that payments will be reduced on a country-by-country basis in the event that there is no market exclusivity in the period. Royalty payments may also be reduced if there is generic competitive product in the period.

We have determined that we have one combined performance obligation for the license to develop and commercialize PH94B in the Territory and related development and regulatory services. In addition, AffaMed has an option that will create manufacturing obligations for us during development upon exercise by AffaMed. This option for manufacturing services was evaluated and determined not to include a material right.

Development and commercialization milestones were not considered probable at inception and therefore were excluded from the initial transaction price. The royalties were excluded from the initial transaction price because they relate to a license of intellectual property and are subject to the royalty constraint.

We recognize revenue as the combined performance obligation is satisfied over time using an output method. The measure of progress is stand-ready straight-line over the period in which we expect to perform the services related to the sublicense of PH94B. Significant management judgment is required to determine the level of effort attributable to the AffaMed Agreement and the period over which we expect to complete our performance obligations under the arrangement. The performance period or measure of progress is estimated at the inception of the arrangement and re-evaluated in subsequent reporting periods. This re-evaluation may shorten or lengthen the period over which we recognize revenue. Changes to these estimates are recorded on a cumulative catch up basis. We currently estimate that we will complete our performance obligations at the end of calendar 2023.

The difference between the revenue recognized to-date under the AffaMed Agreement, $1,089,500, and the consideration received to-date, $5,000,000, is recorded as a contract liability/deferred revenue (cash received exceeds revenue earned). At March 31, 2021, we have recorded deferred revenue of $3,910,500. The following table presents changes in our contract liabilities for our fiscal year ended March 31, 2021:

| | Balance at March 31, 2020 | Additions | Deductions | Balance at March 31, 2021 |
|---|---|---|---|---|
| Deferred Revenue - current portion | $ - | $ 1,420,200 | $ - | $ 1,420,200 |
| Deferred Revenue - non-current portion | - | 3,579,800 | (1,089,500) | 2,490,300 |
| Total | $ - | $ 5,000,000 | $ (1,089,500) | $ 3,910,500 |

For the single combined performance obligation under the AffaMed Agreement, the measure of progress is stand-ready straight-line over the period in which we expect to perform the services related to the sublicense of PH94B. Accordingly, deferred revenue is being recognized on a straight-line basis over the period in which we expect to perform the services.

*Contract Acquisition Costs*

During the quarter ended September 30, 2020, we made cash payments aggregating $345,000 for sublicense fees, which we were obligated to make pursuant to our PH94B license from Pherin, and fees for consulting services exclusively related to the AffaMed Agreement. Additionally, on June 24, 2020, we issued 233,645 unregistered shares of our common stock, valued at $125,000, as partial compensation for consulting services exclusively related to the AffaMed Agreement. These sublicense fees and consulting payments and the fair value of the common stock issued, aggregating $470,000, were incurred solely as a result of obtaining the AffaMed Agreement, and, accordingly, have been capitalized as deferred contract acquisition costs in our Consolidated Balance Sheet at March 31, 2021. Capitalized contract acquisition costs are amortized over the period in which we expect to satisfy the performance obligations under the AffaMed Agreement and the amortization expense of $102,400 has been included in general and administrative expenses in our Consolidated Statement of Operations and Comprehensive Loss for the fiscal year ended March 31, 2021. There has been no impairment loss in relation to the costs capitalized.

Unless earlier terminated due to certain material breaches of the contract, or otherwise, the AffaMed Agreement will expire on a jurisdiction-by-jurisdiction basis until the latest to occur of the expiration of the last valid claim under a licensed patent of PH94B in such jurisdiction, the expiration of regulatory exclusivity in such jurisdiction or ten years after the first commercial sale of PH94B in such jurisdiction.

***License Agreements with Pherin Pharmaceuticals, Inc. (Pherin)***

In September 2018 we issued 1,630,435 shares of our unregistered common stock having a fair market value of $2,250,000 to Pherin to acquire an exclusive worldwide license to develop and commercialize PH94B for social anxiety disorder and an option to acquire a similar license for PH10 for MDD. In October 2018, we exercised our option to acquire an exclusive worldwide license to develop and commercialize PH10 by issuing an additional 925,926 shares of our unregistered common stock having a fair market value of $2,000,000 to Pherin under the terms of the PH10 license agreement. Under the terms of the PH94B and PH10 license agreements, we are obligated to make additional cash payments and pay royalties to Pherin in the event that certain regulatory and performance-based milestones and commercial sales are achieved. Additionally, in connection with the PH94B and PH10 license agreements, we were obligated to pay to Pherin monthly support payments of $10,000 for a term of 18 months, however no monthly support payment was required during the 18-month period identified in the PH10 license agreement if support payments were being made under the terms of the PH94B license agreement. The support payments required under the PH94B license agreement terminated in March 2020 and in April 2020 under the PH10 license agreement. Accordingly, we made support payments of $10,000 under the PH10 license agreement and $120,000 under the PH94B license agreement in the fiscal years ended March 31, 2021 and 2020, respectively.

***BlueRock Therapeutics Sublicense Agreement***

In December 2016, we entered into an Exclusive License and Sublicense Agreement with BlueRock Therapeutics, LP, a next generation regenerative medicine company established in December 2016 by Bayer AG and Versant Ventures (*BlueRock Therapeutics*), pursuant to which BlueRock Therapeutics received exclusive rights to utilize certain technologies exclusively licensed by us from University Health Network (*UHN*) for the production of cardiac stem cells for the treatment of heart disease. As a result of its acquisition of BlueRock Therapeutics in 2019, Bayer AG now holds the rights to develop and commercialize our hPSC technologies relating to the production of heart cells for the treatment of heart disease (the *Bayer Agreement*). We retained rights to cardiac stem cell technology licensed from UHN related to small molecule, protein and antibody drug discovery, drug rescue and drug development, including small molecules with cardiac regenerative potential, as well as small molecule, protein and antibody testing involving cardiac cells. To date, we have recognized $1.25 million in sublicense revenue, in our fiscal year ended March 31, 2017, under the Bayer Agreement.

**13. Stock Option Plans, Employee Stock Purchase Plan, and 401(k) Plan**

At March 31, 2021, we have the following share-based compensation plans, which are described below:

- ***Amended and Restated 2016 Stock Incentive Plan (the 2016 Plan); and***
- ***2019 Omnibus Equity Incentive Plan (the 2019 Plan)***

***Description of the 2016 Plan***

Our Board unanimously approved the Company's Amended and Restated 2016 Stock Incentive Plan, formerly titled the 2008 Stock Incentive Plan (the *2016 Plan*), on July 26, 2016, and the 2016 Plan was approved by our stockholders at our 2016 Annual Meeting of Stockholders on September 26, 2016, and further amended to increase the number of shares authorized for issuance therefrom at our 2017 Annual Meeting of Stockholders on September 15, 2017. The 2016 Plan provided for the grant of stock options, restricted shares of common stock, stock appreciation rights and dividend equivalent rights, collectively referred to as "Awards". Stock options granted under the 2016 Plan were either incentive stock options under the provisions of Section 422 of the Internal Revenue Code of 1986, as amended (the *Code*), or non-qualified stock options. We could grant incentive stock options only to employees of the Company or any parent or subsidiary of the Company. Awards other than incentive stock options could be granted to employees, directors and consultants. A total of 10.0 million shares of our common stock were authorized for issuance under the 2016 Plan, of which options to purchase approximately 7.6 million shares remain outstanding at March 31, 2021. Upon the adoption of our 2019 Plan, no further grants were permissible under the 2016 Plan and approximately 1.4 million authorized shares were transferred to the 2019 Plan and became issuable therefrom. All options granted from the 2016 Plan remain operative under the terms of the respective grants.

***Description of the 2019 Plan***

Our Board approved the VistaGen Therapeutics, Inc. 2019 Omnibus Equity Incentive Plan on May 27, 2019, and our stockholders adopted it and ratified all previously issued grants on September 5, 2019. The principal features of the 2019 Plan are summarized below.

The 2019 Plan provides for the grant of stock options, stock appreciation rights (*SARs*), restricted stock, restricted stock units, and other stock-based awards, and performance awards, collectively referred to as "Awards". Awards may be granted under the 2019 Plan to officers, employees and consultants of the Company and our subsidiaries and to our non-employee directors. Incentive stock options may be granted only to employees of the Company or one of our subsidiaries. The 2019 Plan is administered by the Compensation Committee of the Board. The Compensation Committee, in its discretion, selects the individuals to whom awards may be granted, the time or times at which such awards are granted, and the terms of such awards. The Compensation Committee may delegate its authority to the extent permitted by applicable law.

The Compensation Committee sets stock option exercise prices and terms, except that stock options must be granted with an exercise price not less than 100% of the fair market value of the common stock on the date of grant. The Compensation Committee may grant either incentive stock options, which must comply with Section 422 of the Code, or nonqualified stock options. At the time of grant, the Compensation Committee determines the terms and conditions of stock options, including the quantity, exercise price, vesting periods, term (which cannot exceed ten years) and other conditions on exercise.

The Compensation Committee may grant SARs as a right in tandem with the number of shares underlying stock options granted under the 2019 Plan or as a freestanding award. Upon exercise, SARs entitle the holder to receive payment per share in stock or cash, or in a combination of stock and cash, equal to the excess of the share's fair market value on the date of exercise over the grant price of the SAR.

The Compensation Committee may also grant awards of restricted stock, which are shares of common stock subject to specified restrictions, and restricted stock units, which represent the right to receive shares of the common stock in the future. These awards may be made subject to repurchase, forfeiture or vesting restrictions at the Compensation Committee's discretion. The restrictions may be based on continuous service with the Company or the attainment of specified performance goals, as determined by the Compensation Committee. Stock units may be paid in stock or cash or a combination of stock and cash, as determined by the Compensation Committee.

The Compensation Committee may condition the grant, exercise, vesting, or settlement of any award on such performance conditions as it may specify. We refer to these awards as "performance awards." The Compensation Committee may select such business criteria or other performance measures as it may deem appropriate in establishing any performance conditions. At March 31, 2021, the Compensation Committee has not granted any performance awards.

A total of 7,500,000 shares of common stock were initially authorized for issuance under the 2019 Plan. As noted previously, all awards outstanding under the 2016 Plan at the time the 2019 Plan was adopted remain subject to the 2016 Plan. Upon approval of the 2019 Plan, all shares of common stock remaining authorized and available for issuance under the 2016 Plan, approximately 1.4 million shares, automatically became available for issuance under the 2019 Plan. Additionally, any shares subject to outstanding awards under the 2016 Plan that subsequently expire, terminate, or are surrendered or forfeited for any reason without issuance of shares also become available for issuance under the 2019 Plan. Further, if any award under the 2019 Plan is canceled, terminates, expires or lapses for any reason prior to the issuance of shares or if shares are issued under the 2019 Plan and thereafter are forfeited to us, the shares subject to such awards and the forfeited shares will again be available for grant under the 2019 Plan. At March 31, 2021, a total of 1,843,158 shares remain available for grant under the 2019 Plan.

No more than 25% of any equity-based awards granted under the 2019 Plan may vest on the grant date of such award. This requirement does not apply to (i) substitute awards resulting from acquisitions or (ii) shares delivered in lieu of fully vested cash awards. In addition, the minimum vesting requirement does not apply to the Compensation Committee's discretion to provide for accelerated exercisability or vesting of any award, including in cases of retirement, death, disability or a change in control, in the terms of the award or otherwise. Awards are not transferable other than by will or the laws of descent and distribution, except that in certain instances transfers may be made to or for the benefit of designated family members of the participant for no consideration.

In the event of a change in control of the Company, the Compensation Committee may accelerate the time period relating to the exercise of any award. In addition, the Compensation Committee may take other action, including (a) providing for the purchase of any award for an amount of cash or other property that could have been received upon the exercise of such award had the award been currently exercisable, (b) adjusting the terms of the award in a manner determined by the Compensation Committee to reflect the change in control, or (c) causing an award to be assumed, or new rights substituted therefor, by another entity with appropriate adjustments to be made regarding the number and kind of shares and exercise prices of the award. "Change in Control" is defined under the 2019 Plan and requires consummation of the applicable transaction.

Unless earlier terminated by the Board, the 2019 Plan will terminate, and no further awards may be granted, on September 5, 2029, which is ten years after the date on which it was approved by our stockholders. The Board may amend, suspend or terminate the 2019 Plan at any time. To the extent necessary to comply with applicable provisions of U.S. federal securities laws, state corporate and securities laws, the Code, the rules of any applicable stock exchange or national market system, and the rules of any non-U.S. jurisdiction applicable to Awards granted to residents therein, we will obtain stockholder approval of any such amendment to the 2019 Plan in such a manner and to such a degree as required. The amendment, suspension or termination of the 2019 Plan or the amendment of an outstanding award generally may not, without a participant's consent, materially impair the participant's rights under an outstanding award.

During our fiscal year ended March 31, 2021, we granted options to purchase an aggregate of 4,990,000 shares of our common stock from the 2019 Plan as follows:

- options to purchase an aggregate of 1,580,000 shares of our common stock at a price of $0.398 per share to independent members of our Board, our officers and employees and certain consultants and advisors in April 2020. The options vested 25% upon grant with the remaining shares vesting ratably over two years;

- options to purchase an aggregate of 365,000 shares of our common stock at prices of between $0.42 and $0.55 per share to various investor and public relations and scientific consultants in May and June 2020. The options vested 25% upon grant with the remaining shares vesting ratably monthly over one year;

- options to purchase an aggregate of 195,000 shares of our common stock at prices of between $0.62 and $0.73 per share to various investor and public relations and scientific consultants in August through October 2020. Certain grants vested 25% upon grant with the remaining shares vesting ratably over one year or three years; other options vested monthly over a period of one year or two years;

- options to purchase 200,000 shares of our common stock at a price of $0.7889 per share to a new research and development employee in December 2020. The options vest 25% on the first anniversary of the grant date with the remaining shares vesting ratably monthly over the next 4 years;

- options to purchase an aggregate of 1,375,000 shares of our common stock at a price of $1.77 per share to independent members of our Board, our officers and employees in December 2020 following the December 2020 Public Offering. The options vested 25% upon grant with the remaining shares vesting ratably over two years; and

- options to purchase 1,275,000 shares of our common stock at prices from $1.99 to $2.55 per share to new employees during February and March 2021. The options vest 25% on the first anniversary of the grant date with the remaining shares vesting ratably monthly over the next 3 years.

During our fiscal year ended March 31, 2020, we granted options to purchase an aggregate of 3,455,000 shares of our common stock from the 2019 Plan and the 2016 Plan as follows:

- options from the 2016 Plan to purchase an aggregate of 1,220,000 shares of our common stock at a then above-market exercise price of $1.00 per share to the independent members of our Board, our officers and employees and certain consultants in May 2019. The options vested 25% upon grant with the remaining shares vesting ratably over three years for independent directors, officers and employees, and over two years for consultants;

- options from the 2019 Plan to one of our officers to purchase 170,000 shares of our common stock at a then above-market exercise price of $1.00 per share, which May 2019 grant was contingent upon the approval of the 2019 Plan by our stockholders. Our stockholders approved the 2019 Plan at our Annual Meeting in September 2019 and ratified the contingent grant. The option vested 25% upon approval of the 2019 Plan and the remaining shares are vesting ratably over three years;

- options from our 2019 Plan to the independent members of our Board, our officers and employees and certain consultants to purchase an aggregate of 1,990,000 shares of our common stock at exercise prices ranging from $0.50 per share to $1.41 per share during the quarter ended December 31, 2019. Options granted to Board members, officers, employees and most consultants were vested 25% at grant, with the remaining options vesting ratably over the following 24 months. In the case of options granted to certain consultants, the options were vested 25% at grant but the remaining vesting period was less than 24 months to coincide with remaining contractual terms;

- options from our 2019 Plan to purchase 75,000 shares of our common stock at an exercise price of $0.7074 per share to a consultant as partial compensation under a professional services contract in January 2020. The options were vested 25% upon grant with the remaining shares vesting ratably over the next twelve months.

The following table summarizes stock-based compensation expense related to option grants to our officers, independent directors, consultants and service providers included in the accompanying Consolidated Statement of Operations and Comprehensive Loss for the years ended March 31, 2021 and 2020.

| | Fiscal Years Ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| Research and development expense | $ 746,900 | $ 1,287,200 |
| General and administrative expense | 1,559,200 | 2,533,600 |
| Total stock-based compensation expense | $ 2,306,100 | $ 3,820,800 |

Expense amounts reported above include $7,500 and $2,500 in research and development expense for the fiscal years ended March 31, 2021 and 2020, respectively, and $6,800 and $1,500 in general and administrative expense for the fiscal years ended March 31, 2021 and 2020, respectively, attributable to our 2019 Employee Stock Purchase Plan (the *2019 ESPP*), described below.

We used the Black-Scholes Option Pricing model with the following weighted average assumptions to determine share-based compensation expense related to option grants during the fiscal years ended March 31, 2021 and 2020:

| | Fiscal Years Ended March 31, | |
|---|---|---|
| | 2021 | 2020 |
| | (weighted average) | (weighted average) |
| Exercise price | $ 1.27 | $ 1.14 |
| Market price on date of grant | $ 1.27 | $ 1.05 |
| Risk-free interest rate | 0.53% | 1.79% |
| Expected term (years) | 5.58 | 5.41 |
| Volatility | 83.79% | 86.99% |
| Expected dividend yield | 0.00% | 0.00% |
| | | |
| Fair value per share at grant date | $ 0.87 | $ 0.73 |

The expected term of options represents the period that our share-based compensation awards are expected to be outstanding. We have calculated the weighted-average expected term of the options using the simplified method as prescribed by Securities and Exchange Commission Staff Accounting Bulletins No. 107 and No. 110 (*SAB No. 107 and 110*). The utilization of SAB No. 107 and 110 is based on the lack of relevant historical option exercises and relevant historical data due to the relatively limited period during which our stock has been publicly traded on a major exchange and the historical lack of liquidity in freely-tradable shares of our common stock. Those factors also resulted in our decision to utilize the historical volatilities of a peer group of public companies' stock over the expected term of the option in determining our expected volatility assumptions. The risk-free interest rate for periods related to the expected life of the options is based on the U.S. Treasury yield curve in effect at the time of grant. The expected dividend yield is zero, as we have not paid any dividends and do not anticipate paying dividends in the near future. We recognize the effect of forfeitures as they occur.

The following table summarizes stock option activity for the fiscal years ended March 31, 2021 and 2020 under the 2019 Plan and the 2016 Plan:

| | Fiscal Years Ended March 31, | | | |
|---|---|---|---|---|
| | 2021 | | 2020 | |
| | Number of Shares | Weighted Average Exercise Price | Number of Shares | Weighted Average Exercise Price |
| Options outstanding at beginning of period | 10,003,088 | $ 1.36 | 6,626,088 | $ 1.48 |
| Options granted | 4,990,000 | $ 1.27 | 3,455,000 | $ 1.14 |
| Options exercised | (355,000) | $ 0.89 | - | $ - |
| Options forfeited | - | $ - | - | $ - |
| Options expired | - | $ - | (78,000) | $ 1.50 |
| | | | | |
| Options outstanding at end of period | 14,638,088 | $ 1.34 | 10,003,088 | $ 1.36 |
| Options exercisable at end of period | 10,732,059 | $ 1.29 | 7,936,290 | $ 1.39 |
| | | | | |
| Weighted average grant-date fair value of options granted during the period | | $ 0.87 | | $ 0.73 |

The following table summarizes information on stock options outstanding and exercisable under the 2019 Plan and the 2016 Plan as of March 31, 2021:

| | Options Outstanding | | | Options Exercisable | |
|---|---|---|---|---|---|
| Exercise Price | Number Outstanding | Weighted Average Remaining Years until Expiration | Weighted Average Exercise Price | Number Exercisable | Weighted Average Exercise Price |
| $ 0.398 to $0.89 | 2,590,000 | 9.12 | $ 0.48 | 1,574,795 | $ 0.45 |
| $ 0.90 to $1.18 | 3,240,000 | 7.42 | $ 1.09 | 2,871,049 | $ 1.10 |
| $ 1.19 to $1.46 | 2,500,000 | 8.13 | $ 1.36 | 2,155,468 | $ 1.35 |
| $ 1.47 to $1.63 | 3,177,253 | 5.85 | $ 1.52 | 3,177,253 | $ 1.52 |
| $ 1.64 to $15.00 | 3,130,835 | 9.40 | $ 2.14 | 953,494 | $ 2.38 |
| | 14,638,088 | 7.92 | $ 1.34 | 10,732,059 | $ 1.29 |

At March 31, 2021, there were 1,843,158 registered shares of our common stock remaining available for grant under the 2019 Plan. Two members of our Board and certain consultants exercised options to purchase an aggregate of 355,000 shares of our common stock during the fiscal year ended March 31, 2021. There were no option exercises during the fiscal year ended March 31, 2020.

Aggregate intrinsic value is the sum of the amount by which the fair value of the underlying common stock exceeds the aggregate exercise price of the outstanding options (*in-the-money-options*). Based on the $2.13 per share quoted closing market price of our common stock on March 31, 2021, there was approximately $12,205,000 of intrinsic value in our outstanding options at that date.

As of March 31, 2021, there was approximately $3,852,300 of unrecognized compensation cost related to non-vested share-based compensation awards from the 2019 Plan and the 2016 Plan, which cost is expected to be recognized through November 2023.

***2019 Employee Stock Purchase Plan***

Our Board approved the VistaGen Therapeutics, Inc. 2019 Employee Stock Purchase Plan (the 2019 ESPP) on June 13, 2019. Our stockholders approved the 2019 ESPP at our annual meeting on September 5, 2019. The principal terms of our 2019 ESPP are summarized below.

The 2019 ESPP is intended to qualify as an “employee stock purchase plan” under Section 423 of the Code. The Compensation Committee of the Board administers the 2019 ESPP. The Compensation Committee has authority to construe, interpret and apply the terms of the 2019 ESPP. As approved by our stockholders, a maximum of 1,000,000 shares of our common stock may be purchased under the 2019 ESPP.

The 2019 ESPP is generally expected to operate in consecutive semi-annual periods referred to as “option periods.” The first option period commenced on January 1, 2020 and ended on the last trading day in the semi-annual period ended June 30, 2020, with successive option periods expected to begin on the first day of January and July and to terminate on the last trading day of June and December, respectively. Option periods may not last longer than the maximum period permitted under Section 423 of the Code, which generally limits the length of such offerings to either 5 years or 27 months, depending on the terms of the offering. Generally, all full-time employees of the Company and its subsidiaries are eligible to participate in an option period.

On the first day of each option period (the *Grant Date*), each eligible employee for that option period will be granted an option to purchase shares of our common stock. Each participant’s option will permit the participant to purchase a number of shares determined by dividing the employee’s accumulated payroll deductions for the option period by the applicable purchase price. A participant must designate the percentage (if any) of compensation to be deducted during that option period for the purchase of stock under the 2019 ESPP. The participant’s payroll deduction election will generally remain in effect for future option periods unless terminated by the participant. A participant may elect to withdraw from any option period prior to the last day of the option period, in which case the participant’s payroll deductions will be refunded and the participant’s outstanding options will terminate.

Each participant’s payroll deductions under the 2019 ESPP will be credited to a liability account in his or her name under the 2019 ESPP. The aggregate liability for participant payroll deductions at March 31, 2021 and 2020 was $18,600 and $14,700, respectively, which amounts are included in accrued expenses in the accompanying Consolidated Balance Sheet at those dates.

Each option granted under the 2019 ESPP will automatically be exercised on the last day of the respective option period (referred to as the *Exercise Date*). The number of shares acquired by a participant upon exercise of his or her option will be determined by dividing the participant's 2019 ESPP account balance as of the Exercise Date for the option period by the purchase price of the option. The purchase price for each option is generally equal to the lesser of (i) 85% of the fair market value of a share of our common stock on the applicable Grant Date, or (ii) 85% of the fair market value of a share of our common stock on the applicable Exercise Date. A participant's 2019 ESPP account will be reduced upon exercise of his or her option by the amount used to pay the purchase price of the shares acquired by the participant. Following exercise of the option, any excess amount in a participant's account will be refunded following the Exercise Date. No interest will be paid to any participant under the 2019 ESPP.

Participation in the 2019 ESPP is subject to the following limits:

- A participant cannot contribute less than 1% or more than 15% of his or her compensation to the purchase of stock under the 2019 ESPP in any one payroll period;
- A participant cannot accrue rights to purchase more than $25,000 of stock (valued at the Grant Date of the applicable offering period and without giving effect to any discount reflected in the purchase price for the stock) for each calendar year in which an option is outstanding; and
- A participant will not be granted an option under the 2019 ESPP if it would cause the participant to own stock and/or hold outstanding options to purchase common stock constituting 5.0% or more of the total combined voting power or value of all classes of stock of the Company or of one of its subsidiaries or to the extent it would exceed certain other limits under the Code.

The $25,000 annual purchase and the 5% ownership limitations referred to above are required under the Code.

As is customary, the number of shares of stock available under the 2019 ESPP or subject to outstanding options, is subject to adjustment in the event of certain reorganizations, combinations, recapitalization of shares, stock splits, reverse stock split, subdivision or other similar change in respect of our common stock. A participant's rights with respect to options or the purchase of shares under the 2019 ESPP, as well as payroll deductions credited to his or her 2019 ESPP account, may not be assigned, transferred, pledged or otherwise disposed of in any way except by will or the laws of descent and distribution.

The Board generally may amend, suspend, or terminate the 2019 ESPP at any time and in any manner, except that stockholder approval is required to increase the number of shares authorized for issuance under the 2019 ESPP and for certain other amendments. No amendment to the 2019 ESPP may materially adversely affect the option rights previously granted to a participant under the 2019 ESPP, except as required by law or regulation.

Our 2019 ESPP became effective on January 1, 2020 and will continue in effect until the earlier of such time as all of the shares of the Company's common stock subject to the 2019 ESPP have been sold or December 31, 2030, unless terminated earlier by the Board. During the fiscal year ended March 31, 2021, employees purchased an aggregate of 58,125 shares of common stock under the 2019 ESPP and the Company received proceeds of $26,200.

***401(k) Plan***

Through a third-party agent, we maintain a retirement and deferred savings plan for our employees. This plan is intended to qualify as a tax-qualified plan under Section 401(k) of the Internal Revenue Code. The retirement and deferred savings plan provides that each participant may contribute a portion of his or her pre-tax compensation, subject to statutory limits. Under the plan, each employee is fully vested in his or her deferred salary contributions. Employee contributions are held and invested by the plan's trustee. The retirement and deferred savings plan also permits us to make discretionary contributions, subject to established limits and a vesting schedule. To date, we have not made any discretionary contributions to the retirement and deferred savings plan on behalf of participating employees.

**14. Related Party Transactions**

*Consulting Agreement*

We have we engaged a consulting firm headed by one of the independent members of our Board to provide various market research studies, competitive analyses, and commercial advisory projects for certain of our CNS pipeline candidates pursuant to which we recorded expense of $193,000 and $108,400 for the fiscal years ended March 31, 2021 and 2020, respectively. We recorded no accounts payable or accrued expenses related to such services at March 31, 2021 or 2020.

**15. Commitments, Contingencies, Guarantees and Indemnifications**

From time to time, we may become involved in claims and other legal matters arising in the ordinary course of business. Management is not currently aware of any claims made or other legal matters that will have a material adverse effect on our consolidated financial position, results of operations or our cash flows.

We indemnify our officers and directors for certain events or occurrences while the officer or director is or was serving at our request in such capacity. The term of the indemnification period is for the officer's or director's lifetime. We will indemnify the officers or directors against any and all expenses incurred by the officers or directors because of their status as one of our directors or executive officers to the fullest extent permitted by Nevada law. We have never incurred costs to defend lawsuits or settle claims related to these indemnification agreements. We have a director and officer insurance policy which limits our exposure and may enable us to recover a portion of any future amounts paid. We believe the fair value of these indemnification agreements is minimal. Accordingly, there are no liabilities recorded for these agreements at March 31, 2021 or 2020.

In the normal course of business, we provide indemnifications of varying scopes under agreements with other companies, typically clinical research organizations, investigators, clinical sites, suppliers and others. Pursuant to these agreements, we generally indemnify, hold harmless, and agree to reimburse the indemnified parties for losses suffered or incurred by the indemnified parties in connection with the use or testing of our product candidates or with any U.S. patents or any copyright or other intellectual property infringement claims by any third party with respect to our product candidates. The terms of these indemnification agreements are generally perpetual. The potential future payments we could be required to make under these indemnification agreements is unlimited. We maintain liability insurance coverage that limits our exposure. We believe the fair value of these indemnification agreements is minimal. Accordingly, we have not recorded any liabilities for these agreements at March 31, 2021 or 2020.

***Leases***

**Financing Lease**

At March 31, 2021 and 2020, the following assets are subject to financing lease obligations and included in property and equipment:

| | March 31, 2021 | March 31, 2020 |
|---|---|---|
| Office equipment subject to financing lease | $ 14,700 | $ 14,700 |
| Accumulated depreciation | (12,400) | (9,400) |
| Net book value of office equipment subject to financing lease | $ 2,300 | $ 5,300 |

Amortization expense for assets recorded under financing leases is included in depreciation expense. Future minimum payments, by year and in the aggregate, required under our financing lease are as follows:

| Fiscal Year Ending March 31, | |
|---|---|
| 2022 | $ 3,200 |
| Future minimum lease payments | 3,200 |
| Less imputed interest included in minimum lease payments | (200) |
| Present value of minimum lease payments | 3,000 |
| Less current portion | (3,000) |
| Financing lease obligation - non-current portion | $ - |

**Operating Lease**

We lease our headquarters office and laboratory space in South San Francisco, California under the terms of a lease that expires on July 31, 2022 and that provides an option to renew for an additional five years at then-current market rates. Consistent with the guidance in ASC 842, effective beginning April 1, 2019, we have recorded this lease in our Consolidated Balance Sheet as an operating lease. For the purpose of determining the right-of-use asset and associated lease liability, upon our adoption of ASC 842, we determined that the renewal of this lease was reasonably probable. The lease of our South San Francisco facilities does not include any restrictions or covenants requiring special treatment under ASC 842.

The following table summarizes the presentation of the operating lease in our Condensed Consolidated Balance Sheet at March 31, 2021 and 2020:

| | As of March 31, 2021 | As of March 31, 2020 |
|---|---|---|
| *Assets* | | |
| Right of use asset – operating lease | $ 3,219,600 | $ 3,579,600 |
| *Liabilities* | | |
| Current operating lease obligation | $ 364,800 | $ 313,400 |
| Non-current operating lease obligation | 3,350,800 | 3,715,600 |
| Total operating lease liability | $ 3,715,600 | $ 4,029,000 |

The following table summarizes the effect of operating lease costs in our consolidated statements of operations:

| | For the Fiscal Year Ended March 31, 2021 | For the Fiscal Year Ended March 31, 2020 |
|---|---|---|
| Operating lease cost | $ 838,200 | $ 822,300 |

The minimum (base rental) lease payments related to our South San Francisco operating lease are expected to be as follows:

| Fiscal Years Ending March 31, | |
|---|---|
| 2022 | $ 668,400 |
| 2023 | 726,000 |
| 2024 | 766,000 |
| 2025 | 789,000 |
| 2026 | 812,700 |
| Thereafter | 1,118,700 |
| Total lease expense | 4,880,800 |
| Less imputed interest | (1,165,200) |
| Present value of operating lease liabilities | $ 3,715,600 |

The remaining lease term, including the assumed five-year extension at the expiration of the current lease period, and the discount rate assumption for our South San Francisco operating lease is as follows:

| | As of March 31, 2021 |
|---|---|
| Assumed remaining lease term in years | 6.33 |
| Assumed discount rate | 8.54% |

The interest rate implicit in lease contracts is typically not readily determinable and, as such, we used our estimated incremental borrowing rate based on information available at the adoption of ASC 842, which represents an internally developed rate that would be incurred to borrow, on a collateralized basis, over a similar term, an amount equal to the lease payments in a similar economic environment.

Supplemental disclosure of cash flow information related to our operating leases included in cash flows used by operating activities in the consolidated statements of cash flows is as follows:

| | For the Fiscal Year Ended March 31, 2021 | For the Fiscal Year Ended March 31, 2020 |
|---|---|---|
| Cash paid for amounts included in the measurement of lease liabilities | $ 791,600 | $ 753,900 |

During the fiscal years end March 31, 2021 and 2020, other than the April 1, 2019 initial adoption of ASC 842 that required right of use assets and lease liabilities to be recorded, we recorded no new right of use assets arising from new lease liabilities.

We also lease a small office in the San Francisco Bay Area under a month-to-month arrangement at insignificant cost and have made an accounting policy election not to apply the ASC 842 operating lease recognition requirements to such short-term lease. We recognize the lease payments for this lease in general and administrative expense over the lease term. We recorded rent expense of $14,200 and $14,000 for the fiscal years ended March 31, 2021 and 2020, respectively, attributable to this lease.

**16. Subsequent Events**

We have evaluated subsequent events through the date of this Annual Report and have identified the following material events and transactions that occurred after March 31, 2021:

***Conversion of Series D Preferred Stock***

From April 5, 2021 to April 22,2021, holders of an aggregate of 402,149 shares of our Series D Preferred converted such shares into 9,249,427 shares of our registered common stock, following which no shares of Series D Preferred remained outstanding.

***Exercise of Warrants***

From April 1, 2021 through the date of this Annual Report, holders of outstanding warrants have exercised warrants to purchase an aggregate of 1,508,768 shares of our common stock and we have received cash proceeds of approximately $1,105,700. On May 16, 2021, warrants to purchase 2,705,883 shares of our common stock at $5.30 per share expired unexercised.

***Grant of Options from 2019 Plan***

From April 1, 2021 through the date of this Annual Report, we granted options to purchase 575,000 shares of our common stock under the terms of our 2019 Plan to three newly-hired executives and a new independent member of our Board. The options have an exercise price equal to the quoted closing market price of our common stock on the Nasdaq Capital Market on the respective date of grant, a term of ten years and vest 25% on the first anniversary of the grant date and ratably on a monthly basis for three years thereafter.

***Termination of LPC Agreement***

On June 25, 2021, in accordance with its provisions, we voluntarily terminated the LPC Agreement and we will sell no additional shares of our common stock under that agreement.

**17. Supplemental Financial Information (Unaudited)**

The following table presents the unaudited statements of operations data for each of the eight quarters in the period ended March 31, 2021. The information has been presented on the same basis as the audited financial statements and all necessary adjustments, consisting only of normal recurring adjustments, have been included in the amounts below to present fairly the unaudited quarterly results when read in conjunction with the audited financial statements and related notes. The operating results for any quarter should not be relied upon as necessarily indicative of results for any future period.

**Quarterly Results of Operations (Unaudited)**
**(in thousands, except share and per share amounts)**

| | Three Months Ended | | | | Total |
|---|---|---|---|---|---|
| | June 30, 2020 | September 30, 2020 | December 31, 2020 | March 31, 2021 | Fiscal Year 2021 |
| Sublicense revenue | $ - | $ 334 | $ 314 | $ 442 | $ 1,090 |
| Total revenue | - | 334 | 314 | 442 | 1,090 |
| | | | | | |
| Operating expenses: | | | | | |
| Research and development | $ 1,731 | $ 2,358 | $ 3,496 | $ 4,891 | $ 12,476 |
| General and administrative | 1,391 | 1,270 | 2,117 | 1,770 | 6,548 |
| Total operating expenses | 3,122 | 3,628 | 5,613 | 6,661 | 19,024 |
| Loss from operations | (3,122) | (3,294) | (5,299) | (6,219) | (17,934) |
| | | | | | |
| Other income (expense), net: | | | | | |
| Interest income (expense), net | (3) | (4) | 1 | 8 | 2 |
| Other income | 1 | - | - | - | 1 |
| | | | | | |
| Loss before income taxes | (3,124) | (3,298) | (5,298) | (6,211) | (17,931) |
| Income taxes | (3) | - | - | - | (3) |
| Net loss and comprehensive loss | (3,127) | (3,298) | (5,298) | (6,211) | (17,934) |
| | | | | | |
| Accrued dividend on Series B Preferred stock | (336) | (347) | (354) | (349) | (1,386) |
| Beneficial conversion feature on Series D Preferred stock | - | - | - | (23,000) | (23,000) |
| | | | | | |
| Net loss attributable to common stockholders | $ (3,463) | $ (3,645) | $ (5,652) | $ (29,560) | $ (42,320) |
| | | | | | |
| Basic and diluted net loss per common share attributable to common stockholders | $ (0.07) | $ (0.05) | $ (0.07) | $ (0.20) | $ (0.49) |
| Weighted average shares used in computing basic and diluted net loss per common share attributable to common stockholders | 51,321,355 | 67,082,935 | 81,086,105 | 145,966,502 | 86,133,644 |

| | Three Months Ended | | | | Total |
|---|---|---|---|---|---|
| | June 30, 2019 | September 30, 2019 | December 31, 2019 | March 31, 2020 | Fiscal Year 2020 |
| Operating expenses: | | | | | |
| Research and development | $ 4,314 | $ 4,205 | $ 3,015 | $ 1,840 | $ 13,374 |
| General and administrative | 1,910 | 1,146 | 2,948 | 1,423 | 7,427 |
| Total operating expenses | 6,224 | 5,351 | 5,963 | 3,263 | 20,801 |
| Loss from operations | (6,224) | (5,351) | (5,963) | (3,263) | (20,801) |
| Other expenses, net: | | | | | |
| Interest income (expense), net | 16 | 15 | 2 | (3) | 30 |
| Loss before income taxes | (6,208) | (5,336) | (5,961) | (3,266) | (20,771) |
| Income taxes | (2) | - | - | (1) | (3) |
| Net loss and comprehensive loss | (6,210) | (5,336) | (5,961) | (3,267) | (20,774) |
| Accrued dividend on Series B Preferred stock | (302) | (314) | (322) | (326) | (1,264) |
| Net loss attributable to common stockholders | $ (6,512) | $ (5,650) | $ (6,283) | $ (3,593) | $ (22,038) |
| Basic and diluted net loss per common share attributable to common stockholders | $ (0.15) | $ (0.13) | $ (0.15) | $ (0.08) | $ (0.50) |
| Weighted average shares used in computing basic and diluted net loss per common share attributable to common stockholders | 42,622,965 | 42,622,965 | 43,158,889 | 47,094,781 | 43,869,523 |

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

None.

**Item 9A. Controls and Procedures**

**Disclosure Controls and Procedures.**

As required by Rule 13a-15(b) under the Securities Exchange Act of 1934, as amended, (the *Exchange Act*) our Chief Executive Officer (*CEO*) and our Chief Financial Officer (*CFO*) conducted an evaluation as of the end of the period covered by this Annual Report on Form 10-K, of the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. Based on that evaluation, our CEO and our CFO each concluded that our disclosure controls and procedures are effective to provide reasonable assurance that information required to be disclosed in the reports that we file or submit under the Exchange Act, (i) is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms and (ii) is accumulated and communicated to our management, including our CEO and our CFO, as appropriate to allow timely decisions regarding required disclosure.

**Management's Report on Internal Control Over Financial Reporting.**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Our internal control system is designed to provide reasonable assurance to our management and Board of Directors regarding the reliability of financial reporting and the preparation and fair presentation of financial statements for external purposes in accordance with U.S. generally accepted accounting principles.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance of achieving their control objectives. Smaller reporting companies may face additional limitations in achieving control objectives. Smaller reporting companies typically employ fewer individuals who are often tasked with a wide range of responsibilities, making it difficult to segregate duties. Often, one or two individuals control many, or all, aspects of the smaller reporting company’s general and financial operations, placing such individual(s) in a position to override any system of internal control. Additionally, projections of an evaluation of current 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 controls may deteriorate.

Management has assessed the effectiveness of our internal control over financial reporting for our fiscal year ended March 31, 2021. Management's assessment was based on criteria set forth in *Internal Control - Integrated Framework (2013)*, issued by the Committee of Sponsoring Organizations of the Treadway Commission (*COSO*). Based upon this assessment, management concluded that, as of March 31, 2021, our internal control over financial reporting was not effective, based upon those criteria, as a result of the material weaknesses identified below.

A material weakness is a deficiency or combination of deficiencies in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the annual or interim financial statements will not be prevented or detected on a timely basis.

Specifically, management identified the following control weaknesses existing during our fiscal year ended March 31, 2021: (i) the size of the Company’s staff did not permit appropriate segregation of duties to (a) permit appropriate review of accounting transactions and/or accounting treatment by multiple qualified individuals, and (b) prevent one individual from overriding the internal control system by initiating, authorizing and completing all transactions; and (ii) the Company utilized accounting software that did not prevent erroneous or unauthorized changes to previous reporting periods and/or could be adjusted so as to not provide an adequate audit trail of entries made in the accounting software.

Beginning in April 2021, we have begun to address these material weaknesses by retaining additional accounting staff to facilitate appropriate review of accounting transactions and/or accounting treatment by multiple qualified individuals and by implementing state-of-the-art accounting software to prevent erroneous or unauthorized changes to previous reporting periods and/or adjustments and to provide an adequate auditing trail of entries made in the accounting software.

The Company does not believe that these control weaknesses have resulted in any deficient financial reporting because each of our CEO and CFO is aware of his responsibilities under the SEC's reporting requirements and personally certifies our financial reports. Further, the Company had implemented a series of manual checks and balances to verify that no previous reporting period had been improperly modified and that no unauthorized entries had been made in the current reporting period.

Accordingly, while the Company has identified certain material weaknesses in its system of internal control over financial reporting during its fiscal year ended March 31, 2021, it believes that it has taken reasonable and sufficient steps to ascertain that the financial information contained in this Annual Report is in accordance with U.S. generally accepted accounting principles.

As a result of the enactment of the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, and the resulting amendment of Section 404 of the Sarbanes-Oxley Act of 2002, as a smaller reporting company, we are not required to provide an attestation report by our independent registered public accounting firm regarding internal control over financial reporting for our fiscal year ended March 31, 2021 or thereafter, until such time as we are no longer eligible for the exemption for smaller issuers set forth within the Sarbanes-Oxley Act.

**Item 9B. Other Information**

***Termination of LPC Agreement***

On June 25, 2021, in accordance with its provisions, the Company voluntarily terminated the Purchase Agreement dated March 24, 2020 between the Company and LPC Capital Fund, LLC prior to its March 2022 contractual expiration and will sell no additional shares of its common stock under such agreement.

***Change in Board of Directors Membership***

On June 24, 2021, Dr. H. Ralph Snodgrass notified the Company's Board of Directors of his intention to step down from his position as a member of the Company's Board of Directors, effective June 30, 2021. Dr. Snodgrass will continue to serve as the Company's President and Chief Scientific Officer.

## PART III

### Item 10. Directors, Executive Officers and Corporate Governance

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2021 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission on or before July 29, 2021 pursuant to General Instruction G(3) of Form 10-K.

### Item 11. Executive Compensation

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2021 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission on or before July 29, 2021 pursuant to General Instruction G(3) of Form 10-K.

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

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2021 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission on or before July 29, 2021 pursuant to General Instruction G(3) of Form 10-K.

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

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2021 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission on or before July 29, 2021 pursuant to General Instruction G(3) of Form 10-K.

### Item 14. Principal Accounting Fees and Services

The information required by this Item is incorporated herein by reference to the information that will be contained in our proxy statement related to the 2021 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission on or before July 29, 2021 pursuant to General Instruction G(3) of Form 10-K.

## PART IV

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

**(a)(1) Financial Statements**

See Index to Financial Statements under Item 8 on page 82.

**(a)(2) Consolidated Financial Statement Schedules**

Consolidated financial statement schedules are omitted because they are not applicable or are not required or the information required to be set forth therein is included in the Consolidated Financial Statements or notes thereto.

**(a)(3) Exhibits**

The exhibits listed in the Exhibit Index below are filed or incorporated by reference as part of this report.

**Exhibit Index**

| Exhibit No. | Description |
|---|---|
| 1.1 | Open Market Sale Agreement[SM], dated May 14, 2021, by and between VistaGen Therapeutics, Inc. and Jefferies LLC, incorporated by reference from Exhibit 1.1 to the Company's Current Report on Form 8-K filed on May 14, 2021. |
| 2.1* | Agreement and Plan of Merger by and among Excaliber Enterprises, Ltd., VistaGen Therapeutics, Inc. and Excaliber Merger Subsidiary, Inc. |
| 3.4 | Articles of Merger filed with the Nevada Secretary of State on May 24, 2011, incorporated by reference from Exhibit 3.1 to the Company's Current Report on Form 8-K filed on May 31, 2011. |
| 3.5 | Certificate of Designations Series A Preferred, incorporated by reference from Exhibit 3.1 to the Company's Current Report on Form 8-K filed on December 23, 2011. |
| 3.6 | Certificate of Change filed with the Nevada Secretary of State on August 11, 2014 incorporated by reference from Exhibit 3.1 to the Company's Current Report on Form 8-K filed on August 14, 2014. |
| 3.7 | Certificate of Designation of the Relative Rights and Preferences of the Series B 10% Convertible Preferred Stock of VistaGen Therapeutics, Inc., filed with the Nevada Secretary of State on May 7, 2015, incorporated by reference from Exhibit 3.1 to the Company's Current Report on Form 8-K filed on May 13, 2015. |
| 3.9 | Certificate of Designation of the Relative Rights and Preferences of the Series C Convertible Preferred Stock of VistaGen Therapeutics, Inc., dated January 25, 2016, incorporated by reference from Exhibit 3.1 to the Company's Current Report on Form 8-K filed on January 29, 2016. |
| 3.10 | Restated Articles of Incorporation of VistaGen Therapeutics, Inc., dated August 16, 2016, incorporated by reference from Exhibit 3.1 to the Company's Current Report on Form 8-K, filed on August 17, 2016. |
| 3.11 | Second Amended and Restated Bylaws of VistaGen Therapeutics, Inc., dated August 16, 2016, incorporated by reference from Exhibit 3.2 to the Company's Current Report on Form 8-K, filed on August 16, 2016. |
| 3.12 | Certificate of Amendment to the Restated and Amended Articles of Incorporation of VistaGen Therapeutics, Inc., dated September 15, 2017; incorporated by reference from Exhibit 3.1 to the Company's Current Report on Form 8-K, filed on September 20, 2017. |
| 3.13 | Certificate of Amendment to the Restated and Amended Articles of Incorporation, as amended, of VistaGen Therapeutics, Inc., dated September 6 ,2019; incorporated by reference from Exhibit 3.1 to the Company's Current Report on Form 8-K, filed on September 6, 2019. |
| 3.14 | Certificate of Designation of the Relative Rights and Preferences of the Series D Convertible Preferred Stock of VistaGen Therapeutics, Inc., filed with the Nevada Secretary of State on December 21, 2020, incorporated by reference from Exhibit 3.1 to the Company's Current Report on Form 8-K filed on December 22, 2020. |
| 3.15 | Certificate of Amendment to the Restated and Amended Articles of Incorporation, as amended, of VistaGen Therapeutics, Inc., dated March 5, 2021, incorporated by reference from Exhibit 3.1 to the Company's Current Report on Form 8-K, filed on March 5, 2021. |
| 10.22* | License Agreement by and between Mount Sinai School of Medicine of New York University and the Company, dated October 1, 2004. |
| 10.26* | License Agreement, dated October 24, 2001, by and between the University of Maryland, Baltimore, Cornell Research Foundation and Artemis Neuroscience, Inc. |
| 10.40* | Employment Agreement, by and between, VistaGen and Shawn K. Singh, dated April 28, 2010, as amended May 9, 2011. |

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| 10.41* | Employment Agreement, by and between, VistaGen and H. Ralph Snodgrass, PhD, dated April 28, 2010, as amended May 9, 2011. |
| 10.49 | License Agreement No. 1, dated as of October 24, 2011 between University Health Network and VistaGen Therapeutics, Inc., incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K filed on November 30, 2011. |
| 10.57 | License Agreement No. 2, dated as of March 19, 2012 between University Health Network and VistaGen Therapeutics, Inc., incorporated by reference from Exhibit 10.57 to the Company's Annual Report on Form 10-K filed on July 2, 2012. |
| 10.67 | Note Exchange and Purchase Agreement dated as of October 11, 2012 by and between VistaGen Therapeutics, Inc. and Platinum Long Term Growth VII, LLP, incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K filed on October 16, 2012. |
| 10.73 | Amendment to Note Exchange and Purchase Agreement as of November 14, 2012 between VistaGen Therapeutics Inc. and Platinum Long Term Growth VII, LLP, incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K filed on November 20, 2012. |
| 10.75 | Amendment No. 2 to Note Exchange and Purchase Agreement as of January 31, 2013 between VistaGen Therapeutics Inc. and Platinum Long Term Growth VII, LLP, incorporated by reference from Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on February 14, 2013. |
| 10.76 | Amendment No. 3 to Note Exchange and Purchase Agreement as of February 22, 2013 between VistaGen Therapeutics Inc. and Platinum Long Term Growth VII, LLP, incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K filed on February 28, 2013. |
| 10.77 | Form of Warrant to Purchase Common Stock issued to independent members of the Company's Board of Directors and its executive officers on March 3, 2013, incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K filed on March 6, 2013. |
| 10.83 | Lease between Bayside Area Development, LLC and VistaGen Therapeutics, Inc. (California) dated April 24, 2013, incorporated by reference from Exhibit 10.83 to the Company's Annual Report on Form 10-K filed July 18, 2013. |
| 10.84 | Indemnification Agreement effective May 20, 2013 between the Company and Jon S. Saxe, incorporated by reference from Exhibit 10.84 to the Company's Annual Report on Form 10-K filed on July 18, 2013. |
| 10.85 | Indemnification Agreement effective May 20, 2013 between the Company and Shawn K. Singh, incorporated by reference from Exhibit 10.85 to the Company's Annual Report on Form 10-K filed on July 18, 2013. |
| 10.86 | Indemnification Agreement effective May 20, 2013 between the Company and H. Ralph Snodgrass, incorporated by reference from Exhibit 10.86 to the Company's Annual Report on Form 10-K filed on July 18, 2013. |
| 10.87 | Indemnification Agreement effective May 20, 2013 between the Company and Brian J. Underdown, incorporated by reference from Exhibit 10.87 to the Company's Annual Report on Form 10-K filed on July 18, 2013. |
| 10.88 | Indemnification Agreement effective May 20, 2013 between the Company and Jerrold D. Dotson, incorporated by reference from Exhibit 10.88 to the Company's Annual Report on Form 10-K filed on July 18, 2013. |
| 10.111 | Exchange Agreement, by and between VistaGen Therapeutics, Inc., and Platinum Long Term Growth VII, LLC and Montsant Partners, LLC, dated January 25, 2016, incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K filed on January 29, 2016. |
| 10.112 | Indemnification Agreement effective April 8, 2016 between the Company and Jerry B. Gin, incorporated by reference from Exhibit 10.112 to the Company's Annual Report on Form 10-K filed on June 24, 2016. |
| 10.113 | Underwriting Agreement, by and between Chardan Capital Markets, LLC and WallachBeth Capital, LLC, as representatives of the several underwriters, and VistaGen Therapeutics, Inc., dated May 10, 2016, incorporated by reference from Exhibit 1.1 to the Company's Current Report on Form 8-K filed on May 16, 2016. |
| 10.114 | Warrant Agency Agreement, by and between Computershare, Inc. and VistaGen Therapeutics, Inc., dated May 16, 2016, incorporated by reference from Exhibit 4.1 to the Company's Current Report on Form 8-K filed on May 16, 2016. |
| 10.115 | Form of Warrant; incorporated by reference from Exhibit 4.2 to the Company's Current Report on Form 8-K filed on May 16, 2016. |
| 10.116 | Second Amendment to Employment Agreement by and between VistaGen Therapeutics, Inc. and Shawn K. Singh, dated June 22, 2016, incorporated by reference from Exhibit 10.116 to the Company's Annual Report on Form 10-K filed on June 24, 2016. |
| 10.117 | Second Amendment to Employment Agreement by and between VistaGen Therapeutics, Inc. and H. Ralph Snodgrass, Ph.D., dated June 22, 2016, incorporated by reference from Exhibit 10.117 to the Company's Annual Report on Form 10-K filed on June 24, 2016. |
| 10.118 | Second Amendment to Lease between Bayside Area Development and the Company, effective November 10, 2016, incorporated by reference from Exhibit 10.1 to the Company's Quarterly report on Form 10-Q filed on November 15, 2016. |
| 10.119 | Indemnification Agreement effective November 10, 2016 between the Company and Mark A. Smith, incorporated by reference from Exhibit 10.2 to the Company's Quarterly report on Form 10-Q filed on November 15, 2016. |

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| 10.120+ | Exclusive License and Sublicense Agreement by and between VistaGen Therapeutics, Inc. and Apollo Biologics LP, effective December 9, 2016, incorporated by reference from Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on May 11, 2017. |
| 10.121+ | Patent License Amendment Agreement between VistaGen Therapeutics Inc. and University Health Network effective December 9, 2016, incorporated by reference from Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q/A filed on May 1, 2017. |
| 10.122 | Amended and Restated 2016 Stock Incentive Plan (formerly the VistaGen Therapeutics, Inc. 2008 Stock Incentive Plan), incorporated by reference from Exhibit 10.122 to the Company's Annual Report on Form 10-K filed on June 29, 2017. |
| 10.123 | Underwriting Agreement, dated as of August 31, 2017, by and between VistaGen Therapeutics, Inc. and Oppenheimer & Co. Inc., incorporated by reference from Exhibit 1.1 to the Company's Current Report on Form 8-K filed on August 31, 2017. |
| 10.124 | Form of Series A1 Warrant, incorporated by reference from Exhibit 4.1 to the Company's Current Report on Form 8-K filed on August 31, 2017. |
| 10.126 | Underwriting Agreement, dated as of December 11, 2017, by and between VistaGen Therapeutics, Inc. and Oppenheimer & Co. Inc., incorporated by reference from Exhibit 1.1 to the Company's Current Report on Form 8-K filed on December 13, 2017. |
| 10.127 | Form of Warrant, incorporated by reference from Exhibit 4.1 to the Company's Current Report on Form 8-K filed on December 13, 2017. |
| 10.128 | Form of Summer 2018 Private Placement Subscription Agreement, incorporated by reference from the Company's Current Report on Form 8-K filed on August 9, 2018. |
| 10.129 | Form of Summer 2018 Private Placement Warrant, incorporated by reference from the Company's Current Report on Form 8-K filed on August 9, 2018. |
| 10.130+ | License Agreement (PH94B), by and between VistaGen Therapeutics, Inc. and Pherin Pharmaceuticals, Inc., dated September 11, 2018, incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K filed on September 13, 2018 |
| 10.131+ | Option Agreement, by and between VistaGen Therapeutics, Inc. and Pherin Pharmaceuticals, Inc., dated September 11, 2018, incorporated by reference from Exhibit 10.2 to the Company's Current Report on Form 8-K filed on September 13, 2018. |
| 10.132+ | License Agreement (PH10), by and between VistaGen Therapeutics, Inc. and Pherin Pharmaceuticals, Inc., dated October 24, 2018, incorporated by reference from Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q/A filed on October 30, 2018. |
| 10.133 | Form of Fall 2018 Private Placement Subscription Agreement, incorporated by reference from Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed on October 29, 2018. |
| 10.134 | Form of Fall 2018 Private Placement Warrant, incorporated by reference from Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q filed on October 29, 2018. |
| 10.135 | Indemnification Agreement, dated January 10, 2019, by and between VistaGen Therapeutics, Inc. and Ann Cunningham, incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K filed on January 15, 2019. |
| 10.136 | Indemnification Agreement, dated November 10, 2016, by and between VistaGen Therapeutics, Inc. and Mark A. McPartland, incorporated by reference from Exhibit 10.136 to the Company's Annual Report on Form 10-K filed on June 25, 2019. |
| 10.137 | Underwriting Agreement, dated as of February 26, 2019, by and between VistaGen Therapeutics, Inc. and William Blair & Company, LLC, incorporated by reference from Exhibit 1.1 to the Company's Current Report on Form 8-K filed on March 4, 2019. |
| 10.138 | Master Services Agreement, dated July 11, 2017, by and between VistaGen Therapeutics, Inc. and Cato Research Ltd., incorporated by reference from Exhibit 10.138 to the Company's Annual Report on Form 10-K filed on June 25, 2019. |
| 10.139 | VistaGen Therapeutics, Inc. 2019 Omnibus Equity Incentive Plan, incorporated by reference from Exhibit 99.1 to the Company's Registration Statement on Form S-8 filed on October 1, 2019. |
| 10.140 | VistaGen Therapeutics, Inc. 2019 Employee Stock Purchase Plan, incorporated by reference from Exhibit 99.2 to the Company's Registration Statement on Form S-8 filed on October 1, 2019. |
| 10.141 | Form of Fall 2019 Private Placement Subscription Agreement, incorporated by reference from Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on November 7, 2019. |
| 10.142 | Form of Fall 2019 Private Placement Warrant, incorporated by reference from Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on November 7, 2019. |
| 10.143 | Form of Securities Purchase Agreement, dated January 24, 2020 between the Company and each purchaser named in the signature pages thereto, incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K filed on January 27, 2020. |
| 10.144 | Form of Warrant, dated January 24, 2020, incorporated by reference from Exhibit 10.2 to the Company's Current Report on Form 8-K filed on January 27, 2020. |

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| 10.145 | Purchase Agreement, by and between VistaGen Therapeutics, Inc. and Lincoln Park Capital Fund, LLC, dated March 24, 2020, incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K, filed March 26, 2020. |
| 10.146 | Registration Rights Agreement, by and between VistaGen Therapeutics, Inc. and Lincoln Park Capital Fund, LLC, dated March 24, 2020, incorporated by reference from Exhibit 10.2 to the Company's Current Report on Form 8-K, filed March 26, 2020 |
| 10.147 | Note Payable Agreement by and between VistaGen Therapeutics, Inc. and Silicon Valley Bank, dated April 22, 2020, incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K, filed April 27, 2020. |
| 10.148# | License and Collaboration Agreement between VistaGen Therapeutics, Inc. and EverInsight Therapeutics Inc. incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K, filed June 26, 2020. |
| 10.149 | Underwriting Agreement, dated August 2, 2020, by and between VistaGen Therapeutics, Inc. and Maxim Group, LLC incorporated by reference from Exhibit 1.1 to the Company's Current Report on Form 8-K filed on August 6, 2020. |
| 10.150 | Underwriting Agreement, dated December 18, 2020 by and among VistaGen Therapeutics, Inc., Jefferies LLC and William Blair & Company, L.L.C. incorporated by reference from Exhibit 1.1 to the Company's Current Report on Form 8-K filed on December 22, 2020. |
| 10.151 | Indemnification Agreement, dated April 26, 2021, by and between VistaGen Therapeutics, Inc. and Joanne Curley, Ph.D. incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K filed on April 27, 2021. |
| 21.1 | List of Subsidiaries, filed herewith. |
| 23.1 | Consent of Independent Registered Public Accounting Firm, filed herewith. |
| 31.1 | Certification of the Company's Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002, filed herewith. |
| 31.2 | Certification of the Company's Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002, filed herewith. |
| 32.1 | Certification of the Company's Chief Executive Officer and Chief Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, filed herewith. |
| 101.INS | XBRL Instance Document, filed herewith |
| 101.SCH | XBRL Taxonomy Extension Schema, filed herewith |
| 101.CAL | XBRL Taxonomy Extension Calculation Linkbase, filed herewith |
| 101.DEF | XBRL Taxonomy Extension Definition Linkbase, filed herewith |
| 101.LAB | XBRL Taxonomy Extension Label Linkbase, filed herewith |
| 101.PRE | XBRL Taxonomy Extension Presentation Linkbase, filed herewith |

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* Incorporated by reference from the like-numbered exhibit filed with our Current Report on Form 8-K on May 16, 2011.

\+ Confidential treatment has been granted for certain confidential portions of this agreement.

\# Pursuant to Item 601(b)(10) of Regulation S-K, certain confidential portions of this exhibit (indicated by "[*****]") have been omitted as the Company has determined (i) the omitted information is not material and (ii) the omitted information would likely cause harm to the Company if publicly disclosed.

**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, in the City of South San Francisco, State of California, on the 29th day of June, 2021.

**VistaGen Therapeutics, Inc.**

Date: June 29, 2021 By: /s/ *Shawn K. Singh*

**Shawn K. Singh, J.D.**
***Chief Executive Officer***

In accordance with the Exchange Act, 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/ Shawn K. Singh<br>**Shawn K. Singh, JD** | Chief Executive Officer, and Director<br>*(Principal Executive Officer)* | June 29, 2021 |
| /s/ Jerrold D. Dotson<br>**Jerrold D. Dotson** | Vice President and Chief Financial Officer<br>*(Principal Financial and Accounting Officer)* | June 29, 2021 |
| /s/ H. Ralph Snodgrass<br>**H. Ralph Snodgrass, Ph.D** | President, Chief Scientific Officer and Director | June 29, 2021 |
| /s/ Jon S. Saxe<br>**Jon S. Saxe** | Chairman of the Board of Directors | June 29, 2021 |
| /s/ Ann M. Cunningham<br>**Ann M. Cunningham** | Director | June 29, 2021 |
| /s/ Joanne Curley, Ph.D<br>**Joanne Curley, Ph.D.** | Director | June 29, 2021 |
| /s/ Jerry B. Gin, Ph.D<br>**Jerry B. Gin, Ph.D.** | Director | June 29, 2021 |
| /s/ Brian J. Underdown<br>**Brian J. Underdown, Ph. D** | Director | June 29, 2021 |

**Exhibit 21.1**

**List of Subsidiaries**

VistaGen Therapeutics, Inc., a California corporation d/b/a VistaStem Therapeutics, Inc.

VistaStem Canada, Inc. (Ontario, Canada)

Artemis Neuroscience, Inc. (Maryland)

**Exhibit 23.1**

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (File Nos. 333-234026, 333-223556 and 333-208354), Form S-3 (File Nos. 333-254299, 333-237968, 333-234025 and 333-215671) and Form S-1 (No. 333-237514) of VistaGen Therapeutics, Inc. of our report dated June 29, 2021 relating to the consolidated financial statements of VistaGen Therapeutics, Inc., which appears in this Annual Report on Form 10-K.

/s/ OUM & CO. LLP

San Francisco, California
June 29, 2021

**EXHIBIT 31.1**

**CERTIFICATION**

I, Shawn K. Singh, certify that;

1. I have reviewed this Annual Report on Form 10-K of VistaGen Therapeutics, Inc., a Nevada corporation;

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

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

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

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

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

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

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

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

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

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

June 29, 2021

/s/ Shawn K. Singh
Shawn K. Singh, JD
Principal Executive Officer

**EXHIBIT 31.2**

**CERTIFICATION**

I, Jerrold D. Dotson, certify that:

1. I have reviewed this Annual Report on Form 10-K of VistaGen Therapeutics, Inc., a Nevada corporation;

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

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

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

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

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

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

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

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

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

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

June 29, 2021

/s/ Jerrold D. Dotson
Jerrold D. Dotson
Principal Financial Officer

**EXHIBIT 32**

**CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,**
**AS ADOPTED PURSUANT TO**
**SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

Pursuant to 18 U.S.C. § 1350, as created by Section 906 of the Sarbanes-Oxley Act of 2002, the undersigned officer of VistaGen Therapeutics, Inc. (the "*Company* ") hereby certifies, to such officer's knowledge, that:

(i) the accompanying Annual Report on Form 10-K of the Company for the annual period ended March 31, 2021 (the "*Report*") fully complies with the requirements of Section 13(a) or Section 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(ii) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

June 29, 2021

/s/ Shawn K. Singh
Shawn K. Singh, JD
Principal Executive Officer

/s/ Jerrold D. Dotson
Jerrold D. Dotson
Principal Financial Officer