

**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, 2023

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

(State or other jurisdiction of
incorporation or organization)

20-5093315

(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

<u>Title of each class</u>	<u>Trading Symbol(s)</u>	<u>Name of each exchange on which registered</u>
Common Stock, par value \$0.001 per share	VTGN	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 every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes No

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

Large accelerated filer Accelerated filer Non-accelerated filer Smaller reporting company Emerging Growth company

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

Indicate by check mark whether the registrant 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

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. Yes No

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). 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, 2022, the last business day of the registrant's second fiscal quarter, was: \$31,202,662.

As of June 27, 2023, there were 7,872,479 shares of the registrant's common stock, \$0.001 par value per share, outstanding.

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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 availability of capital to satisfy our working capital requirements and development objectives for our product candidates;
- the accuracy of our estimates regarding future expenses, future revenues and future capital requirements;
- our plans to develop our product candidates, including, among other things, fasedienol (PH94B) as a potential acute treatment of anxiety in adults with social anxiety disorder (SAD) and other anxiety disorders, itruvone and (PH10) as a potential treatment for major depressive disorder (MDD) and other depression-related disorders, as well as development programs for our other product candidates- PH15, PH80, PH284 and AV-101;
- our ability to initiate and complete necessary preclinical and clinical studies in accordance with applicable regulatory requirements to advance the development of our product candidates 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 and other consultants on whose services we rely from time to time 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, commercial, and/or other 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. 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 our 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 statement 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 late clinical-stage biopharmaceutical company aiming to transform the treatment landscape for individuals living with anxiety, depression and other central nervous system (CNS) disorders. We are advancing therapeutics with the potential to be faster-acting, and with fewer side effects and safety concerns, than those currently available for treating anxiety, depression and multiple CNS disorders. Our pipeline includes six clinical-stage product candidates, including five investigational agents belonging to a new class of neuroactive drugs known as pherines, in addition to AV-101, an oral prodrug of an antagonist of the glycine site of the N-methyl-D-aspartate receptor (NMDAR). Pherines, which are administered as nasal sprays, are designed with an innovative rapid-onset mechanism of action that activates chemosensory neurons in the nasal cavity and can selectively and beneficially impact key neural circuits in the brain without requiring systemic uptake or direct activity on CNS neurons. AV-101 inhibits the activity of the ion channel of the NMDAR but does not block it, unlike some approved NMDAR antagonists having significant side effects.

Our CNS product candidates are set forth below. Each has an innovative potential mechanism of action (MOA), has been safe and well-tolerated in all clinical studies to date, and has therapeutic potential in multiple CNS markets.



(1) Indicates U.S. Investigational New Drug (IND) application-enabling work necessary to facilitate further clinical development in the U.S.

Our goal is to develop and commercialize, on our own and with multiple global and regional strategic partners, innovative therapies for anxiety, depression, and other CNS indications where current treatment options are inadequate to meet the needs of millions of patients in the U.S. and worldwide. First and foremost, we are passionate about transforming mental health care and redefining what is possible in the treatment of anxiety and depression disorders – *One Mind at a Time*TM.

Our Product Candidates

Pherine Product Candidates

Five of our product candidates – fasedienol (PH94B), itruvone (PH10), PH15, PH80 and PH284 – belong to a new class of synthetic neuroactive steroids referred to as pherines. Pherines, administered in ultra-low microgram level doses as odorless and tasteless nasal sprays, are designed to selectively engage chemosensory neurons in the nasal cavity and induce rapid-onset pharmacologic and behavioral benefits. Specifically, each of our pherine product candidates is a distinct chemical entity that selectively modulates particular areas of the brain, such as the limbic amygdala (the main fear and anxiety center of the brain), the hypothalamus, the hippocampus, the locus ceruleus, and the prefrontal cortex. We believe each of our pherine product candidates has the potential to be a fast-acting therapy for one or more CNS disorders, including social anxiety disorder (fasedienol), major depressive disorder (itruvone), cognitive impairment (PH15), vasomotor syndrome (hot flashes) due to menopause, as well as migraine headaches (PH80) and disorders related to appetite loss (cachexia) (PH284), all without requiring apparent systemic uptake or binding to classic abuse liability receptors or steroidal hormone receptors.

Fasedienol Nasal Spray

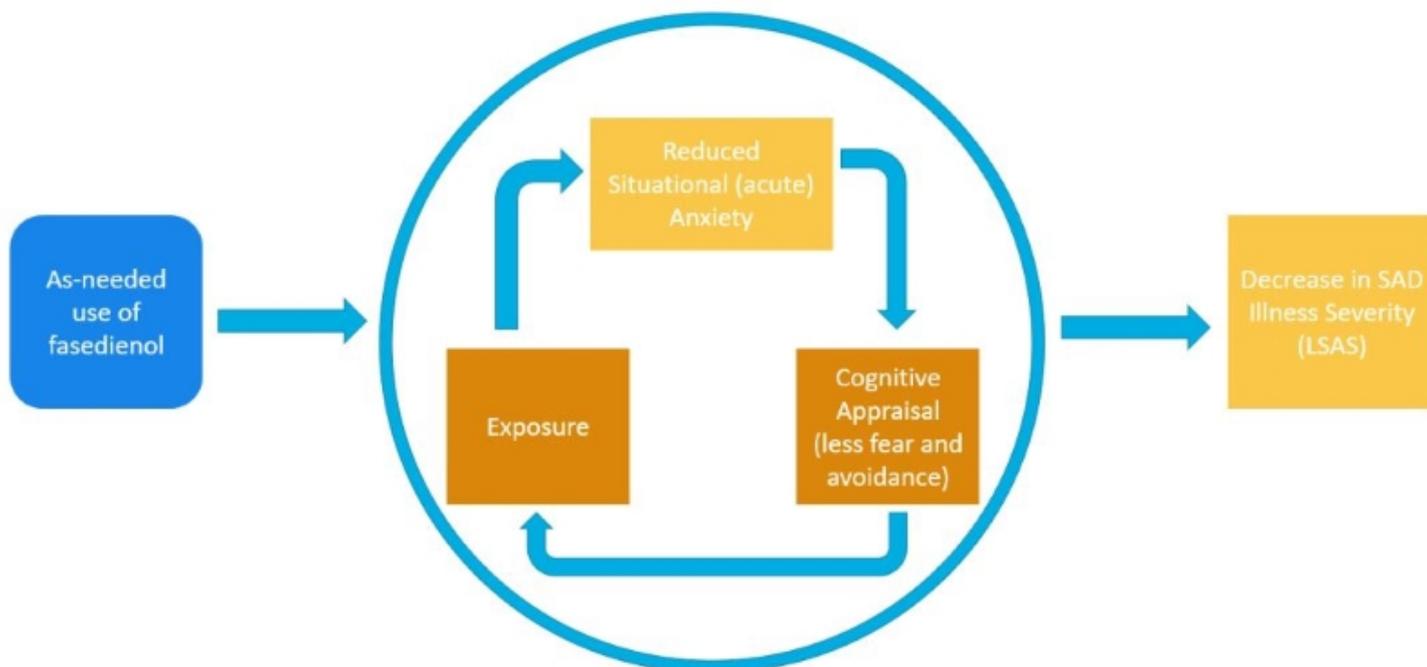
Fasedienol (PH94B) is a synthetic investigational pherine from the androstane family in Phase 3 clinical development in the U.S. for treatment of social anxiety disorder (SAD). When administered intranasally in microgram doses, fasedienol activates receptors of peripheral nasal chemosensory neurons connected to subsets of neurons in the olfactory bulbs that, in turn, connect to neurons in the limbic amygdala involved in the pathophysiology of SAD and potentially other anxiety and mood disorders. Fasedienol is pharmacologically active without requiring apparent systemic uptake and distribution of the compound to the brain to achieve its rapid-onset and short duration of anxiolytic effects.

Social Anxiety Disorder (SAD). Based on the 2021 National Health and Wellness Survey, over 25 million adults or 10% of the adult population in the U.S. have experienced SAD. SAD can be viewed as a series of acute, socially stressful events in which patients exhibit excessive fear of embarrassment, humiliation, scrutiny, evaluation, or rejection by others (Liebowitz, Gorman, Fyer, & Klein, 1985). The avoidance, fear, or anxious anticipation of these situations interferes significantly with the person's daily routine, having a marked impact on occupational functioning and social life. The disorder has a lifetime prevalence estimated at up to 13%, with onset typically in the mid-teens or earlier, and is diagnosed slightly more frequently in females than males. In the absence of anxiety-provoking social or performance events, generally, patients with SAD are asymptomatic.

SAD typically does not resolve naturally, oftentimes leading to alcohol use disorder and major depressive disorder (MDD) as sequelae. A key psychotherapy mechanism by which individuals with SAD overcome this condition, or lessen their symptoms, is believed to be by exposing themselves to feared or avoided situations. This is the basis of cognitive-behavioral treatment (CBT) for SAD. However, it is difficult for most individuals with SAD to even consider entering stressful, anxiety-provoking social or performance situations, preventing initiation of CBT as a psychotherapeutic approach with its gradual increase in exposure to stress, which is necessary for successful CBT.

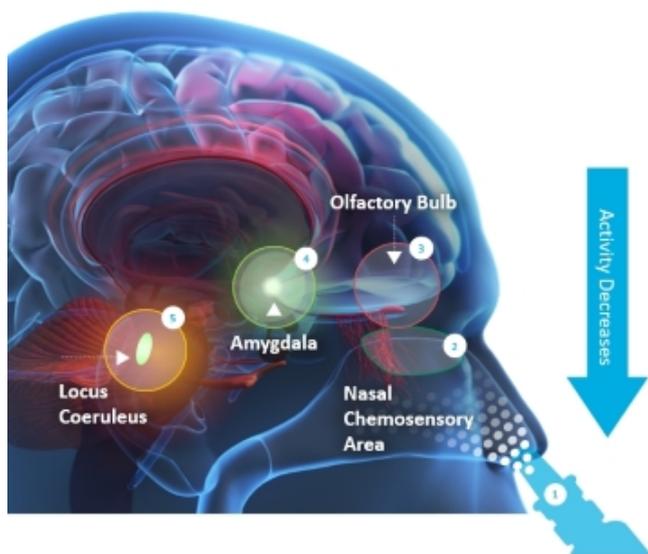
The three antidepressants currently FDA-approved for treatment of SAD exert their therapeutic effect by gradually and over time reducing the anxiety and physical symptoms that SAD patients experience when they find themselves in feared or avoided situations. Once these products begin to produce a clinical therapeutic benefit, usually at least three to six weeks following the start of daily systemic dosing, the approved treatments for SAD may work by controlling anxiety when SAD patients enter stressful, anxiety-provoking situations. However, these products require long-term daily maintenance dosing, regardless of whether the patient actually experiences social anxiety on a given day, and chronic treatment is typically associated with a range of bothersome side effects, such as gastrointestinal symptoms, agitation, sleep disturbances, weight changes, and sexual dysfunction.

Fasedienol and SAD. We believe fasedienol allows individuals affected by SAD to enter stressful or previously avoided social or performance situations with fewer or less severe symptoms when they have been pre-treated with fasedienol. A key and substantial difference between fasedienol and each of the three antidepressants approved by the FDA for the treatment of SAD is that fasedienol is used only on an as-needed basis prior to or during a socially stressful situation because of its rapid-onset pharmacological effect. Nor does fasedienol require systemic uptake and chronic daily maintenance dosing. Hence, fasedienol has the potential to reduce the wave of anxiety usually experienced by SAD patients when in a feared situation and is designed to be used on an as-needed basis prior to or during these stressful or often-avoided social or performance situations. Through more frequent exposure to socially stressful events, SAD subjects gain new insight about their social and performance situations and begin to cognitively separate the negative physiological symptoms of anxiety from specific anxiety-provoking events. By engaging in new situations previously avoided as a result of less severe and frequent waves of anxiety following treatment, subjects experience increased confidence, leading to an overall reduction in SAD illness severity, decreased burden of disease, improved workplace productivity, educational attainment, and satisfaction with social life.



Fasedienol does not exert effects on certain cellular receptors that are associated with known drug abuse potential (for example, dopamine, nicotinic, and opiate receptors) when activated by some other pharmaceutical compounds. It also does not produce agonistic or antagonistic effects on GABA_A α1/β2/γ2 ion channels. Fasedienol is pharmacologically active without requiring apparent systemic uptake and distribution to achieve its rapid-onset and short duration of anxiolytic effects. The U.S. Food and Drug Administration (FDA) has designated fasedienol as a Fast Track product candidate, and we are currently developing fasedienol for the treatment of anxiety symptoms in adult subjects with SAD.

Fasedienol's MOA via Olfactory-Amygdala Circuit



- ① Microgram-level intranasal dose of fasedienol (3.2 mcg) is administered.
- ② Fasedienol engages peripheral receptors in nasal chemosensory neurons (NCNs).
- ③ Once stimulated with fasedienol, NCNs then trigger subsets of interneurons in the olfactory bulbs (OB).
- ④ Neurons in the OB then stimulate inhibitory GABAergic "Fear Off" neurons in the limbic amygdala, the main fear and anxiety center of the brain.
- ⑤ The stimulation of the limbic amygdala DECREASES the activity of the sympathetic nervous system which facilitates fear extinction activity of the limbic-hypothalamic system, as well as in other parts of the brain.

Sources: Monti L, and Liebowitz MR (2020). Neural circuits of anxiolytic and antidepressant phetine molecules. CNS Spectrums <https://doi.org/10.1017/S109285292000190X>

The proposed MOA of fasedienol is fundamentally differentiated from all currently approved anti-anxiety medications, including the three antidepressants approved by the FDA for the treatment of SAD, as well as all benzodiazepines and beta blockers, which, although not FDA-approved for the treatment of SAD, are prescribed for treatment of SAD on an off-label basis. Pre-clinical and Phase 2 clinical studies completed to date suggest that fasedienol has the potential to achieve rapid-onset anti-anxiety effects without systemic uptake or transport into the brain, significantly reducing the risk of side effects and other safety concerns such as potential drug-drug interactions, abuse, misuse and addiction associated with certain other systemic pharmaceuticals that act directly on the CNS and are sometimes prescribed for anxiety disorders.

SAD Phase 1 Studies. Fasedienol's rapid-onset and short-acting properties are supported by Phase 1 clinical trials conducted in healthy male and female subjects. In these trials, fasedienol was intranasally administered to subjects via a noninvasive nasal spray device, and changes in bioelectric transmucosal potentials of the nasal septum chemosensory epithelium were measured. These trials demonstrated that: (i) the nasal chemosensory epithelium has receptors that are selective for fasedienol, and (ii) fasedienol produces an immediate local electrogram response (i.e., EVG or EGNR), as illustrated by electrograms recorded from the surface of the sensory neuroepithelial lining of the vomeronasal organ. Additional studies evaluated the effect of fasedienol on the EVG amplitude and duration. Collectively, these studies show that fasedienol produces a short-duration electrogram response at the level of the peripheral receptor sites. Systemic exposure to fasedienol was evaluated following escalating doses of fasedienol in healthy female subjects. No measurable plasma concentrations of fasedienol were observed in the blood samples taken following the two highest single intranasal doses of 4.8 and 19.2 µg. In all samples (taken at 15 minutes, 30 minutes, and one hour after dosing), the levels were below the level of detection of 0.1 ng/mL. For exploration, a more sensitive research bioanalytical method (non-validated) was used on a selection of samples. Using this method, with a limit of quantitation of 0.025 ng/mL, no fasedienol could be detected. A study was conducted in human subjects to establish the bioavailability of fasedienol administered intranasally and repeatedly with the maximal therapeutic dose. However, it was not possible to characterize the actual bioavailability of fasedienol due to the absence of quantifiable concentrations of fasedienol in plasma. With respect to fasedienol's safety profile, the totality of nonclinical data and clinical data in over 800 human subjects exposed to fasedienol to date continue to demonstrate that fasedienol appears to be safe and is well-tolerated, as well as the lack of abuse potential of fasedienol.

SAD Phase 2 Studies

Positive Phase 2 Results in Public Speaking and Social Interaction-Induced Stressors in a Clinical Setting. Phase 2 development of fasedienol began with a two-part public speaking and social interaction challenge study. In this published randomized, double-blind, placebo-controlled Phase 2 clinical trial (n=91) conducted at three clinical sites, 91 adult female subjects diagnosed with SAD underwent a placebo-only baseline public speaking and social interaction challenges in a clinical setting followed a week later by a randomized placebo-controlled treatment period and intranasal administration of fasedienol. Fasedienol (1.6 µg) was administered intranasally 15 minutes prior to both the public speaking and social interaction challenge simulations. The two challenges were separated by a 30-minute rest period. The primary outcome measure was the Subjective Units of Distress Scale (SUDS). Peer-reviewed results published in the *American Journal of Psychiatry* (Monti, et al., *Am. J. Psychiatry* (2014) 171:675-682) showed statistically significant results for reducing anxiety during a public speaking performance and during social interactions in a clinical setting. During the public speaking challenge, subjects randomized to treatment with fasedienol (n = 45) showed a 26.7-point improvement in mean SUDS scores following the treatment visit with fasedienol as compared to the SUDS scores during the baseline visit (placebo treatment). In comparison, subjects randomized to treatment with placebo (n = 46) showed an improvement of only 14.0 points in mean SUDS scores compared to baseline. The fasedienol treatment group's improvement in the public speaking challenge significantly exceeded that of the placebo group's improvement (t = 3.16, p = 0.002).

Mild or moderate adverse events were infrequent and did not differ significantly between the fasedienol and placebo groups. No severe or serious adverse events were reported.

Positive Phase 2 Results in a Real-World Setting. A second peer-reviewed Phase 2 study of fasedienol in SAD was published in the *Journal of Depression and Anxiety* (Monti, et al., *Depress Anxiety* (2016); 33: 1081–1089). In the randomized, double-blind, placebo-controlled crossover study that included both adult males and females 18 to 65 years of age, subjects self-administered fasedienol or placebo nasal spray on an as-needed basis, just prior to stressful, anxiety-provoking encounters in their daily lives, up to four times a day. Following two weeks of treatment, the subjects were crossed over to the other nasal spray for another two weeks. The primary efficacy measure in the study was the SUDS and the secondary efficacy measure was the Liebowitz Social Anxiety Scale (LSAS). The LSAS was created by Dr. Michael Liebowitz and was the primary efficacy endpoint in all Phase 3 registration trials for the three antidepressants approved by the FDA for treatment of SAD. Dr. Liebowitz was the Principal Investigator of this Phase 2 study of fasedienol.

The change from baseline SUDS scores was significantly greater for all subjects while taking fasedienol compared with the placebo group. The average change from baseline SUDS score was 15.6 points for all subjects while on PH94B and 8.3 points while on placebo (paired t-test = 3.09; $p = 0.006$; effect size 0.658). The LSAS was recorded at weekly visits. Looking between groups at just the group treated first with fasedienol for two weeks, fasedienol showed a positive trend in the LSAS scores ($p = 0.07$, Cohen's $d = 0.812$, change from baseline 23.3 vs 8.2 points fasedienol vs placebo, respectively). Interestingly, subjects receiving fasedienol first also had a significantly greater decrease in their avoidance score on the LSAS as compared to those who received placebo first ($p = 0.02$, Cohen's $d = 1.078$). After the crossover, fasedienol showed less of an effect as compared to placebo, likely due to a confidence carryover effect from treatment with fasedienol during the previous two weeks. Importantly, self-administration of fasedienol on an as-needed basis prior to anxiety-provoking encounters in a real-world setting was accompanied by a persistent change in overall SAD symptoms, reduction in fear and anxiety, and less frequent avoidance, as measured by the LSAS over the course of fasedienol usage. Notably, the amount of separation between fasedienol and placebo at the end of the first two weeks on the LSAS in this study was comparable to what was observed in the registration trials for the current FDA-approved antidepressants after 12 weeks. A large effect size (0.78) and trend to significance ($p = 0.083$) in favor of fasedienol also was observed when comparing overall the Clinical Global Impression (CGI) score means for fasedienol and placebo during the first two weeks of treatment. Patient Global Impression of Change (PGI-C) ratings also showed improvement for fasedienol after two weeks of treatment ($p = 0.024$).

No drug-related serious adverse events (SAEs) were reported during the study. All adverse events (AEs) were mild or moderate and the frequencies of their occurrence did not differ meaningfully between active and placebo treatments.

We believe this multiple-administration, placebo-controlled assessment Phase 2 study conducted in a real-world setting outside a clinical environment indicates the potential for cumulative functional improvement with longer use of fasedienol, while still being used on an as-needed basis, as subjects are increasingly able to engage in previously difficult social and performance situations in their daily lives more frequently and with less fear and anxiety.

SAD Phase 3 Studies

PALISADE-1. In May 2021, we initiated our PALISADE Phase 3 Program for fasedienol in SAD with PALISADE-1, a single-administration assessment Phase 3 public speaking challenge clinical study of fasedienol for the acute treatment of anxiety in adults with SAD. Following discussions with the FDA in mid-2020 during the acute phase of the COVID-19 pandemic, we agreed to design PALISADE-1 in a manner substantially similar to the single-administration assessment Phase 2 public speaking challenge study of fasedienol, which involved self-administration of only a single dose of fasedienol by subjects randomized to the treatment arm. All subjects were given an anxiety-provoking public speaking challenge, conducted only in a clinical setting, and their change in a Subjective Units of Distress Scale (SUDS) score was determined.

In July 2022, we announced top line results from PALISADE-1. Although the safety and tolerability of fasedienol in PALISADE-1 were favorable and consistent with previously reported results from previous clinical trials, PALISADE-1 did not achieve its primary efficacy endpoint, as measured by change from baseline using the SUDS as compared to placebo. We believe the following hypotheses are potential explanations for the unexpected outcome in PALISADE-1: (i) the study was conducted during the acute phase of the COVID-19 pandemic, introducing significant systemic variability in terms of changing social dynamics, subject stress, study site and contract research organization (CRO) personnel turnover and mask wearing regulations; (ii) given the foregoing, the public speaking challenge study design may not have been scalable to a large Phase 3 study, particularly during the acute phase of the COVID-19 pandemic; and (iii) some subjects in the study may have had reduced potential to respond to fasedienol due to impaired olfactory cell function potentially caused by the COVID-19 virus, nasal swab testing for COVID-19, respiratory syncytial virus (RSV) or influenza, and/or heavy cannabis use, smoking or vaping.

PALISADE-2. In October 2021, near the end of the acute phase of the COVID-19 pandemic, we initiated PALISADE-2, which involved the same clinic-based, single-administration assessment public speaking challenge study design and use of the SUDS as the primary efficacy endpoint as PALISADE-1. In July 2022, after receiving top line results from PALISADE-1, we paused recruitment and enrollment in PALISADE-2 to allow independent third-party biostatisticians to conduct an interim analysis of available data from subjects randomized in PALISADE-2 up to the date we paused the study. In September 2022, based on their review of unblinded data from the 140 subjects who had completed PALISADE-2, the independent third-party biostatisticians recommended that we continue PALISADE-2 as planned, without revealing the underlying data to us.

Although the results of the interim analysis of PALISADE-2 indicated that continuation of the study would not be futile, after considering the expense, time, and challenges associated with PALISADE-1, as well as the potential methodological complexities involved in resuming PALISADE-2, we closed the PALISADE-2 study. Topline results from the 140 subjects who completed PALISADE-2 are expected in the second half of 2023.

PALISADE Open Label Study. The PALISADE Open Label Study (*OLS*) was a Phase 3, open-label safety trial designed to evaluate the safety and tolerability of multiple, as-needed administrations (up to four times a day) of fasedienol in adults with SAD. The PALISADE OLS also evaluated the change from baseline in monthly standard clinical measurements and behavioral assessment scales (LSAS, Clinician Global Impression of Improvement scale (*CGI-I*) and Patient Global Impression of Change scale (*PGI-C*)) in response to anxiety-provoking social situations in daily-life after the administration of fasedienol. The key exploratory efficacy endpoint in the study included evaluation of the change from baseline on the LSAS, which measures SAD patients' response to anxiety-provoking social and performance situations experienced in their daily lives. Following the completion of PALISADE-1, we terminated the PALISADE OLS early, solely for strategic business reasons, and not due to any safety concerns with fasedienol.

Safety and tolerability of fasedienol were assessed and summarized during monthly visits from baseline to end of treatment in AEs, laboratory values, 12-lead electrocardiograms (*ECGs*), physical examinations, and vital sign assessments following exposure to fasedienol. Long-term administration of 3.2 µg of fasedienol, as-needed up to four times per day, was safe and well-tolerated, with no new safety findings or trends identified, regardless of the number of doses administered by each subject (safety population: n=481). Headache was the most common treatment-emergent adverse event (*TEAE*) (17.0%), and, except for COVID-19 *TEAEs* (11.4%) which were not considered related to fasedienol, no other *TEAE* occurred in more than 5.0% of subjects. Over 30,000 doses of fasedienol were administered by patients during the study, with a mean duration of four months and a maximum study duration of over ten months.

The final data set from PALISADE OLS demonstrates clinically meaningful functional improvement, as measured by the LSAS, and total LSAS scores, in both men and women, continued to decline in consecutive months during the study, as follows:

- After 1 month, the mean reduction on the LSAS was 16 points (n=385);
- After 2 months, the mean reduction on the LSAS was 20 points (n=324); and
- After 3 months, the mean reduction on the LSAS was 24 points (n=218).

For subjects who continued in the study, total LSAS scores continued to decline from baseline, with improvements observed each month on the LSAS through nine months. The continued improvement in LSAS scores is indicative of the therapeutic potential of multiple, patient-tailored, as-needed administrations of fasedienol over time to help patients build confidence to engage in anxiety-provoking social and performance situations in their daily lives more frequently and with less fear and anxiety.

In addition, the *CGI-I* results indicated 43% of the 218 patients assessed after three months were “much” or “very much” improved, and *PGI-C* results indicated 44% of the 218 patients assessed after three months considered themselves “much” or “very much” improved.

FDA Feedback on Path Forward; FEARLESS-1. We believe data from approximately 400 subjects in the PALISADE OLS over a period of one month and beyond, combined with the data from the previous Phase 2 randomized, double-blind, placebo-controlled, crossover study of fasedienol after two weeks of use, as discussed above, demonstrate the potential for fasedienol to achieve robust overall reduction in symptoms of SAD and improvement in severity of the disorder over time, as measured by the LSAS. These data also appear to suggest that studies involving multiple administrations of fasedienol over time on an as-needed basis, up to four times per day, when subjects experience daily, real-life, socially stressful situations may most accurately reflect the true efficacy of fasedienol in patients with SAD and represent the actual way in which they would use fasedienol, if approved. Utilizing the LSAS as the primary efficacy outcome measure in our next Phase 3 study is consistent with the pivotal registration trials for all three currently approved treatments for SAD. As those studies indicate, the LSAS is capable of measuring a drug's efficacy in patients with SAD due to its ability to capture patient feedback on fear and anxiety regarding various social situations, as well avoidance of such situations. Hence, we believe using the LSAS as the primary efficacy endpoint for our further Phase 3 development of fasedienol has the potential to demonstrate its efficacy and true impact on patients' lives.

In the first quarter of calendar 2023, we met with the FDA to discuss next steps in our Phase 3 development plan for fasedienol in SAD, which plan includes, among other things, conducting, on our own or with collaborators, a multiple-assessment, randomized, double-blind, placebo-controlled Phase 3 study of fasedienol in adults in a real-world setting, using the LSAS as the primary efficacy outcome measure to evaluate the efficacy of fasedienol over time in patients with SAD to support a potential fasedienol New Drug Application (NDA). Positive feedback from the FDA at this meeting confirmed the acceptable use of the LSAS as a primary efficacy endpoint. Accordingly, we are positioned to finalize key components of FEARLESS, our potential NDA-enabling Phase 3 development program for fasedienol for treatment of SAD.

Unlike the PALISADE Phase 3 studies, which involved assessment of only a single, self-administered dose of fasedienol in a clinic-based public speaking challenge using the SUDS as the primary outcome measure, our FEARLESS program will assess multiple administrations of fasedienol, on a patient-tailored as-needed basis, up to six times per day, in a real-world setting over a multiple week period, with the LSAS as the primary efficacy endpoint, consistent with the FDA's three precedent-setting approvals of antidepressants for treatment of SAD. Dr. Michael R. Liebowitz, a Columbia University psychiatrist, former director and founder of the Anxiety Disorders Clinic at the New York State Psychiatric Institute and current Managing Director of The Medical Research Network LLC in New York City, is the innovator of the LSAS and will be the Principal Investigator for our FEARLESS program in SAD.

Exploratory Phase 2A Study in AjDA and Future Development Opportunities. During the acute phase of the COVID-19 pandemic, we conducted a small exploratory Phase 2A clinical study of fasedienol designed to assess its therapeutic potential in adults experiencing adjustment disorder with anxiety (AjDA). Adjustment disorder (AjD) occurs within three months of exposure to a stressor as evidenced by marked distress that is out of proportion to the socially or culturally expected reactions to the stressor, or that represents significant impairment in social, occupational or other important areas of daily functioning. Our small exploratory study in AjDA is believed to be the first ever randomized, double-blind, placebo-controlled Phase 2A study in the U.S. aimed at exploring the pharmacological treatment of AjDA, and the first clinical trial that evaluated the effects of a fixed dosing regimen of fasedienol, involving intranasal administration of 3.2 µg of fasedienol four times per day over four weeks. A total of 71 subjects were screened for the study, 41 were randomized, 7 discontinued, and 34 completed four weeks of treatment. The study, which was not designed to achieve statistical significance, did not demonstrate a clinically significant difference between fasedienol and placebo as measured on the clinician-rated Hamilton Anxiety Scale (HAM-A). Site variances and both a high drug response rate and high placebo response rate were observed, likely related to the various aspects of AjDA that make it a challenging indication to study. The study of AjDA is complicated because the disorder is, by definition, temporary and self-resolving, making it difficult to identify the cause of clinical improvement or whether placebo played a role in any improvement observed. AjDA is a temporary stress reaction. The stress reaction typically starts within three months of an identifiable stressful situation, but because the disorder is directly linked to a stressor, once the stressor ends, the anxiety reaction may also end, with or without treatment.

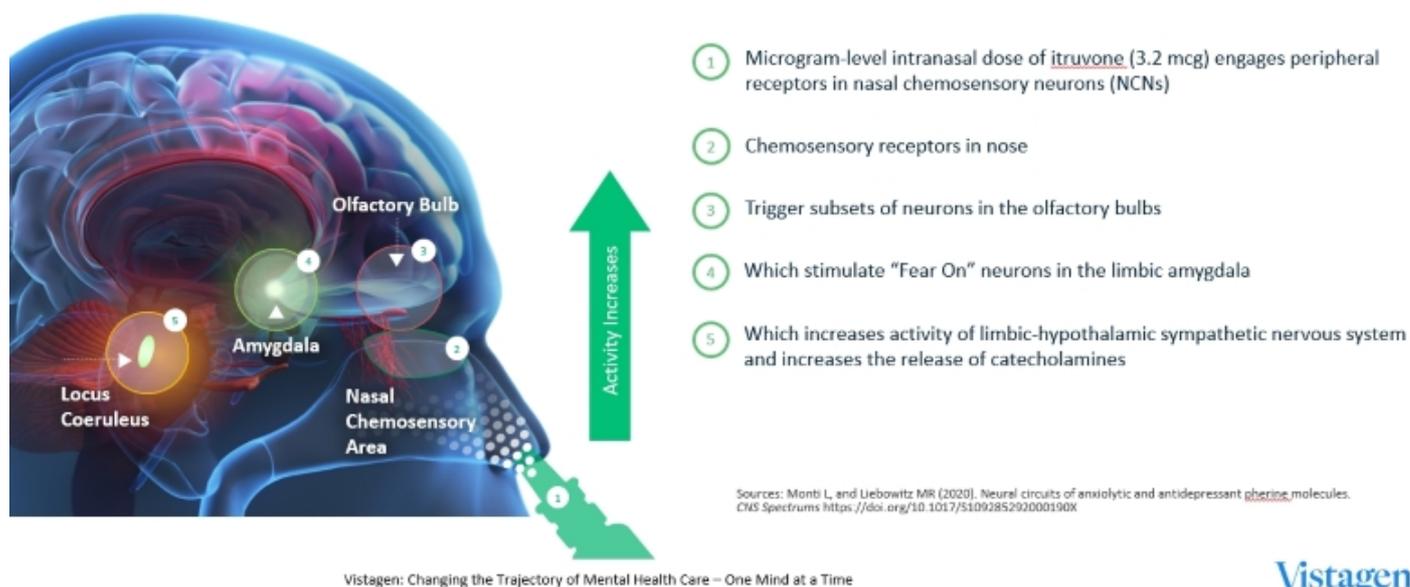
Fixed dosing of fasedienol four times per day, over four weeks, was well tolerated, with no appreciable differences in TEAEs between fasedienol and placebo. All reported TEAEs were of mild or moderate severity, with no severe or serious TEAEs reported during the study. Headache was the most commonly reported TEAE, reported by 3 subjects (15.8%) on fasedienol and 2 subjects (9.1%) on placebo.

Despite the methodological challenges inherent in the exploratory Phase 2A study in AjDA, we believe fasedienol builds resilience against anxiety and reduces the cognitive and physical paralysis that occurs during moments of heightened anxiety and stressful situations. Results of the AjDA study may provide support for an as-needed fasedienol dosing approach over time as the preferred mode of treatment.

We may also have potential opportunities to explore the development of fasedienol for other anxiety-related disorders, including postpartum anxiety, post-traumatic stress disorder, panic disorder, and procedural anxiety.

Itruvone Nasal Spray

Itruvone (PH10) is an odorless, tasteless synthetic investigational pherine from the pregnane family with a novel, rapid-onset potential MOA that is fundamentally differentiated from the MOA of all currently approved treatments for depression disorders. Itruvone, which is administered as a nasal spray at microgram-level doses, is designed to engage and activate chemosensory neurons in the nasal cavity, which are connected to neural circuits in the brain that produce antidepressant effects. Specifically, in a manner similar to fasedienol, itruvone's proposed MOA involves the regulation of the olfactory-amygdala neural circuits believed to increase activity of the limbic-hypothalamic sympathetic nervous system and increase the release of catecholamines. Importantly, unlike all currently approved oral antidepressants (ADs) and rapid-onset ketamine-based therapy, including both intravenous ketamine and intranasal ketamine (esketamine), we believe itruvone does not require systemic uptake and distribution of the compound to the brain to produce rapid-onset of antidepressant effects. In all clinical studies completed to date, itruvone has been well-tolerated and has not caused psychological side effects (such as dissociation and hallucinations) or other safety concerns that may be associated with ketamine-based therapy.



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 250 million people. Statistics reported by the U.S. National Institute of Health (NIMH) indicate that approximately 21 million adults in the U.S., or approximately 8.4% of all adults in the U.S., had at least one major depressive episode in 2020. While most people will experience a 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 antidepressants 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 antidepressant, and the likelihood of achieving remission of depressive symptoms declines with each successive treatment attempt. Even after multiple treatment attempts with current antidepressants, approximately one-third of depression sufferers still fail to find an adequately effective therapy. In addition, this trial and error process and the systemic effects of the various antidepressants involved may increase the risk of patient tolerability issues and serious side effects, including suicidal thoughts and behaviors in certain groups. Inadequate response to current treatments 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.

MDD Clinical Studies. In a peer-reviewed, published exploratory Phase 2A clinical study (n=30), itruvone, self-administered at a daily 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 antidepressants or intravenous or intranasal ketamine-based therapy. With its potential for rapid-onset activity at a 6.4 microgram-level dose that we believe does not require systemic uptake to achieve sustained antidepressant effects, as well as a safety profile in studies completed to date that is differentiated from current therapeutics, we believe itruvone has transformative potential as an innovative stand-alone treatment for MDD and potential opportunities for development in multiple additional depression disorders, including postpartum depression, treatment-resistant depression, and suicidal ideation.

In January 2023, we launched a small U.S. single center, randomized, double-blinded, placebo-controlled Phase 1 study to investigate the safety and tolerability of itruvone in healthy adult subjects (n=12). The study was designed to confirm the favorable safety profile of itruvone established in three previous clinical studies conducted in Mexico, including the Phase 2 study noted above, as well as facilitate our plans for Phase 2B development of itruvone in the U.S. as a fast-acting stand-alone treatment for MDD. In June 2023, we announced positive data from this study. There were no reported SAEs or discontinuations due to adverse events in the trial. Two AEs were reported during the treatment period, fatigue and headache, which occurred in the same subject. Both AEs resolved without sequelae and were mild in severity. Following itruvone administration, there were no clinically significant findings in ECGs, vital signs, and laboratory parameters. Overall, itruvone was well-tolerated and continued to demonstrate a favorable safety profile.

The FDA has granted Fast Track designation for development of itruvone as a potential adjunctive treatment for MDD.

PH80 Nasal Spray

PH80 is an odorless, tasteless synthetic investigational piperine with a novel, rapid-onset potential MOA that is fundamentally differentiated from the MOA of all currently approved treatments for both vasomotor symptoms (hot flashes) due to menopause and migraine headaches. PH80, which is administered as a nasal spray at microgram-level doses, engages and activates chemosensory neurons in the nasal cavity, which are connected to neural circuits in the brain that modulate neural circuits in the basal forebrain associated with the control of body temperature, as well as premonitory and aura symptoms of migraines.

PH80 for Acute Management of Vasomotor Symptoms (Hot Flashes) due to Menopause. Approximately 60% to 80% of women entering menopause suffer from hot flashes and associated symptoms lasting up to ten years, according to the Massachusetts General Hospital Center for Women's Mental Health. Menopausal symptoms are triggered by hormonal fluctuations that develop at the onset of menopause and affect areas of the brain involved in the control of core body temperature. Sudden changes in core body temperature result in hot flashes, sweating, reddening of the face and upper thorax, rapid heartbeat and general feelings of discomfort that can have an impact on the quality of life.

In a small exploratory Phase 2A clinical study (n=36), PH80 showed a profile compatible with the acute management of menopausal hot flashes. The randomized, double-blind, placebo-controlled exploratory Phase 2A study was designed to explore the efficacy, safety, and tolerability of intranasal administration of PH80 for the acute management of vasomotor symptoms hot flashes due to menopause. In the study, PH80 nasal spray containing PH80 in a dose of 0.8 micrograms/50 microliters (0.8 µg/50 µL) was self-administered by subjects intranasally, two sprays in each nostril (total dose = 3.2µg) up to four times daily, as-needed for four consecutive weeks. One additional dose was allowed at night if subjects were awakened by hot flashes. Through the course of the study, subjects recorded the number, severity, disruption in function, and sweating related to hot flashes. PH80 was well-tolerated with no serious adverse events, and the adverse event profiles were comparable between PH80 and placebo. All 36 subjects completed four weeks of treatment and no subject discontinued participation in the study as a result of TEAEs.

PH80 induced significant reduction in the daily number of hot flashes compared to placebo at the end of the first week of treatment, and the improvement was maintained through each treatment week until the end of the four-week treatment period. At baseline, subjects reported a mean daily number of hot flashes of 7.7 (PH80, n=18) and 8.0 (placebo, n=18). After one week of treatment, the number of hot flashes dropped to 2.8 (PH80) and 6.4 (placebo) ($p<.001$), and after four weeks of treatment the number of hot flashes dropped to 1.5 (PH80) and 5.1 (placebo) ($p<.001$). PH80 treatment also significantly reduced the severity, disruption in function, and sweating related to hot flashes during the treatment period as compared with placebo.

We are currently preparing, on our own or with collaborators, to submit an U.S. IND for a Phase 2B clinical study of PH80 as a treatment for hot flashes due to menopause.

PH80 for Acute Treatment of Migraine Headaches. Migraine headaches are a common and debilitating neurological disorder experienced by approximately 4% to 9% of men and 11% to 25% of women, according to the American Headache Society. A migraine is characterized by unilateral, pulsating headaches of moderate to severe intensity lasting four to 72 hours. Symptoms are aggravated by routine physical activity and are associated with nausea, photophobia and phonophobia. Usually, migraine headaches are preceded by premonitory symptoms (fatigue neck discomfort, gastrointestinal symptoms and mood changes, and these are followed by an aura of sensory and language disturbance (Headache, 58: 4-16, 2018. American Headache Society).

PH80 initiates neural impulses in the olfactory bulb transmitted by pathways that rapidly affect the function of multiple structures in the brain, including the amygdala and hypothalamus that have been linked to the pathology of migraine. Due to its MOA and a small proof of concept study, we believe PH80 may have therapeutic potential to relieve premonitory and aura symptoms of migraines.

PH15 Nasal Spray

Cognitive impairment has many potential causes, including mental fatigue, and is often associated with hypersomnia or excessive daytime sleepiness (EDS). EDS is commonly caused by sleep-related disorders such as sleep apnea, circadian rhythm disorder, or narcolepsy but may also be caused by psychiatric disorders, neurological conditions, or medications. In the U.S., it is estimated that 12.7% of adults, or approximately 30 million people suffer from EDS (Ford et al, 2015).

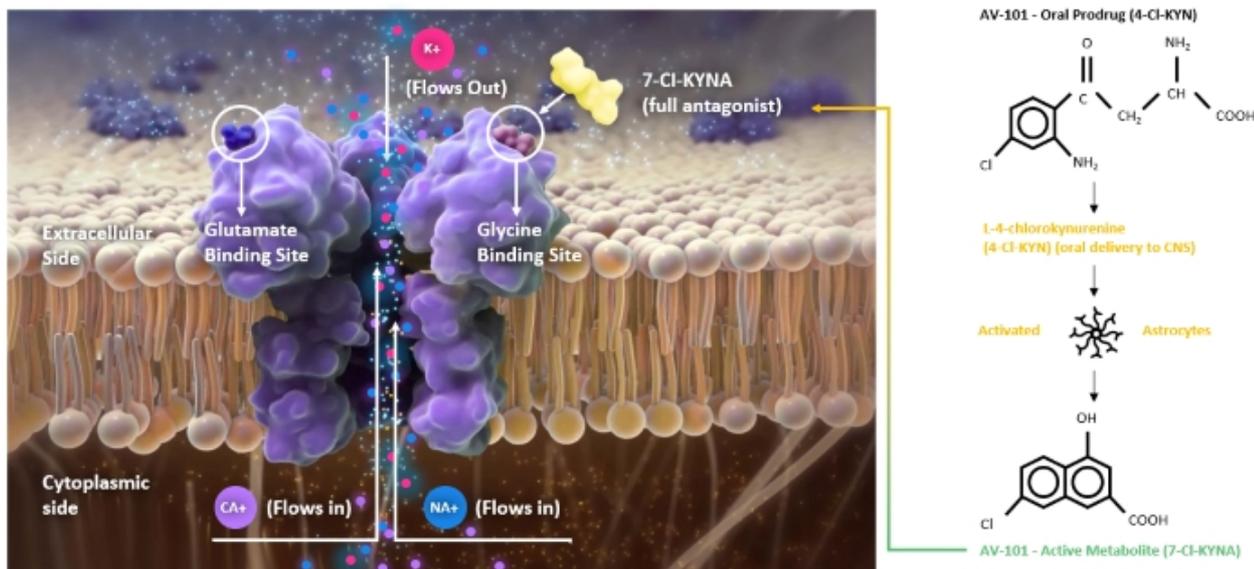
PH15 is an odorless, tasteless synthetic investigational piperine with a novel, rapid-onset potential MOA that is fundamentally differentiated from the MOA of all currently approved treatments to improve cognitive impairment caused by mental fatigue and potentially other disorders. Early functional MRI studies in human volunteers at Stanford University revealed that intranasal administration of PH15 induced rapid activation of brain areas related to cognition (Sobel et al, Brain, 1999). In a small double blind, placebo-controlled study Phase 2 study of human subjects who were sleep deprived to induce mental fatigue, intranasal PH15 showed rapid and significant improvement in cognitive and psychomotor performance and improvement of reaction time that was better than the effect of a placebo and 400 mg of oral caffeine. We are currently evaluating the path forward to submitting an U.S. IND for a Phase 2 clinical study, on our own or with collaborators, and the appropriate indication for demonstrating improvement of cognitive function.

PH284 Nasal Spray

PH284 is an odorless, tasteless synthetic investigational piperine with a novel, rapid-onset potential MOA that is fundamentally differentiated from the MOA of all currently approved treatments for the loss of appetite associated with chronic disorders such as cancer. Cachexia is a serious but under recognized consequence of many chronic diseases with body mass loss of >10% and a prevalence of 5 to 15 %. We believe PH284 may have therapeutic potential for improving subjective feelings of hunger in patients with cachexia. We are currently evaluating the path forward to submitting an U.S. IND for cachexia, on our own or with collaborators, and the appropriate patient populations for demonstrating increase in appetite and weight gain in a second Phase 2 study.

AV-101

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 binding 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 completed to date, AV-101 has demonstrated good oral bioavailability and an excellent pharmacokinetic (PK) profile. No binding of AV-101 or 7-Cl-KYNA to off-site targets was identified by an extensive receptor screening study. Moreover, in all clinical trials completed 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. 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.



Vistagen: Changing the Trajectory of Mental Health Care – One Mind at a Time

Vistagen

Based on observations and findings from preclinical studies, we believe AV-101 has the potential to become a new oral treatment alternative for multiple CNS disorders. We are currently preparing for Phase 2A development of AV-101, on our own or with collaborators, as a treatment for one or more neurological disorders involving the NMDAR receptor. Multiple studies have shown AV-101 to be safe and well-tolerated, and a range of preclinical studies indicate potential in multiple indications, including levodopa-induced dyskinesia, neuropathic pain, seizures, MDD, and suicidal ideation.

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.

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 timely 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 pharmaceutical compositions, methods of use, including treatment and patient selection, formulations, nasal administration devices, 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:

Fasedienol (PH94B) for the treatment of social anxiety disorder:

- Granted U.S. patents and corresponding foreign patents related to the treatment of anticipatory anxiety or social phobic response.

The granted U.S. patents related to fasedienol to treat social anxiety disorder will nominally expire either in 2025 or 2028, respectively, and foreign patents will nominally expire in 2026, subject to patent term extensions that may be available on a country-by-country basis, including in the U.S.

Fasedienol (PH94B) for the treatment of adjustment disorder:

- Pending U.S. and corresponding foreign patent applications related to the treatment of adjustment disorder with anxiety.

Patents that may be granted on these applications related to fasedienol to treat adjustment disorder will nominally expire in 2041, subject to patent term extensions that may be available on a country-by-country basis, including in the U.S.

Itruvone (PH10) for the treatment of depression:

- Granted U.S. patent and corresponding foreign patents related to the treatment of depressive disorders.

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

PH80 for the treatment of menopausal hot flashes:

Granted U.S. patent and corresponding foreign patents related to the treatment of menopausal hot flashes. The U.S. and foreign patents related to PH80 to treat menopausal hot flashes nominally expire in 2029, subject to extensions that may be available on a country-by-country basis, including in the U.S.

PH80 for the treatment of migraine:

- Granted U.S. patent and corresponding pending foreign patent applications related to the treatment of migraine.

The U.S. and foreign patents that may be granted on these patent applications related to PH80 to treat migraine nominally expire in 2040, subject to extensions that may be available on a country-by-country basis, including in the U.S.

PH15 for the improvement of psychomotor and cognitive performance:

- Pending U.S. patent applications related to the improvement of psychomotor and cognitive performance.

U.S. and foreign patents that may be granted on these applications related to PH15 to improve psychomotor and cognitive performance will nominally expire in 2044, 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-101.

The U.S. and foreign patents related to AV-101 nominally expire between 2034 and 2040, depending on the particular subject matter claimed in each patent, subject to extensions that may be available on a country-by-country basis, 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*). The FDA may reduce this patent term restoration period if it finds that an 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 an 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 extension or restoration of patent term for our applicable patents, if any, to extend patent life beyond their base expiration dates depending on the length of the clinical trials and other factors involved in the filing of the relevant NDA.

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.

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 for an NDA for a new chemical entity (*NCE*). An *NCE* 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 to the FDA for evaluation after four years from the original NDA approval 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 moiety 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.

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 employment or other contractual 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

Given the depth of clinical development across our CNS pipeline, as well as new potential to elevate additional preclinical candidates from our pherine platform, we are pursuing multiple strategic development and commercialization partnerships, both global and regional, across our clinical-stage pipeline to efficiently unlock the full value of our product candidate portfolio. We believe regional and global partnerships designed to amplify our internal activities can efficiently accelerate key development timelines and regulatory milestones for our product candidates.

In addition, 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, accounting, manufacturing, nonclinical development, clinical development and regulatory affairs support.

We have entered into, and plan to seek multiple additional global and regional strategic collaborations and relationships focused on development and/or commercialization of our product candidates in key pharmaceutical markets worldwide, including the U.S.

Commercial Agreements

We have customary clinical supply agreements with multiple contract development and manufacturing organizations (*CDMOs*) 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 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 fasedienol 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 fasedienol 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 fasedienol 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 fasedienol 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 fasedienol in such jurisdiction, the expiration of regulatory exclusivity in such jurisdiction or ten years after the first commercial sale of fasedienol in such jurisdiction.

Manufacturing and Supply

Manufacturing of the drug substance and drug product for our product candidates is performed by CMOs who must comply with current good manufacturing practice (*cGMP*) regulations. Our product candidates are comprised of synthetic small molecules that are manufactured 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, manufacturing facilities for the production of our drug substance and drug product candidates for nonclinical, clinical or commercial use. We conduct manufacturing and analytical testing activities under individual project work orders with independent CMOs to supply all of our nonclinical and clinical trial needs. We conduct periodic quality audits of each of the CMO's facilities to ensure that they are fully compliant with *cGMPs*. We believe that all of our existing CMOs are, or will be, capable of providing sufficient quantities of both drug substance and drug product to meet our nonclinical and clinical development needs. New CMOs may be added to our supply chain strategy in the future to ensure that our nonclinical, clinical and, subject to NDA approval, commercial manufacturing and testing needs are met.

By design, we do not currently have any fixed contractual arrangements in place with any CMOs, for either long-term supply or redundant supply, of drug substance or drug product for our drug product candidates. If our product candidates are approved for commercial distribution, we intend to execute long-term commercial supply agreement(s) with our CMOs to produce 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 drug substance and/or drug product.

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. 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 large and established research and development and commercial 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, tolerability, convenience, price, the level of branded and generic competition, and the availability of reimbursement from government and other third-party payers.

Currently there is no FDA-approved acute treatment of anxiety for adults with SAD with the proposed mechanism of action of fasedienol, and we are aware of no company developing a potential treatment of anxiety for adults with SAD that is a nasal spray and involves the same mechanism of pharmacological action as fasedienol. We are aware of several companies that are developing therapies targeting acute treatment in the SAD market, including, among others, Bionomics, Vanda Pharmaceuticals, and Receptor Life Sciences, Ananda Scientific, EmpowerPharm and PureTech. In addition, we may face competition to fasedienol for treatment of anxiety in adult and adolescent patients with SAD from generic antidepressants as well as off-label use of generic benzodiazepines and generic beta blockers even though no drug in either of such generic drug classes has been systematically developed for treatment of SAD and thus no drug in either of such generic drug classes has been FDA-approved for the treatment of anxiety in adults with SAD. Although there are three oral antidepressants approved by the FDA for the treatment of SAD, such drugs do not achieve rapid-onset therapeutic effects and are associated with undesirable side effects. Cognitive behavioral therapy is also an important treatment approach to SAD that may be used along with or instead of pharmacological treatments, including antidepressants, benzodiazepines, beta blockers, fasedienol and other drug candidates in clinical development.

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 venlafaxine (Effexor), both previously marketed by Pfizer, Inc.; and paroxetine (Paxil) and bupropion (Wellbutrin), both previously marketed by GlaxoSmithKline (now GSK). Treatments may also include currently marketed proprietary branded medications indicated for MDD such as: Trintellix, which is marketed by Takeda Pharmaceuticals America, Inc and H. Lundbeck A/S; Viibryd and Vraylar, which are marketed by Abbvie; and Rexulti which is marketed by Otsuka America. Although currently there are no FDA-approved therapies for MDD with the mechanism of pharmacological action of itruvone, we are aware of numerous companies that are developing and commercializing therapies targeting the MDD market, including, among others, Axsome Therapeutics, Sage Therapeutics, Relmada Therapeutics, Xenon, Intra-Cellular Therapies, Johnson & Johnson, Usona Institute, Boehringer Ingelheim, and Sirtsei Pharmaceuticals. 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.

We are still assessing our competition for PH80 for the treatment of hot flashes due to menopause and for migraine headaches, PH15 to improve cognitive impairment and PH284 for the loss of appetite.

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 Good Manufacturing Practices (*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 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 NDA, it will determine within 60 days whether the application 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.

Types of Marketing Applications

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.

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

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. 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 granted, 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 designated product may be eligible for Accelerated Approval or Priority Review.

The FDA may grant an NDA Priority Review designation for 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 NDA 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 may 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 additional 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 (*VA*), the Department of Defense (*DOD*), 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.

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 payers, 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 statute 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 payer 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 may 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 payer, 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 will depend in part on the extent to which governmental payer programs at the federal and state levels, including Medicare and Medicaid, private health insurers, and other third-party payers 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 payers 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 payers 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 payers 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 payers are developing increasingly sophisticated methods of controlling healthcare costs. Third-party payers 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 payers 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 payers 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 payers 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 payers.

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 payers often rely on the lead of the governmental payers 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 payers 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 payers.

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 payers continue to demand discounted fee structures, and the trend toward consolidation among third-party payers tends to increase their bargaining power over price structures. If third-party payers reduce their rates for our products, then our revenue and profitability may decline and our operating margins will be reduced. Because some third-party payers 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 payers. Our inability to maintain suitable financial arrangements with third-party payers could have a material adverse impact on our business. Additionally, the reimbursement process is complex and can involve lengthy delays. Third-party payers 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 payers. 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 payer'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 payers 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 payers 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 payers 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 payers.

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 payers, 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 payers 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 payer 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 U.S. 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 U.S. 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 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 payers 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, payers 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.

As in the past, there may be other efforts to repeal or materially modify various aspects of ACA. The results and effects of such efforts, including judicial and Congressional challenges, could affect our business operations and prospects in unknown ways. Also, it is unclear how ACA and other laws ultimately will be fully implemented or modified. 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, which vacated the judgment and instructed the lower court 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, payer 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 U.S. The FCPA also obligates companies whose securities are listed in the U.S. 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. Whether or not we obtain U.S. 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 U.S. 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

As of March 31, 2023, we had two wholly-owned subsidiaries, Pherin Pharmaceuticals, Inc., a Delaware corporation, and Vistastem Inc., a California corporation. The operations of these subsidiaries are managed by our senior management team based in South San Francisco, California.

Corporate History

Vistastem, Inc., a California corporation (formerly VistaGen Therapeutics, Inc.) was incorporated on May 26, 1998, and 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.

On December 20, 2022, we entered into an Agreement and Plan of Merger (the *Merger Agreement*) along with VTGN Merger Sub, Inc., our wholly-owned subsidiary (*Merger Sub*), Pherin Pharmaceuticals, Inc. (*Pherin*), and Kevin McCarthy in his capacity of Stockholder Representative, in order to acquire Pherin (the *Pherin Acquisition*). On February 2, 2023 (the *Closing Date*), we completed the Pherin Acquisition and Pherin is now a wholly-owned subsidiary of the Company. Immediately prior to the consummation of the Pherin Acquisition, each of Pherin’s directors and officers resigned, and no employees or other affiliates of Pherin on the Closing Date are serving or will serve in their previous roles or in any other capacity with Pherin or with the Company. Following the completion of the Pherin Acquisition, we now have full ownership of intellectual property rights to all five of our pherine drug candidates.

The Consolidated Financial Statements included in Item 8 of this Annual Report represent the activity of Vistastem from May 26, 1998, 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, 2023, and the activity of Pherin Pharmaceuticals, Inc. from February 2, 2023 (the date of the Pherin Acquisition) through March 31, 2023. For the relevant periods, the Consolidated Financial Statements included in Item 8 of this Annual Report also include the accounts of Vistastem’s two wholly owned inactive subsidiaries, Artemis Neuroscience, Inc., a Maryland corporation which was dissolved in April 2022, and VistaStem Canada, Inc., a corporation organized under the laws of Ontario, Canada which was dissolved in June 2022.

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 approximately \$44.4 million and \$35.4 million for the fiscal years ended March 31, 2023 and 2022, respectively. We expect that our research and development expenses will remain a significant portion of our total operating costs for the foreseeable future as we seek to complete the development of fasedienol, itrivone, and AV-101 and our other recently acquired pherine product candidates.

Environmental, Social, Governance, and Human Capital

We believe corporate responsibility is fundamental to our mission and we are committed to holding ourselves to high ethical standards. Beyond our quest to develop innovative therapeutic solutions that combat CNS disorders affecting so many lives and to improve healthcare outcomes, we strive to have a positive impact on our employees, our local communities, our patients, our shareholders, the health care ecosystem and society as a whole.

Governance and Leadership

As a late-clinical stage company that is passionate about transforming mental health care, we believe creating an environment that allows our team to collectively thrive and achieve its full potential begins with our Board of Directors, which consists of directors with diverse and dynamic backgrounds in pharmaceutical development, commercialization, and corporate governance. Applying the Nasdaq Stock Market’s continued listing standards for director independence, five of our seven directors are currently independent. At the management level, we have built a team of highly experienced professionals that we believe provide us with a diverse and inclusive culture, while also providing the know-how necessary to allow us to achieve our short- and long-term goals. Among these goals is to develop a formal environmental, social and governance (*ESG*) strategic roadmap and framework that will guide our operations, so as to ensure that we are operating in a manner that is consistent with our mission of transforming mental health care – *One Mind at a Time*.

Core Values and Ethics

We are committed to driving improvement and innovation in the care of patients suffering from CNS disorders. In this pursuit, our core values of integrity, compassion, teamwork, and excellence while on our journey to change the way we approach mental healthcare guide our internal processes and define our mission to radically improve mental health and well-being worldwide. In addition, all of our directors, officers and employees are responsible for upholding these values as set forth in our Code of Business Conduct and Ethics, which forms the foundation of our policies and practices. Our Code of Business Conduct and Ethics is available on our website at www.vistagen.com.

Environmental Commitment

We are committed to protecting the environment and attempt to mitigate any negative impact of our operations. We strive to address the environmental impacts of the building in which we operate and minimize waste by reducing our use of paper by operating primarily in a digital environment. We have safety protocols in place for handling biohazardous waste in our labs, and we use third-party vendors for biohazardous waste and chemical disposal.

Human Capital and Employees

We believe that our people are one of our greatest assets. We make diversity and inclusion priorities because they are key to unlocking the potential of our people. With colleagues who can contribute unique viewpoints and diverse perspectives to all aspects of the business, we believe that our culture can be more collaborative, more accepting of difference and more prepared for overall success on our journey to reimagine medicine.

As of June 28, 2023, we employed 33 full-time employees and one part-time employee. Twenty-one full-time employees work in research and development and laboratory support services and twelve full-time employees work in management, business development, legal, human resources, 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, 2027 which also provides a five-year option to renew.

Legal Proceedings

None.

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:

- we require substantial additional financing to execute our long-term business plan either on our own or with collaborators, including further development of our product candidates;
- We have incurred significant net losses since inception and we will continue to incur substantial operating losses for the foreseeable future;
- we are a development stage biopharmaceutical company with no revenues from product sales or approved products, and limited experience developing new drug candidates, which makes it difficult to assess our future viability;
- failures of our current and/or future clinical studies of our product candidates, or delays in the commencement of completion of our clinical trials, could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business;
- we depend heavily on the success of our product candidates 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;
- if we are unable to retain or attract key management and scientific personnel, we may be unable to successfully produce and develop our product candidates;
- the successful completion of clinical or nonclinical studies in any of our development programs may not be sufficient to cause the FDA to approve of any NDA that we may submit or cause any other agency to provide regulatory approval of any of our product candidates and, even if approved, does not ensure acceptance of such product candidates by clinicians leading to a revenue stream to support our operations;
- 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;
- raising additional capital in equity-based financing transactions is likely to 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;
- if we fail to comply with the continued listing requirements of the Nasdaq Capital Market, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted; 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 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.

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 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 revenue 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 any of our product candidates;
- maintain, leverage and expand our intellectual property portfolio;
- 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 and regulatory approval of product candidates.

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

From our inception through 2019, a substantial portion of our resources were dedicated to research and development of AV-101 and Vistastem's stem cell technology platform. Since 2019, we have expended a considerable portion of our resources for research, clinical development, manufacturing and regulatory expense related to fasedienol and itruvone, including costs related to the PALISADE Phase 3 Program and our Phase 1 study of itruvone in MDD. We expect to continue to expend substantial resources for the foreseeable future developing fasedienol, itruvone, AV-101 and our other product candidates, PH15, PH80 and PH284, on our own and 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 should the FDA approve any of such product candidates for sale.

Although we had cash and cash equivalents of approximately \$16.6 million at March 31, 2023, 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, subject to availability of adequate working capital, we plan to (i) continue to advance our FEARLESS Phase 3 Program, on our own or with a collaborator, to develop and commercialize fasedienol as a new acute treatment of anxiety in adults with SAD, (ii) complete preparations, on our own or with a collaborator, for and initiate further Phase 2B clinical development of itruvone as a potential stand-alone treatment for MDD, (iii) complete IND-enabling activities, either on our own with a collaborator, for Phase 2B development of PH80, PH15 and PH284 and Phase 2A development of AV-101 for one or more neurological disorders involving the NMDAR, and (iv) conduct various nonclinical studies involving each of our product candidates.

Although we received the \$5 million upfront payment under the AffaMed Agreement in August 2020 and expect to recognize that amount as revenue in future periods, we have no other 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 transactions involving our stem cell technology, or (iii) obtain approval from the FDA and other regulatory authorities and successfully commercialize fasedienol, or one of our other product candidates, on our own or through collaborations.

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 any of our product candidates, on our own or in collaboration with others. As in prior periods, we will continue to incur substantial costs associated with other clinical and nonclinical development programs for our product candidates. 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 fasedienol and our other 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 intend to pursue and complete additional financing arrangements in the future.

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, developing and commercializing 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 manufacturing and formulating our product candidates;
- 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 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 may also seek funds through arrangements with collaborative partners in certain territories, including the U.S., or at an earlier stage than otherwise would be desirable or aligned with our business plan, 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 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.

Our future success is highly dependent upon our ability to successfully develop, on our own or with collaborators, any of our current CNS product candidates or acquire or license additional CNS product candidates, and we cannot provide any assurance that we will successfully develop and obtain regulatory approval of any of our current CNS product candidates or future product candidates, or that, if approved, any of our CNS product candidates 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. If beneficial, we may seek to collaborate with others to develop and commercialize any of our current or future CNS product candidates, if and when they are acquired and developed. 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 our 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.

Risks Related to Product Development, Regulatory Approval

Failures of our current and/or future clinical studies of 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.

Our PALISADE-1 Phase 3 clinical study of fasedienol for the acute treatment of anxiety in adults with SAD did not achieve its primary endpoint, as measured by change from baseline using the SUDS as compared to placebo. 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. Failure of any of our current and/or future clinical and nonclinical trials to achieve the planned endpoints, such as our PALISADE-1 Phase 3 clinical trial of fasedienol, could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business.

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 any of our product candidates.

We currently have no drug products for sale and may never be able to develop marketable drug products. Our business currently depends heavily on the successful development, manufacturing and regulatory approval of one or more of our current CNS drug candidates, as well as our ability to acquire, license or produce and develop additional product candidates. Each of our current investigational 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. 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 an *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 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, certain of our product candidates, including fasedienol and itruvone, 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.

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 caused considerable uncertainty about the potential effects of the virus and its variants, and the extent of and effectiveness of responses taken on international, national and local levels. Measures taken to limit the impact of the pandemic, 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. The *COVID-19* pandemic has impacted our business and may continue to do so. Additionally, future outbreaks may have several adverse effects on our business, results of operations and financial condition.

- ***Adverse impact on product development:*** Recent medical literature has reported that the SARS-COV-2 virus, which causes *COVID-19*, may cause long-term and reversible olfactory dysfunction (*OD*) in approximately 30% of affected individuals. *OD* may occur in cases where the SARS-COV-2 virus damages the nasal chemosensory epithelium, a structure in the nose where the types of cells are found that respond to pherines such as fasedienol, itruvone, PH15, PH80 and PH284. Accordingly, there is a risk that the prevalence of *OD* caused by *COVID-19* infections may interfere with the ability of our pherine nasal sprays to provide a therapeutic benefit, which, may, in turn, have a materially adverse impact on results of our clinical trials designed to assess the efficacy of these product candidates or a negative impact on potential future sales should any of our pherine nasal sprays be approved for commercialization.
- ***Negative impacts on our employees, collaborators and suppliers:*** *COVID-19* has impacted, and variant and subvariant strains of *COVID-19* or another highly transmissible and pathogenic infectious disease may impact or continue to impact, the health of our employees, collaborators, 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 fasedienol and itruvone. 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 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, clinical sites involved in our clinical studies and other contractors. The *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.

We have been granted Fast Track designation from the FDA for development of fasedienol 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 fasedienol or AV-101. Further, there is no guarantee the FDA will grant Fast Track designation for fasedienol 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 fasedienol 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 fasedienol or AV-101 and the FDA may withdraw Fast Track designation of fasedienol 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 fasedienol, AV-101 and any of our other product candidates 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 our 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 our current and/or our other future product candidates, if any, including positive results, may not be predictive of the results of later-stage clinical trials. Each of our current 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, as is the case for results from our PALISADE-1 clinical trial. 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 future nonclinical or clinical studies fail to produce positive results, the development timeline and regulatory approval and commercialization prospects for these candidates and, correspondingly, our business and financial prospects, could be materially adversely affected.

Any changes in planned timing or nature of clinical trials compared to completed clinical trials could impede our ability to meet our clinical development objectives for our product candidates.

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 timing of planned clinical trials may be affected by delays caused by the ongoing COVID-19 pandemic, including potential delays in recruitment and enrollment in our planned clinical and nonclinical studies or supply chain disruptions experienced by certain of our CMOs and/or CROs. 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 clinical and/or nonclinical trials.

If serious adverse events or other undesirable side effects or safety concerns attributable to our product candidates occur, the clinical development of our product candidates may be delayed or adversely affected.

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 reported in any clinical trials of any of our product candidates completed to date, if treatment-related SAEs or other undesirable side effects or safety concerns, or unexpected characteristics attributable to any of our product candidates are reported in any future 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 drug safety program 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 expense, 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 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.

We will need to successfully complete at least two Phase 3 clinical trials and certain other clinical and nonclinical studies prior to our potential submission of an NDA for regulatory approval of fasedienol as an as needed, over time, treatment of anxiety in adults with SAD, or for any other anxiety disorder such as AjDA. For itruvone, at present, we believe we will need to complete at least one additional Phase 2B clinical study, two adequate and well-controlled Phase 3 clinical trials, as well as standard nonclinical and long-term clinical safety studies, as well as other smaller clinical studies prior to the potential submission of a NDA for regulatory approval of itruvone as a stand-alone rapid-onset treatment for MDD, or any other depression disorder. For AV-101, we believe we will need to complete our ongoing exploratory Phase 1B clinical study, two Phase 2 clinical studies, two adequate and well-controlled Phase 3 clinical trials, additional toxicology and other standard nonclinical and long-term clinical safety studies, as well as certain standard smaller clinical studies prior to the potential submission of an NDA for regulatory approval in any CNS indication. For PH15, PH80 and PH284, we are in the process of determining the work required to successfully complete the clinical and nonclinical development of each of these product candidates. 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 any of our product candidates 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:

- 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 our 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 any of our 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 our 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 our current and/or future CNS product candidates may be delayed and we may not be able to obtain regulatory approval for our current or 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 efficient 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 and inefficiencies in coordinating activities. CROs and other outside parties may:

- experience disruptions to their operations, such as staff attrition, reduced staffing and supply chain disruptions;
- 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 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 API and formulate final drug product for any of our product candidates 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 due to supply chain disruptions, or successfully manufacture our product candidates, including 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 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 any of our product candidates 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.

We do not yet have long-term supply agreements in place with our CMOs and each batch manufactured of our product candidates 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 fasedienol, itruvone, PH15, PH80 and PH284, and the current and projected supply of API and finished drug product for each of our product candidates will be adequate to support our planned nonclinical and clinical studies, no assurance can be given that unanticipated supply shortages or CMO-related delays in the manufacture and formulation of API and/or finished drug product for any or all of our product candidates will not occur in the future.

Additionally, fasedienol, itruvone, PH15, PH80 and PH284 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 any of our CNS product candidate in the U.S., we may never receive regulatory approval to market the same CNS product candidate outside of the U.S.

In order to market any of our 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 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 distributors, 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 from product sales.

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 such 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. Moreover, creating broad sales and marketing capabilities will require substantial capital, which we may not be able to obtain.

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 payers. 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 payers, we may not generate sufficient revenue from our product candidates to become or remain profitable. Before granting reimbursement approval, healthcare payers 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 payers 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 drug safety program. Any REMS or comparable drug 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, treatment of anxiety in adults with SAD having the same mechanism of pharmacological action and safety profile as fasedienol. 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 itruvone 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 itruvone or AV-101 in combination with probenecid may have therapeutic potential. Additionally, other non-pharmaceutical treatment options, such as psychotherapy and electroconvulsive therapy (ECT) are used before or instead of standard antidepressant medications to treat patients with MDD.

With respect to fasedienol 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, and certain investigational oral drug candidates in Phase 2 development. 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. We are still assessing our competition for PH80 for the treatment of hot flashes due to menopause and for migraine headaches, PH15 to improve cognitive impairment and PH284 for the loss of appetite.

Many of our potential competitors, alone or with their collaborators, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development, obtaining FDA and other regulatory approvals, and the commercialization of investigational product candidates. With respect to fasedienol, 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, and two oral drug candidates in Phase 2 development that act on the alpha-7 nicotinic acetylcholine receptor, one in development by Bionomics and the other in development by Vanda. With respect to itruvone 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 new 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, Takeda and Xenon, 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 investigational product candidates will require substantial additional cash to fund expenses. We may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates, such as the AffaMed Agreement.

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 U.S., 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 therapeutic and commercial potential. We may fail to pursue additional development opportunities for our current CNS product candidates 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 fasedienol and itruvone. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other potential CNS-related indications for fasedienol and/or itruvone 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 payers 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 payers, 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, 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 fasedienol as an needed treatment of anxiety in adults with SAD, physicians may prescribe fasedienol 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 payers, 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 payers 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 fasedienol 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.

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 \$59.2 million and \$47.8 million during our fiscal years ended March 31, 2023 and 2022, respectively. At March 31, 2023, we had an accumulated deficit of approximately \$326.9 million and our auditors have included a qualification to their opinion on our Financial Statements at March 31, 2023 as a result of the uncertainty of our ability to continue as a going concern. 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 expense to significantly increase in connection with planned nonclinical and clinical studies, and out-sourced manufacturing, of our product candidates. 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, 2023, 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 remains recorded as deferred revenue at March 31, 2023, 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 our current and/or future CNS product candidate, or we enter into one or more development and commercialization agreements with respect our current CNS product candidates 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 and/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 payers.

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 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. 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 previously identified material weaknesses in our internal control over financial reporting, and we may identify future material weaknesses in our internal control over financial reporting. If we are unable to remediate these material weaknesses, or if we fail to establish and maintain adequate internal control over financial reporting, we may not be able to produce timely and accurate financial statements, and we may conclude that our internal control over financial reporting is not effective, which may adversely affect our business.

We previously identified material weaknesses in our internal control over financial reporting that, as of March 31, 2022, were remediated. 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 our annual or interim condensed consolidated financial statements will not be prevented or detected on a timely basis.

Although we have determined that the previously identified material weaknesses have been remediated as of March 31, 2022, we cannot assure you that we will not identify other material weaknesses in the future, which could negatively impact our results of operations in future periods.

Ensuring that we have adequate internal control over financial reporting so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles.

Implementing any future changes to our internal control over financial reporting may entail substantial costs to hire additional personnel, modify our existing processes and will take significant time to fully implement. These changes may not, however, be effective in establishing and maintaining the adequacy of our internal control, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business.

Any failure to maintain or implement required effective internal control over financial reporting, or any difficulties we encounter in their implementation, could result in additional material weaknesses, cause us to fail to meet our reporting obligations or result in material misstatements in our financial statements. Furthermore, if we cannot provide reliable financial reports or prevent material misstatements due to fraud or error, our business and results of operations could be harmed, and investors could lose confidence in our reported financial information. We also could become subject to investigations by The Nasdaq Stock Market, the Securities and Exchange Commission or other regulatory authorities, which could require additional financial and management resources.

Raising additional capital is likely to 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, and strategic acquisitions, 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 or in the context of strategic acquisitions, we issue shares of 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 the rights of our stockholders. Debt financing, if available, would increase our fixed payment obligations and would 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 acquisitions, 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 substantial additional financing to fund future operations, including research and development activities for our CNS product candidates, assuming our clinical development programs are successful and we receive necessary regulatory 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, 2023, we had federal and state net operating loss carryforwards of approximately \$191.9 million and \$65.2 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 prior or future offerings of our debt and/or equity securities, private placements, sales of our common stock by our existing stockholders or additional sales of our common stock by us could have a material adverse effect on our results of operations in future years. We have not yet 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 retain and attract senior management and key scientific personnel, we may be unable to successfully produce and develop our product candidates.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management and technical personnel across multiple key functions, including, but not limited to clinical operations, finance, legal, human resources, information technology, CMC and quality assurance, regulatory affairs and medical affairs. We are highly dependent upon our Chief Executive Officer and Chief Financial Officer, as well as our other senior management personnel, advisors, consultants and scientific and clinical collaborators. As of the date of this Report, we have 33 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 following our change in business plans as a result of the negative results of our PALISADE-1 clinical trial or in the future. As of the date of this Report, a total of nine employees have voluntarily resigned from their positions within the Company since the PALISADE-1 outcome was reported, including our Chief Commercial Officer and Chief Medical Officer. Work conducted by these individuals that furthers our current business plan has assumed by other employees and, when appropriate, based on clinical, regulatory and financial considerations, may be resumed by personnel hired in the future. However, competition for qualified personnel in the pharmaceuticals field is intense, and 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 will need to further expand our research and development capabilities and our contractual arrangements 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 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, development and regulatory efforts effectively, and hire, train and integrate additional management, administrative, research and development, regulatory and other 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 any of the product candidates 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 currently 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 economic downturn triggered by the 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 fasedienol, itruvone, 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.

Remote working arrangements could significantly increase the Company's digital and cybersecurity risks.

Most of our employees are geographically dispersed from our headquarters facility in South San Francisco and now routinely work remotely. With the continuing shift to remote working, and the use of virtual board and executive management meetings, cybersecurity risks are exponentially greater, including increased risk of phishing and other cybersecurity attacks as well as increased risk of unauthorized dissemination of sensitive personal information or proprietary or confidential information about us or our customers, employees, or business partners. Despite our cybersecurity measures, we may be more susceptible to security breaches and other security incidents because we have less capability to implement, monitor, and enforce our information security and data protection policies. Techniques or software used to gain unauthorized access, and/or disable, degrade, or harm our systems may be difficult to detect for prolonged periods of time, and we may be unable to anticipate these techniques or put in place protective or preventive measures. The damage or disruption of our systems, or the theft or compromise of our technology, data, or intellectual property, may negatively impact our business, financial condition and results of operations, reputation, stock price and long-term value, which could adversely affect our Company's business.

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. These proposals may 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, delivery devices, 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 patents and patent applications related to product candidates fasedienol (PH94B), itruvone (PH10), PH80, PH15 and AV-101 and have licensed patents and patent applications related to certain stem cell technology.

Although we own and have licensed issued and patents and pending patent applications relating to our product candidates in the U.S. and selected countries in other markets, we cannot provide any assurances that our pending U.S. and corresponding 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 product candidates and may have filed or may file patent applications and may have granted or may be granted patents that 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 and may limit or eliminate our ability to commercialize our product candidates.

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 biopharmaceutical 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 the 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 vary among the countries in which we pursue patents.

In addition, some patent-related uncertainty exists because of the challenge of 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 the 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 rejections 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 satisfy 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 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 the 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 the patent may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Even if a patent is granted 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, 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, and non-enablement. Grounds for unenforceability assertions include allegations that someone connected with the 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 by 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 we initiate, and the damages or other remedies awarded if we prevailed 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 could 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 could also be materially and adversely impacted.

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

- any granted patents related to our product candidates or any pending patent applications, if granted and challenged by others, will include or maintain claims having a scope sufficient to these product candidates 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 may 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 proprietary 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 biopharmaceutical 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 their 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 kinds of legal actions than we or our licensors or collaborators can dedicate. 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, the 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 the 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 litigation and other types of intellectual property litigation can involve complex factual and legal questions, and litigation 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 are unable to obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing our product candidates.

Patent litigation and other types of intellectual property 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 commercially 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 U.S., 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 U.S. or other jurisdictions. The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority filing date of each of our patent applications and the time periods allowed for filing related applications in a given country. Thus, for each of the patent families that we believe provide coverage for our lead product candidates or technologies, we will need to decide where and when 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 in relevant foreign jurisdictions 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 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 the 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 that 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 an 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 that 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 considered, particularly as they relate to changes in what types of inventions are eligible for patent protection. Foreign patent and intellectual property laws are also 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 another 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 to defend 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.

Risks Related to our Securities

If we fail to comply with the continued listing requirements of the Nasdaq Capital Market, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.

On September 6, 2022, we were notified by the Nasdaq Stock Market, LLC (*Nasdaq*) that we were not in compliance with the minimum bid price requirements set forth in Nasdaq Listing Rule 5550(a)(2) for continued listing on the Nasdaq Capital Market. Nasdaq Listing Rule 5550(a)(2) requires listed securities to maintain a minimum bid price of \$1.00 per share, and Nasdaq Listing Rule 5810(c)(3)(A) provides that a failure to meet the minimum bid price requirement exists if the deficiency continues for a period of 30 consecutive business days. The notification provided that we had 180 calendar days, or until March 6, 2023, to regain compliance with Nasdaq Listing Rule 5550(a)(2). To regain compliance, the bid price of our common stock must have a closing bid price of at least \$1.00 per share for a minimum of 10 consecutive business days. Based on our written notification to Nasdaq of our intention to cure the deficiency by implementing a previously stockholder-authorized reverse stock split, if necessary, on March 7, 2023, Nasdaq granted us a second 180-day period, through September 5, 2023, in which to regain compliance. On June 6, 2023, we effected a one-for-thirty reverse split of our issued and outstanding common stock which caused the trading price of our common stock to regain compliance with the minimum bid price rule as of June 21, 2023.

Although we are currently in compliance with Nasdaq's continued listing standards, no assurance can be given that we will continue to meet applicable Nasdaq continued listing standards. Failure to meet applicable Nasdaq continued listing standards could result in a delisting of our common stock, which could materially reduce the liquidity of our common stock and result in a corresponding material reduction in the price of our common stock. In addition, delisting could harm our ability to raise capital through alternative financing sources on terms acceptable to us, or at all, and may result in the inability to advance our drug development programs, potential loss of confidence by investors and employees, and fewer business development opportunities.

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;
- 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, including under our Sales Agreement, 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.

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. As a result, our Board could authorize the issuance of additional series of preferred stock in the futures 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 significant 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 expense 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, 2027, 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, 2023		
First quarter ended June 30, 2022	\$ 53.70	\$ 25.80
Second quarter ended September 30, 2022	\$ 32.10	\$ 4.16
Third quarter ended December 31, 2022	\$ 5.10	\$ 2.30
Fourth quarter ended March 31, 2023	\$ 10.30	\$ 3.09
Year Ended March 31, 2022		
First quarter ended June 30, 2021	\$ 95.10	\$ 57.30
Second quarter ended September 30, 2021	\$ 106.50	\$ 76.80
Third quarter ended December 31, 2021	\$ 83.40	\$ 48.00
Fourth quarter ended March 31, 2022	\$ 63.30	\$ 31.80

We completed a stockholder approved 1-for-30 reverse split of our issued and outstanding common stock effective on June 6, 2023 (the *Reverse Stock Split*). The per share high and low prices in the table above and other references to shares and per share prices elsewhere in this Report have been adjusted retrospectively to reflect the Reverse Stock Split.

On June 27, 2023 the closing price of our common stock on the Nasdaq Capital Market was \$1.69 per share.

At June 27, 2023, we had 7,872,479 shares of common stock outstanding held by approximately 13,000 stockholders. At June 27, 2023, no shares of our preferred stock were outstanding.

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.

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 (Report) includes forward-looking statements. All statements contained in this 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 substantial additional financing, the results of our research and development efforts, the results of nonclinical and clinical testing, the effect of regulation by the U.S. Food and Drug Administration (FDA) and other domestic and foreign regulatory agencies, the impact of competitive products, product development and technological difficulties, the effect of our accounting policies, and other risks as detailed in the section entitled "Risk Factors" in this 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 (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 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 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 late clinical-stage biopharmaceutical company aiming to transform the treatment landscape for individuals living with anxiety, depression and other CNS disorders. We are advancing therapeutics with the potential to be faster-acting, and with fewer side effects and safety concerns, than those currently available for treating anxiety, depression and multiple CNS disorders. Our pipeline includes six clinical-stage product candidates, including five investigational agents belonging to a new class of neuroactive drugs known as pherines, in addition to AV-101, an oral prodrug of an antagonist of the glycine site of the N-methyl-D-aspartate receptor (NMDAR). Pherines, administered as nasal sprays, are designed with an innovative rapid-onset mechanism of action that activates chemosensory neurons in the nasal cavity and can selectively and beneficially impact key neural circuits in the brain without requiring systemic uptake or direct activity on CNS neurons. AV-101 inhibits the activity of the ion channel of the NMDAR but does not block it, unlike some approved NMDAR antagonists having significant side effects.

Our goal is to develop and commercialize, on our own and with multiple global and regional strategic partners, innovative therapies for anxiety, depression, and other CNS indications where current treatment options are inadequate to meet the needs of millions of patients in the U.S. and worldwide. First and foremost, we are passionate about transforming mental health care and redefining what is possible in the treatment of anxiety and depression disorders – *One Mind at a Time*[™].

Our Product Candidates

Pherine Product Candidates

Five of our product candidates – fasedienol (PH94B), itruvone (PH10), PH15, PH80 and PH284 – belong to a new class of synthetic neuroactive steroids referred to as pherines. Pherines, which are administered in ultra-low microgram level doses as odorless and tasteless nasal sprays, are designed to selectively engage chemosensory neurons in the nasal cavity and induce rapid-onset pharmacologic and behavioral benefits. Specifically, each of our pherine product candidates is a distinct chemical entity that selectively modulates particular areas of the brain, such as the limbic amygdala (the main fear and anxiety center of the brain), the hypothalamus, the hippocampus, the locus ceruleus, and the prefrontal cortex. We believe each of our pherine product candidates has the potential to be a fast-acting therapy for one or more CNS disorders, including social anxiety disorder (fasedienol), major depressive disorder (itruvone), cognitive impairment (PH15), vasomotor syndrome (hot flashes) due to menopause, as well as migraine headaches (PH80) and disorders related to appetite loss (cachexia) (PH284), all without requiring apparent systemic uptake or binding to classic abuse liability receptors or steroidal hormone receptors.

Fasedienol Nasal Spray

Fasedienol (PH94B) is a synthetic investigational pherine from the androstane family in Phase 3 clinical development in the U.S. for treatment of social anxiety disorder (SAD). When administered intranasally in microgram doses, fasedienol activates receptors of peripheral nasal chemosensory neurons connected to subsets of neurons in the olfactory bulbs that, in turn, connect to neurons in the limbic amygdala involved in the pathophysiology of SAD and potentially other anxiety and mood disorders. Fasedienol is pharmacologically active without requiring apparent systemic uptake and distribution of the compound to the brain to achieve its rapid-onset and short duration of anxiolytic effects.

The proposed MOA of fasedienol is fundamentally differentiated from all currently approved anti-anxiety medications, including the three antidepressants approved by the FDA for the treatment of SAD, as well as all benzodiazepines and beta blockers, which, although not FDA-approved for the treatment of SAD, are prescribed for treatment of SAD on an off-label basis. Pre-clinical and Phase 2 clinical studies completed to date suggest that fasedienol has the potential to achieve rapid-onset anti-anxiety effects without systemic uptake or transport into the brain, significantly reducing the risk of side effects and other safety concerns such as potential drug-drug interactions, abuse, misuse and addiction associated with certain other systemic pharmaceuticals that act directly on the CNS and are sometimes prescribed for anxiety disorders.

SAD PALISADE Phase 3 Program

PALISADE-1. In May 2021, we initiated our PALISADE Phase 3 Program for fasedienol in SAD with PALISADE-1, a single-administration assessment Phase 3 public speaking challenge clinical study of fasedienol for the acute treatment of anxiety in adults with SAD. Following discussions with the FDA in mid-2020 during the acute phase of the COVID-19 pandemic, we agreed to design PALISADE-1 in a manner substantially similar to the single-administration assessment Phase 2 public speaking challenge study of fasedienol, which involved self-administration of only a single dose of fasedienol by subjects randomized to the treatment arm. All subjects were given an anxiety-provoking public speaking challenge, conducted only in a clinical setting, and their change in a SUDS score was determined.

In July 2022, we announced top line results from PALISADE-1. Although the safety and tolerability of fasedienol in PALISADE-1 were favorable and consistent with previously reported results from previous clinical trials, PALISADE-1 did not achieve its primary efficacy endpoint, as measured by change from baseline using the SUDS as compared to placebo. We believe the following hypotheses are potential explanations for the unexpected outcome in PALISADE-1: (i) the study was conducted during the acute phase of the COVID-19 pandemic, introducing significant systemic variability in terms of changing social dynamics, subject stress, study site and CRO personnel turnover and mask wearing regulations; (ii) given the foregoing, the public speaking challenge study design may not have been scalable to a large Phase 3 study, particularly during the acute phase of the COVID-19 pandemic; and (iii) some subjects in the study may have had reduced potential to respond to fasedienol due to impaired olfactory cell function potentially caused by the COVID-19 virus, nasal swab testing for COVID-19, RSV or influenza, and/or heavy cannabis use, smoking or vaping.

PALISADE-2. In October 2021, near the end of the acute phase of the COVID-19 pandemic, we initiated PALISADE-2, which involved the same clinic-based, single-administration assessment public speaking challenge study design and use of the SUDS as the primary efficacy endpoint as PALISADE-1. In July 2022, after receiving top line results from PALISADE-1, we paused recruitment and enrollment in PALISADE-2 to allow independent third-party biostatisticians to conduct an interim analysis of available data from subjects randomized in PALISADE-2 up to the date we paused the study. In September 2022, based on their review of unblinded data from the 140 subjects who had completed PALISADE-2, the independent third-party biostatisticians recommended that we continue PALISADE-2 as planned, without revealing the underlying data to us.

Although the results of the interim analysis of PALISADE-2 indicated that continuation of the study would not be futile, after considering the expense, time, and challenges associated with PALISADE-1, as well as the potential methodological complexities involved in resuming PALISADE-2, we closed the PALISADE-2 study. Topline results from the 140 subjects who completed PALISADE-2 are expected in the second half of 2023.

PALISADE Open Label Study. The PALISADE OLS was a Phase 3, open-label safety trial designed to evaluate the safety and tolerability of multiple, as-needed administrations (up to four times a day) of fasedienol in adults with SAD. The PALISADE OLS also evaluated the change from baseline in monthly standard clinical measurements and behavioral assessment scales (LSAS, CGI-I, and PGI-C) in response to anxiety-provoking social situations in daily-life after the administration of fasedienol. The key exploratory efficacy endpoint in the study included evaluation of the change from baseline on the LSAS, which measures SAD patients' response to anxiety-provoking social and performance situations experienced in their daily lives. Following the completion of PALISADE-1, we terminated the PALISADE OLS early, solely for strategic business reasons, and not due to any safety concerns with fasedienol.

Safety and tolerability of fasedienol were assessed and summarized during monthly visits from baseline to end of treatment in AEs, laboratory values, 12-lead electrocardiograms (ECGs), physical examinations, and vital sign assessments following exposure to fasedienol. Long-term administration of 3.2 µg of fasedienol, as-needed up to four times per day, was safe and well-tolerated, with no new safety findings or trends identified, regardless of the number of doses administered by each subject (safety population: n=481). Headache was the most common treatment-emergent adverse event (TEAE) (17.0%), and, except for COVID-19 TEAEs (11.4%) which were not considered related to fasedienol, no other TEAE occurred in more than 5.0% of subjects. Over 30,000 doses of fasedienol were administered by patients during the study, with a mean duration of four months and a maximum study duration of over ten months.

The final data set from PALISADE OLS demonstrates clinically meaningful functional improvement, as measured by the LSAS, and total LSAS scores, in both men and women, continued to decline in consecutive months during the study, as follows:

- After 1 month, the mean reduction on the LSAS was 16 points (n=385);
- After 2 months, the mean reduction on the LSAS was 20 points (n=324); and
- After 3 months, the mean reduction on the LSAS was 24 points (n=218).

For subjects who continued in the study, total LSAS scores continued to decline from baseline, with improvements observed each month on the LSAS through nine months. The continued improvement in LSAS scores is indicative of the therapeutic potential of multiple, patient-tailored, as-needed administrations of fasedienol over time to help patients build confidence to engage in anxiety-provoking social and performance situations in their daily lives more frequently and with less fear and anxiety.

In addition, the CGI-I results indicated 43% of the 218 patients assessed after three months were “much” or “very much” improved, and PGI-C results indicated 44% of the 218 patients assessed after three months considered themselves “much” or “very much” improved.

FDA Feedback on Path Forward; FEARLESS-1. We believe data from approximately 400 subjects in the PALISADE OLS over a period of one month and beyond, combined with the data from the previous Phase 2 randomized, double-blind, placebo-controlled, crossover study of fasedienol after two weeks of use, as discussed above, demonstrate the potential for fasedienol to achieve robust overall reduction in symptoms of SAD and improvement in severity of the disorder over time, as measured by the LSAS. These data also appear to suggest that studies involving multiple administrations of fasedienol over time on an as-needed basis, up to four times per day, when subjects experience daily, real-life, socially stressful situations may most accurately reflect the true efficacy of fasedienol in patients with SAD and represent the actual way in which they would use fasedienol, if approved. Utilizing the LSAS as the primary efficacy outcome measure in our next Phase 3 study is consistent with the pivotal registration trials for all three currently approved treatments for SAD. As those studies indicate, the LSAS is capable of measuring a drug’s efficacy in patients with SAD due to its ability to capture patient feedback on fear and anxiety regarding various social situations, as well avoidance of such situations. Hence, we believe using the LSAS as the primary efficacy endpoint for our further Phase 3 development of fasedienol has the potential to demonstrate its efficacy and true impact on patients’ lives.

In the first quarter of calendar 2023, we met with the FDA to discuss next steps in our Phase 3 development plan for fasedienol in SAD, which plan includes, among other things, conducting, on our own or with collaborators, a multiple-assessment, randomized, double-blind, placebo-controlled Phase 3 study of fasedienol in adults in a real-world setting, using the LSAS as the primary efficacy outcome measure to evaluate the efficacy of fasedienol over time in patients with SAD to support a potential fasedienol New Drug Application (NDA). Positive feedback from the FDA at this meeting confirmed the acceptable use of the LSAS as a primary efficacy endpoint. Accordingly, we are positioned to finalize key components of FEARLESS, our potential NDA-enabling Phase 3 development program for fasedienol for treatment of SAD.

Unlike the PALISADE Phase 3 studies, which involved assessment of only a single, self-administered dose of fasedienol in a clinic-based public speaking challenge using the SUDS as the primary outcome measure, our FEARLESS program will assess multiple administrations of fasedienol, on a patient-tailored as-needed basis, up to six times per day, in a real-world setting over a multiple week period, with the LSAS as the primary efficacy endpoint, consistent with the FDA’s three precedent-setting approvals of antidepressants for treatment of SAD. Dr. Michael R. Liebowitz, a Columbia University psychiatrist, former director and founder of the Anxiety Disorders Clinic at the New York State Psychiatric Institute and current Managing Director of The Medical Research Network LLC in New York City, is the innovator of the LSAS and will be the Principal Investigator for our FEARLESS program in SAD.

Exploratory Phase 2A Study in AjDA and Future Development Opportunities. During the acute phase of the COVID-19 pandemic, we conducted a small exploratory Phase 2A clinical study of fasedienol designed to assess its therapeutic potential in adults experiencing adjustment disorder with anxiety (AjDA). Adjustment disorder (AjD) occurs within three months of exposure to a stressor as evidenced by marked distress that is out of proportion to the socially or culturally expected reactions to the stressor, or that represents significant impairment in social, occupational or other important areas of daily functioning. Our small exploratory study in AjDA is believed to be the first ever randomized, double-blind, placebo-controlled Phase 2A study in the U.S. aimed at exploring the pharmacological treatment of AjDA, and the first clinical trial that evaluated the effects of a fixed dosing regimen of fasedienol, involving intranasal administration of 3.2 µg of fasedienol four times per day over four weeks. A total of 71 subjects were screened for the study, 41 were randomized, 7 discontinued, and 34 completed four weeks of treatment. The study, which was not designed to achieve statistical significance, did not demonstrate a clinically significant difference between fasedienol and placebo as measured on the clinician-rated Hamilton Anxiety Scale (HAM-A). Site variances and both a high drug response rate and high placebo response rate were observed, likely related to the various aspects of AjDA that make it a challenging indication to study. The study of AjDA is complicated because the disorder is, by definition, temporary and self-resolving, making it difficult to identify the cause of clinical improvement or whether placebo played a role in any improvement observed. AjDA is a temporary stress reaction. The stress reaction typically starts within three months of an identifiable stressful situation, but because the disorder is directly linked to a stressor, once the stressor ends, the anxiety reaction may also end, with or without treatment.

Fixed dosing of fasedienol four times per day, over four weeks, was well tolerated, with no appreciable differences in TEAEs between fasedienol and placebo. All reported TEAEs were of mild or moderate severity, with no severe or serious TEAEs reported during the study. Headache was the most commonly reported TEAE, reported by 3 subjects (15.8%) on fasedienol and 2 subjects (9.1%) on placebo.

Despite the methodological challenges inherent in the exploratory Phase 2A study in AjDA, we believe fasedienol builds resilience against anxiety and reduces the cognitive and physical paralysis that occurs during moments of heightened anxiety and stressful situations. Results of the AjDA study may provide support for an as-needed fasedienol dosing approach over time as the preferred mode of treatment.

We may also have potential opportunities to explore the development of fasedienol for other anxiety-related disorders, including postpartum anxiety, post-traumatic stress disorder, panic disorder, and procedural anxiety.

Itruvone Nasal Spray

Itruvone (PH10) is an odorless, tasteless synthetic investigational piperine from the pregnane family with a novel, rapid-onset potential MOA that is fundamentally differentiated from the MOA of all currently approved treatments for depression disorders. Itruvone, which is administered as a nasal spray at microgram-level doses, is designed to engage and activate chemosensory neurons in the nasal cavity, which are connected to neural circuits in the brain that produce antidepressant effects. Specifically, in a manner similar to fasedienol, itruvone's proposed MOA involves the regulation of the olfactory-amygdala neural circuits believed to increase activity of the limbic-hypothalamic sympathetic nervous system and increase the release of catecholamines. Importantly, unlike all currently approved oral antidepressants (ADs) and rapid-onset ketamine-based therapy, including both intravenous ketamine and intranasal ketamine (esketamine), we believe itruvone does not require systemic uptake and distribution of the compound to the brain to produce rapid-onset of antidepressant effects. In all clinical studies completed to date, itruvone has been well-tolerated and has not caused psychological side effects (such as dissociation and hallucinations) or other safety concerns that may be associated with ketamine-based therapy.

In January 2023, we launched a small U.S. single center, randomized, double-blinded, placebo-controlled Phase 1 study to investigate the safety and tolerability of itruvone in healthy adult subjects (n=12). The study was designed to confirm the favorable safety profile of itruvone established in three previous clinical studies conducted in Mexico, as well as facilitate our plans for Phase 2B development of itruvone in the U.S. as a fast-acting stand-alone treatment for MDD. In June 2023, we announced positive data from this study. There were no reported SAEs or discontinuations due to adverse events in the trial. Two AEs were reported during the treatment period, fatigue and headache, which occurred in the same subject. Both AEs resolved without sequelae and were mild in severity. Following itruvone administration, there were no clinically significant findings in ECGs, vital signs, and laboratory parameters. Overall, itruvone was well-tolerated and continued to demonstrate a favorable safety profile.

The FDA has granted Fast Track designation for development of itruvone as a potential adjunctive treatment for MDD.

PH80 Nasal Spray

PH80 is an odorless, tasteless synthetic investigational piperine with a novel, rapid-onset potential MOA that is fundamentally differentiated from the MOA of all currently approved treatments for both vasomotor symptoms (hot flashes) due to menopause and migraine headaches. PH80, which is administered as a nasal spray at microgram-level doses, engages and activates chemosensory neurons in the nasal cavity, which are connected to neural circuits in the brain that modulate neural circuits in the basal forebrain associated with the control of body temperature, as well as premonitory and aura symptoms of migraines. Results from a previously unpublished exploratory randomized, double-blind, placebo-controlled Phase 2A study of PH80 for the acute treatment of vasomotor symptoms (hot flashes) due to menopause demonstrated a statistically significant reduction in the daily number of menopausal hot flashes compared to placebo at the end of the first week of treatment ($p < .001$), and the improvement was maintained through each treatment week until the end of the four-week treatment period. We are currently preparing, on our own or with collaborators, to submit an U.S. IND for a Phase 2B clinical study of PH80 as a treatment for hot flashes due to menopause.

In addition, PH80 initiates neural impulses in the olfactory bulb transmitted by pathways that rapidly affect the function of multiple structures in the brain, including the amygdala and hypothalamus that have been linked to the pathology of migraine. Due to its MOA and a small proof of concept study, we believe PH80 may have therapeutic potential to relieve premonitory and aura symptoms of migraines.

PH15 Nasal Spray

PH15 is an odorless, tasteless synthetic investigational piperine with a novel, rapid-onset potential MOA that is fundamentally differentiated from the MOA of all currently approved treatments to improve cognitive impairment caused by mental fatigue and potentially other disorders. Early functional MRI studies in human volunteers at Stanford University revealed that intranasal administration of PH15 induced rapid activation of brain areas related to cognition (Sobel et al, Brain, 1999). In a small double blind, placebo-controlled study Phase 2 study of human subjects who were sleep deprived to induce mental fatigue, intranasal PH15 showed rapid and significant improvement in cognitive and psychomotor performance and improvement of reaction time that was better than the effect of a placebo and 400 mg of oral caffeine. We are currently evaluating the path forward to submitting an U.S. IND for a Phase 2 clinical study, on our own or with collaborators, and the appropriate indication for demonstrating improvement of cognitive function.

PH284 Nasal Spray

PH284 is an odorless, tasteless synthetic investigational pherine with a novel, rapid-onset potential MOA that is fundamentally differentiated from the MOA of all currently approved treatments for the loss of appetite associated with chronic disorders such as cancer. Cachexia is a serious but under recognized consequence of many chronic diseases with body mass loss of >10% and a prevalence of 5 to 15 %. We believe PH284 may have therapeutic potential for improving subjective feelings of hunger in patients with cachexia. We are currently evaluating the path forward to submitting an U.S. IND for cachexia, on our own or with collaborators, and the appropriate patient populations for demonstrating increase in appetite and weight gain in a second Phase 2 study.

AV-101

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 binding 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 completed to date, AV-101 has demonstrated good oral bioavailability and an excellent pharmacokinetic (PK) profile. No binding of AV-101 or 7-Cl-KYNA to off-site targets was identified by an extensive receptor screening study. Moreover, in all clinical trials completed 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. 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.

Based on observations and findings from preclinical studies, we believe AV-101 has the potential to become a new oral treatment alternative for multiple CNS disorders. We are currently preparing for Phase 2A development of AV-101, on our own or with collaborators, as a treatment for one or more neurological disorders involving the NMDAR receptor. Multiple studies have shown AV-101 to be safe and well-tolerated, and a range of preclinical studies indicate potential in multiple indications, including levodopa-induced dyskinesia, neuropathic pain, seizures, MDD, and suicidal ideation.

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.

Acquisition of Pherin Pharmaceuticals, Inc.

On December 20, 2022, we entered into an Agreement and Plan of Merger (the *Merger Agreement*) along with VTGN Merger Sub, Inc., our wholly owned subsidiary (*Merger Sub*), Pherin Pharmaceuticals, Inc. (*Pherin*), and Kevin McCarthy in his capacity of Stockholder Representative, to acquire Pherin (the *Pherin Acquisition*). On February 2, 2023 (the *Closing Date*), we completed the Pherin Acquisition and Pherin is now a wholly owned subsidiary of the Company. Immediately prior to the consummation of the Pherin Acquisition, each of Pherin's directors and officers resigned, and no employees or other affiliates of Pherin on the Closing Date are serving or will serve in their previous roles or in any other capacity with Pherin or with the Company.

As consideration for the Pherin Acquisition, we (i) issued an aggregate of 413,670 unregistered shares of our common stock to the exchange agent for the Pherin Acquisition, which shares were issued to approximately 96.07% of Pherin stockholders eligible to receive common stock in exchange for their outstanding shares of Pherin common stock (the *Stock Consideration*), and (ii) paid to the exchange agent for the Pherin Acquisition, an aggregate of approximately \$126,100 for the approximately 3.93% remaining Pherin stockholders who were not eligible to receive Stock Consideration in exchange for their outstanding shares of Pherin common stock (the *Cash Consideration* and, together with the Stock Consideration, the *Merger Consideration*). We have accounted for the Pherin Acquisition as an asset acquisition.

Following the completion of the Pherin Acquisition, we now have full ownership of intellectual property rights to fasedienol and itruvone, as well as PH15, PH80 and PH284.

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 (*U.S. 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

The AffaMed Agreement, involving clinical development and commercialization of fasedienol for acute treatment of anxiety in adults with SAD, and potentially other anxiety-related disorders, in Greater China, South Korea, and Southeast Asia, has been the basis of our reported revenue for both our fiscal year ending March 31, 2023 (*Fiscal 2023*) and 2022 (*Fiscal 2022*). In prior years, we occasionally generated revenue from collaborative research and development arrangements, licensing and technology access fees and government grants. We recognize revenue following the guidance of 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.

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 account for our leases following the guidance of Accounting Standards Update No. 2016-02, “Leases (Topic 842)” (ASU 2016-02). 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. 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 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. We do not carry any capitalized intellectual property or product licenses as assets subject to impairment on our Consolidated Balance Sheets.

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 fasedienol, itruvone, and AV-101. 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 CROs 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, at acquisition, the product or technology licensed has not achieved regulatory approval or reached technical feasibility and has no alternative future uses. We treated the Pherin Acquisition as an acquisition of assets for accounting purposes. Since, at the date of the acquisition, neither fasedienol, itrivone nor the other three pherines acquired had achieved regulatory approval and each required significant additional development and expense and were without alternative future use, we recorded the costs related to acquiring the assets as research and development expense in our Consolidated Statement of Operations and Comprehensive Loss for our fiscal year ended March 31, 2023.

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. 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 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, as we do not believe that the historical volatility of our common stock will be indicative of its future performance.

Warrants Issued in Connection with Equity Financing

We evaluate the appropriate balance sheet classification of warrants we issue as either equity or as a derivative liability. In accordance with ASC 815-40, *Derivatives and Hedging-Contracts in the Entity's Own Equity (ASC 815-40)*, we classify a warrant as equity if it is "indexed to the Company's equity" and meets several specific conditions for equity classification. A warrant is not considered "indexed to the Company's equity," in general, when it contains certain types of exercise contingencies or potential adjustments to its exercise price. If a warrant is not indexed to the Company's equity or it has net cash settlement that results in the warrants to be accounted for under ASC 480, *Distinguishing Liabilities from Equity* or ASC 815-40, it is classified as a derivative liability which is carried on the consolidated balance sheet at fair value with any changes in its fair value recognized immediately in the Statement of Operations and Comprehensive Loss. At March 31, 2023 and 2022, we had both investor warrants and share-based compensation warrants outstanding that were classified as equity.

Income Taxes

We account for income taxes using the asset and liability approach promulgated by ASC 740, *Income Taxes*, 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.

See Note 3 to the Consolidated Financial Statements included in Item 8 in this Report (*Financial Statements*) for information on recent accounting pronouncements.

Financial Operations Overview and Results of Operations

Net Loss

We have not yet achieved recurring revenue-generating status from any of our product candidates or technologies in amounts sufficient to sustain our operations and enable our strategic business plans. Since acquiring our exclusive worldwide licenses in 2018, we have devoted substantial resources to advance initiatives related to research, development, and contract manufacturing of our intranasal investigational product candidates, fasedienol (PH94B) and itruvone (PH10), including initiatives related to manufacturing processes, analytical methods and production programs for drug substance and finished drug product, as well as for preclinical studies and clinical studies focused on potential commercialization of these product candidates for neuropsychiatry indications. During Fiscal 2022 and Fiscal 2023, we allocated significant resources to our PALISADE Phase 3 Program evaluating fasedienol for the acute treatment of anxiety in adults with SAD. We conducted, and are continuing to conduct, various preclinical studies and manufacturing activities that enabled submission of our U.S. IND for itruvone in MDD in late September 2022 and our initiation of a small Phase 1 clinical study of itruvone in December 2022 to facilitate potential Phase 2B clinical development of itruvone in the U.S. as a stand-alone treatment for MDD. With respect to AV-101, our current focus is evaluating AV-101 in combination with probenecid, which may provide opportunities to explore the therapeutic potential of the combination for certain CNS indications involving the NMDAR. We have on-going initiatives for creating, protecting and patenting intellectual property (*IP*) related to our product candidates and technologies and raising sufficient working capital to fund these studies, initiatives and other activities. At March 31, 2023, we had an accumulated deficit of approximately \$326.9 million. Our net loss for Fiscal 2023 and Fiscal 2022 was approximately \$59.2 million and \$47.8 million, respectively. We expect losses to continue for the foreseeable future as we engage in further research, development and regulatory activities related to fasedienol, itruvone and AV-101 and, potentially, the new pherines acquired in the Pherin Acquisition.

Summary of the Fiscal Year Ended March 31, 2023

Throughout Fiscal 2022 and Fiscal 2023, we have continued to advance our nonclinical and clinical development, manufacturing, and regulatory activities necessary for (i) Phase 3 clinical development of fasedienol as a potential treatment of anxiety in adults with SAD, (ii) advancing our Phase 2A clinical study of fasedienol in adults experiencing AjDA, (iii) submitting our itruvone IND and initiating a small Phase 1 study of itruvone in the U.S. to facilitate potential Phase 2B development as a stand-alone treatment of MDD and (iv) exploratory Phase 1B development of AV-101 in combination with probenecid to assess potential opportunities to develop the combination for treatment of certain CNS indications.

We initiated our PALISADE Phase 3 Program for fasedienol in SAD with PALISADE-1 in May 2021 and PALISADE-2 in August 2021. During Fiscal 2022, we also initiated the PALISADE OLS and advanced our Phase 2A clinical study of fasedienol in adults experiencing AjDA. We achieved last patient out of PALISADE-1 in June 2022 and commenced analysis of the data generated throughout the study. As noted above, in July 2022 we determined that PALISADE-1 did not achieve its primary efficacy endpoint. Accordingly, we have actively investigated, on multiple fronts, potential contributors to that outcome and will apply our learnings to all future clinical studies of fasedienol in SAD and/or other anxiety indications. In July 2022, after receiving the results from PALISADE-1, we paused recruitment and enrollment in PALISADE-2 to allow independent biostatisticians to conduct an interim analysis of available data from 140 subjects randomized in PALISADE-2 up to the date we paused the study and subsequently closed the study. We also ended enrollment in our PALISADE OLS in August 2022. In February 2023, we met with the FDA to discuss our broader Phase 3 development plan for fasedienol, which includes a multiple-assessment, randomized, double-blind, placebo-controlled Phase 3 study of fasedienol in adults, using the LSAS as the primary outcome measure to evaluate the efficacy of fasedienol over time in patients with SAD. FDA feedback confirmed the acceptable use of the LSAS as a primary efficacy endpoint in future fasedienol studies. Near-term, we plan to focus our resources primarily on the planning and preparation for FEARLESS-1, an LSAS-based Phase 3 study of fasedienol for treatment of SAD. We believe data from the earlier Phase 2 study of fasedienol and unpublished preliminary data from PALISADE OLS support continued late-stage clinical development of fasedienol as a potential treatment for SAD when used as-needed, over an extended period of time in an outpatient (real world) setting.

Throughout Fiscal 2022 and Fiscal 2023, we have expanded our employee infrastructure with experienced personnel across multiple functional areas, including clinical operations, clinical research, data management, chemistry, manufacturing and controls (*CMC*) and quality assurance, biostatistics and clinical analytics, regulatory affairs, medical affairs, translational medicine, legal, contracts and corporate affairs, development operations, and investor and public relations. We have paused further additions to our employee base until we are able to secure additional financial resources and finalize our broader Phase 3 development plan for fasedienol in SAD.

Throughout Fiscal 2022 and during Fiscal 2023, strains of SARS-CoV-2, commonly referred to as COVID-19 and multiple variants of the virus, have spread globally and the outbreak was declared a pandemic by the World Health Organization and a public health emergency in the U.S. by the U.S. Secretary of Health and Human Services. Operations at our headquarters in South San Francisco were significantly curtailed during the first half of Fiscal 2022, and, to some extent, periodically thereafter, while state and local restrictions required remote working conditions. Most of our employee additions during Fiscal 2022 and thereafter are geographically located away from our headquarters facility in South San Francisco and routinely work remotely. Our employees have worked efficiently and productively while remotely located and working from home, whether as a result of the COVID-19 pandemic or otherwise. From time to time during the COVID-19 pandemic, however, the efficiency and productivity of certain preclinical and clinical development programs and our third-party collaborators, including, among others, CROs, CMOs and other third-party service providers have been impacted by surges in the spread of variants of COVID-19, such as spreads induced by the Delta and Omicron variants and their sub-variants during Fiscal 2022 and thereafter, shelter-in-place orders, social distancing measures, travel bans and restrictions, and certain business and government closures or reductions in service. Moreover, during the COVID-19 pandemic, we experienced delays in the delivery of supplies of active pharmaceutical product (*API*) or other key materials required to continue development of fasedienol and itruvone, as well as temporary disruptions in the availability of third-party personnel and others involved in the conduct of our preclinical and clinical programs. In addition, we believe conditions resulting from the COVID-19 pandemic may have negatively impacted the outcome of at least PALISADE-1. Future unexpected delays may result in a significant, material delay or disruption to our current clinical and nonclinical development plans, programs, and operations.

We did not complete any capital-raising or other significant financing activities during Fiscal 2023. In May 2021, we entered into an Open Market Sale Agreement SM (the *Sales Agreement*) with Jefferies LLC (*Jefferies*) as sales agent, with respect to an at-the-market offering program (the *ATM*) under which we may, at our option, offer and sell, from time to time, shares of our common stock having an aggregate offering price of up to \$75.0 million through Jefferies as our sales agent. During September and early October 2021, we sold an aggregate of 50,593 shares of our common stock and received gross cash proceeds of approximately \$4.45 million under the ATM. We did not sell any shares of our common stock under the ATM during Fiscal 2023. From June 12, 2023 through the date of this Report we sold an aggregate of 561,418 shares of our common stock and received approximately \$1.15 million in gross proceeds under the ATM. Subject to certain restrictions, our Registration Statement on Form S-3 (the *S-3 Shelf Registration Statement*) remains available for future sales of our equity securities in one or more public offerings, including under the ATM, from time to time.

Since we received the results of PALISADE-1, we have been carefully monitoring our cash resources and critically evaluating our internal and external research and development and general and administrative expenditures, which has included (i) reassessing our Phase 3 clinical development plan for fasedienol in SAD, (ii) terminating the PALISADE OLS study of fasedienol, (iii) continuing to completion our Phase 2A clinical study of fasedienol in adults experiencing AjDA and (iv) commencing and completing our Phase 1 clinical study of itruvone as a treatment for adults suffering from MDD.

Comparison of Fiscal Years Ended March 31, 2023 and 2022

The following table summarizes the results of our operations for the fiscal years ended March 31, 2023 and 2022 (amounts in thousands).

	Fiscal Year Ended March 31,	
	2023	2022
Sublicense revenue	\$ (227)	\$ 1,109
Operating expenses:		
Research and development	44,377	35,408
General and administrative	14,664	13,480
Total operating expenses	59,041	48,888
Loss from operations	(59,268)	(47,779)
Interest income, net	26	20
Loss before income taxes	(59,242)	(47,759)
Income taxes	(6)	(3)
Net loss	(59,248)	(47,762)
Accrued dividend on Series B Preferred Stock	-	(945)
Net loss attributable to common stockholders	\$ (59,248)	\$ (48,707)

Revenue

We derecognized \$227,300 in sublicense revenue pursuant to the AffaMed Agreement during Fiscal 2023 compared to recognizing revenue of \$1,108,900 during Fiscal 2022. As described more completely in Note 3 and Note 11 to our Financial Statements in Item 8 of this Report, on June 24, 2020, we entered into the AffaMed Agreement, pursuant to which we received a non-refundable upfront license fee payment of \$5.0 million on August 3, 2020, which payment commenced our revenue recognition under the AffaMed Agreement. We recognize revenue on a straight-line basis over the period during which we expect to perform our obligation under the AffaMed Agreement, essentially the development and regulatory approval in the U.S. of fasedienol in adults with SAD. Revenue related to our performance obligation, which is satisfied over time, could be materially impacted because of changes in our estimates of the time or effort necessary to satisfy the performance obligation. Due to the failure of PALISADE-1 to meet its primary efficacy endpoint and the resulting anticipated delays in subsequent clinical and regulatory processes for fasedienol in SAD, at September 30, 2022, we estimated that completion of our performance obligation under the AffaMed Agreement would be delayed until mid-calendar 2027. As a result of the change in our estimate of the time required to complete our performance obligation under the AffaMed Agreement, we recorded a cumulative catch-up adjustment at September 30, 2022 pursuant to which we derecognized previously recorded revenue of \$892,500, resulting in negative revenue of \$227,300 for Fiscal 2023. Following the cumulative catch-up adjustment, through March 31, 2023, we have recognized an aggregate of \$1,971,100 as revenue under the AffaMed Agreement and expect to recognize the remaining \$3,028,900 as revenue over the estimated performance period as our obligation is completed. We have not subsequently modified our September 30, 2022 estimate of the timing to complete our performance obligation, however, we will adjust our estimates, as necessary, in subsequent periods should more definitive information on which to base our projections become available. 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 any additional revenue beyond that noted or cash payments to us in the near term, or at all.

In December 2016, we entered into an Exclusive License and Sublicense Agreement with BlueRock Therapeutics, LP, a 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. We recognized \$1.25 million in sublicense revenue in our fiscal year ended March 31, 2017, under the agreement. In May 2023, BlueRock Therapeutics notified us that the Exclusive License and Sublicense Agreement would be terminated effective July 10, 2023.

Research and Development Expense

Research and development (*R&D*) expense increased by approximately \$9.0 million, from \$35.4 million in Fiscal 2022 to \$44.4 million in Fiscal 2023. Activities related to our PALISADE Phase 3 Program for fasedienol, including PALISADE-1, PALISADE-2 and the PALISADE OLS study, and the fasedienol Phase 2 Study in AjDA, as well as nonclinical development, outsourced manufacturing and regulatory activities for both fasedienol and itruvone, accounted for increased expenses of approximately \$5.1 million during Fiscal 2023 in comparison to the activities conducted during Fiscal 2022. Additionally, we expensed approximately \$3.6 million of costs related to the Pherin Acquisition, including approximately \$3.1 million representing the fair market value of the common stock issued in the Pherin Acquisition. In addition to the noncash fair value of the common stock issued in the Pherin Acquisition in Fiscal 2023, other noncash research and development expenses, primarily stock-based compensation and depreciation in both periods, accounted for approximately \$1.5 million in both Fiscal 2023 and Fiscal 2022.

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

	Fiscal Years Ended March 31,	
	2023	2022
Salaries and benefits	\$ 6,255	\$ 6,040
Stock-based compensation	1,365	1,457
Consulting and other professional services	817	834
Clinical and nonclinical studies and development expenses:		
Fasedienol and Itruvone	30,326	25,184
AV-101	1,163	999
All other	72	129
	<u>31,561</u>	<u>26,312</u>
Cost of Pherin Acquisition as an asset purchase	3,559	-
Rent	556	483
Depreciation	102	97
All other	162	185
Total Research and Development Expense	<u>\$ 44,377</u>	<u>\$ 35,408</u>

The increase in salaries and benefits expense in Fiscal 2023 primarily reflects the addition of seven new management and staff positions across multiple functional disciplines, including biostatistics and clinical analytics, clinical operations, chemistry, manufacturing and controls, and regulatory affairs since the end of Fiscal 2022, as well as the impact of salary increases effective in January 2022 granted to our R&D management and staff. These increases are partially offset by the impact of six terminations during Fiscal 2023. Further, there were no payments or accruals of additional compensation expense for R&D officers and employees as a result of the outcome of the PALISADE-1 study and delay or termination of other clinical trials and nonclinical activities related to calendar year 2022 corporate operational objectives, compared to approximately \$1,075,800 of expense in Fiscal 2022 related to attainment of calendar year 2021 corporate objectives.

Stock-based compensation expense for Fiscal 2023 reflects the amortization of option grants made to our R&D staff and certain clinical and scientific consultants since May 2019, in addition to grants to new employees as indicated above. All outstanding options granted to R&D employees and consultants prior to May 2019 became fully vested and amortized during or prior to the end of Fiscal 2022 and the May 2019 grants became fully vested during Fiscal 2023. Grants awarded during Fiscal 2023, including those granted to new employees, account for approximately \$89,000 of expense during Fiscal 2023, offset by an expense reduction of approximately \$294,000 attributable to certain options granted between May 2019 and May December 2020 that became fully vested and amortized prior to or during Fiscal 2023. Grants made during Fiscal 2022 reflected a full twelve months of vesting and amortization during Fiscal 2023, or became fully vested and amortized, decreasing expense for such options by approximately \$47,000. FY 2023 expense was reduced by approximately \$47,000 as a result of employee terminations noted earlier. The extension of option exercisability by approximately six months for a terminated employee accounted for approximately \$109,000 of additional expense during Fiscal 2023. 2019 ESPP expense in Fiscal 2023 decreased by approximately \$10,000 compared to Fiscal 2022 expense.

Consulting and other professional services in both periods reflects fees incurred, generally on an as-needed basis, for project-based scientific, CMC, nonclinical and clinical development and regulatory advisory and analytical services rendered to us by third parties, primarily in support of our fasedienol and itruvone development initiatives. Expense in both periods includes contract recruiting services for certain specialized R&D positions.

Fasedienol and itruvone project expenses increased by approximately \$5.1 million in Fiscal 2023 compared to Fiscal 2022. Fasedienol expense for Fiscal 2023 reflects (i) the costs associated with conducting and completing the PALISADE-1 study, including data analysis, site closures and root cause investigations, (ii) costs associated with the PALISADE-2 study both during its conduct, for the interim analysis of PALISADE-2 data and during its pause from August 2022 through March 2023, when it was closed, (iii) costs associated with the PALISADE OLS study during its conduct and following its termination, including site closure costs, and (iv) costs for conducting the Phase 2A study of fasedienol in AjDA which was completed late in the third quarter of Fiscal 2023, as well as various other clinical, nonclinical, regulatory and manufacturing activities. The PALISADE OLS study commenced in July 2021, PALISADE-2 commenced in August 2021 and the fasedienol AjDA study commenced in mid-June 2021, and each of those studies was actively enrolling during at least a portion of Fiscal 2022. Throughout both Fiscal 2023 and 2022, manufacturing, formulation, process validation and analysis of sufficient quantities of drug substance and drug product for clinical trials and other developmental requirements were significant initiatives for advancing both fasedienol and itruvone. Additionally, there was significant regulatory activity during the second quarter of Fiscal 2023 leading to the late-September 2022 submission to the FDA of the IND for itruvone in MDD, followed by the small Phase 1 study conducted during the fourth quarter of Fiscal 2023. Due to its later stage of development, costs for fasedienol initiatives have significantly exceeded those for itruvone during both Fiscal 2023 and Fiscal 2022. In both Fiscal 2023 and Fiscal 2022, AV-101 project expense includes costs for certain preclinical and nonclinical studies related to the use of AV-101 with adjunctive probenecid and certain AV-101 manufacturing stability studies. Fiscal 2023 expense also includes the costs of our ongoing exploratory Phase 1B AV-101 and probenecid clinical trial.

Rent expense for both Fiscal 2023 and Fiscal 2022 reflects our implementation of ASC 842 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. As disclosed in Note 14, *Commitments and Contingencies*, in the Financial Statements in Item 8 of this Report, in October 2021, we entered into an amendment to this lease, pursuant to which the term of the lease was extended from August 1, 2022 to July 31, 2027 and the base rent under the lease for the five-year extension period was specified. We allocate total rent expense for our South San Francisco facility between R&D expense and G&A expense based generally on square footage dedicated to each function. In both periods reported, rent expense includes charges for 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 increased by approximately \$1.2 million to approximately \$14.7 million in Fiscal 2023 compared to approximately \$13.5 million in Fiscal 2022. Primary components of the change include:

- (i) Expensing professional services incurred in anticipation of a potential credit facility offering that we opted to forego as a result of the PALISADE-1 outcome;
- (ii) Increased insurance coverage limits and new coverages added to our insurance portfolio;
- (iii) Expanded investor and public relations and corporate awareness initiatives;
- (iv) The impact of new G&A employees hired since the end of Fiscal 2022, offset by the absence of payment or accrual for additional compensation expense for G&A officers and employees as a result of the outcome of PALISADE-1 and the delay or conclusion of other clinical trials and nonclinical activities related to calendar year 2022 corporate operational objectives; offset by
- (v) Customary pre-commercialization studies, analyses, projections, strategic modeling and awareness services, primarily for fasedienol in SAD, initiated in Fiscal 2022 in expectation of positive clinical trial results from the PALISADE Phase 3 program and curtailed in Fiscal 2023 as a result of the PALISADE-1 outcome.

Noncash general and administrative expenses, approximately \$2,065,000 and \$2,379,000 in Fiscal 2023 and Fiscal 2022, respectively, primarily reflect stock-based compensation and depreciation in both periods, expense attributable to the modification of an outstanding warrant to purchase our common stock in Fiscal 2023 and the write-off of deferred offering costs in Fiscal 2022.

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

	Fiscal Years Ended March 31,	
	2023	2022
Salaries and benefits	\$ 4,313	\$ 4,082
Stock-based compensation	1,972	2,023
Board fees and other consulting services	678	453
Legal, accounting and other professional fees	2,424	1,791
Investor and public relations	1,160	707
Pre-launch marketing studies and analyses	1,904	2,796
Insurance	1,379	578
Travel expenses	107	42
Rent and utilities	419	377
Sublicense contract amortized acquisition expense	(21)	105
Warrant modification expense	77	-
Write off of deferred offering costs	-	232
All other expenses	252	294
	<u>\$ 14,664</u>	<u>\$ 13,480</u>

The increase in salaries and benefits expense for Fiscal 2023 primarily reflects the addition of four additional management and staff positions including our Vice President, Human Resources in January 2022, our Chief Legal Officer in May 2022, our Vice President, Associate General Counsel in August 2022 and an additional administrative employee, as well as the impact of salary increases effective in January 2022 granted to our G&A management and staff. These increases are offset by (i) the absence in Fiscal 2023 of payment or accrual for additional compensation expense for G&A officers and employees as a result of the outcome of the PALISADE-1 study and the delay or conclusion of other clinical trials and nonclinical activities related to calendar year 2022 corporate objectives compared to payment of approximately \$938,000 in Fiscal 2022 related to achievement of calendar 2021 corporate objectives, and (ii) the impact of the voluntary resignation in November 2022 of our Chief Commercial Officer, who remains a member of our Board.

Fiscal 2023 stock-based compensation expense reflects the amortization of option grants made to our internal management and administrative staff, independent members of our Board and certain consultants since May 2019, in addition to grants to new senior management and other new employees as indicated above. All outstanding options granted to G&A employees, Board members and consultants prior to May 2019 were fully vested and amortized at the end of Fiscal 2022. Options granted in May 2019, September 2019 and April 2020 became fully vested and amortized in May 2022, September 2022 and April 2022, respectively, so that all outstanding options granted to G&A employees and consultants prior to October 2020 are fully vested and amortized at the end of Fiscal 2023. Grants awarded after March 31, 2022, including those granted to new employees indicated above, account for approximately \$78,000 of Fiscal 2023 expense, offset by an expense reduction of approximately \$791,000 attributable to certain options granted between May 2019 and June 2020 that became fully vested and amortized in Fiscal 2023. Grants made in March 2022 reflected a full year of expense during Fiscal 2023 increasing Fiscal 2023 expense by approximately \$498,000 compared to the expense in Fiscal 2022. Other than the new-hire grant to our Chief Legal Officer, there were no option grants to senior executives or independent members of our Board in Fiscal 2023. 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 2023 and Fiscal 2022, 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 represents, in both periods, fees paid as consideration for Board and Board Committee services to the independent members of our Board of Directors. We modified our cash compensation policy for our independent Board members at the beginning of Fiscal 2022, increasing payments to reflect current market conditions and we added one new independent Board member in April 2021 and two additional independent members during July 2021. Expenses for Fiscal 2023 also include recruiting fees for certain administrative positions and fees paid to our former Chief Commercial Officer pursuant to a consulting agreement following her voluntary resignation.

Legal, accounting and other professional fees for Fiscal 2023 and Fiscal 2022 includes expense related to routine corporate legal and compliance fees as well as 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 necessarily occur ratably throughout the year or between years. In both Fiscal 2023 and Fiscal 2022, 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 fasedienol and itruvone intellectual property portfolios. Accounting expenses include costs related to the annual audit of our prior year financial statements and the three quarterly reviews of our current year financial statements. Fiscal 2023 and Fiscal 2022 accounting expense also includes the cost of certain outsourced financial and accounting services which commenced at the beginning of Fiscal 2022 and, in Fiscal 2022, implementation of new accounting software. Both years reflect expense related to an expanded service level from our information technology service provider and a contracted head of Information Technology, all of which commenced at the beginning of Fiscal 2022. Both years also reflect certain recruiting fees incurred in connection with searches for certain specialized positions.

Investor and public relations expense in both Fiscal 2023 and Fiscal 2022 includes the fees of our various external service providers for a broad spectrum of investor relations, public relations and social media services, and, particularly in Fiscal 2023, additional market awareness and strategic advisory and support functions and initiatives. During both years, we conducted numerous virtual meetings 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.

Throughout Fiscal 2022 and through the second quarter of Fiscal 2023, we incurred expenses for a number of customary pre-commercialization studies, analyses, projections, strategic modeling and awareness services, primarily attributable to Fasedienol as a potential acute treatment of anxiety in adults with SAD. Given the outcome of PALISADE-1 and the resulting delay to our anticipated commercialization timeline for fasedienol, these activities were significantly reduced during the third and fourth quarters of Fiscal 2023. We have evaluated the extent and timing of such future activities, and anticipate that such expenditures will, for the short term, remain at the modest level similar to that expended during the second half of Fiscal 2023.

The increase in Fiscal 2023 insurance expense is primarily attributable to the increased coverage obtained under our directors' and officers' liability insurance upon renewal of our policy in May 2022 and additional coverages, including cybersecurity and employment practices liability, added to our insurance program during Fiscal 2022.

As a result of periodic shelter-in-place restrictions and travel and workplace precautions and restrictions associated with the COVID-19 pandemic during calendar 2020 and 2021, management presentations and historically in-person 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, generally occurred remotely without requiring in-person business travel by our executives. During Fiscal 2023, we incurred modest travel expense for attendance at seminars, and for vendor audits, clinical trial site visits and certain investor-focused events, as conditions have permitted, with in-person travel still reasonably limited.

Rent expense for both Fiscal 2023 and Fiscal 2022 reflects our implementation of ASC 842 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. As disclosed in Note 14, *Commitments and Contingencies*, in the Financial Statements included in Item 8 of this Report, in October 2021, we entered into an amendment to this lease, pursuant to which the term of the lease was extended from August 1, 2022 to July 31, 2027 and the base rent under the lease for the five-year extension period was specified. We allocate total rent expense for our South San Francisco facility between R&D expense and G&A expense based generally on square footage dedicated to each function. In both years, rent expense includes charges for such items as common area maintenance fees, taxes and insurance which are generally assessed to us by our landlord.

Beginning in the quarter ended September 30, 2020, we began to amortize the deferred contract acquisition costs related to our acquisition of the AffaMed Agreement, composed of the cash payment of \$220,000 for sublicense fees which we were obligated to make pursuant to our PH94B license from Pherin, and the \$125,000 cash payment 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. As described above in the section entitled *Revenue*, the outcome of the PALISADE-1 study resulted in an estimated extension of the period over which we will recognize both revenue under the AffaMed Agreement and the period over which we will amortize the deferred contract acquisition costs. Our extended estimate of the time required to satisfy our performance obligation required a cumulative catch-up adjustment to amortization of the contract acquisition costs at September 30, 2022, pursuant to which we reversed previously recorded expense of approximately \$84,000, resulting in negative contract acquisition amortization expense of \$21,000 for Fiscal 2023.

In December 2022, we modified outstanding warrants to purchase an aggregate of 33,333 registered shares of our common stock exercisable at \$15.00 per share that were due to expire during December 2022 to extend the exercisability of such warrants for a period of two years. No other term of the warrants, including exercise price, was modified. We recognized the incremental fair value of \$77,400 resulting from the modification as a noncash warrant modification expense in Fiscal 2023.

In June 2021, we terminated a financing arrangement pursuant to which we had recorded legal, accounting and securities registration filing fees as deferred offering costs. Upon termination of the agreement, we expensed the remaining \$232,100 of deferred offering costs related to the agreement as a noncash charge to G&A expense in Fiscal 2022.

Interest and Other Income, Net

Interest income, net totaled \$26,200 in Fiscal 2023 compared to \$19,900 in Fiscal 2022. 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,	
	2023	2022
Interest income	\$ 49	\$ 20
Interest expense on financing lease and insurance premium financing note	(23)	-
Interest income, net	<u>\$ 26</u>	<u>\$ 20</u>

In both Fiscal 2023 and Fiscal 2022, interest income relates to cash deposits in interest-bearing cash equivalent accounts. Although interest rates increased during Fiscal 2023, our cash deposit balances have declined as we used such amounts to fund our operations. Interest expense for Fiscal 2023 relates to interest paid on the insurance premium financing note executed in May 2022 and, in both periods, on our financing lease of office equipment subject to ASC 842. We did not finance insurance premiums for policies that renewed in May 2021 or February 2022.

We recognized approximately \$945,000 during Fiscal 2022 attributable to the 10% cumulative dividend accrued on outstanding shares of our Series B 10% Convertible Preferred Stock (*Series B Preferred*) prior to its conversion in November 2021 as an additional deduction in arriving at net loss attributable to common stockholders. In November 2021, the custodial holder of 1,131,669 outstanding shares of our Series B Preferred exercised its rights for conversion into common stock under the terms of the Certificate of Designation of the Relative Rights and Preferences of the Series B 10% Convertible Preferred Stock (*Series B Certificate of Designation*) and we issued 37,722 shares of our common stock upon conversion. From initial issuance in May 2015 through the time of conversion in November 2021, the Series B Preferred had accrued 10% dividends aggregating \$7,217,800 and, in accordance with the terms of the Series B Certificate of Designation, we issued 109,860 shares of our unregistered common stock in payment of the accrued dividends. Following this conversion there were no additional shares of Series B Preferred outstanding and no further accrual of dividends on the Series B Preferred.

Liquidity and Capital Resources

Since our inception in May 1998 through March 31, 2023 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 \$208.7 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 \$41.3 million in noncash acquisitions of product licenses, the Pherin Acquisition, and in settlements of certain liabilities, including liabilities for professional services rendered to us or as compensation for such services.

We did not complete any capital-raising or other significant financing activities during Fiscal 2023. During Fiscal 2022, holders of outstanding warrants to purchase an aggregate of 243,293 shares of our common stock exercised such warrants, and we received cash proceeds of approximately \$6.2 million. Additionally, in May 2021, we entered into an Open Market Sale Agreement SM (the *Sales Agreement*) with Jefferies LLC (*Jefferies*) as sales agent, with respect to an at-the-market offering program (the *ATM*) under which we may, at our option, offer and sell, from time to time, shares of our common stock having an aggregate offering price of up to \$75.0 million through Jefferies as our sales agent. During September and early October 2021, we sold an aggregate of 50,593 shares of our common stock and received gross cash proceeds of approximately \$4.45 million under the ATM. We did not sell any shares of our common stock under the ATM during Fiscal 2023. From June 12, 2023 through the date of this Report we sold an aggregate of 561,418 shares of our common stock and received approximately \$1.15 million in gross proceeds under the ATM.

During our fiscal year ended March 31, 2021 (*Fiscal 2021*), we received approximately \$119 million in net cash proceeds primarily from various public sales of our equity securities and \$5.0 million gross proceeds from the AffaMed Agreement. These earlier transactions continued to provide necessary capital resources and liquidity throughout Fiscal 2023, during which we also received approximately \$167,500 in cash proceeds from the exercise of outstanding stock options and sales under our 2019 Employee Stock Purchase Plan (the *2019 ESPP*).

We had cash and cash equivalents of approximately \$16.6 million at March 31, 2023, which we do not believe will be sufficient to fund our planned operations for the twelve months following the issuance of these Consolidated Financial Statements, which raises substantial doubt regarding our ability to continue as a going concern. We are continuing to evaluate our cash resources as we prepare for the next steps in our development of our product candidates, either on our own or with collaborators, including Phase 3 development of fasedienol for the treatment of SAD, Phase 2B development of itruvone as a potential stand-alone rapid-onset treatment for MDD, IND-enabling and Phase 2B development of PH80 for treatment of vasomotor symptoms (hot flashes) due to menopause, IND-enabling and Phase 2B development of PH15 for cognition improvement, IND-enabling and Phase 2B development of PH284 for treatment of cachexia and Phase 2A development of AV-101 for one or more neurological disorders involving the NMDAR. We are continuing to evaluate the potential implications for the conduct and timing of these and other clinical trials and strategies for the development and commercialization, on our own or with collaborators, of all of our product candidates. However, as we have not yet developed products that generate recurring revenue and, in the event we successfully complete future clinical and/or nonclinical programs, we will need to obtain and invest substantial additional capital resources to develop and commercialize our drug candidates.

When necessary and advantageous, we will seek additional financial resources to fund our planned operations through (i) sales of our equity and/or debt securities in one or more public offerings and/or private placements, (ii) non-dilutive government grants and research awards and (iii) non-dilutive strategic partnering collaborations to advance development and commercialization of our product candidates. For example, we may seek to enter research, development and/or commercialization collaborations similar to the AffaMed Agreement, which applies only to development and commercialization of PH94B in Greater China, South Korea and Southeast Asian territories, to provide non-dilutive funding for our operations, while also reducing a portion of our future cash outlays and working capital requirements. Although we may seek additional collaborations that could generate revenue and/or provide non-dilutive funding for development and commercialization of our product candidates, no assurance can be provided that any such collaborations, awards or agreements will occur in the future. Subject to certain restrictions, our S-3 Shelf Registration Statement 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 Shelf Registration Statement and/or under the Sales Agreement, we do not have an obligation to do so.

During the next twelve months, subject to availability of adequate working capital, we plan to (i) continue to advance our FEARLESS Phase 3 Program, on our own or with a collaborator, to develop and commercialize fasedienol as a new acute treatment of anxiety in adults with SAD, (ii) complete preparations, on our own or with a collaborator, for and initiate further Phase 2B clinical development of itruvone as a potential stand-alone treatment for MDD, (iii) complete IND-enabling activities, either on our own with a collaborator, for Phase 2B development of PH80, PH15 and PH284 and Phase 2A development of AV-101 for one or more neurological disorders involving the NMDAR, and (iv) conduct various nonclinical studies involving each of our product candidates.

Our future working capital requirements will depend on many factors, including, without limitation, potential impacts related to adjustments in the size of our staff, the scope and nature of opportunities related to our success or failure and the success or failure of certain other companies in nonclinical and clinical trials, including the development and commercialization of our current product candidates, and the availability of, and our ability to enter into financing transactions and research, development and commercialization collaborations on terms acceptable to us. In the future, to further advance the clinical development of our product candidates, as well as support our operating activities, we plan to seek additional financing, including both equity-based capital and funding from non-dilutive sources, and continue to carefully manage our operating costs, including, but not limited to, our clinical and nonclinical programs.

Notwithstanding the foregoing, there can be no assurance that future financings will be available to us in sufficient amounts, in a timely manner, or on terms acceptable to us, if at all, or that our current development and commercialization collaboration under the AffaMed Agreement or other potential strategic partnering collaborations will generate revenue from future potential milestone payments or otherwise. In addition, although the Listing Qualifications Staff of The Nasdaq Stock Market, LLC (*Nasdaq*) advised us on June 22, 2023 that we regained compliance with the minimum bid price requirement of the Nasdaq Capital Market, there can be no assurance that our common stock will maintain a closing bid price sufficient to remain in compliance with the minimum bid price requirement or that we will maintain compliance with other continued listing standards for the Nasdaq Capital Market.

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,	
	2023	2022
Net cash used in operating activities	\$ (49,715)	\$ (45,257)
Net cash used in investing activities	(740)	(200)
Net cash provided by (used in) financing activities	(1,042)	10,484
Net decrease in cash and cash equivalents	(51,497)	(34,973)
Cash and cash equivalents at beginning of period	68,135	103,108
Cash and cash equivalents at end of period	<u>\$ 16,638</u>	<u>\$ 68,135</u>

As discussed above, the combination of the net proceeds we received from public offerings in Fiscal 2021, from transactions under our ATM in Fiscal 2022 and from warrant exercises in both Fiscal 2021 and Fiscal 2022, have been the primary sources of our available cash during both Fiscal 2022 and Fiscal 2023. The increase in cash used in operations during Fiscal 2023 reflects our conduct, completion, pause or termination of fasedienol clinical trials including PALISADE-1, PALISADE-2, the PALISADE OLS, and the Phase 2 AjDA study, as previously described, as well as ongoing manufacturing and regulatory initiatives and other nonclinical studies of our product candidates. Additionally, during Fiscal 2022, we expanded our internal capabilities with the addition of numerous senior personnel with significant expertise in disciplines critical to the advancement of our product pipeline. In both Fiscal 2023 and Fiscal 2022, but to a much greater extent during the first half of Fiscal 2023, in parallel with our clinical and regulatory initiatives, and in expectation of positive results from the PALISADE Phase 3 Program, we engaged in customary pre-commercialization analyses, modeling, planning and awareness initiatives. Given the outcome of the PALISADE-1 study, we terminated most of such activities.

Cash used in investing activities during Fiscal 2023 reflects laboratory analytical equipment acquired for our internal studies and experiments with both fasedienol and itrivone. Cash used in investing activities during Fiscal 2022 primarily reflects the cost of laboratory analytical equipment acquired for use by our CMO in connection with the development and production of fasedienol drug product. As discussed previously, the Pherin Acquisition was treated as an asset purchase; however, we issued shares of our common stock rather than cash as the primary component of payment for the in-process R&D assets acquired and expensed.

Cash used by financing activities during Fiscal 2023 primarily reflects the proceeds of option exercises and the sales of common stock under our ESPP, net of principal payments on our insurance premium financing note and expenditures related to the Sales Agreement with Jefferies which are recorded as deferred offering costs. Cash provided by financing activities during Fiscal 2022 primarily reflects the proceeds of warrant exercises, net of expenditures related to the Sales Agreement with Jefferies that are recorded as deferred offering costs.

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. Throughout Fiscal 2022 and for a portion of Fiscal 2023, Vistastem had two inactive, wholly owned subsidiaries, Artemis Neuroscience, a Maryland corporation, and VistaStem Canada, Inc., an Ontario corporation. VistaStem Canada was dissolved in April 2022 and Artemis Neuroscience was dissolved in June 2022.

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

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Vistagen Therapeutics, Inc. (the “Company”) as of March 31, 2023 and 2022, the related consolidated statements of operations and comprehensive loss, cash flows, and stockholders’ equity for each of the two years in the period ended March 31, 2023, and the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of March 31, 2023 and 2022, and the results of its operations and its cash flows for each of the two years in the period ended March 31, 2023, in conformity with accounting principles generally accepted in the United States of America.

Substantial Doubt Regarding Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 2 to the consolidated financial statements, the Company has suffered negative cash flows from operations and recurring losses from operations since inception, resulting in an accumulated deficit of \$326.9 million as of March 31, 2023, that raise substantial doubt about its ability to continue as a going concern. Management’s plans in regard to these matters are also described in Note 2. The accompanying consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

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) relate 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 a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Revenues from Contract with Customers

Description of the Matter

As discussed in Note 11 to the consolidated financial statements, the Company derecognized approximately \$0.9 million in revenue under the sublicense agreement with AffaMed Therapeutics, Inc. (“AffaMed”) during the fiscal year ended March 31, 2023.

Auditing management’s timing of revenue recognition attributed to the single combined performance obligation was challenging, as significant judgment is required in the evaluation of the period in which the combined performance obligation is satisfied.

We identified sublicense revenue recognition as a critical audit matter because of the judgments necessary for management to determine the timing of recognition for such revenue. Because of the complexity associated with applying the recognition criteria of Accounting Standards Codification, Topic 606, *Revenue Recognition*, notably related to the 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 We Addressed the Matter in Our Audit

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

- We evaluated the Company’s revenue recognition for the sublicense agreement through an inspection of the agreement and an evaluation of management’s revenue recognition analysis corresponding to the sublicense agreement. Our objective was to validate that revenue from the sublicense agreement was recognized in a manner commensurate with the terms of the established agreement and the relevant accounting guidance.
- We analyzed the sublicense 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 tested the measurement of efforts toward satisfaction of the combined performance obligation which included, among other procedures:
 - o Reviewed management’s revenue schedules for accuracy and completeness by agreeing data to the underlying agreement.
 - o Evaluated the manner in which the combined performance obligation was satisfied, and corroborated management estimates and judgments through a review of press releases and third-party data as a potential source of corroborating or contradictory evidence.
 - o Discussed management’s judgments with the Company’s research and development personnel that oversee aspects of the license agreement.

/s/ WithumSmith+Brown, PC

We have served as the Company's auditor since 2006.

San Francisco, California
June 28, 2023
PCAOB ID Number 100

VISTAGEN THERAPEUTICS, INC.

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

	March 31, 2023	March 31, 2022
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 16,637,600	\$ 68,135,300
Prepaid expenses and other current assets	802,700	2,745,800
Deferred contract acquisition costs - current portion	67,100	116,900
Total current assets	17,507,400	70,998,000
Property and equipment, net	507,300	414,300
Right-of-use asset - operating lease	2,260,300	2,662,000
Deferred offering costs	495,700	321,800
Deferred contract acquisition costs - non-current portion	217,600	146,400
Security deposits	100,900	100,900
Total assets	\$ 21,089,200	\$ 74,643,400
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	\$ 2,473,100	\$ 2,758,600
Accrued expenses	787,400	1,329,200
Note payable	105,300	-
Deferred revenue - current portion	714,300	1,244,000
Operating lease obligation - current portion	485,600	433,300
Financing lease obligation - current portion	1,700	-
Total current liabilities	4,567,400	5,765,100
Non-current liabilities:		
Deferred revenue - non-current portion	2,314,600	1,557,600
Operating lease obligation - non-current portion	2,119,800	2,605,400
Financing lease obligation - non-current portion	7,400	-
Total non-current liabilities	4,441,800	4,163,000
Total liabilities	9,009,200	9,928,100
Commitments and contingencies (Note 14)		
Stockholders' equity:		
Preferred stock, \$0.001 par value; 10,000,000 shares authorized at March 31, 2023 and March 31, 2022; no shares outstanding at March 31, 2023 and March 31, 2022	-	-
Common stock, \$0.001 par value; 325,000,000 shares authorized at March 31, 2023 and March 31, 2022; 7,315,404 and 6,889,221 shares issued at March 31, 2023 and March 31, 2022, respectively	7,300	6,900
Additional paid-in capital	342,892,500	336,280,500
Treasury stock, at cost, 4,522 shares of common stock held at March 31, 2023 and March 31, 2022	(3,968,100)	(3,968,100)
Accumulated deficit	(326,851,700)	(267,604,000)
Total stockholders' equity	12,080,000	64,715,300
Total liabilities and stockholders' equity	\$ 21,089,200	\$ 74,643,400

See accompanying notes to consolidated financial statements, including Note 15, *Subsequent Events*, for information on reverse split of common stock effective on June 6, 2023.

VISTAGEN THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(Amounts in dollars, except share amounts)

	Fiscal Years Ended	
	March 31,	
	2023	2022
Revenues:		
Sublicense revenue	\$ (227,300)	\$ 1,108,900
Total revenues	<u>(227,300)</u>	<u>1,108,900</u>
Operating expenses:		
Research and development	44,377,100	35,407,800
General and administrative	14,663,600	13,480,000
Total operating expenses	<u>59,040,700</u>	<u>48,887,800</u>
Loss from operations	(59,268,000)	(47,778,900)
Other income, net:		
Interest income, net	26,200	19,900
Loss before income taxes	(59,241,800)	(47,759,000)
Income taxes	(5,900)	(3,400)
Net loss and comprehensive loss	<u>(59,247,700)</u>	<u>(47,762,400)</u>
Accrued dividend on Series B Preferred stock	-	(945,100)
Net loss attributable to common stockholders	<u>\$ (59,247,700)</u>	<u>\$ (48,707,500)</u>
Basic and diluted net loss attributable to common stockholders per common share	<u>\$ (8.51)</u>	<u>\$ (7.38)</u>
Weighted average shares used in computing basic and diluted net loss attributable to common stockholders per common share	<u>6,958,749</u>	<u>6,599,287</u>

See accompanying notes to consolidated financial statements, including Note 15, *Subsequent Events*, for information on reverse split of common stock effective on June 6, 2023.

VISTAGEN THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(Amounts in dollars)

	Fiscal Years Ended March 31,	
	2023	2022
Cash flows from operating activities:		
Net loss	\$ (59,247,700)	\$ (47,762,400)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	129,500	153,500
Stock-based compensation	3,336,400	3,480,700
Expense related to acquisition of Pherin Pharmaceuticals, Inc. recorded as an asset acquisition	3,559,400	-
Warrant modification expense	77,400	-
Amortization of operating lease right-of-use asset	401,700	557,600
Expense related to write-off of deferred offering costs	-	232,000
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	3,188,400	(1,870,100)
Security deposits	-	(53,100)
Operating lease liability	(433,300)	(677,000)
Deferred sublicense revenue, net of deferred contract acquisition costs	205,900	(1,004,600)
Accounts payable and accrued expenses	(932,800)	1,686,900
Net cash used in operating activities	<u>(49,715,100)</u>	<u>(45,256,500)</u>
Cash flows from investing activities:		
Purchases of laboratory and other equipment	(212,000)	(200,400)
Cash used in acquisition of Pherin Pharmaceuticals, Inc. as an asset acquisition	(528,300)	-
Net cash used in investing activities	<u>(740,300)</u>	<u>(200,400)</u>
Cash flows from financing activities:		
Net proceeds from issuance of common stock, including option exercises	104,400	139,900
Net proceeds from exercise of warrants, net of underlying share registration expenses	-	5,948,500
Net proceeds (expenses) from sale of common stock under At the Market (ATM) facility, net of deferred offering costs	(173,900)	4,299,000
Net proceeds from sale of common stock under Employee Stock Purchase Plan	63,100	99,500
Repayment of financing lease obligations	(1,500)	(3,000)
Repayment of note payable	(1,034,400)	-
Net cash (used in) provided by financing activities	<u>(1,042,300)</u>	<u>10,483,900</u>
Net decrease in cash and cash equivalents	(51,497,700)	(34,973,000)
Cash and cash equivalents at beginning of year	68,135,300	103,108,300
Cash and cash equivalents at end of year	<u>\$ 16,637,600</u>	<u>\$ 68,135,300</u>
Supplemental disclosure of noncash activities:		
Insurance premiums settled by issuing note payable	\$ 1,139,700	\$ -
Acquisition of office equipment subject to financing lease	\$ 10,600	\$ -
Fair value of common stock issued for acquisition of Pherin Pharmaceuticals, Inc.	\$ 3,076,500	\$ -
Accrued dividends on Series B Preferred	\$ -	\$ 945,100
Accrued dividends on Series B Preferred settled upon conversion by issuance of common stock	\$ -	\$ 7,217,800

See accompanying notes to consolidated financial statements, including Note 15, *Subsequent Events*, for information on reverse split of common stock effective on June 6, 2023.

VISTAGEN THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

Fiscal Years Ended March 31, 2022 and 2023
(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	Treasury Stock	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Capital			
Balances at March 31, 2021	500,000	\$ 500	1,131,669	\$ 1,100	2,318,012	\$ 2,300	402,149	\$ 400	6,025,042	\$ 6,000	\$315,777,900	\$(3,968,100)	\$(219,841,600)	\$ 91,978,500
Net proceeds from exercise of warrants	-	-	-	-	-	-	-	-	243,293	200	6,207,200	-	-	6,207,400
Conversion of Series D Preferred stock to common stock	-	-	-	-	-	-	(402,149)	(400)	308,314	300	100	-	-	-
Conversion of Series A Preferred stock to common stock	(500,000)	(500)	-	-	-	-	-	-	25,000	-	500	-	-	-
Conversion of Series B Preferred stock to common stock and payment of accrued dividends in common stock	-	-	(1,131,669)	(1,100)	-	-	-	-	147,582	200	7,218,700	-	-	7,217,800
Conversion of Series C Preferred Stock to common stock	-	-	-	-	(2,318,012)	(2,300)	-	-	77,267	100	2,200	-	-	-
Accrued dividends on Series B Preferred stock	-	-	-	-	-	-	-	-	-	-	(945,100)	-	-	(945,100)
Stock-based compensation expense	-	-	-	-	-	-	-	-	-	-	3,480,700	-	-	3,480,700
Sale of common stock pursuant to 2019 Employee Stock Purchase Plan	-	-	-	-	-	-	-	-	1,907	-	99,300	-	-	99,300
Issuance of common stock upon cashless exercise of stock options	-	-	-	-	-	-	-	-	4,204	-	-	-	-	-
Net proceeds from exercise of stock options for cash	-	-	-	-	-	-	-	-	6,019	-	140,000	-	-	140,000
Net proceeds from issuance of common stock under ATM facility	-	-	-	-	-	-	-	-	50,593	100	4,299,000	-	-	4,299,100
Net loss for the fiscal year ended March 31, 2022	-	-	-	-	-	-	-	-	-	-	-	-	(47,762,400)	(47,762,400)
Balances at March 31, 2022	-	-	-	-	-	-	-	-	6,889,221	6,900	336,280,500	\$(3,968,100)	\$(267,604,000)	64,715,300
Stock-based compensation expense	-	-	-	-	-	-	-	-	-	-	3,336,400	-	-	3,336,400
Sale of common stock pursuant to 2019 Employee Stock Purchase Plan	-	-	-	-	-	-	-	-	5,167	-	63,100	-	-	63,100
Issuance of common stock upon cashless exercise of stock options	-	-	-	-	-	-	-	-	3,646	-	-	-	-	-
Net proceeds from exercise of stock options for cash	-	-	-	-	-	-	-	-	3,700	-	104,400	-	-	104,400
Increase in fair value attributable to warrant modification	-	-	-	-	-	-	-	-	-	-	77,400	-	-	77,400
Fair value of common stock issued for acquisition of Pherin Pharmaceuticals, Inc. as an asset acquisition, net of registration expenses	-	-	-	-	-	-	-	-	413,670	400	3,030,700	-	-	3,031,100
Net loss for the fiscal year ended March 31, 2023	-	-	-	-	-	-	-	-	-	-	-	-	(59,247,700)	(59,247,700)
Balances at March 31, 2023	-	\$ -	-	\$ -	-	\$ -	-	\$ -	7,315,404	\$ 7,300	\$342,892,500	\$(3,968,100)	\$(326,851,700)	\$ 12,080,000

See accompanying notes to consolidated financial statements, including Note 15, *Subsequent Events*, for information on reverse split of common stock effective on June 6, 2023.

1. Description of Business

Overview

Vistagen Therapeutics, Inc., a Nevada corporation (which may be referred to as *Vistagen*, the *Company*, *we*, *our*, or *us*), late clinical-stage biopharmaceutical company aiming to transform the treatment landscape for individuals living with anxiety, depression and other central nervous system (CNS) disorders. We are advancing therapeutics with the potential to be faster-acting, and with fewer side effects and safety concerns, than those currently available for treating anxiety, depression and multiple CNS disorders. Our pipeline includes six clinical-stage product candidates, including five investigational agents belonging to a new class of neuroactive drugs known as pherines, in addition to AV-101, an oral prodrug of an antagonist of the glycine site of the N-methyl-D-aspartate receptor (NMDAR). Pherines, which are administered as nasal sprays, are designed with an innovative rapid-onset mechanism of action that activates chemosensory neurons in the nasal cavity and can selectively and beneficially impact key neural circuits in the brain without requiring systemic uptake or direct activity on CNS neurons. AV-101 inhibits the activity of the ion channel of the NMDAR but does not block it, unlike some approved NMDAR antagonists having significant side effects. Our goal is to develop and commercialize, on our own and with multiple global and regional strategic partners, innovative therapies for anxiety, depression, and other CNS indications where current treatment options are inadequate to meet the needs of millions of patients in the U.S. and worldwide.

Our Product Candidates

Pherine Product Candidates

Five of our product candidates – fasedienol (PH94B), itruvone (PH10), PH15, PH80 and PH284 – belong to a new class of synthetic neuroactive steroids referred to as pherines. Pherines, administered in ultra-low microgram level doses as odorless and tasteless nasal sprays, are designed to selectively engage chemosensory neurons in the nasal cavity and induce rapid-onset pharmacologic and behavioral benefits. Specifically, each of our pherine product candidates is a distinct chemical entity that selectively modulates particular areas of the brain, such as the limbic amygdala (the main fear and anxiety center of the brain), the hypothalamus, the hippocampus, the locus ceruleus, and the prefrontal cortex. We believe each of our pherine product candidates has the potential to be a fast-acting therapy for one or more CNS disorders, including social anxiety disorder (fasedienol), major depressive disorder (itruvone), cognitive impairment (PH15), vasomotor syndrome (hot flashes) due to menopause, as well as migraine headaches (PH80) and disorders related to appetite loss (cachexia) (PH284), all without requiring apparent systemic uptake or binding to classic abuse liability receptors or steroidal hormone receptors.

Fasedienol Nasal Spray

Fasedienol (PH94B) is a synthetic investigational pherine from the androstane family in Phase 3 clinical development in the U.S. for treatment of social anxiety disorder (SAD). When administered intranasally in microgram doses, fasedienol activates receptors of peripheral nasal chemosensory neurons connected to subsets of neurons in the olfactory bulbs that, in turn, connect to neurons in the limbic amygdala involved in the pathophysiology of SAD and potentially other anxiety and mood disorders. Fasedienol is pharmacologically active without requiring apparent systemic uptake and distribution of the compound to the brain to achieve its rapid-onset and short duration of anxiolytic effects.

The proposed MOA of fasedienol is fundamentally differentiated from all currently approved anti-anxiety medications, including the three antidepressants approved by the FDA for the treatment of SAD, as well as all benzodiazepines and beta blockers, which, although not FDA-approved for the treatment of SAD, are prescribed for treatment of SAD on an off-label basis. Pre-clinical and Phase 2 clinical studies completed to date suggest that fasedienol has the potential to achieve rapid-onset anti-anxiety effects without systemic uptake or transport into the brain, significantly reducing the risk of side effects and other safety concerns such as potential drug-drug interactions, abuse, misuse and addiction associated with certain other systemic pharmaceuticals that act directly on the CNS and are sometimes prescribed for anxiety disorders.

SAD PALISADE Phase 3 Program

PALISADE-1. In May 2021, we initiated our PALISADE Phase 3 Program for fasedienol in SAD with PALISADE-1, a single-administration assessment Phase 3 public speaking challenge clinical study of fasedienol for the acute treatment of anxiety in adults with SAD. Following discussions with the FDA in mid-2020 during the acute phase of the COVID-19 pandemic, we agreed to design PALISADE-1 in a manner substantially similar to the single-administration assessment Phase 2 public speaking challenge study of fasedienol, which involved self-administration of only a single dose of fasedienol by subjects randomized to the treatment arm. All subjects were given an anxiety-provoking public speaking challenge, conducted only in a clinical setting, and their change in a Subjective Units of Distress Scale (SUDS) score was determined.

VISTAGEN THERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

In July 2022, we announced top line results from PALISADE-1. Although the safety and tolerability of fasedienol in PALISADE-1 were favorable and consistent with previously reported results from previous clinical trials, PALISADE-1 did not achieve its primary efficacy endpoint, as measured by change from baseline using the SUDS as compared to placebo. We believe the following hypotheses are potential explanations for the unexpected outcome in PALISADE-1: (i) the study was conducted during the acute phase of the COVID-19 pandemic, introducing significant systemic variability in terms of changing social dynamics, subject stress, study site and contract research organization (CRO) personnel turnover and mask wearing regulations; (ii) given the foregoing, the public speaking challenge study design may not have been scalable to a large Phase 3 study, particularly during the acute phase of the COVID-19 pandemic; and (iii) some subjects in the study may have had reduced potential to respond to fasedienol due to impaired olfactory cell function potentially caused by the COVID-19 virus, nasal swab testing for COVID-19, respiratory syncytial virus (RSV) or influenza, and/or heavy cannabis use, smoking or vaping.

PALISADE-2. In October 2021, near the end of the acute phase of the COVID-19 pandemic, we initiated PALISADE-2, which involved the same clinic-based, single-administration assessment public speaking challenge study design and use of the SUDS as the primary efficacy endpoint as PALISADE-1. In July 2022, after receiving top line results from PALISADE-1, we paused recruitment and enrollment in PALISADE-2 to allow independent third-party biostatisticians to conduct an interim analysis of available data from subjects randomized in PALISADE-2 up to the date we paused the study. In September 2022, based on their review of unblinded data from the 140 subjects who had completed PALISADE-2, the independent third-party biostatisticians recommended that we continue PALISADE-2 as planned, without revealing the underlying data to us.

Although the results of the interim analysis of PALISADE-2 indicated that continuation of the study would not be futile, after considering the expense, time, and challenges associated with PALISADE-1, as well as the potential methodological complexities involved in resuming PALISADE-2, we closed the PALISADE-2 study. Topline results from the 140 subjects who completed PALISADE-2 are expected in the second half of 2023.

PALISADE Open Label Study. The PALISADE Open Label Study (OLS) was a Phase 3, open-label safety trial designed to evaluate the safety and tolerability of multiple, as-needed administrations (up to four times a day) of fasedienol in adults with SAD. The PALISADE OLS also evaluated the change from baseline in monthly standard clinical measurements and various behavioral assessment scales in response to anxiety-provoking social situations in daily-life after the administration of fasedienol. The final data set from PALISADE OLS demonstrates clinically meaningful functional improvement, as measured by the LSAS, and total LSAS scores, in both men and women, continued to decline in consecutive months during the study. In addition, long-term administration of fasedienol was well-tolerated, with no new safety findings or trends identified, regardless of the number of doses administered by each subject. Following the completion of PALISADE-1, we terminated the PALISADE OLS early, solely for strategic business reasons, and not due to any safety concerns with fasedienol.

FDA Feedback on Path Forward; FEARLESS Program. In the first quarter of calendar 2023, we met with the FDA to discuss next steps in our Phase 3 development plan for fasedienol in SAD, which plan includes, among other things, conducting, on our own or with collaborators, a multiple-assessment, randomized, double-blind, placebo-controlled Phase 3 study of fasedienol in adults in a real-world setting, using the Liebowitz Social Anxiety Scale (LSAS) as the primary efficacy outcome measure to evaluate the efficacy of fasedienol over time in patients with SAD to support a potential fasedienol New Drug Application (NDA). Positive feedback from the FDA at this meeting confirmed the acceptable use of the LSAS as a primary efficacy endpoint. Accordingly, we are positioned to finalize key components of FEARLESS, our potential NDA-enabling Phase 3 development program for fasedienol for treatment of SAD.

Unlike the PALISADE Phase 3 studies, which involved assessment of only a single, self-administered dose of fasedienol in a clinic-based public speaking challenge using the SUDS as the primary outcome measure, our FEARLESS program will assess multiple administrations of fasedienol, on a patient-tailored as-needed basis, up to six times per day, in a real-world setting over a multiple week period, with the LSAS as the primary efficacy endpoint, consistent with the FDA's three precedent-setting approvals of antidepressants for treatment of SAD.

Exploratory Phase 2A Development for AjDA. In January 2023, we completed our small exploratory Phase 2A clinical study of fasedienol designed to assess its therapeutic potential in adults experiencing adjustment disorder with anxiety (AjDA). Our small randomized, double-blind, placebo-controlled Phase 2A exploratory study in AjDA was aimed at exploring the pharmacological treatment of AjDA and evaluating the effects of a fixed dosing regimen of fasedienol, involving intranasal administration of 3.2 µg of fasedienol four times per day over four weeks. A total of 71 subjects were screened for the study, 41 were randomized, and 34 completed four weeks of treatment. The study, which was not designed to achieve statistical significance, did not demonstrate a clinically significant difference between fasedienol and placebo as measured on the clinician-rated Hamilton Anxiety Scale (HAM-A). Site variances and both a high drug response rate and high placebo response rate were observed, likely related to the various aspects of AjDA that make it challenging to study. Fixed dosing of fasedienol four times per day over four weeks appeared to be safe and well tolerated.

Despite the methodological challenges inherent in the exploratory Phase 2A study in AjDA, we believe fasedienol builds resilience against anxiety and reduces the cognitive and physical paralysis that occurs during moments of heightened anxiety and stressful situations. The AjDA study's results may support an as-needed fasedienol dosing approach over time as the preferred mode of treatment.

Itruvone Nasal Spray

Itruvone (PH10) is an odorless, tasteless synthetic investigational piperine from the piperidine family with a novel, rapid-onset potential MOA that is fundamentally differentiated from the MOA of all currently approved treatments for depression disorders. Itruvone, which is administered as a nasal spray at microgram-level doses, is designed to engage and activate chemosensory neurons in the nasal cavity, which are connected to neural circuits in the brain that produce antidepressant effects. Specifically, in a manner similar to fazedienol, itruvone's proposed MOA involves the regulation of the olfactory-amygdala neural circuits believed to increase activity of the limbic-hypothalamic sympathetic nervous system and increase the release of catecholamines. Importantly, unlike all currently approved oral antidepressants (ADs) and rapid-onset ketamine-based therapy, including both intravenous ketamine and intranasal ketamine (esketamine), we believe itruvone does not require systemic uptake and distribution of the compound to the brain to produce rapid-onset of antidepressant effects. In all clinical studies completed to date, itruvone has been well-tolerated and has not caused psychological side effects (such as dissociation and hallucinations) or other safety concerns that may be associated with ketamine-based therapy.

In January 2023, we launched a small U.S. single center, randomized, double-blinded, placebo-controlled Phase 1 study to investigate the safety and tolerability of itruvone in healthy adult subjects. The study was designed to confirm the favorable safety profile of itruvone established in three previous clinical studies conducted in Mexico, as well as facilitate our plans for Phase 2B development of itruvone in the U.S. as a fast-acting stand-alone treatment for MDD. In June 2023, we announced positive data from this study. There were no reported SAEs or discontinuations due to adverse events in the trial. Overall, itruvone was well-tolerated and continued to demonstrate a favorable safety profile.

The FDA has granted Fast Track designation for development of itruvone as a potential adjunctive treatment for MDD.

PH80 Nasal Spray

PH80 is an odorless, tasteless synthetic investigational piperine with a novel, rapid-onset potential MOA that is fundamentally differentiated from the MOA of all currently approved treatments for both vasomotor symptoms (hot flashes) due to menopause and migraine headaches. PH80, which is administered as a nasal spray at microgram-level doses, engages and activates chemosensory neurons in the nasal cavity, which are connected to neural circuits in the brain that modulate neural circuits in the basal forebrain associated with the control of body temperature, as well as premonitory and aura symptoms of migraines. Results from a previously unpublished exploratory randomized, double-blind, placebo-controlled Phase 2A study of PH80 for the acute treatment of vasomotor symptoms (hot flashes) due to menopause demonstrated a statistically significant reduction in the daily number of menopausal hot flashes compared to placebo at the end of the first week of treatment ($p < .001$), and the improvement was maintained through each treatment week until the end of the four-week treatment period. We are currently preparing, on our own or with collaborators, to submit an U.S. IND for a Phase 2B clinical study of PH80 as a treatment for hot flashes due to menopause.

In addition, PH80 initiates neural impulses in the olfactory bulb transmitted by pathways that rapidly affect the function of multiple structures in the brain, including the amygdala and hypothalamus that have been linked to the pathology of migraine. Due to its MOA and a small proof of concept study, we believe PH80 may have therapeutic potential to relieve premonitory and aura symptoms of migraines.

PH15 Nasal Spray

PH15 is an odorless, tasteless synthetic investigational piperine with a novel, rapid-onset potential MOA that is fundamentally differentiated from the MOA of all currently approved treatments to improve cognitive impairment caused by mental fatigue and potentially other disorders. Early functional MRI studies in human volunteers at Stanford University revealed that intranasal administration of PH15 induced rapid activation of brain areas related to cognition (Sobel et al, Brain, 1999). In a small double blind, placebo-controlled study Phase 2 study of human subjects who were sleep deprived to induce mental fatigue, intranasal PH15 showed rapid and significant improvement in cognitive and psychomotor performance and improvement of reaction time that was better than the effect of a placebo and 400 mg of oral caffeine. We are currently evaluating the path forward to submitting an U.S. IND for a Phase 2 clinical study, on our own or with collaborators, and the appropriate indication for demonstrating improvement of cognitive function.

PH284 Nasal Spray

PH284 is an odorless, tasteless synthetic investigational piperine with a novel, rapid-onset potential MOA that is fundamentally differentiated from the MOA of all currently approved treatments for the loss of appetite associated with chronic disorders such as cancer. Cachexia is a serious but under recognized consequence of many chronic diseases with body mass loss of >10% and a prevalence of 5 to 15 %. We believe PH284 may have therapeutic potential for improving subjective feelings of hunger in patients with cachexia. We are currently evaluating the path forward to submitting an U.S. IND for cachexia, on our own or with collaborators, and the appropriate patient populations for demonstrating increase in appetite and weight gain in a second Phase 2 study.

VISTAGEN THERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

AV-101

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 binding 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 completed to date, AV-101 has demonstrated good oral bioavailability and an excellent pharmacokinetic (PK) profile. No binding of AV-101 or 7-Cl-KYNA to off-site targets was identified by an extensive receptor screening study. Moreover, in all clinical trials completed 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. 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.

Based on observations and findings from preclinical studies, we believe AV-101 has the potential to become a new oral treatment alternative for multiple CNS disorders. We are currently preparing for Phase 2A development of AV-101, on our own or with collaborators, as a treatment for one or more neurological disorders involving the NMDAR receptor. Multiple studies have shown AV-101 to be safe and well-tolerated, and a range of preclinical studies indicate potential in multiple indications, including levodopa-induced dyskinesia, neuropathic pain, seizures, MDD, and suicidal ideation.

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.

Acquisition of Pherin Pharmaceuticals, Inc.

On December 20, 2022, we entered into an Agreement and Plan of Merger (the *Merger Agreement*) along with VTGN Merger Sub, Inc., our wholly owned subsidiary (*Merger Sub*), Pherin Pharmaceuticals, Inc. (*Pherin*), and Kevin McCarthy in his capacity of Stockholder Representative, to acquire Pherin (the *Pherin Acquisition*). On February 2, 2023 (the *Closing Date*), we completed the Pherin Acquisition, and Pherin is now a wholly owned subsidiary of the Company. Immediately prior to the consummation of the Pherin Acquisition, each of Pherin's directors and officers resigned, and no employees or other affiliates of Pherin on the Closing Date are serving or will serve in their previous roles or in any other capacity with Pherin or with us.

As consideration for the Pherin Acquisition, we (i) issued an aggregate of 413,670 unregistered shares of our common stock having a fair value of approximately \$3,076,550 at issuance to the exchange agent for the Pherin Acquisition, which shares were to approximately 96.07% of Pherin stockholders eligible to receive common stock in exchange for their outstanding shares of Pherin common stock (the *Stock Consideration*), and (ii) paid to the exchange agent for the Pherin Acquisition, an aggregate of approximately \$126,100 for the approximately 3.93% remaining Pherin stockholders who were not eligible to receive Stock Consideration in exchange for their outstanding shares of Pherin common stock (the *Cash Consideration* and, together with the Stock Consideration, the *Merger Consideration*). In addition to the Cash Consideration, we paid certain transaction related expenses specified under the terms of the Merger Agreement and other expenses associated with the registration of the shares underlying the Stock Consideration, aggregating \$402,200. We have accounted for the Pherin Acquisition as an asset acquisition and the associated costs, including the fair value of the Stock Consideration, totaling approximately \$3,559,400, were expensed as in-process research and development expense. We charged approximately \$45,400 to additional paid-in-capital related to costs of registering the common stock underlying the Stock Consideration.

Subsidiaries

In addition to Pherin, as described above, Vistastem, Inc., a California corporation founded in 1998 (*Vistastem*), is also our wholly owned subsidiary. For the relevant periods, our Condensed Consolidated Financial Statements in this Annual Report on Form 10-K (*Report*) also include the accounts of Vistastem's two wholly owned inactive subsidiaries, Artemis Neuroscience, Inc., a Maryland corporation (*Artemis*), which was dissolved in April 2022, and VistaStem Canada, Inc., a corporation organized under the laws of Ontario, Canada (*VistaStem Canada*), which was dissolved in June 2022.

2. Basis of Presentation and Going Concern

The accompanying Consolidated Financial Statements have been prepared in conformity with U.S. generally accepted accounting principles (*U.S. GAAP*) and include the Company's accounts, as well as those of Vistastem and, for the relevant periods, those of Pherin and of Vistastem's two wholly owned inactive subsidiaries, Artemis and VistaStem Canada. All material intercompany accounts and transactions have been eliminated in consolidation. The Consolidated Financial Statements have been prepared assuming that we will continue as a going concern.

As discussed more completely in Note 15, *Subsequent Events*, we completed a stockholder approved 1-for-30 reverse split of our issued and outstanding common stock effective on June 6, 2023 (the *Reverse Split*). All share and per share data for all periods presented in the accompanying financial statements and related disclosures in this Report have been adjusted retrospectively to reflect the Reverse Split.

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As a late-stage 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 \$326.9 million accumulated from inception (May 1998) through March 31, 2023. We expect losses and negative cash flows from operations to continue for the foreseeable future as we engage in further development of fasedienol, itrivone, AV-101, and the newly-acquired pherine product candidates.

Since our inception in May 1998 through March 31, 2023 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 \$208.7 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 \$41.3 million in noncash acquisitions of product licenses, the Pherin Acquisition, and in settlements of certain liabilities, including liabilities for professional services rendered to us or as compensation for such services.

Recent Developments

We did not complete any capital-raising or other significant financing activities during our fiscal year ended March 31, 2023 (*Fiscal 2023*). During our fiscal year ended March 31, 2022 (*Fiscal 2022*), holders of outstanding warrants to purchase an aggregate of 243,293 shares of our common stock exercised such warrants, and we received cash proceeds of approximately \$6.2 million. Additionally, in May 2021, we entered into an Open Market Sale Agreement SM (the *Sales Agreement*) with Jefferies LLC (*Jefferies*) as sales agent, with respect to an at-the-market offering program (the *ATM*) under which we may, at our option, offer and sell, from time to time, shares of our common stock having an aggregate offering price of up to \$75.0 million through Jefferies as our sales agent. During September and early October 2021, we sold an aggregate of 50,593 shares of our common stock and received gross cash proceeds of approximately \$4.45 million under the ATM. We did not sell any shares of our common stock under the ATM during Fiscal 2023. As discussed more completely in Note 15, *Subsequent Events*, from June 12, 2023 through the date of this Report we sold an aggregate of 561,418 shares of our common stock and received approximately \$1.15 million in gross proceeds under the ATM.

During our fiscal year ended March 31, 2021 (*Fiscal 2021*), we received approximately \$119 million in net cash proceeds primarily from various public sales of our equity securities and \$5.0 million gross proceeds from a strategic licensing and collaboration agreement (the *AffaMed Agreement*, discussed more completely in Note 11, *Licensing, Sublicensing and Collaborative Agreements*.) These earlier transactions continued to provide necessary capital resources and liquidity throughout Fiscal 2023, during which we also received approximately \$167,500 in cash proceeds from the exercise of outstanding stock options and sales under our 2019 Employee Stock Purchase Plan (the *2019 ESPP*).

We had cash and cash equivalents of approximately \$16.6 million at March 31, 2023, which we do not believe will be sufficient to fund our planned operations for the twelve months following the issuance of these Consolidated Financial Statements, which raises substantial doubt regarding our ability to continue as a going concern. We are continuing to evaluate our cash resources as we prepare for the next steps in our late-stage development of fasedienol for the treatment of SAD, consider clinical and nonclinical requirements to advance Itrivone in potential Phase 2B development, on our own or with a collaborator, as a potential stand-alone rapid-onset treatment for MDD and finalize our Phase 1 study of AV-101 in combination with probenecid to facilitate potential exploratory Phase 2A development of AV-101. We are continuing to evaluate the potential implications for the conduct and timing of other clinical trials and strategies for the development and commercialization, on our own or with collaborators, of all of our product candidates. However, as we have not yet developed products that generate recurring revenue and, in the event we successfully complete future clinical and/or nonclinical programs, we will need to obtain and invest substantial additional capital resources to develop and commercialize our drug candidates.

When necessary and advantageous, we will seek additional financial resources to fund our planned operations through (i) sales of our equity and/or debt securities in one or more public offerings and/or private placements, (ii) non-dilutive government grants and research awards and (iii) non-dilutive strategic partnering collaborations to advance development and commercialization of our product candidates. For example, we may seek to enter research, development and/or commercialization collaborations similar to the AffaMed Agreement, which applies only to development and commercialization of PH94B in Greater China, South Korea and Southeast Asian territories, to provide non-dilutive funding for our operations, while also reducing a portion of our future cash outlays and working capital requirements. Although we may seek additional collaborations that could generate revenue and/or provide non-dilutive funding for development and commercialization of our product candidates, no assurance can be provided that any such collaborations, awards or agreements will occur in the future. Subject to certain restrictions, our Registration Statement on Form S-3 (the *S-3 Shelf Registration Statement*) 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 Shelf Registration Statement and/or under the Sales Agreement, we do not have an obligation to do so.

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During the next twelve months, subject to availability of adequate working capital, we plan to (i) continue to advance our FEARLESS Phase 3 Program, on our own or with a collaborator, to develop and commercialize fasedienol as a new acute treatment of anxiety in adults with SAD, (ii) complete preparations, on our own or with a collaborator, for and initiate further Phase 2B clinical development of itruvone as a potential stand-alone treatment for MDD, (iii) complete IND-enabling activities, either on our own with a collaborator, for Phase 2B development of PH80, PH15 and PH284 and Phase 2A development of AV-101 for one or more neurological disorders involving the NMDAR, and (iv) conduct various nonclinical studies involving each of our product candidates.

Our future working capital requirements will depend on many factors, including, without limitation, potential impacts related to adjustments in the size of our staff, the scope and nature of opportunities related to our success or failure and the success or failure of certain other companies in nonclinical and clinical trials, including the development and commercialization of our current product candidates, and the availability of, and our ability to enter into financing transactions and research, development and commercialization collaborations on terms acceptable to us. In the future, to further advance the clinical development of our product candidates, as well as support our operating activities, we plan to seek additional financing, including both equity-based capital and funding from non-dilutive sources, and continue to carefully manage our operating costs, including, but not limited to, our clinical and nonclinical programs.

Notwithstanding the foregoing, there can be no assurance that future financings will be available to us in sufficient amounts, in a timely manner, or on terms acceptable to us, if at all, or that our current development and commercialization collaboration under the AffaMed Agreement or other potential strategic partnering collaborations will generate revenue from future potential milestone payments or otherwise. Further, on September 6, 2022, we received a letter from the Listing Qualifications Staff of The Nasdaq Stock Market, LLC (*Nasdaq*) indicating that, based upon the closing bid price of our common stock for the previous 30 consecutive business days, we were not in compliance with the requirement to maintain a minimum bid price of \$1.00 per share for continued listing on the Nasdaq Capital Market. At March 6, 2023, the expiration of the initial 180-day period in which to regain compliance, we had not regained compliance with the minimum bid price requirement. Based on our written notification to Nasdaq of our intention to cure the deficiency by implementing a previously stockholder-authorized reverse stock split, if necessary, on March 7, 2023, Nasdaq granted us a second 180-day period, through September 5, 2023, in which to regain compliance. To regain compliance with the minimum bid price requirement, our common stock was required to have a closing bid price of at least \$1.00 per share for a minimum of 10 consecutive trading days. As a result of the Reverse Split, our common stock has maintained a closing bid price in excess of \$1.00 since June 7, 2023. Although the Listing Qualifications Staff of Nasdaq advised us on June 22, 2023 that we regained compliance with the minimum bid price requirement of the Nasdaq Capital Market, there can be no assurance that our common stock will maintain a closing bid price sufficient to remain in compliance with the Minimum Bid Price Requirement or that we will maintain compliance with other continued listing standards for the Nasdaq Capital Market.

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.

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, net of accumulated depreciation. 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.

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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. We do not carry any capitalized intellectual property or product licenses as assets subject to impairment in our Consolidated Financial Statements.

Deferred Offering Costs

Deferred offering costs include registration expenses related to our current S-3 Registration Statement (the *Shelf Registration*), which became effective on March 26, 2021, and expenses related to the Sales Agreement for the ATM (as described in Note 8, *Capital Stock*). These expenses consist primarily of legal, accounting, SEC filing fees, and, as appropriate, Nasdaq filing fees. Upon the completion or partial completion of an applicable equity offering, the deferred expenses are charged to additional paid-in capital. If there are any deferred offering costs remaining at the expiration of the Shelf Registration or the equity financing agreement, such costs are charged to expense. Upon termination of a financing agreement in June 2021, we expensed the remaining \$232,100 of deferred offering costs associated with the agreement as a noncash component of our general and administrative expenses in our Consolidated Statement of Operations and Comprehensive Loss for the fiscal year ended March 31, 2022.

Revenue Recognition

The AffaMed Agreement, involving clinical development and commercialization of fasedienol for acute treatment of anxiety in adults with SAD, and potentially other anxiety-related disorders, in Greater China, South Korea, and Southeast Asia, has been the basis of our reported revenue for both Fiscal 2023 and Fiscal 2022. 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. In prior years, we have occasionally generated revenue from collaborative research and development arrangements, licensing and technology transfer agreements, including strategic licenses or sublicenses, and government grants.

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.

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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 fasedienol, itruvone and AV-101. 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 (CROs) 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, at acquisition, the product or technology licensed has not achieved regulatory approval or reached technical feasibility and has no alternative future uses. We treated the Pherin Acquisition as an acquisition of assets for accounting purposes. Since, at the date of the acquisition, neither fasedienol, itruvone nor the other three pherines acquired had achieved regulatory approval and each required significant additional development and expense and were without alternative future use, we recorded the costs related to acquiring the assets as research and development expense in our Consolidated Statement of Operations and Comprehensive Loss for our fiscal year ended March 31, 2023.

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. 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.

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Income Taxes

We account for income taxes using the asset and liability approach promulgated by ASC 740, *Income Taxes*, 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 account for our leases following the guidance of Accounting Standards Update No. 2016-02, “*Leases (Topic 842)*” (ASU 2016-02). 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. 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 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 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.

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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. Our only financial assets that are measured on a recurring basis at fair value were \$5,010,800 and \$65,094,900 held in money market funds and classified as cash equivalents at March 31, 2023 and 2022, respectively. Our money market funds are classified within Level 1 of the fair value hierarchy and are valued based on quoted prices in active markets for identical securities. We had no financial liabilities that are measured on a recurring basis at fair value at March 31, 2023 or March 31, 2022.

Warrants Issued in Connection with Equity Financing

We evaluate the appropriate balance sheet classification of warrants we issue as either equity or as a derivative liability. In accordance with ASC 815-40, *Derivatives and Hedging-Contracts in the Entity's Own Equity (ASC 815-40)*, we classify a warrant as equity if it is "indexed to the Company's equity" and meets several specific conditions for equity classification. A warrant is not considered "indexed to the Company's equity," in general, when it contains certain types of exercise contingencies or potential adjustments to its exercise price. If a warrant is not indexed to the Company's equity or it has net cash settlement provisions that result in the warrants being accounted for under ASC 480, *Distinguishing Liabilities from Equity* or ASC 815-40, it is classified as a derivative liability which is carried on the consolidated balance sheet at fair value with any changes in its fair value recognized immediately in the Statement of Operations and Comprehensive Loss. At March 31, 2023 and 2022 all of our outstanding warrants were classified as equity.

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 has historically been 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*) prior to its conversion during the third quarter of Fiscal 2022, 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.

As a result of our net loss for both years presented and the conversion of all series of our preferred stock prior to March 31, 2022, potentially dilutive securities were excluded from the computation of diluted net loss per share, as their effect would be antidilutive. Potentially dilutive securities excluded in determining diluted net loss attributable to common stockholders per common share at March 31, 2023 and 2022 are as follows:

	At March 31, 2023	At March 31, 2022
Outstanding options under the Company's Amended and Restated 2016 (formerly 2008) Stock Incentive Plan and 2019 Omnibus Equity Incentive Plan	702,545	646,213
Outstanding warrants to purchase common stock	45,685	309,195
Total	748,230	955,408

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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. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets are composed of the following:

	<u>March 31,</u> <u>2023</u>	<u>March 31,</u> <u>2022</u>
Clinical and nonclinical materials and contract services	\$ 166,700	\$ 2,139,600
Insurance	206,000	196,500
Receivable from CRO for cancelled project	-	337,900
Receivable from collaboration partner	274,700	-
All other	155,300	71,800
	<u>\$ 802,700</u>	<u>\$ 2,745,800</u>

The amount reported as receivable from CRO for cancelled project at March 31, 2022 represents the amount of prepayments on a cancelled project net of expenses incurred by the CRO prior to project cancellation and was refunded to us in July 2022. The amount reported as receivable from collaboration partner at March 31, 2023 represents payments we made to two CROs and another service provider for clinical trial services on behalf of our collaboration partner. At the date of this Report, our collaboration partner has reimbursed us for \$174,700 of these amounts.

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5. Property and Equipment, Net

Property and equipment, net is composed of the following:

	<u>March 31,</u> <u>2023</u>	<u>March 31,</u> <u>2022</u>
Laboratory equipment	\$ 1,234,800	\$ 1,181,300
Tenant improvements	214,400	214,400
Office furniture and equipment	40,300	76,200
Manufacturing equipment	211,200	211,200
	<u>1,700,700</u>	<u>1,683,100</u>
Accumulated depreciation and amortization	(1,193,400)	(1,268,800)
Property and equipment, net	<u>\$ 507,300</u>	<u>\$ 414,300</u>

The amounts reported above for manufacturing equipment at March 31, 2023 and 2022 reflect the cost of certain process equipment acquired in connection with the manufacture of fasedienol drug product and placed in service at our CRO's facilities in the fourth quarter of Fiscal 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, 2023 and 2022 are as follows:

	<u>March 31,</u> <u>2023</u>	<u>March 31,</u> <u>2022</u>
Office equipment subject to financing lease	\$ 10,600	\$ 14,700
Accumulated depreciation	(2,000)	(14,700)
Net book value of office equipment subject to financing lease	<u>\$ 8,600</u>	<u>\$ -</u>

The fully depreciated office equipment reported at March 31, 2022 was subject to a lease that expired in January 2022. That equipment was replaced subject to a new lease in April 2022. The new lease requires a monthly payment of approximately \$200 through June 2027. Other than certain leased office equipment, none of our assets were subject to third party security interests at March 31, 2023 or 2022.

The following table summarizes depreciation and amortization expense attributable to owned and leased property and equipment for the fiscal years ended March 31, 2023 and 2022:

	<u>Fiscal Years Ended March 31,</u>	
	<u>2023</u>	<u>2022</u>
Owned assets	\$ 127,500	\$ 151,200
Leased assets	2,000	2,300
Total depreciation and amortization	<u>\$ 129,500</u>	<u>\$ 153,500</u>

6. Accrued Expenses

Accrued expenses are composed of the following:

	<u>March 31,</u> <u>2023</u>	<u>March 31,</u> <u>2022</u>
Accrued expenses for clinical and nonclinical materials, development and contract services	\$ 412,100	\$ 1,070,800
Accrued compensation	337,200	66,200
Accrued professional services	38,100	159,500
All other	-	32,700
	<u>\$ 787,400</u>	<u>\$ 1,329,200</u>

In both periods, accrued expenses for clinical and nonclinical services includes accrued clinical trial expenses and other amounts accrued for contract manufacturing and product development services. Accrued compensation at March 31, 2023 includes an accrual of \$300,000 representing an estimated liability associated with matters related to a terminated former employee.

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7. Note Payable

The following table summarizes our outstanding note payable at March 31, 2023 and 2022:

	March 31, 2023			March 31, 2022		
	Principal Balance	Accrued Interest	Total	Principal Balance	Accrued Interest	Total
3.88% Note payable to insurance premium financing company (current)	\$ 105,300	\$ -	\$ 105,300	\$ -	\$ -	\$ -

In May 2022, we executed a 3.88% promissory note in the principal amount of \$1,139,700 in connection with certain insurance policy premiums. The note is payable in monthly installments of \$105,600, including principal and interest, through April 2023.

8. 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. 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 was convertible at the option of the holder into one-twentieth (1/20) of one restricted share of our common stock. The Series A Preferred ranked prior to the common stock for purposes of liquidation preference.

At March 31, 2021, there were 500,000 restricted shares of Series A Preferred outstanding, convertible into 25,000 shares of our common stock at the option of the holders. In November 2021, the custodial holder of the 500,000 outstanding shares of our Series A Preferred exercised its rights for conversion into common stock and we issued 25,000 unregistered shares of our common stock. In November 2022, the Company filed a Certificate of Withdrawal of the Relative Rights and Preferences of the Series A Convertible Preferred Stock with the Nevada Secretary of State and the Series A Preferred was retired.

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 (*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.

Each share of Series B Preferred was convertible, at the option of the holder (*Conversion*), into one-thirtieth (1/30) of one share of our common stock. Approximately 2.4 million shares of Series B Preferred were converted into approximately 80,000 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.

Prior to Conversion, shares of Series B Preferred accrued in-kind dividends (payable only in unregistered shares of our common stock) at a rate of 10% per annum (*Accrued Dividends*). The Accrued Dividends were payable on the date of a Conversion in that number of shares of common stock equal to the Accrued Dividends. At March 31, 2021, there remained 1,131,669 shares of Series B Preferred outstanding, which were exchangeable by the remaining holder by Conversion into 37,722 shares of our common stock, excluding shares of our common stock which would have been issued in payment of Accrued Dividends upon conversion. In November 2021, the custodial holder of the 1,131,669 outstanding shares of our Series B Preferred exercised its rights for conversion into common stock and we issued 37,722 shares of our common stock, of which 13,151 shares were registered and 24,571 were unregistered. From initial issuance in May 2015 through the time of conversion in November 2021, the remaining Series B Preferred shares had accrued dividends aggregating \$7,217,800 and, in accordance with the terms of the Series B Certificate of Designation, we issued 109,860 shares of our unregistered common stock in payment of the Accrued Dividends. We recognized a deduction from net loss of \$945,100 related to Accrued Dividends on the outstanding Series B Preferred for the period of April 2021 through November 2021 in arriving at net loss attributable to common stockholders in the Consolidated Statement of Operations and Comprehensive Loss for the fiscal year ended March 31, 2022. In November 2022, the Company filed a Certificate of Withdrawal of the Relative Rights and Preferences of the Series B 10% Preferred Stock with the Nevada Secretary of State and the Series B Preferred was retired.

VISTAGEN THERAPEUTICS, INC.
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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*).

Each share of Series C Preferred was convertible, at the option of the holder into one-thirtieth (1/30) of one share of our common stock. At March 31, 2021, one custodial holder held all 2,318,012 outstanding shares of Series C Preferred. In October 2021, the custodial holder of 2,318,012 outstanding shares of our Series C Preferred exercised its rights for conversion into common stock and we issued 77,267 unregistered shares of our common stock. In November 2022, the Company filed a Certificate of Withdrawal of the Relative Rights and Preferences of the Series C Convertible Preferred Stock with the Nevada Secretary of State and the Series C Preferred was retired.

Series D Preferred Stock

On December 17, 2020, in connection with the a public offering of our equity securities, 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 Nevada Secretary of State on December 21, 2020.

Each share of our Series D Preferred was initially convertible into approximately 0.7667 (23/30) of one share of our common stock at any time at the option of the holder, provided that, the Series D Preferred was not convertible prior to the date on which we 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 became effective (the *Approval Date*). We obtained such approval from our stockholders at a special meeting of stockholders held on March 5, 2021. 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 1,225,019 registered shares of our common stock. At March 31, 2021, there were 402,149 shares of Series D Preferred outstanding, which were convertible into 308,314 shares of our common stock. During April 2021, the remaining investors in the December 2020 public offering converted their 402,149 outstanding shares of Series D Preferred into an aggregate of 308,314 registered shares of our common stock. In November 2022, the Company filed a Certificate of Withdrawal of the Relative Rights and Preferences of the Series D Convertible Preferred Stock with the Nevada Secretary of State and the Series D Preferred was retired.

At March 31, 2022 and 2023, and through the date of this Report, we have 10 million shares of preferred stock authorized and no preferred shares outstanding.

Financing Transactions

We did not complete any financing transactions during Fiscal 2023. We initiated the Open Market Sales Agreement, as described below, during Fiscal 2022.

Open Market Sale Agreement

In May 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 (the *ATM*) under which we may, at our sole discretion, offer and sell, from time to time, shares of our common stock having an aggregate offering price of up to \$75.0 million (the *Shares*) through Jefferies. We will pay Jefferies a commission equal to three percent (3.0%) of the aggregate gross proceeds from any sales of the Shares under the Sales Agreement. If and when we direct Jefferies to offer and sell Shares under the Sales Agreement, Jefferies may sell the Shares by any method permitted by law and deemed to be an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, including block transactions, sales made directly on the Nasdaq Capital Market or any other trading market for our common stock. In addition, with our consent, Jefferies may sell the Shares in negotiated transactions. Under certain circumstances, we may instruct Jefferies not to sell the Shares if the sales cannot be effected at or above the price we may designate from time to time. Shares offered and sold under the Sales Agreement will be issued and sold pursuant to our Shelf Registration Statement on Form S-3 filed with the SEC on March 15, 2021 and declared effective on March 26, 2021.

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In transactions occurring during September 2021 and on October 1, 2021, we sold an aggregate of 50,593 shares of our common stock and received gross cash proceeds of approximately \$4.45 million under the ATM. We did not sell any shares of our common stock under the ATM during Fiscal 2023. Refer to Note 15, *Subsequent Events*, for information regarding additional sales of our common stock under the ATM after March 31, 2023. We record transactions under the Sales Agreement on a settlement date basis. All legal fees and accounting expenses incurred in connection with the Sales Agreement are recorded as Deferred Offering Costs and are amortized to Additional Paid-in Capital as costs of the offering as sales of Shares are made under the Sales Agreement. Between execution of the Sales Agreement in May 2021 and March 31, 2023, we incurred legal fees and accounting expenses aggregating approximately \$450,300 in connection with the Sales Agreement, of which approximately \$16,400 had been amortized to Additional Paid-in Capital during Fiscal 2022 and none in Fiscal 2023. The Sales Agreement will terminate upon the earlier of (i) the sale of all Shares subject to the Sales Agreement or (ii) the termination of the Sales Agreement by Jefferies or by us, as permitted.

Stock Option Exercises and Employee Stock Purchase Plan Purchases

During Fiscal 2023, holders of outstanding stock options, including members of management, exercised such options to purchase an aggregate of 9,533 shares of our common stock at a weighted average exercise price of \$18.30 per share and we received cash proceeds of \$104,400. Certain of the options were exercised on a net exercise basis as permitted by the option plans and we issued an aggregate of 7,346 shares of our common stock pursuant to the exercises. During Fiscal 2022, holders of outstanding stock options, including members of management, exercised such options to purchase an aggregate of 11,873 shares of our common stock at a weighted average exercise price of \$24.30 per share and we received cash proceeds of \$140,000. Certain of the exercises were on a net exercise basis and we issued an aggregate of 10,223 shares of our common stock pursuant to the exercises. On June 30, 2022 and December 30, 2022, participants in our 2019 ESPP completed purchase periods pursuant to which we issued 2,500 shares and 2,667 shares of our registered common stock and received proceeds of \$56,100 and \$7,000, respectively. On June 30, 2021 and December 31, 2021, participants in our 2019 ESPP completed purchase periods pursuant to which we issued 542 shares and 1,365 shares of our common stock and received proceeds of \$31,600 and \$67,800, respectively.

Warrant Exercises, Expirations and Modifications

There were no warrant exercises during Fiscal 2023; however, warrants to purchase 263,510 shares of our common stock at a weighted average exercise price of \$48.94 per share expired unexercised during Fiscal 2023. During Fiscal 2022, holders of outstanding warrants to purchase an aggregate of 243,293 shares of our common stock exercised such warrants, and we received cash proceeds of approximately \$6.2 million.

On December 5, 2022, our Board modified outstanding warrants to purchase an aggregate of 33,333 registered shares of our common stock exercisable at \$15.00 per share that were due to expire on December 9, 2022 to extend the exercisability of such warrants for a period of two years. No other term of the warrants, including exercise price, was modified. We calculated the fair value of the modified warrants immediately before and after the modification using the Black Scholes Option Pricing Model and the assumptions indicated in the table below. We recognized the incremental fair value, \$77,400, as a component of general and administrative expense in our Consolidated Statements of Operations and Comprehensive Loss for the fiscal year ended March 31, 2023 and as an increase in additional paid-in capital in our Consolidated Statements of Changes in Stockholders' Equity for the same period.

Assumption:	Pre-modification	Post-modification
Market price per share	\$ 3.74	\$ 3.74
Exercise price per share	\$ 15.00	\$ 15.00
Risk-free interest rate	3.93%	4.41%
Remaining contractual term in years	0.011	2.012
Volatility	65.60%	175.27%
Dividend rate	0.0%	0.0%
Number of warrant shares	33,333	33,333
Weighted average fair value per share	\$ 0.00	\$ 2.40

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The following table summarizes outstanding and exercisable warrants to purchase shares of our common stock as of March 31, 2023. The weighted average exercise price of outstanding and exercisable warrants at March 31, 2023 was \$16.87 per share.

Exercise Price per Share	Expiration Date	Warrants Outstanding and Exercisable at March 31, 2023
\$15.00	12/9/2024	33,333
\$21.90	7/25/2025	12,352
		45,685

At March 31, 2023, all shares of common stock underlying the outstanding warrants have been registered for resale by the warrant holders. No outstanding warrant is subject to any down round anti-dilution protection feature. All outstanding warrants are exercisable by the holders only by payment in cash of the stated exercise price per share.

Reserved Shares

At March 31, 2023, we have reserved shares of our common stock for future issuance as follows:

Pursuant to warrants to purchase common stock:		
Subject to outstanding warrants		45,685
Pursuant to stock incentive plans:		
Subject to outstanding options under the Amended and Restated 2016 Stock Incentive Plan and the Amended and Restated 2019 Omnibus Equity Incentive Plan		702,545
Available for future grants under the Amended and Restated 2019 Omnibus Equity Incentive Plan		179,260
Available for future issuance under the 2019 Employee Stock Purchase Plan		24,322
		906,127
Reserved for issuance under the Sales Agreement		858,498
Total		1,810,310

At March 31, 2023, we have 315,878,808 authorized shares of our common stock not subject to reserves and available for future issuance.

9. Research and Development Expenses

We recorded research and development expenses of approximately \$44.4 million and \$35.4 million in Fiscal 2023 and Fiscal 2022, respectively, including approximately \$4.6 million and \$1.5 million of noncash expense in Fiscal 2023 and Fiscal 2022, respectively, including stock-based compensation and depreciation expense in both periods and, in Fiscal 2023, approximately \$3.1 million representing the fair market value of our common stock issued in the Pherin Acquisition. Research and development expense is composed of employee compensation expenses, including stock-based compensation, both internal and external direct project expenses, notably including costs related to our various clinical trials of fasedienol and itruvone and other preclinical and nonclinical projects for fasedienol, itruvone and AV-101 in both years.

10. 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, North Carolina and Utah income tax.

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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,	
	2023	2022
Computed expected tax benefit	(21.00)%	(21.00)%
State income taxes, net of federal benefit	0.00%	0.01%
Tax effect of warrant modifications	0.03%	0.00%
Tax effect of research and development credits	(0.78)%	(0.73)%
Tax effect of stock compensation	0.50%	0.59%
Tax effect of other non-deductible items	1.27%	0.11%
Expired net operating loss carryforwards	0.17%	0.74%
Change in valuation allowance (federal only)	18.57%	20.40%
All other	1.24%	0.00%
Income tax expense	<u>0.00%</u>	<u>0.12%</u>

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 and liabilities are as follows:

	March 31,	
	2023	2022
Deferred tax assets:		
Net operating loss carryovers	\$ 43,602,800	\$ 41,924,800
Basis differences in property and equipment	-	47,000
Research and development credit carryforwards	3,591,100	3,032,800
Stock based compensation	2,985,600	3,469,300
Operating lease Right-of-Use asset	73,200	79,700
Capitalized research and development costs	8,214,700	-
Deferred revenue	642,500	-
Accruals and reserves	146,300	66,700
Total deferred tax assets	59,256,100	48,620,300
Valuation allowance	(59,251,300)	(48,620,300)
Total deferred tax assets net of valuation allowance	4,800	-
Deferred tax liabilities:		
Basis differences in property and equipment	(4,800)	-
Total deferred tax liabilities	(4,800)	-
Net deferred tax asset (liability)	<u>\$ -</u>	<u>\$ -</u>

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 \$10,631,000 and \$8,743,700 during the fiscal years ended March 31, 2023 and 2022, respectively.

As of March 31, 2023, we had U.S. federal net operating loss carryforwards of approximately \$191,935,600. Federal net operating loss carryforwards of approximately \$84,111,700 generated through our fiscal year ended March 31, 2018 will expire in our fiscal years ending March 31, 2024 through March 31, 2038. Federal net operating loss carryforwards of approximately \$107,823,900 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, 2023, we had state net operating loss carryforwards of approximately \$65,195,200, which will expire in fiscal years ending in 2029 through 2043. We also have federal and state research and development tax credit carryforwards of approximately \$3,495,500 and \$1,636,200, 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.

The Tax Cuts and Jobs Act of 2017 (*TCJA*) made a significant change to Internal Revenue Code Section 174 that went into effect for taxable years beginning after December 31, 2021. The change eliminated the ability to currently deduct research and development costs. Instead, these costs must be capitalized and amortized over a period of five years for domestic activity and a period of 15 years for foreign activity. As a result, we capitalized research and development costs of approximately \$42,755,300 for tax purposes for the year ended March 31, 2023.

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On March 27, 2020 the U.S. enacted the Coronavirus Aid, Relief, and Economic Security Act (the CARES Act). On December 21, 2020, The U.S. Congress passed the Consolidation Appropriations Act, 2021 (the CAA Act). The Company evaluated the provisions of the CARES Act and CCA Act and determined that it did not result in a significant impact on its tax provision.

On June 29, 2020, California Assembly Bill 85 (AB 85) was signed into law, which suspended the use of California net operating losses and limits the use of California research tax credits for tax years beginning in 2020 and before 2023. However, on February 9, 2022, California Senate Bill 113 (SB 113) was signed into law and removed the limitation on the net operating losses and credits for the 2022 year and allows, after taxable years beginning on or after January 1, 2022, the ability to utilize net operating losses and credits. These changes did not result in a significant impact on the value of the Company's 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, and various U.S. state jurisdictions. We are subject to U.S. federal and state income tax examinations by tax authorities for tax years 2004 through 2023 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, 2023 and 2022 relate entirely to research and development tax credits. The total amount of unrecognized tax benefits at March 31, 2023 and 2022 is \$1,283,000 and \$1,088,100, 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,	
	2023	2022
Unrecognized benefit - beginning of period	\$ 1,088,100	\$ 931,900
Current period tax position increases	194,900	156,200
Unrecognized benefit - end of period	\$ 1,283,000	\$ 1,088,100

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, 2023 or 2022. We do not anticipate any significant changes in our uncertain tax positions within twelve months of this reporting date.

11. Licensing, Sublicensing and Collaborative Agreements

Fasedienol Sublicense Agreement with EverInsight Therapeutics, Inc. (now AffaMed Therapeutics, Inc.)

On June 24, 2020, we entered into a license and collaboration agreement with EverInsight Therapeutics Inc. (*EverInsight*). Subsequent to entering into the agreement with EverInsight, in October 2020, EverInsight merged with AffaMed Therapeutics, Inc., which as a combined entity is focusing on developing and commercializing therapeutics to address ophthalmologic and CNS disorders in Greater China (which includes Mainland China, Hong Kong, Macau and Taiwan) and beyond. Accordingly, we are now referring to EverInsight as AffaMed and the agreement originally entered into with EverInsight as the AffaMed Agreement. Under the AffaMed Agreement, we granted AffaMed an exclusive license to develop and commercialize fasedienol for SAD and other anxiety-related disorders in Greater China, South Korea and Southeast Asia (which includes Indonesia, Malaysia, Philippines, Thailand and Vietnam) (collectively, the *Territory*). We retain exclusive development and commercialization rights for fasedienol in the U.S. and throughout 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 fasedienol 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 fasedienol in the Territory.

We are responsible for pursuing clinical development and regulatory submissions of fasedienol 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. AffaMed will participate in the Phase 3 global clinical trial of fasedienol 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 fasedienol 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.

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Under the terms of the AffaMed Agreement, AffaMed paid us a non-refundable upfront license payment of \$5.0 million in August 2020. Additionally, upon successful development and commercialization of fasedienol 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 fasedienol 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 fasedienol. Significant management judgment is required to determine the level of effort attributable to the performance obligation included in the AffaMed Agreement and the period over which we expect to complete our performance obligation under the arrangement. The performance period or measure of progress was estimated at the inception of the arrangement and is re-evaluated in subsequent reporting periods. This re-evaluation may shorten or lengthen the period over which we recognize revenue. Due to the failure of PALISADE-1 to meet its primary efficacy endpoint and the resulting anticipated delay in subsequent clinical and regulatory processes for PH94B, at September 30, 2022, we estimated that our performance obligation under the AffaMed Agreement will be completed in mid-calendar 2027 rather than mid-calendar 2024. We have not subsequently revised our estimate, however, we will further adjust our estimates, as necessary, in subsequent periods as we obtain additional information on which to base our projections, including our ability to finance future clinical trials and satisfy other NDA-enabling requirements and/or our prospects for partnering future development of fasedienol in SAD with other entities. As described in Note 3, *Summary of Significant Accounting Policies*, as a result of the change in our estimate of the time required to complete our performance obligation, we recorded a cumulative catch-up adjustment for the quarter ending September 30, 2022 pursuant to which we derecognized \$892,600 of previously recognized revenue, resulting in a \$227,300 net derecognition of income for Fiscal 2023. Following the cumulative catch-up adjustment and subsequent amortization, through March 31, 2023, we have recognized an aggregate of \$1,971,100 in revenue under the AffaMed Agreement. We recognized \$1,108,900 as revenue during Fiscal 2022. At March 31, 2023, the aggregate amount of the transaction price allocated to the remaining performance obligation (deferred revenue) is \$3,028,900 which will be recognized as revenue as our performance obligation is completed.

The following table presents changes in our contract liabilities for Fiscal 2022 and Fiscal 2023:

	Balance at March 31, 2021	Revenue Recognition Amortization	Derecognition	Balance at March 31, 2022
Deferred revenue - current portion	\$ 1,420,200	\$ (176,200)	\$ -	\$ 1,244,000
Deferred revenue - non-current portion	2,490,300	(932,700)	-	1,557,600
Total	\$ 3,910,500	\$ (1,108,900)	\$ -	\$ 2,801,600

	Balance at March 31, 2022	Revenue Recognition Amortization	Derecognition	Balance at March 31, 2023
Deferred revenue - current portion	\$ 1,244,000	\$ (665,300)	\$ 135,600	\$ 714,300
Deferred revenue - non-current portion	1,557,600	-	757,000	2,314,600
Total	\$ 2,801,600	\$ (665,300)	\$ 892,600	\$ 3,028,900

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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 fasedienol license from Pherin, and fees for consulting services exclusively related to the AffaMed Agreement. Additionally, on June 24, 2020, we issued 7,788 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 capitalized as deferred contract acquisition costs in our Consolidated Balance Sheet. Similar to the related deferred revenue, capitalized contract acquisition costs are amortized over the periods during which we expect to satisfy the performance obligation under the AffaMed Agreement. As with deferred revenue, we recorded a cumulative catch-up adjustment in September 2022 pursuant to which we reversed \$83,900 of previously recognized contract acquisition cost expense related to the reassessment of the timeline for satisfying our performance obligation. Accordingly, amortization expense of approximately (\$21,400) and \$104,100 has been included in general and administrative expenses in our Consolidated Statement of Operations and Comprehensive Loss for Fiscal 2023 and Fiscal 2022, respectively. 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 fasedienol in such jurisdiction, the expiration of regulatory exclusivity in such jurisdiction or ten years after the first commercial sale of fasedienol in such jurisdiction.

License Agreements with Pherin Pharmaceuticals, Inc. (Pherin)

In September 2018, we issued 54,348 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 fasedienol for social anxiety disorder and an option to acquire a similar license for itruvone for MDD. In October 2018, we exercised our option to acquire an exclusive worldwide license to develop and commercialize itruvone by issuing an additional 30,864 shares of our unregistered common stock having a fair market value of \$2,000,000 to Pherin under the terms of the itruvone license agreement. Under the terms of the fasedienol and itruvone license agreements, we were 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. As a result of the Pherin Acquisition, we are no longer obligated to pay such milestone or royalty payments.

12. Stock Option Plans, Employee Stock Purchase Plan, and 401(k) Plan

At March 31, 2023, we have the following stock-based compensation plans, which are described below:

- ***Amended and Restated 2016 Stock Incentive Plan (the 2016 Plan); and***
- ***Amended and Restated 2019 Omnibus Equity Incentive Plan (the Amended 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 333,333 shares of our common stock were authorized for issuance under the 2016 Plan, of which options to purchase 215,773 shares remain outstanding at March 31, 2023. Upon the adoption of our 2019 Plan, no further grants were permissible under the 2016 Plan and 46,280 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 Amended 2019 Plan

Our Board approved the Vistagen Therapeutics, Inc. 2019 Omnibus Equity Incentive Plan (the *2019 Plan*) on May 27, 2019, and our stockholders adopted it and ratified all previously issued grants on September 5, 2019. On June 28, 2021 our Board approved and at our Annual Meeting of Stockholders on September 17, 2021, our stockholders approved certain amendments to the 2019 Plan (*Amended 2019 Plan*). The principal features of the Amended 2019 Plan are summarized below.

VISTAGEN THERAPEUTICS, INC.
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Awards and Eligible Participants

The Amended 2019 Plan is designed to secure and retain the services of our employees, non-employee directors and consultants, to provide incentives for such persons to exert maximum efforts for the success of the Company and our affiliates, and to provide a means by which such persons may be given an opportunity to benefit from increases in the value of our common stock. The Amended 2019 Plan is also designed to align employees' interests with stockholder interests.

The Amended 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 Amended 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.

Plan Administration

The Amended 2019 Plan is administered by the Compensation Committee of the Board (the *Committee*). The 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 Committee may delegate its authority to the extent permitted by applicable law.

The 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 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 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 Committee may grant SARs as a right in tandem with the number of shares underlying stock options granted under the Amended 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 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 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 Committee. Stock units may be paid in stock or cash or a combination of stock and cash, as determined by the Committee.

The 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 Committee may select such business criteria or other performance measures as it may deem appropriate in establishing any performance conditions. At March 31, 2023, the Committee has not granted any performance awards.

Authorized Shares

A total of 250,000 shares of our common stock was initially authorized for issuance under the 2019 Plan. Upon approval of the Amended 2019 Plan by our stockholders, a total of 600,000 shares of our common stock became available for issuance under the Amended 2019 Plan.

In the event any award under the Amended 2019 Plan is canceled, terminates, expires or lapses for any reason prior to the issuance of shares or if shares are issued under the Amended 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 Amended 2019 Plan.

Vesting

No more than 25% of any equity-based awards granted under the Amended 2019 Plan may vest on the grant date of such award. The Board believes this requirement provides the Company the necessary flexibility to issue Awards that will both attract new talent, particularly as the Company advances its clinical development plans for its drug candidates, and provide incentives sufficient to retain the Company's existing employees and directors.

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 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.

VISTAGEN THERAPEUTICS, INC.
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Option Repricing

The Amended 2019 Plan does not permit repricing of outstanding stock options.

Change of Control

In the event of a change in control of the Company, the Committee may accelerate the time period relating to the exercise of any outstanding Award, including stock options or restricted stock units. In addition, the 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) subject to certain limitations, adjusting the terms of the award in a manner determined by the 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 Amended 2019 Plan and requires consummation of the applicable transaction.

Termination

Unless earlier terminated by the Board, the Amended 2019 Plan will terminate, and no further awards may be granted, on September 5, 2029, which is ten years after the date on which the 2019 Plan was initially approved by our stockholders. The Board may amend, suspend or terminate the Amended 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 Amended 2019 Plan in such a manner and to such a degree as required. The amendment, suspension or termination of the Amended 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 Fiscal 2023, we granted from the Amended 2019 Plan options to purchase an aggregate of 143,900 shares of our common stock at exercise prices equal to the closing market price of our common stock on each respective grant date, including:

- Options to purchase 96,667 shares granted to all of our employees except executive officers and members of our Board in November 2022, at an exercise price of \$4.4370 per share. The options vest 25% on the first anniversary of the grant date with the remaining shares vesting ratably monthly over the next three years;
- Options to purchase 33,900 shares granted to newly hired employees at exercise prices ranging from \$3.57 per share to \$45.30 per share. Options granted to new employees vest 25% on the first anniversary of the grant date with the remaining shares vesting ratably monthly over the next three years;
- Options to purchase 13,333 shares granted to consultants, which options vested 25% on the grant date and ratably monthly over the next twelve months.

During Fiscal 2022, we granted from the Amended 2019 Plan options to purchase an aggregate of 173,500 shares of our common stock at exercise prices equal to or above the closing market price of our common stock on each respective grant date, including:

- Options to purchase 136,333 shares of our common stock granted to our officers and employees, of which options to purchase 55,000 shares were granted to newly-hired employees upon commencement of their employment. Options granted to newly-hired employees vest 25% on the first anniversary of the grant date with the remaining shares vesting ratably monthly over the next three years. General option grants to employees in March 2022, aggregating options to purchase 81,333 shares, including to employees who may have received new-hire grants earlier in Fiscal 2022, vest 25% upon grant with the remaining shares vesting ratably over two years;
- Options to purchase 24,167 shares of our common stock granted to the independent members of our Board, of which 7,500 were granted to three newly appointed independent members. Options granted to independent Board members vest ratably over one year following the respective grant dates;
- Options to purchase 13,000 shares of our common stock granted to certain consultants, which options were vested 25% upon grant with the balance generally vesting over one to two years following the grant date.

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On September 12, 2022, the Committee modified outstanding options to purchase an aggregate of 44,071 shares of our common stock exercisable at prices between \$11.94 per share and \$53.10 per share previously granted to a terminated employee and otherwise set to expire on September 13, 2022, to extend the exercisability of such options for a period of 90 days. No other term of the options, including exercise price, was modified. We calculated the fair value of the modified options 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, \$108,600, as a component of research and development stock compensation expense in our Consolidated Statements of Operations and Comprehensive Loss for Fiscal 2023.

Assumption:	Pre-modification	Post-modification
Market price per share	\$ 6.156	\$ 6.156
Exercise price per share	\$ 38.10	\$ 38.10
Risk-free interest rate	2.62%	3.17%
Remaining contractual term in years	0.003	0.249
Volatility	138.31%	412.67%
Dividend rate	0.0%	0.0%
Number of option shares	44,071	44,071
Weighted average fair value per share	\$ 0.00	\$ 2.46

On December 12, 2022, the Committee again modified the options to extend the exercisability of such options through March 31, 2023. No other term of the options was modified. We calculated the fair value of the modified options 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, \$100, as a component of research and development stock compensation expense in our Consolidated Statement of Operations and Comprehensive Loss for Fiscal 2023, bringing the aggregate modification expense for these options to \$108,700 for Fiscal 2023.

Assumption:	Pre-modification	Post-modification
Market price per share	\$ 3.57	\$ 3.57
Exercise price per share	\$ 38.10	\$ 38.10
Risk-free interest rate	3.86%	4.38%
Remaining contractual term in years	0.0	0.299
Volatility	92.75%	99.54%
Dividend rate	0.0%	0.0%
Number of option shares	44,071	44,071
Weighted average fair value per share	\$ 0.00	\$ 0.002

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 Statements of Operations and Comprehensive Loss for the years ended March 31, 2023 and 2022, including the effect of the option modifications described above.

	Fiscal Years Ended March 31,	
	2023	2022
Research and development expense	\$ 1,364,800	\$ 1,457,600
General and administrative expense	1,971,600	2,023,100
Total stock-based compensation expense	\$ 3,336,400	\$ 3,480,700

Expense amounts reported above include \$37,000 and \$47,000 in research and development expense for the fiscal years ended March 31, 2023 and 2022, respectively, and \$14,500 and \$19,500 in general and administrative expense for the fiscal years ended March 31, 2023 and 2022, respectively, attributable to our 2019 Employee Stock Purchase Plan (the 2019 ESPP), described below.

VISTAGEN THERAPEUTICS, INC.
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We used the Black-Scholes Option Pricing model with the following weighted average assumptions to determine stock-based compensation expense related to option grants during the fiscal years ended March 31, 2023 and 2022:

	Fiscal Years Ended March 31,	
	2023	2022
	(weighted average)	(weighted average)
Exercise price	\$ 10.20	\$ 53.40
Market price on date of grant	\$ 10.20	\$ 53.40
Risk-free interest rate	3.55%	1.42%
Expected term (years)	6.03	5.60
Volatility	158.03%	80.27%
Expected dividend yield	0.00%	0.00%
Fair value per share at grant date	\$ 8.10	\$ 36.00

The expected term of options represents the period that our stock-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 minimal number of relevant historical option exercises and lack of other meaningful historical data due to the relatively limited period during which our stock has been publicly traded with significant volume on a major exchange and the historical lack of liquidity in freely tradable shares of our common stock. Those factors also informed 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 as we do not believe that the historical volatility of our common stock will be indicative of its future performance. 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, 2023 and 2022 under the Amended 2019 Plan and the 2016 Plan:

	Fiscal Years Ended March 31,			
	2023		2022	
	Number of Shares	Weighted Average Exercise Price	Number of Shares	Weighted Average Exercise Price
Options outstanding at beginning of period	646,213	\$ 44.10	487,936	\$ 40.20
Options granted	143,900	\$ 10.20	173,500	\$ 53.40
Options exercised	(9,533)	\$ 18.30	(11,873)	\$ 24.30
Options forfeited	(32,660)	\$ 42.30	(3,333)	\$ 59.70
Options expired	(45,374)	\$ 40.80	(17)	\$ 240.00
Options outstanding at end of period	<u>702,545</u>	\$ 37.80	<u>646,213</u>	\$ 44.10
Options exercisable at end of period	<u>496,257</u>	\$ 42.00	<u>452,309</u>	\$ 39.60
Weighted average grant-date fair value of options granted during the period		<u>\$ 8.10</u>		<u>\$ 36.00</u>

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The following table summarizes information on stock options outstanding and exercisable under the Amended 2019 Plan and the 2016 Plan as of March 31, 2022:

Exercise Price	Options Outstanding			Options Exercisable	
	Number Outstanding	Weighted Average Remaining Years until Expiration	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price
\$ 3.57 to \$12.30	151,773	8.96	\$ 6.47	43,710	\$ 11.24
\$12.60 to \$36.30	128,521	6.06	\$ 29.35	117,097	\$ 29.41
\$38.10 to \$41.10	130,833	8.26	\$ 40.40	93,042	\$ 40.31
\$42.30 to \$51.00	147,833	4.95	\$ 44.74	144,500	\$ 44.72
\$52.50 to \$277.50	143,585	7.89	\$ 68.76	97,908	\$ 68.34
	<u>702,545</u>	7.24	\$ 37.76	<u>496,257</u>	\$ 41.99

At March 31, 2023, there were 179,260 registered shares of our common stock remaining available for grant under the Amended 2019 Plan.

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 \$3.74 per share quoted closing market price of our common stock on March 31, 2023, there was approximately \$4,800 of intrinsic value in our outstanding options at that date.

As of March 31, 2023, there was approximately \$3,775,500 of unrecognized compensation cost related to non-vested stock-based compensation awards from the Amended 2019 Plan and the 2016 Plan, which cost is expected to be recognized through May 2025.

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 Committee also administers the 2019 ESPP. The Committee has authority to construe, interpret and apply the terms of the 2019 ESPP. As approved by our stockholders, a maximum of 33,333 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, 2023 and 2022 was \$17,400 and \$66,200, 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.

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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 Fiscal 2023, employees purchased an aggregate of 5,167 shares of our common stock under the 2019 ESPP and we received proceeds of \$63,100. During Fiscal 2022, employees purchased an aggregate of 1,907 shares of our common stock and we received proceeds of \$99,500.

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.

13. Related Party Transactions

During the fourth quarter of Fiscal 2022, we entered into a consulting agreement with FitzPatrick & Co LLC, a consulting firm for which Margaret FitzPatrick, an independent member of our Board, is the Managing Director, to provide corporate development and public relations advisory services. We recorded expense of \$45,000 during the quarter ended March 31, 2022 related to this agreement, all of which was included in accounts payable at that date. The agreement continued throughout Fiscal 2023, during which we recorded general and administrative expense of \$165,000, including an accrued expense of \$10,000 at March 31, 2023. In June 2023, we extended the agreement through December 31, 2023.

On November 11, 2022, Ann Cunningham resigned as our Chief Commercial Officer, but remains a member of our Board. Following Ms. Cunningham's resignation as Chief Commercial Officer, i3 Strategy Partners, a consulting firm for which Ms. Cunningham is the Managing Partner, began providing certain advisory services to us pursuant to a consulting agreement. The initial term of the consulting agreement will end on March 31, 2024, and, pursuant to the agreement, i3 Strategy Partners received a fee of \$120,000 for the period from the effective date of the agreement through March 31, 2023 and will receive \$10,000 per month thereafter through the end of the consulting agreement's initial term. The payment of \$120,000 was completed during our fiscal quarter ended December 31, 2022 and we recorded that amount as general and administrative expense during Fiscal 2023. In June 2023, we extended the agreement through December 31, 2023.

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On December 1, 2022, Mark Smith resigned as our Chief Medical Officer. Following his departure, Dr. Smith serves as a member of our Clinical and Regulatory Advisory Board and provides consulting services to us regarding the development of our product candidates pursuant to a consulting agreement. Under the terms of the consulting agreement, Dr. Smith was paid \$50,000 prior to December 31, 2022, and will receive \$10,000 per month through the contract term ending December 31, 2023. We recorded \$80,000 as research and development expense during Fiscal 2023, including \$10,000 as accounts payable at March 31, 2023 pursuant to the consulting agreement.

During the quarter ended December 31, 2021, we entered into a consulting agreement with Joanne Curley, another independent member of our Board, to assist us in developing a phase-appropriate research and development human resources staffing plan to support our development of fasedione, itrivone and AV-101. We recorded expense of \$6,800 during the quarter ended December 31, 2021 related to this agreement and an accounts payable balance of \$1,800 at December 31, 2021, which was settled in the fourth quarter of Fiscal 2022.

14. 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, 2023 or 2022.

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, 2023 or 2022.

Leases

Financing Lease

Assets subject to financing lease obligations at March 31, 2023 and 2022 that are included in property and equipment are reflected in the table below:

	<u>March 31,</u> <u>2023</u>	<u>March 31,</u> <u>2022</u>
Office equipment subject to financing lease	\$ 10,600	\$ 14,700
Accumulated depreciation	(2,000)	(14,700)
Net book value of office equipment subject to financing lease	<u>\$ 8,600</u>	<u>\$ -</u>

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The fully depreciated office equipment reported at March 31, 2022 was subject to a lease that expired in January 2022. That equipment was replaced subject to a new lease in April 2022. Future minimum lease payments under the new financing lease are as follows:

Fiscal Year Ending March 31,	
2024	\$ 2,900
2025	2,900
2026	2,900
2027	2,900
2028	600
Future minimum lease payments	12,200
Less imputed interest included in minimum lease payments	(3,100)
Present value of minimum lease payments	9,100
Less current portion	(1,700)
Financing lease obligation - non-current portion	<u>\$ 7,400</u>

Amortization expense for assets recorded under financing leases is included in depreciation expense.

Operating Lease

We lease our headquarters office and laboratory space in South San Francisco, California under the terms of a lease that was set to expire on July 31, 2022 but which provided an option to renew for an additional five years at then-current market rates. For the purpose of determining the right-of-use asset and associated lease liability, we determined that the renewal of this lease for the period from August 2022 through July 2027 was reasonably probable at the time we adopted ASC 842. On October 14, 2021, we entered into an amendment to the lease (the *Lease Amendment*), pursuant to which the term of the lease was extended from August 1, 2022 to July 31, 2027 and the base rent under the lease for the five-year extension period was specified. Under the terms of the Lease Amendment, we have the option to renew the lease for an additional five-year term commencing on August 1, 2027. Consistent with our adoption of ASC 842, beginning April 1, 2019, we recorded this lease in our Consolidated Balance Sheet as an operating lease. 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 Consolidated Balance Sheets at March 31, 2023 and 2022:

	As of March 31, 2023	As of March 31, 2022
<i>Assets</i>		
Right-of-use asset – operating lease	<u>\$ 2,260,300</u>	<u>\$ 2,662,000</u>
<i>Liabilities</i>		
Current operating lease obligation	\$ 485,600	\$ 433,300
Non-current operating lease obligation	2,119,800	2,605,400
Total operating lease liability	<u>\$ 2,605,400</u>	<u>\$ 3,038,700</u>

The following table summarizes the effect of operating lease costs in our consolidated statements of operations:

	For the Fiscal Year Ended March 31, 2023	For the Fiscal Year Ended March 31, 2022
Operating lease cost	\$ 851,700	\$ 725,000

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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,	Amount
2024	\$ 689,500
2025	710,200
2026	731,500
2027	753,500
2028	253,600
Total lease expense	3,138,300
Less imputed interest	(532,900)
Present value of operating lease liabilities	<u>\$ 2,605,400</u>

The remaining lease term, which does not include the optional five-year extension at the expiration of the lease period ending July 31, 2027, and the discount rate assumption for our South San Francisco operating lease are as follows:

	As of March 31, 2023
Assumed remaining lease term in years	4.33
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, 2023	For the Fiscal Year Ended March 31, 2022
Cash paid for amounts included in the measurement of lease liabilities	\$ 883,200	\$ 844,300

During Fiscal 2023 and Fiscal 2022, we did not record any new right-of-use assets arising from new operating 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 expenses over the lease term. We recorded rent expense of \$14,200 for both Fiscal 2023 and Fiscal 2022 attributable to this lease.

15. 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, 2023:

Reverse Split of Common Stock

On June 6, 2023, we implemented a one-for-thirty (1-for-30) reverse split of our common stock (the *Reverse Stock Split*). At our 2022 Annual Meeting of Stockholders held on October 28, 2022, our stockholders authorized our Board to effect a reverse stock split of our issued and outstanding shares of common stock at a ratio of up to one-for-thirty, with the exact ratio to be determined at the discretion of the Board. The Board subsequently unanimously approved the ratio of one-for-thirty. Our common stock began trading on the Nasdaq Capital Market on a split-adjusted basis on June 7, 2023. The Reverse Stock Split reduced the number of shares of our common stock outstanding. Additionally, the number of shares and exercise prices of outstanding options to purchase common stock granted under our stockholder-approved 2016 Plan, 2019 Plan and our 2019 ESPP and outstanding warrants to purchase common stock have been adjusted proportionately. Our authorized shares of common stock remain at 325,000,000 and our authorized shares of preferred stock remain at 10,000,000. The par value of each of our common stock and preferred stock remains at \$0.001 per share. All share and per share data for all periods presented in the accompanying financial statements and related disclosures in this Report have been adjusted retrospectively to reflect the Reverse Stock Split.

VISTAGEN THERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Sales of Common Stock under the Sales Agreement

During June 2023 through the date of this Report, we sold an aggregate of 561,418 shares of our common stock under the Sales Agreement at a weighted average price of \$2.05 per share and received gross cash proceeds of \$1,151,884.

Grant of Options from 2019 Plan

In June 2023, we granted options to purchase 10,000 shares of our common stock under our 2019 Plan in accordance with the terms of a settlement with a former employee. The options have an exercise price equal to the quoted closing market price of our common stock on the Nasdaq Capital Market on the date of grant, a term of five years and vest 25% on the grant date with the remaining 75% vested 30 days thereafter.

16. 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, 2023. 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 Fiscal Year 2023
	June 30, 2022	September 30, 2022	December 31, 2022	March 31, 2023	
Sublicense revenue	\$ 310	\$ (893)	\$ 180	\$ 176	\$ (227)
Total revenue	310	(893)	180	176	(227)
Operating expenses:					
Research and development	15,291	12,895	6,854	9,337	44,377
General and administrative	4,792	3,702	3,092	3,078	14,664
Total operating expenses	20,083	16,597	9,946	12,415	59,041
Loss from operations	(19,773)	(17,490)	(9,766)	(12,239)	(59,268)
Other income and expenses, net:					
Interest income, net	2	6	5	13	26
Loss before income taxes	(19,771)	(17,484)	(9,761)	(12,226)	(59,242)
Income taxes	(5)	-	-	(1)	(6)
Net loss and comprehensive loss	(19,776)	(17,484)	(9,761)	(12,227)	(59,248)
Basic and diluted net loss per common share	\$ (2.87)	\$ (2.54)	\$ (1.42)	\$ (1.71)	\$ (8.51)
Weighted average shares used in computing basic and diluted net loss per common share	6,886,557	6,893,708	6,894,603	7,163,799	6,958,749

VISTAGEN THERAPEUTICS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

	Three Months Ended				Total Fiscal Year 2022
	June 30, 2021	September 30, 2021	December 31, 2021	March 31, 2022	
Sublicense revenue	\$ 354	\$ 358	\$ 358	\$ 39	\$ 1,109
Total revenue	354	358	358	39	1,109
Operating expenses:					
Research and development	5,458	9,937	7,779	12,234	35,408
General and administrative	2,643	3,221	3,118	4,498	13,480
Total operating expenses	8,101	13,158	10,897	16,732	48,888
Loss from operations	(7,747)	(12,800)	(10,539)	(16,693)	(47,779)
Other income and expenses, net:					
Interest income, net	5	5	5	5	20
Loss before income taxes	(7,742)	(12,795)	(10,534)	(16,688)	(47,759)
Income taxes	(3)	-	-	-	(3)
Net loss and comprehensive loss	(7,745)	(12,795)	(10,534)	(16,688)	(47,762)
Accrued dividend on Series B Preferred stock	(362)	(375)	(208)	-	(945)
Net loss attributable to common stockholders	\$ (8,107)	\$ (13,170)	\$ (10,742)	\$ (16,688)	\$ (48,707)
Basic and diluted net loss per common share attributable to common stockholders	\$ (1.28)	\$ (2.04)	\$ (1.59)	\$ (2.42)	\$ (7.38)
Weighted average shares used in computing basic and diluted net loss per common share attributable to common stockholders	6,330,805	6,440,928	6,744,289	6,884,403	6,599,287

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

None.

Item 9A. Controls and Procedures

Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer (*CEO*) and principal financial officer (*CFO*), evaluated the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) as of March 31, 2023. Based upon that evaluation, our CEO and CFO concluded that, as of such date, our disclosure controls and procedures were effective to ensure that information required to be disclosed in reports filed by us under the Securities Exchange Act of 1934 is recorded, processed, summarized and reported within the required time periods and is accumulated and communicated to our management, including our CEO and CFO, as appropriate, to allow timely decisions regarding required disclosure.

Management's Report on Internal Control Over Financial Reporting

Management of the Company is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in the U.S. Securities Exchange Act of 1934, Rules 13a-15(f) and 15d-15(f). Our internal control system was designed to provide reasonable assurance to our management and board of directors regarding the preparation and fair presentation of published financial statements. Management assessed the effectiveness of our internal control over financial reporting for our fiscal year ended March 31, 2023 based on criteria set forth in *Internal Control - Integrated Framework (2013)*, issued by the Committee of Sponsoring Organizations of the Treadway Commission (*COSO*) (the *COSO Framework*). Based upon this assessment, management concluded that, as of March 31, 2023, our internal control over financial reporting was effective, based upon those criteria.

Limitations on Effectiveness of Controls

It should be noted that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment and makes assumptions about the likelihood of future events. There can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions, regardless of how remote. Management believes that the Financial Statements included in this Annual Report fairly present in all material respects our financial condition, results of operations and cash flows for the periods presented.

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 persons 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.

Attestation Report of Registered Public Accounting Firm

This Annual Report does not include an attestation report of our registered independent public accounting firm regarding internal control over financial reporting pursuant to SEC rules for smaller reporting companies that permit us to provide only management's report in this Annual Report.

Item 9B. Other Information

None.

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 2023 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission on or before July 29, 2023 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 2023 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission on or before July 29, 2023 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 2023 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission on or before July 29, 2023 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 2023 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission on or before July 29, 2023 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 2023 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission on or before July 29, 2023 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 85.

(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.
2.2	Agreement and Plan of Merger, by and among Vistagen Therapeutics, Inc., VTGN Merger Sub, Inc., Pherin Pharmaceuticals, Inc. and Kevin McCarthy dated December 20, 2022, incorporated by reference from Exhibit 2.1 to the Company's Current Report on Form 8-K, dated December 21, 2022.
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.
3.5.1	Certificate of Withdrawal of Certificate of Designation of the Relative Rights and Preferences of the Series A Convertible Preferred Stock, dated November 9, 2022, incorporated by reference from Exhibit 3.2 to the Company's Quarterly Report on Form 10-Q, filed on November 10, 2022.
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.
3.7.1	Certificate of Withdrawal of Certificate of Designation of the Relative Rights and Preferences of the 10% Convertible Series B Preferred Stock, dated November 9, 2022, incorporated by reference from Exhibit 3.3 to the Company's Quarterly Report on Form 10-Q, filed on November 10, 2022.
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.
3.9.1	Certificate of Withdrawal of Certificate of Designation of the Relative Rights and Preferences of the Series C Convertible Preferred Stock, dated November 9, 2022, incorporated by reference from Exhibit 3.4 to the Company's Quarterly Report on Form 10-Q, filed on November 10, 2022.
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 17, 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.
3.14.1	Certificate of Withdrawal of Certificate of Designation of the Relative Rights and Preferences of the Series D Convertible Preferred Stock, dated November 9, 2022, incorporated by reference from Exhibit 3.5 to the Company's Quarterly Report on Form 10-Q, filed on November 10, 2022.
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.
3.16	Amendment No. 2 to the Second Amended and Restated Bylaws of Vistagen Therapeutics, Inc., incorporated by reference from Exhibit 3.1 to the Company's Current Report on Form 8-K, filed on August 31, 2022.
3.17	Certificate of Amendment to the Restated and Amended Articles of Incorporation, as amended, of Vistagen Therapeutics, Inc., dated June 6, 2023, incorporated by reference from Exhibit 3.1 to the Current Report on Form 8-K, filed June 6, 2023.
10.40*	Employment Agreement, by and between, Vistagen and Shawn K. Singh, dated April 28, 2010, as amended May 9, 2011.
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.
10.88	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.
10.112	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.
10.116	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.

10.118	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.
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.
10.130+	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.
10.135	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.
10.138	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.
10.143	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.
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.
10.151	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.
10.152	Indemnification Agreement, dated July 6, 2021, by and between Vistagen Therapeutics, Inc. and Mary L. Rotunno, J.D. incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K, filed on July 8, 2021.
10.153	Indemnification Agreement, dated July 21, 2021, by and between Vistagen Therapeutics, Inc. and Margaret M. FitzPatrick incorporated by reference from Exhibit 10.1 to the Company's Current Report on Form 8-K filed on July 22, 2021.

10.154	Third Amendment to Lease, by and between Bayside Area Development, LLC and Vistagen Therapeutics, Inc. dated October 14, 2021, incorporated by reference from Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on November 10, 2021.
10.155	Indemnification Agreement, dated May 13, 2022, by and between Vistagen Therapeutics, Inc. and Reid G. Adler, J.D., incorporated by reference from Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on August 11, 2022.
10.156	Consulting Services Agreement between Vistagen Therapeutics, Inc and FitzPatrick & Co. LLC, dated January 21, 2022, incorporated by reference from Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on November 10, 2022.
10.157	Amendment No. 1 to Consulting Services Agreement between Vistagen Therapeutics, Inc and FitzPatrick & Co. LLC, effective June 1, 2022, incorporated by reference from Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q, filed on November 10, 2022.
10.158	Amendment No 2. to Consulting Services Agreement between Vistagen Therapeutics, Inc. and FitzPatrick & Co. LLC effective January 1, 2023, incorporated by reference from Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on February 7, 2023.
10.159	Amendment No 3. to Consulting Services Agreement between Vistagen Therapeutics, Inc. and FitzPatrick & Co. LLC effective July 1, 2023, filed herewith.
10.160	Consulting Agreement between Vistagen Therapeutics, Inc and i3 Strategy, dated November 10, 2022, incorporated by reference from Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed on November 10, 2022.
10.161	Consulting Services Agreement between Vistagen Therapeutics, Inc. and Mark Smith, dated November 16, 2022, filed herewith.
10.162	Amendment No. 1 to Master Services Agreement by and between Vistagen Therapeutics, Inc. and Allucent, dated June 24, 2022, filed herewith.
21.1	List of Subsidiaries, filed herewith.
23.1	Consent of WithumSmith+Brown, PC, 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	The instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.
101.SCH	Inline XBRL Taxonomy Extension Schema, filed herewith
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase, filed herewith
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase, filed herewith
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase, filed herewith
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase, filed herewith
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

- * 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 28th day of June, 2023.

Vistagen Therapeutics, Inc.

Date: June 28, 2023

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
<u>/s/ Shawn K. Singh</u> Shawn K. Singh, J.D.	Chief Executive Officer, and Director <i>(Principal Executive Officer)</i>	June 28, 2023
<u>/s/ Jerrold D. Dotson</u> Jerrold D. Dotson	Vice President and Chief Financial Officer <i>(Principal Financial and Accounting Officer)</i>	June 28, 2023
<u>/s/ Jon S. Saxe</u> Jon S. Saxe, J.D., LL.M	Chairman of the Board of Directors	June 28, 2023
<u>/s/ Ann M. Cunningham</u> Ann M. Cunningham	Director	June 28, 2023
<u>/s/ Joanne Curley</u> Joanne Curley, Ph.D.	Director	June 28, 2023
<u>/s/ Margaret M. FitzPatrick</u> Margaret M. FitzPatrick	Director	June 28, 2023
<u>/s/ Jerry B. Gin</u> Jerry B. Gin, Ph.D.	Director	June 28, 2023
<u>/s/ Mary L. Rotunno</u> Mary L. Rotunno, J.D.	Director	June 28, 2023

AMENDMENT NO. 3
TO
CONSULTING SERVICES AGREEMENT

This Amendment (“Amendment No. 3”) is made between **Vistagen Therapeutics, Inc.**, a Nevada corporation having an address at 343 Allerton Avenue, South San Francisco, California 94080 (“Vistagen”), and **FitzPatrick & Co. LLC**, a Delaware limited liability company, having an address at 2023 Allen Place, NW, Washington DC 20009 (“Consultant”), effective as of July 1, 2023.

WHEREAS, Vistagen and Consultant entered into a Consulting Services Agreement dated January 21, 2022, Amendment No. 1 to the Consulting Agreement dated June 1, 2022, and Amendment No. 2 to the Consulting Agreement dated January 1, 2023 (collectively, the “Agreement”); and

WHEREAS, the parties wish to amend the Agreement to extend its term.

Vistagen and Consultant, therefore, agree as follows:

AMENDMENT

1. The term of this Agreement shall be extended and continue until December 31, 2023.

Except as expressly provided in this Amendment No. 3, the Agreement remains unchanged and in full force and effect.

[Remainder of page intentionally left blank]

Each party is signing this agreement with the party's authorized signature.

AGREED TO:

VISTAGEN THERAPEUTICS, INC.

AGREED TO:

FITZPATRICK & CO., LLC

By: /s/ Shawn K. Singh

Name: Shawn K. Singh, J.D.

Title: Chief Executive Officer

Date: June 22, 2023

By: /s/ Maggie FitzPatrick

Name: Margaret Mary FitzPatrick

Title: Managing Director

Date: June 22, 2023

CONSULTING AGREEMENT

This Consulting Agreement (“Agreement”) is made and entered into as of November 17, 2022, by and between Vistagen Therapeutics, Inc., a Nevada corporation with principal offices located at 343 Allerton Avenue, South San Francisco, CA 94080 (“Vistagen”), and Mark A. Smith, M.D., Ph.D. (“Consultant”). In this Agreement, Vistagen and Consultant are sometimes referred to individually as a “Party” and together as the “Parties.”

WHEREAS, Consultant has substantial expertise in the biopharmaceutical industry relating to the clinical development of therapeutic products; and

WHEREAS, Vistagen wishes to engage Consultant to provide consulting services in their area of expertise.

NOW, THEREFORE, the Parties, intending to be legally bound, agree as follows:

1. **SERVICES.** Consultant agrees to provide Vistagen with the consulting services (“Services”) described in Appendix A to this Agreement. Consultant will perform the Services in good faith, with all due care, skill, and ability, and to the highest standards of professional and ethical competence and integrity. Consultant will keep accurate records of their Services including authorized expenditures. For clarity, this Agreement shall be applied in case of any conflict between this Agreement and the proposal at Appendix A.
 2. **COMPENSATION.** In consideration for the Services performed by Consultant, Vistagen agrees to compensate Consultant as set forth in Appendix A. Monthly invoices will be submitted by Consultant via email to: accountspayable@vistagen.com, with a copy to jdotson@vistagen.com
 3. **WORK PRODUCT AND DELIVERABLES.** Any work product and deliverables to be provided pursuant to the Services are described in Appendix A. Consultant agrees to treat as for the sole benefit of Vistagen and to fully and promptly disclose and assign to Vistagen, without additional compensation, all right, title and interest in and to any and all intellectual property embodied in such work product and deliverables. Works of authorship that are protectable by copyright are “works made for hire,” as that term is defined in the United States Copyright Act. As required by California law, the foregoing provision regarding intellectual property, specifically including any assignment obligations, shall not apply to any invention developed outside of the Services. Consultant agrees to sign all papers and take other actions, at Vistagen’s expense and reasonable request, to assign, secure and enforce rights to such intellectual property.
 4. **RELATIONSHIP OF THE PARTIES.** Consultant is an independent contractor to and not an employee of Vistagen. Vistagen will not withhold taxes or provide any benefits to Consultant, such as health insurance, leave, or any other employee benefits. Consultant will have no management activities, authority or responsibilities on behalf of Vistagen.
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5. **CONFIDENTIAL INFORMATION.** Subject to the limitations set forth in Section 6, all information disclosed by one Party to the other shall be deemed to be "Confidential Information." Confidential Information may include, without limitation, any trade secret, patent application, technique, invention, idea, process, or formula; any sample, compound, extract, media, vector and/or cell line; any procedures and formulations for producing the foregoing; any data or information relating to any past, current and contemplated research and development activities, clinical trials, and the like; and any commercial, engineering, manufacturing, marketing, partnering, regulatory, servicing, financing or personnel matter, plan, program or strategy, suppliers, clients, customers, employees, investors, partners or business opportunities of a Party, whether in oral, written, visual, graphic or electronic form. All Confidential Information (including all copies thereof) shall remain at all times the property of the Party that discloses it ("Disclosing Party").
6. **EXCLUSIONS FROM CONFIDENTIAL INFORMATION.** Confidential Information shall not include information that the Party which receives it ("Receiving Party") can demonstrate by competent written proof: (a) is now, or hereafter, becomes generally known or available in the public domain through no act or failure to act by Receiving Party; (b) is already known by Receiving Party at the time of receiving such information; (c) is hereafter furnished to Receiving Party by a third party, as a matter of right and without restriction on disclosure; (d) is independently developed by Receiving Party without any use of the Confidential Information; or (e) is approved in writing for disclosure by Disclosing Party.
7. **DISCLOSURE DUE TO OPERATION OF LAW.** Notwithstanding any other provision of this Agreement to the contrary, disclosure of Confidential Information by Receiving Party will not be precluded if such disclosure: (a) is made in response to a valid order of a court or other governmental body of the United States or any political subdivision thereof having competent jurisdiction; or (b) is otherwise required by law or regulation; provided, however, that Receiving Party shall first have given reasonable prior notice to Disclosing Party, to the extent legally permissible, and shall have made a reasonable effort to obtain a protective order requiring that the Confidential Information so disclosed be used only for the purposes for which the order was issued.
8. **LIMITATIONS ON USE.** Receiving Party may use the Confidential Information only to the extent required to provide the Services and for no other purpose. Receiving Party shall maintain all Confidential Information in trust and strict confidence and shall not disclose any of the Confidential Information to any other third party without Disclosing Party's prior written consent.
9. **MAINTENANCE OF CONFIDENTIALITY.** Receiving Party agrees to take reasonable measures to protect the secrecy of and avoid disclosure and unauthorized use of the Confidential Information. Without limiting the foregoing, Receiving Party will take at least those measures taken to protect their own confidential information of a similar nature.
10. **NO LICENSE OR IMPLIED RIGHTS.** No rights or licenses to copyrights, inventions, know-how, patents, trademarks, trade secrets, or any other intellectual property rights, are implied or granted under this Agreement except as expressly set forth.

11. **TERM, TERMINATION AND SURVIVAL.** This term of this Agreement will extend from December 2, 2022 (“Effective Date”) to December 31, 2023, unless earlier terminated or extended by mutual agreement. Each Party reserves the right, in its sole discretion, to terminate the Agreement at any time and for any reason, including no reason. Either Party may terminate this Agreement if the other Party commits a material breach of this Agreement that is not remedied within thirty (30) days after receiving written notice of such breach or within such other period as is reasonable under the circumstances. Receiving Party’s obligations regarding confidentiality under this Agreement will continue for a period of five (5) years after any expiration or termination of this Agreement. The provisions of this Agreement that expressly or by implication are intended to come into or remain in force on or after its expiration or termination shall remain in full force and effect, including Sections 4 – 8 and 10.
12. **TREATMENT OF CONFIDENTIAL INFORMATION UPON TERMINATION.** Upon expiration or termination of this Agreement, Receiving Party shall promptly return or destroy, as directed by Disclosing Party, all copies of Confidential Information and provide Disclosing Party with all work product and deliverables described in the Services and confirm such actions in writing. Notwithstanding the foregoing, Receiving Party may retain copies of Confidential Information as is reasonably required to comply with their internal document retention policies or applicable law or to ensure compliance with the provisions of this Agreement. In addition, Receiving Party will not be obligated to destroy copies of such information remaining on their standard computer back-up systems. Any Confidential Information so retained will continue to be subject to the terms of this Agreement for the period set forth.
13. **REMEDIES.** Consultant understands and agrees that money damages may not be a sufficient remedy for a breach of this Agreement and that Vistagen will be entitled to seek specific performance, injunctive relief and/or other equitable relief as a remedy for any such breach. Such remedy shall not be deemed to be the exclusive remedy for a breach of this Agreement but shall be in addition to other remedies available at law or in equity.
14. **SECURITIES LAWS.** Vistagen is a publicly traded company. Consultant acknowledges that: (i) trading in securities of Vistagen is subject to applicable securities legislation; (ii) as a result of the disclosure of the Confidential Information by Vistagen to Consultant, Consultant may possess material, non-public information of Vistagen; and (iii) any trading by Consultant or its Representatives in the securities of Vistagen while in possession of such material, non-public information may be a violation of applicable securities legislation and is at all times prohibited.
15. **NOTICE.** All demands, notices and requests under this Agreement, other than routine communications, shall be in writing, in each case to the attention of the other Party’s signatory at the address above. Either Party may give any notice under this Agreement by customary means (including personal delivery, overnight courier, or by certified postal delivery but expressly not including fax or email), and such notice or other communication shall not be deemed duly given when the Party for whom it is intended receives it. Any Party may change the address to which notices and other communications are to be delivered.

16. **MISCELLANEOUS.**

- (a) Each of the undersigned warrants that they have the authority to enter into this Agreement and to disclose the Confidential Information provided hereunder.
- (b) In the performance of their permitted activities under this Agreement, each Party shall comply with all applicable laws, including all applicable export control, anti-corruption and anti-bribery laws and regulations.
- (c) This Agreement shall bind and inure to the benefit of the Parties and their successors and permitted assigns.
- (d) Neither Party shall have the right to use the other Party's name or likeness in any publications, publicity or other materials or presentations without obtaining the prior written consent of the other Party.
- (e) Neither this Agreement nor any rights or obligations under this Agreement are assignable by either Party without the prior written approval of the other Party, except that either Party may assign this Agreement to an Affiliate without such consent and Vistagen may assign this Agreement in the context of a sale of all or substantially all of its assets that relate to this Agreement without such consent.
- (f) This Agreement shall be governed by the laws of the State of California as applied to disputes involving parties located entirely within the State and without giving effect to its choice of law provisions. Any claim or controversy arising out of or related to this Agreement, or any breach hereof, shall be submitted to a court of competent jurisdiction in the State of California, and each Party hereby consents to the jurisdiction and venue of such court.
- (g) This Agreement has been prepared in the English language and the English language shall control its interpretation.
- (h) This Agreement constitutes the final, complete and exclusive agreement of the Parties relative to its subject matter and supersedes all prior and contemporaneous understandings and agreements relating to its subject matter. This Agreement may not be changed, modified, amended or supplemented except by a written instrument signed by both Parties.
- (i) Section headings are included for convenience only and will not be deemed to be a part of this Agreement.
- (j) Any failure to enforce any provision of this Agreement shall not constitute a waiver of any provision, nor will any single or partial exercise of any provision preclude any other or further exercise or the exercise of any other right, power or privilege under this Agreement. To be effective, any waiver of any right, power, or privilege under this Agreement shall be in writing and signed by the Party against whom the waiver is sought to be enforced.

(k) If any one or more of the provisions of this Agreement is held to be invalid or unenforceable by any court of competent jurisdiction from which no appeal can be or is taken, the provision shall be considered severed from this Agreement and shall not serve to invalidate any remaining provisions. The Parties shall make a good faith effort to replace any invalid or unenforceable provision with a valid and enforceable one such that the objectives contemplated by the Parties when entering into this Agreement may be realized.

(l) Neither Party shall be deemed to have defaulted under or to be in breach of this Agreement for failure or delay in fulfilling material obligations when such failure or delay is directly caused by an event outside of their reasonable control, including but not limited to war, acts of war, insurrections, acts of terrorism, epidemics or pandemics, or acts of God (a "Force Majeure Event"). Each Party shall inform the other promptly and in writing of any such Force Majeure Event and the Parties will discuss the situation, and acting in good faith, agree on the appropriate course of action under the circumstances.

(m) For the convenience of the Parties, this Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. This Agreement may be executed in PDF form or by other electronically transmitted signatures and such signatures will be deemed to bind each Party as if they were the original signatures.

[Remainder of page intentionally blank]

IN WITNESS WHEREOF, EACH PARTY HAS CAUSED THE AGREEMENT TO BE EXECUTED EFFECTIVE AS OF THE DATE SET FORTH ABOVE.

AGREED TO:

AGREED TO:

VISTAGEN THERAPEUTICS, INC.

CONSULTANT

By: /s/ Shawn K. Singh

By: /s/ Mark A. Smith

Name: Shawn K. Singh, J.D.

Name: Mark A. Smith, M.D., Ph.D.

Title: Chief Executive Officer

Date: November 17, 2022

Date: November 17, 2022

Tax ID:

(Appendix A is attached)

Appendix A

1. Description of Services to be Provided by Consultant to Vistagen:

- Serve on the Company's Clinical and Regulatory Advisory Board.
- Provide preclinical and clinical development advisory services to senior management and the Company's Tiger Teams regarding development of the Company's drug candidates, including, but not limited to its current drug candidates, PH94B, PH10 and AV-101, for central nervous system (CNS) disorders.

2. Compensation from Vistagen to Consultant:

Vistagen agrees to provide compensation to Consultant as follows, by check or wire to a U.S. bank account:

- \$50,000 from the Effective Date through December 31, 2022
- \$10,000 per month to be paid in arrears per invoices to be submitted by Consultant, from January 1, 2023 to December 31, 2023, or upon termination of this Agreement if that occurs prior to December 31, 2023
- Reasonable expenses will be reimbursed by Vistagen at cost. Substantial expenses not in the usual course of business, airfare and hotel accommodations must be pre-approved by Vistagen.

3. Stock Options and Continuation of Service:

Consultant's issued and outstanding stock options as of the Effective Date will continue to vest until expiration or termination of this Agreement; vested options as of the expiration or termination date of this Agreement will be exercisable for up to 90 days thereafter.

AMENDMENT NO. 1

TO

**MASTER SERVICES AGREEMENT
(For All CRO Services)**

This Amendment (“Amendment No. 1”) is made between **VistaGen Therapeutics, Inc.**, a Nevada corporation having an address at 343 Allerton Avenue, South San Francisco, California 94080 (“VistaGen”) and **Allucent (formerly known as Cato Research Ltd.)** a North Carolina corporation having an address at 2000 Centregreen Way, Suite 300, Cary, North Carolina 27513 (“Allucent”), and is effective as of June 23, 2022.

WHEREAS, VistaGen and Allucent entered into a Master Services Agreement dated July 11, 2017 (the “Agreement”); and

WHEREAS, the parties wish to amend the Agreement to extend its term.

VistaGen and Allucent therefore agree as follows:

AMENDMENT

1. The term of the Agreement shall be extended and continue until the later of July 31, 2027, or the expiration or termination of any Work Orders that are active as of that date.
2. The automatic renewal provision in Section 5.1 of the Agreement is deleted going forward as of the effective date of this Amendment No. 1.

Except as expressly provided in this Amendment No. 1, the Agreement remains unchanged and in full force and effect.

[Remainder of page intentionally left blank]

Each party is signing this agreement with the party's authorized signature.

AGREED TO:

VISTAGEN THERAPEUTICS, INC.

By: /s/ Shawn K. Singh

Name: Shawn K. Singh, J.D.

Title: Chief Executive Officer

Date: June 23, 2022

AGREED TO:

ALLUCENT

By: /s/ Richard Shimota

Name: Richard Shimota

Title: Chief Financial Officer

Date: 6/24/2022

List of Subsidiaries

Vistastem, Inc., a California corporation

Pherin Pharmaceuticals, Inc., a Delaware corporation

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. 333-259799, 333-234026, 333-223556 and 333-208354), Form S-3 (File Nos. 333-270232, 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 28, 2023, which includes an explanatory paragraph relating to Vistagen Therapeutics, Inc.'s ability to continue as a going concern, relating to the consolidated financial statements, which appears in this Annual Report on Form 10-K.

/s/ WithumSmith+Brown, PC

San Francisco, California
June 28, 2023

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 28, 2023

/s/ Shawn K. Singh
Shawn K. Singh, JD
Principal Executive Officer

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 28, 2023

/s/ Jerrold D. Dotson
Jerrold D. Dotson
Principal Financial Officer

**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, 2023 (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 28, 2023

/s/ Shawn K. Singh
Shawn K. Singh, JD
Principal Executive Officer

/s/ Jerrold D. Dotson
Jerrold D. Dotson
Principal Financial Officer