Vistagen Announces Positive Results from Exploratory Phase 2A Study of PH80 in Women Diagnosed with Menopausal Hot Flashes

June 7, 2023

PH80 nasal spray demonstrates statistically significant efficacy versus placebo in exploratory double-blind, placebo-controlled Phase 2A study (n=36) in women diagnosed with menopausal hot flashes

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

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jun. 7, 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 efficacy versus placebo in an exploratory Phase 2A study for the acute treatment of hot flashes (vasomotor symptoms) in women diagnosed with menopausal hot flashes.

The randomized, double-blind, placebo-controlled exploratory 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 menopausal hot flashes in women. In the study, PH80 nasal spray containing epoxyestrenolone 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 adverse events.

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 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.

"The previously unreported results of this exploratory Phase 2A clinical study of PH80 for treatment of menopausal hot flashes are yet another part of the promising larger body of evidence regarding the potential of our innovative pherine nasal spray pipeline," said Shawn Singh, Chief Executive Officer of Vistagen. "There is clearly a need for an alternative treatment option for menopausal hot flashes that provides rapid relief without the safety, side effects, and treatment burden of the currently available options. We are encouraged by the potential that PH80 holds to improve the treatment paradigm for hot flashes and reduce the serious physical burden on the quality of life experienced by millions of women worldwide."

This exploratory Phase 2A study of PH80 was conducted in a real-world setting in Mexico and was sponsored by Pherin Pharmaceuticals (Pherin), now a wholly owned subsidiary of Vistagen, prior to Vistagen's acquisition of Pherin in February 2023. Ellen Freeman, Ph.D. of the University of Pennsylvania served as the Principal Investigator of the study. Vistagen's pipeline now includes six clinical-stage drug candidates, including its most advanced pherine nasal spray, fasedienol (PH94B), which is in Phase 3 development for treatment of social anxiety disorder.

About PH80

PH80 is a first-in-class, rapid-onset product candidate, designed to be used in a manner analogous to a rescue inhaler for asthma, with user-friendly, patient-tailored intranasal administration as-needed up to multiple times daily. The proposed mechanism of action of PH80 nasal spray does not require systemic uptake or direct action on CNS neurons 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 menopausal hot flashes and, potentially, acute treatment of migraine. Designed for intranasal administration in low microgram doses, the proposed novel MOA of PH80 is fundamentally differentiated from all currently approved treatment options and has potential to be a rapid-onset intervention that is safe to use for patients who choose not to be treated with presently available therapies, including hormone replacement therapy, certain antidepressants, and a neurokinin 3 (NK3) receptor antagonist.

About Hot Flashes

Hot flashes are vasomotor symptoms commonly experienced by women in menopause and are accompanied by hallmark symptoms such as sudden feelings of warmth, night sweats, and flushed skin. Presentation of hot flashes is directly linked to changes in hormone levels due to menopause, or menopause induced by other medical treatments or co-existing conditions, and the causal mechanism is unclear. Hot flashes are the most common symptom of the menopausal transition, affecting about 75% of menopausal women and about 40% of women in perimenopause. Prevalence of hot flashes is estimated to be about 20 million women in the U.S. with 9 million women estimated to be suffering from severe hot flashes. Current pharmacotherapies to treat hot flashes include hormonal therapy (estrogen with or without progesterone, or a synthetic progestin), gabapentins, certain antidepressants, clonidine, and fezolinetant, a neurokinin 3 (NK3) receptor antagonist, all of which are associated with certain side effects and safety concerns.

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 that are currently available for treatment of anxiety, depression and multiple CNS disorders. Vistagen's pipeline includes six clinical-stage product candidates, including five investigational agents belonging to a new class of drugs known as pherines, in addition to AV-101, an oral 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 passages and can selectively and beneficially impact key neural circuits in the brain without requiring systemic uptake or direct activity on CNS neurons. Vistagen's AV-101 inhibits activity of the ion channel of the NMDAR but does not block it. 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, 2022, and in the Company's most recent Quarterly Report on Form 10-Q for the quarter ended December 31, 2022, 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20230607005382/en/

Investors:
Mark McPartland
Senior Vice President, Investor Relations
(650) 577-3606
markmcp@vistagen.com

Media:
Nate Hitchings
SKDK
nhitchings@skdknick.com

Source: Vistagen