Vistagen Announces Positive Data in Fasedienol (PH94B) Phase 3 Open-Label Study in Adults with Social Anxiety Disorder

March 22, 2023

Long-term intranasal administration of fasedienol, used as-needed up to four times a day in daily life, was safe and well-tolerated in nearly 500 patients with social anxiety disorder (SAD)

Patients self-administered over 30,000 doses of fasedienol in real-world settings, with a mean study duration of 4 months, and a maximum study duration of over 10 months

Fasedienol demonstrated clinically meaningful reductions in fear, anxiety and avoidance of anxiety-provoking social and performance situations in daily life, as measured by the Liebowitz Social Anxiety Scale (LSAS), building on LSAS data from a previous placebo-controlled Phase 2 study of fasedienol in SAD

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Mar. 22, 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 positive data from its Phase 3 open-label study designed to evaluate the safety and tolerability of multiple, as-needed intranasal administrations of fasedienol (PH94B) over time in adults with social anxiety disorder (SAD). For the primary endpoint of safety and tolerability (safety population: n=481), the long-term administration of 3.2 µg of fasedienol, up to four times a day, as-needed, was safe and well-tolerated, with no new safety findings or trends identified, regardless of the number of doses administered by each subject. Secondary endpoints in the study included evaluation of the change from baseline on the Liebowitz Social Anxiety Scale (LSAS), which measures SAD patients' response to anxiety-provoking social and performance situations experienced in their daily lives. Analysis of the final data set demonstrates clinically meaningful functional improvement, as measured by the LSAS, and total LSAS scores continued to decline in consecutive months during the study.

The safety and exploratory LSAS results of this Phase 3 open label study build on the safety and LSAS efficacy results from a previous randomized, double-blind, placebo-controlled Phase 2 study of fasedienol in a real-world setting. Results from that study suggested that self-administration of fasedienol on an as-needed basis prior to anxiety-provoking situations 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, in the placebo-controlled Phase 2 study, the amount of separation between fasedienol and placebo at the end of the first 2 weeks on the LSAS was comparable to what was observed after 12 weeks in the registration trials for the three medications currently approved by the FDA for the treatment of SAD, two SSRIs and one SNRI. All prior registration studies for these medications were positive, and all studies used the LSAS as the primary efficacy endpoint.

"The safety profile and potential for fasedienol to achieve overall reduction in symptoms of SAD and improvement in severity of the disorder, as measured by the LSAS, have now been demonstrated in a placebo-controlled Phase 2 study after two weeks of use, as well as in this open-label study over a period of one month and beyond," said Shawn Singh, Chief Executive Officer of Vistagen. "We believe these data suggest that studies involving multiple administrations of fasedienol over time, on an as-needed basis at moments when subjects experience real-life, socially stressful situations, most accurately demonstrate the safety and efficacy potential of fasedienol in patients with SAD and reflect the way we believe fasedienol would be used by SAD patients, if approved. Each SAD patient is unique, and we believe an optimal SAD treatment is one that is individualized and tailored-to-fit by patients, as-needed, to help them engage in the anxiety-provoking situations they encounter in their daily lives with less fear and anxiety."

Study Details

The fasedienol Phase 3 open-label study was designed to evaluate the safety and tolerability of multiple, as-needed intranasal administrations (up to four times a day) of fasedienol in adults with SAD. The study also evaluated the change from baseline in monthly standard clinical measurements and behavioral assessment scales (LSAS, CGI-S, CGI-I and PGI-C) in response to anxiety-provoking social situations in their daily lives after the administration of fasedienol. Safety and tolerability of fasedienol were assessed and summarized during monthly visits from baseline to end of treatment in adverse events (AEs), laboratory values, 12-lead electrocardiograms (ECGs), physical examinations, and vital sign assessments following exposure to fasedienol. The study was closed early due to business reasons. At the time of study closure, study participants had a mean trial exposure of 120 days and a maximum exposure of 320 days.

Safety Results

- The long-term intranasal administration of 3.2 µg of fasedienol, up to four times a day, as-needed, was safe and well-tolerated in adult SAD patients (n=481).
- Of the 481 SAD patients in the study who received at least one dose of fasedienol, at least one treatment-emergent adverse event (TEAE) was reported by 56.8% of subjects, with 54.9% of the 481 patients reporting mild or moderate TEAEs and only 1.9% of patients reporting severe TEAEs.
- Headache was the most common TEAE (17.0%); no other TEAE occurred in more than 5.0% of subjects, except for COVID-19 TEAEs (11.4%), which were not considered related to fasedienol.
- Fourteen patients (2.9%) experienced a TEAE leading to discontinuation from the study.
- Six patients (1.2%) experienced a treatment-emergent serious adverse event, none of which were considered related to

fasedienol.

Exploratory Efficacy Results

Liebowitz Social Anxiety Scale

- At 1 month, mean reduction on the LSAS was 16 points, with 36% experiencing a 20-point or greater reduction (n=385).
- At 2 months, mean reduction on the LSAS was 20 points, with 44% experiencing a 20-point or greater reduction (n=324).
- At 3 months, mean reduction on the LSAS was 24 points, with 55% experiencing a 20-point or greater reduction, and with 36% experiencing a 30-point or greater reduction (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 9 months. The continued improvement in LSAS scores is indicative of the value of multiple, as-needed administrations of fasedienol over time.

Clinician-rated Severity and Improvement

At baseline, half (50.3%) of the 481 SAD patients assessed in the study were rated as “severely ill” or “among the most extremely ill patients” on the Clinician Global Impression – Severity of Illness Scale (CGI-S). After one month, 21.8% of the 385 patients assessed remained in that category. The Clinician Global Impression of Improvement (CGI-I) indicated 28.6% of the 385 patients assessed after one month were “much” or “very much” improved.

Patient-rated Improvement

The Patient Global Impression of Change (PGI-C) indicated 26.8% of the 385 patients assessed after one month considered themselves “much” or “very much” improved. Importantly, the data show good congruence between clinician and patient assessments of improvement. Moreover, both clinician-observed (CGI-I) and patient-rated improvements (PGI-C) support the data shown by the reduction in LSAS scores, indicating that the LSAS is a clinically useful tool for measuring the severity of SAD.

About Fasedienol (PH94B)

Vistagen’s fasedienol (PH94B) is a first-in-class, rapid-onset investigational pherine nasal spray with a novel proposed mechanism of action (MOA) that regulates the olfactory-amygdala neural circuits of fear and anxiety and attenuates the tone of the sympathetic autonomic nervous system, without systemic distribution, potentiation of GABA-A or direct activity on CNS neurons in the brain. Vistagen is developing fasedienol in a Phase 3 program for the treatment of social anxiety disorder. Designed for intranasal administration in low microgram doses, the proposed novel MOA of fasedienol is fundamentally differentiated from all currently approved anti-anxiety medications, including all antidepressants and benzodiazepines.

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. The Company 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 and depression disorders. Several of Vistagen’s product candidates belong to a new class of drugs known as pherines, which are designed with a novel rapid-onset mechanism of action that activates chemosensory neurons in the nasal passages and can beneficially impact key neural circuits without systemic uptake or direct activity on CNS neurons in the brain. Vistagen is passionate about transforming mental health care and redefining what is possible in the treatment of anxiety and depression. 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 the Company’s drug candidates, including fasedienol (PH94B) and/or itruvone (PH10), or any other pherine drug candidate will successfully complete ongoing or future clinical trials, receive regulatory approval or be commercially successful. These risks, along with additional 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. 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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