Vistagen Announces Positive Results from Exploratory Phase 2A Study of PH80 for Acute Management of the Symptoms of Premenstrual Dysphoric Disorder

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PH80 nasal spray demonstrated statistically and clinically significant improvement versus placebo in an exploratory double-blind, placebo-controlled Phase 2A study (n=52) in subjects with a history of premenstrual dysphoric disorder (PMDD)

PH80 was well-tolerated with an adverse event profile similar to placebo

Data builds on the previously reported vasomotor symptoms (hot flashes) due to menopause study, reinforcing the potential of PH80 to treat multiple aspects of women's health

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Sep. 12, 2023-- Vistagen (Nasdaq: VTGN), 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, today announced that PH80, one of the Company's five investigational neuroactive nasal sprays, demonstrated statistically significant improvement versus placebo in an exploratory Phase 2A study for acute management of the symptoms of premenstrual dysphoric disorder (PMDD), including negative mood and physical and behavioral symptoms.

The previously unreported randomized, double-blind, placebo-controlled Phase 2A clinical study of PH80 was designed to explore the efficacy, safety, and tolerability of intranasal administration of PH80 for the acute management of PMDD in subjects with a regular menstrual cycle and at least a one-year history of PMDD. The initial study visit occurred after the onset of symptoms. All subjects were administered placebo nasal spray and those who showed no symptom improvement were eligible to return for the second visit, which occurred after the onset of symptoms during the next menstrual cycle. At the second study visit, subjects were randomized to receive a single dose of 0.9 µg PH80 nasal spray or placebo in the clinic. Subsequent doses of PH80 or placebo were then self-administered at home as-needed, up to four times per day for six consecutive days prior to the estimated day of menses onset.

PH80 demonstrated statistically and clinically significant improvement versus placebo in symptoms of PMDD using the subject-rated Penn Daily Symptom Report (DSR) as early as Day 4 and continuing to Day 6. At Day 6, change from baseline was -12.1 for PH80 (n=29) versus -7.6 for placebo (n=23) (p=0.008), showing significant and clinically meaningful improvement. PH80 also demonstrated statistically and clinically significant improvement versus placebo at Day 6 on the clinician-rated Premenstrual Tension Scale (PMTS) total score where the PH80 change from baseline was -12.0 versus -7.7 for placebo (p=0.006). PH80 was well-tolerated with no serious adverse events (AEs). The most common AE was headache, reported by 17% in the placebo group and 7% in the PH80 group. No other treatment-emergent AE occurred more than once per subject.

Analysis of the data revealed that mood symptoms seemed to be the most sensitive to PH80:

- Depression/feeling sad or blue was reported by 0% of PH80 and 68% of placebo-treated subjects;
- Irritability/persistent anger was reported by <3% of PH80 and 43% of placebo-treated subjects;
- Anxiety/tension/on edge was reported by 0% of PH80 and 35% of placebo-treated subjects; and
- Difficulty concentrating was reported by 0% of PH80 and 18% of placebo-treated subjects.

"Symptoms of PMDD affect 5% to 8% of menarcheal individuals and there are limited effective treatment options that help with both physical and mood symptoms. The previously unreported results of this exploratory Phase 2A clinical study of PH80 signal a potential revolutionary method for treating premenstrual mood symptoms," said Shawn Singh, Chief Executive Officer of Vistagen. "PMDD symptoms can be extremely limiting to daily functioning and PH80 demonstrated the potential to alleviate these symptoms. Interestingly, improvements in the mood items of depression and dysphoria were observed both by subject- and clinician-rated scales. Along with the previously reported efficacy of PH80 for the treatment of hot flashes due to menopause, PH80 efficacy in PMDD further supports its potential as a valuable and differentiated treatment option for multiple indications in women's healthcare."

This previously unreported exploratory Phase 2A study of PH80 was sponsored by Pherin Pharmaceuticals (Pherin), now a wholly owned subsidiary of Vistagen, and conducted in a real-world setting in Mexico in 2005 and 2006. Vistagen gained access to the results of the study in connection with its acquisition of Pherin in February 2023. Ellen Freeman, Ph.D., formerly of the University of Pennsylvania, served as the Principal Investigator of the study. Vistagen recently entered into an exclusive negotiation agreement with Fuji Pharma Co., Ltd. regarding a potential license to develop and commercialize PH80 in Japan, including for the acute treatment of moderate to severe hot flashes due to menopause and potentially other indications.

Vistagen's pipeline includes six clinical-stage drug candidates, including its most advanced neuroactive pherine nasal spray, fasedienol (PH94B), for which Vistagen recently reported positive top-line results from its PALISADE-2 Phase 3 trial in social anxiety disorder.

About PH80

PH80 is a first-in-class, neuroactive pherine nasal spray. The proposed mechanism of action of PH80 nasal spray does not require systemic absorption or direct activity on neurons in the brain and has demonstrated an excellent safety profile in all clinical trials to date. Vistagen is developing PH80 as a potential new treatment for the acute management of vasomotor symptoms (hot flashes) due to menopause, PMDD, and potentially other disorders. Designed for intranasal administration in low microgram doses, the proposed novel mechanism of action of PH80 is fundamentally differentiated from all currently approved treatment options in women's healthcare.

About Premenstrual Dysphoric Disorder

According to the National Institutes of Health (NIH), 5% to 8% of menarcheal individuals have moderate-to-severe symptoms that can cause significant distress and functional impairment, suggestive of premenstrual dysphoric disorder (PMDD). PMDD is a severe, sometimes disabling extension of premenstrual syndrome (PMS). PMDD symptoms usually begin in the luteal phase (approximately seven to 10 days before a person's period starts) and continue for the first few days of the period. Like PMS, PMDD can cause bloating, breast tenderness, fatigue, and changes in sleep and eating habits, but distinctively, it can also cause extreme mood shifts that can disrupt daily life and damage relationships. The cause of PMDD is not clearly understood, but it is thought that neurotransmitter systems may trigger PMDD. Brain areas that regulate emotion and behavior are studded with receptors for estrogen, progesterone, and other sex hormones. These hormones affect the functioning of neurotransmitter systems that influence mood and thinking, possibly triggering PMDD. Treatment of PMDD is aimed at preventing or minimizing symptomology.

About Vistagen

Vistagen (Nasdaq: VTGN) is a late clinical-stage biopharmaceutical company aiming to transform the treatment landscape for individuals living with anxiety, depression, and other CNS disorders. Vistagen is advancing therapeutics with the potential to be faster-acting, and with fewer side effects and safety concerns, than those currently available for the treatment of anxiety, depression, and multiple CNS disorders. Vistagen's pipeline includes six clinical-stage product candidates, including fasedienol (PH94B), itruvone (PH10), PH80, PH15, and PH284, each an investigational agent belonging to a new class of drugs known as pherines, as well as AV-101, which is an oral prodrug of an antagonist of the N-methyl-D-aspartate receptor (NMDAR). Pherines are neuroactive nasal sprays designed with an innovative proposed mechanism of action that activates chemosensory neurons in the nasal cavity and can beneficially impact key neural circuits in the brain without systemic absorption or direct activity on neurons in the brain. Vistagen is passionate about transforming mental health care and redefining what is possible in the treatment of anxiety, depression, and several other CNS disorders. Connect at www.Vistagen.com.

Forward Looking Statements

This press release contains certain forward-looking statements within the meaning of the federal securities laws. These forward-looking statements involve known and unknown risks that are difficult to predict and include all matters that are not historical facts. In some cases, you can identify forward-looking statements by the use of words such as "may," "could," "expect," "project," "outlook," "strategy," "intend," "plan," "seek," "anticipate," "believe," "estimate," "predict," "potential," "strive," "goal," "continue," "likely," "will," "would" and variations of these terms and similar expressions, or the negative of these terms or similar expressions. Such forward-looking statements are necessarily based upon estimates and assumptions that, while considered reasonable by Vistagen and its management, are inherently uncertain. As with all pharmaceutical products, there are substantial risks and uncertainties in the process of development and commercialization and actual results or development may differ materially from those projected or implied in these forward-looking statements. Among other things, there can be no guarantee that any of the Company's drug candidates will successfully complete ongoing or future clinical trials, receive regulatory approval or be commercially successful, or that the Company will be able to successfully replicate the result of past studies of its product candidates, including PH80. Other factors that may cause such a difference include, without limitation, risks and uncertainties relating to the Company's ability to secure adequate financing for its operations, including financing or collaborative support for continued clinical development of the Company's product candidates; other risks and uncertainties related to delays in launching, conducting and/or completing ongoing and planned clinical trials; the scope and enforceability of the Company's patents, including patents related to the Company's pherine drug candidates; fluctuating costs of materials and other resources and services required to conduct the Company's ongoing and/or planned clinical and non-clinical trials; market conditions; the impact of general economic, industry or political conditions in the United States or internationally; and other technical and unexpected hurdles in the development, manufacture and commercialization of the Company's drug candidates. These risks are more fully discussed in the section entitled "Risk Factors" in the Company's most recent Annual Report on Form 10-K for the fiscal year ended March 31, 2023, and in the Company's most recent Quarterly Report on Form 10-Q for the quarter ended June 30, 2023, as well as discussions of potential risks, uncertainties, and other important factors in our other filings with the U.S. Securities and Exchange Commission (SEC). The Company's SEC filings are available on the SEC's website at www.sec.gov. Additionally, you should not place undue reliance on these forward-looking statements in the future, because they apply only as of the date of this press release and should not be relied upon as representing the Company's views as of any subsequent date. The Company explicitly disclaims any obligation to update any forward-looking statements, other than as may be required by law. If the Company does update one or more forward-looking statements, no inference should be made that the Company will make additional updates with respect to those or other forward-looking statements.

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