Vistagen Announces Results of Successful U.S. Phase 1 Study of Itruvone (PH10), Enabling U.S. Phase 2B Development for Treatment of Major Depressive Disorder

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The U.S. Phase 1 data build on successful Phase 1 and Phase 2A clinical studies of itruvone previously conducted outside the U.S.

Itruvone was well-tolerated and demonstrated a favorable safety and tolerability profile across single and multiple dose intranasal administrations

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jun. 21, 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 favorable safety and tolerability data from its U.S. Phase 1 clinical trial of itruvone (PH10), the Company's investigational rapid-onset pherine nasal spray for the treatment of major depressive disorder (MDD). Results from the U.S. Phase 1 study build on successful Phase 1 studies and a positive randomized, double-blind, placebo-controlled Phase 2A study of itruvone nasal spray in MDD previously conducted in Mexico and enable Phase 2B development of itruvone in the U.S. as an innovative stand-alone rapid-onset product candidate for treatment of MDD.

The U.S. Phase 1 study was a randomized, double-blind, placebo-controlled clinical study investigating the safety and tolerability of a single dose and of multiple doses of itruvone nasal spray in healthy adult subjects. There were no reported serious adverse events (SAEs) or discontinuations due to adverse events (AEs) in the study. Two AEs were reported during the treatment period, fatigue and headache, which occurred in the same subject. Both AEs were mild in severity and resolved without sequelae. Overall, itruvone nasal spray was well-tolerated and demonstrated a favorable safety profile, consistent with the three prior clinical studies of itruvone, including a positive randomized, double-blind, placebo-controlled Phase 2A study in MDD.

"According to a recent Gallup survey, more than a quarter of American adults have been diagnosed with depression at some point in their lifetime. The need for faster-acting, safer and more effective medications is unrelenting, especially in an environment where the gap between innovative treatment options and the prevalence of depressive disorders is increasing," stated Shawn Singh, Chief Executive Officer of Vistagen. "With a successful Phase 1 study in the U.S. and a positive Phase 2A study conducted outside the U.S. in hand, we look forward to advancing itruvone into Phase 2B development in the U.S., on our own or with a partner."

Itruvone Published Phase 2A Results in Major Depressive Disorder

The confirmation of itruvone's safety profile demonstrated in the U.S. Phase 1 study, along with the results of Vistagen's nonclinical studies and three prior clinical studies, inform Phase 2B development of itruvone as a potential rapid-onset stand-alone treatment of MDD with a favorable safety profile. In the published randomized, double-blind, placebo-controlled parallel design Phase 2A study of itruvone in MDD, itruvone was administered intranasally at a daily dose of 3.2µg and 6.4µg for 8 weeks.

After one week of treatment, the mean reduction on the 17-item Hamilton Depression Scale (HAM-D-17) scores for the itruvone 6.4µg group was 10.1 points, which was statistically greater ($p = 0.03$) than the mean reduction in the placebo group of 4.2 points from baseline. Also, at the end of the last week of treatment (Week 8), the itruvone 6.4µg group showed a mean HAM-D-17 score reduction of 17.8, which was statistically greater than the mean reduction in the placebo group of 10.9 points from baseline ($p = 0.02$). Thus, in the itruvone 6.4µg treatment group, the HAM-D-17 score improved significantly from the baseline within one week and this effect was sustained until the Week 8 study endpoint. Notably, both the itruvone 3.2µg and 6.4µg treatment groups showed strong effect sizes after one week of treatment (0.72 for the 3.2µg dose and 1.01 for the 6.4µg dose) and at the Week 8 study endpoint (0.74 for the 3.2µg dose and 0.95 for the 6.4µg dose). There were no reports of SAEs. Itruvone was well-tolerated and did not cause psychological side effects (such as dissociation or hallucinations) or other safety concerns that may be associated with other approved pharmacological therapies for MDD.

More information about the itruvone Phase 2A study in MDD can be found in the peer-reviewed article, "A Placebo Controlled Trial of PH10: Test of a New Rapidly Acting Intranasally Administered Antidepressant," published in the November- December 2019 edition of the British Journal of Pharmaceutical and Medical Research.

About Itruvone (PH10)

Itruvone (PH10) is an investigational pherine nasal spray designed with a potential rapid-onset mechanism of action (MOA) that is fundamentally differentiated from the MOA of all currently approved treatments for depression disorders. Itruvone nasal spray, which is administered at microgram-level doses, is designed to engage and activate chemosensory neurons in the nasal passages connected to neural circuits in the brain that produce antidepressant effects. Specifically, itruvone's proposed MOA involves binding to receptors of chemosensory neurons in the nasal passages that regulate the olfactory-amygdala neural circuits believed to increase the activity of the limbic-hypothalamic sympathetic nervous system and increase the release of catecholamines. Importantly, unlike all currently approved oral antidepressants and rapid-onset ketamine-based therapy (KBT), including both intravenous ketamine and intranasal ketamine, our data show itruvone does not require systemic uptake or brain penetration to produce rapid-onset of antidepressant effects, potentially avoiding side effects and safety concerns associated with KBT and longer acting oral antidepressants.

The FDA has granted Fast Track designation for development of itruvone as a potential treatment for major depressive disorder.

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 and an oral prodrug of 7-Cl-CYNA, which is a full 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 selectively impact key neural circuits in the brain without requiring systemic uptake or direct activity on CNS neurons. 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 developments may differ materially from those projected or implied in these forward-looking statements. Among other things, there can be no guarantee that any of Vistagen's drug candidates will successfully complete 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 itruvone. 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 itruvone and/ or the Company's other product candidates; other risks and uncertainties related to delays in launching, conducting and/or completing ongoing and planned clinical trials; fluctuating costs of materials and other resources required to conduct the Company's ongoing and/or planned clinical and non-clinical trials; that the scope and enforceability of protection provided by patents issued for any of the Company's drug candidates will be sufficient to deter competition; 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 any of the Company's product candidates. Certain of these risks and others 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. You should not place undue reliance on these forward-looking statements, which 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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