Vistagen Announces Preliminary Positive Data from Open-Label Extension Portion of PALISADE-4 Phase 3 Study of Fasedienol for the Acute Treatment of Social Anxiety Disorder

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Fasedienol nasal spray was well-tolerated in patients with social anxiety disorder with no new drug-related safety findings after as-needed use for up to 12 months

Clinically relevant improvement in social anxiety over time was observed on both clinician-administered and patient-reported scales over four months

PALISADE-4 OLE data add to growing body of evidence supporting fasedienol's potential to address social anxiety disorder in anxiety-provoking social and performance situations in everyday life

SOUTH SAN FRANCISCO, Calif., Sept. 22, 2026 (GLOBE NEWSWIRE) -- Vistagen (Nasdaq: VTGN), a late clinical-stage biopharmaceutical company leveraging nose-to-brain neurocircuitry to develop and commercialize a new class of intranasal product candidates called pherines, today announced preliminary positive data from the open-label extension (OLE) portion of its PALISADE-4 Phase 3 study of fasedienol for the acute treatment of social anxiety disorder.

In a recent analysis of subjects who elected to participate in the OLE portion of PALISADE-4 (safety population: N=322), administration of 3.2 µg of fasedienol, taken as needed up to six times per day in anxiety-provoking social and performance situations in everyday life for up to 12 months, was well-tolerated with no new drug-related safety findings. Exploratory efficacy data over the first four months of as-needed treatment demonstrated improvement over time on both the Liebowitz Social Anxiety Scale (LSAS) and the Social Phobia Inventory (SPIN).

"These preliminary PALISADE-4 OLE results are important because they reflect the potential impact of repeated, as-needed use of fasedienol in everyday life settings where social anxiety symptoms occur," said Angel S. Angelov, M.D., Chief Medical Officer of Vistagen. "These findings contribute to the deep clinical dataset informing our understanding of fasedienol's potential clinical utility to help patients experience less fear, anxiety, and avoidance in social and performance situations over time."

Preliminary Safety Data

In the OLE portion of PALISADE-4, as of a July 24, 2026 data cut-off[1], fasedienol nasal spray, taken as needed up to six times per day, was well-tolerated in adults with social anxiety disorder.

- The rate of discontinuation due to adverse events was 1.6% (5/322), with no discontinuations attributed to fasedienol.
- More than 95% of treatment-emergent adverse events (TEAEs) were mild or moderate in severity.
- The TEAEs occurring in more than 5% of subjects were headache (18.0%; 58/322), upper respiratory tract infection (9.9%; 32/322), rhinorrhoea (7.1%; 23/322), and oropharyngeal pain (5.3%; 17/322).
- There were no serious adverse events related to fasedienol.
- No safety signals of concern were identified related to laboratory values, ECGs, physical examinations, and vital sign assessments following exposure to fasedienol.

Preliminary Exploratory Efficacy Data

Liebowitz Social Anxiety Scale (LSAS)

The OLE portion of PALISADE-4 explored the change from baseline (study entry) on the LSAS, a clinician-administered scale (range 0-144) which assesses both fear or anxiety and avoidance across 24 standardized anxiety-provoking social-interaction and performance situations, with the goal of capturing not only how distressing situations are, but also whether patients entered, tolerated, remained in, or avoided them. Preliminary analysis of the data cut (July 24, 2026) from the initial four-month period in the OLE portion of PALISADE-4 demonstrated a clinically relevant improvement from repeated as-needed use of fasedienol over time on the LSAS for subjects participating in the OLE[1]:

- At study entry, the mean baseline LSAS score (99.3, n=320) indicated very severe social anxiety (≥95).
- At Month 1, mean improvement on the LSAS was 20.2 points (n=298, 44% had a ≥ 20 point-improvement).
- At Month 2, mean improvement on the LSAS was 24.6 points (n=273, 54% had a ≥ 20 point-improvement).
- At Month 3, mean improvement on the LSAS was 29.1 points (n=240, 60% had a ≥ 20 point-improvement).

- At Month 4, mean improvement on the LSAS was 31.4 points (n=197, 65% had ≥ 20 point-improvement).

Continued improvements were observed through each month on both the fear or anxiety and avoidance subscales of the LSAS, suggesting that participants engaging in everyday life experienced less fear or anxiety and avoidance of anxiety-provoking situations. The mean change in LSAS achieved by month 2 showed a clinically meaningful improvement of two social anxiety disorder severity categories, which was maintained through month 4. The percentage of participants who improved by two social anxiety disorder severity categories also increased steadily over 4 months. Social anxiety disorder severity categories based on the LSAS are defined as: 0-29 minimal (remission, patient does not suffer social anxiety disorder); 30-49 (mild); 50-64 (moderate); 65-79 (marked); 80-94 (severe); ≥95 (very severe)[2].

Social Phobia Inventory (SPIN)

The OLE portion of PALISADE-4 also explored the change from baseline on the SPIN, a 17-item patient-reported scale (range 0-64) which measures fear, avoidance, and physiological components of social phobia over time. The recent preliminary analysis of the initial four-month data cut from the OLE portion of PALISADE-4 demonstrated consistent improvement over time on the SPIN for subjects participating in the OLE:

- At study entry, the mean baseline SPIN score (48.5, n=321) indicated severe social anxiety (≥41).
- At Month 1, mean improvement on the SPIN was 10.5 points (n=299, 45% had a ≥ 10-point improvement).
- At Month 4, mean improvement on the SPIN was 14.9 points (n=199, 59% had a ≥ 10-point improvement).

The Company believes that results from a placebo-controlled Phase 2 crossover study of fasedienol and the open-label extensions of the PALISADE Phase 3 studies conducted to date in everyday life settings suggest that acute treatment with fasedienol, administered as-needed at the patient's discretion, was accompanied by a persistent change in the overall severity of social anxiety disorder, including observed reductions in fear, anxiety, and avoidance as measured by the LSAS over the course of fasedienol usage. The Company is preparing to meet with the FDA during the current quarter to consider a proposed new registrational Phase 3 clinical trial of fasedienol in social anxiety disorder.

About the OLE Portion of PALISADE-4
The OLE portion of PALISADE-4 was a voluntary extension of the randomized, double-blind, placebo-controlled portion of the PALISADE-4 Phase 3 study of fasedienol for the acute treatment of social anxiety disorder, available to participants who chose to continue in the study per the study protocol[1]. It was designed to evaluate the safety and tolerability of multiple, as-needed intranasal administrations of fasedienol (up to six times daily, maximum daily dose of 19.2 µg fasedienol) in adults with social anxiety disorder over time in an everyday life setting. Monthly safety and tolerability assessments included change in adverse events, laboratory values, 12-lead electrocardiograms, physical examinations, and vital sign assessments. The study evaluated change from baseline over time in standard clinical measurements, including the LSAS and SPIN, as participants used fasedienol in anxiety-provoking social and performance situations in their everyday lives. Endpoints of the OLE portion of PALISADE-4 included monthly evaluation of change from baseline at study entry on the LSAS and Month 1 and Month 4 evaluation of change from baseline at study entry on the SPIN patient self-report questionnaire. Both scales provide validated psychological assessments of the severity of social anxiety disorder, with a focus on fear, avoidance, and physiological discomfort in social and performance situations.

About PALISADE-4
PALISADE-4 was a U.S. multi-center, randomized, double-blind, placebo-controlled Phase 3 public speaking challenge study designed to evaluate the efficacy and safety of fasedienol in reducing anxiety symptoms during a simulated single-dose, clinic-based public speaking challenge using the Subjective Units of Distress Scale (SUDS). PALISADE-4 subjects who chose to continue with the OLE portion of the study could use fasedienol as needed in their daily lives up to six times per day for up to 12 months[1].

In June 2026, Vistagen announced topline results from the randomized portion of PALISADE-4. The single-dose randomized portion of the study did not achieve its primary endpoint in the overall study population, as measured by the least squares mean change from baseline on the SUDS for fasedienol compared with placebo. The favorable safety results observed for fasedienol were consistent with those observed in previously completed clinical trials. In a post-hoc analysis of a subpopulation of patients with very severe social anxiety defined by a baseline score at screening of 95 or greater on the Liebowitz Social Anxiety Scale (LSAS) (n=123), fasedienol was nominally statistically significant as measured by the LS mean change from baseline on the SUDS score for fasedienol (-12.8+/-3.4 SE) compared with placebo (-3.7 +/-3.4 SE), with a difference in the LS means of -9.1 (p=0.036).

About Vistagen
Vistagen (Nasdaq: VTGN) is a late clinical-stage biopharmaceutical company leveraging a deep understanding of nose-to-brain neurocircuitry to develop and commercialize a new class of rapid-onset neurocircuitry-focused intranasal product candidates called pherines. Vistagen's pherine product candidates are designed to achieve therapeutic benefits without requiring absorption into the blood or uptake into the brain, giving them the potential to be a safer alternative to other pharmacological options, if successfully developed and approved. Vistagen's most advanced intranasal pherine product candidates are fasedienol for the acute treatment of social anxiety disorder, itruvone for treatment of major depressive disorder, and refisolone for treatment of vasomotor symptoms (hot flashes) due to menopause. Connect at www.vistagen.com

Forward-looking Statements
This press release contains certain forward-looking statements within the meaning of the federal securities laws, including, without limitation, statements regarding indications of improvements observed over time by patients in the OLE portion of PALISADE-4; the ability of preliminary findings from the OLE portion of PALISADE-4 to support potential clinical meaningfulness; indications of safety data from the OLE portion of PALISADE-4; the Company's belief that the results of the PALISADE-4 OLE are consistent with, supportive of, or complementary to previously reported fasedienol clinical data; Vistagen's other beliefs about the understandings drawn from the preliminary OLE data and other fasedienol clinical studies; Vistagen's plans to meet with FDA and the potential regulatory path forward for fasedienol; and Vistagen's belief that its fasedienol development program could support a potential New Drug Application submission to the FDA for the acute treatment of social anxiety disorder. 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. There can be no guarantee that any of Vistagen's product candidates, including fasedienol, will successfully complete ongoing or future clinical trials within estimated timelines or at all, receive regulatory approval, or be commercially successful. Other factors that may cause such a difference include, without limitation, risks and uncertainties relating to conducting and/or completing ongoing and future clinical trials, Vistagen's ability to secure adequate financing or collaborative support for continued clinical development of its product candidates, Vistagen's dependence on third-party collaborators for the development, regulatory approval, and/or commercialization of its product candidates and other aspects of its business, the scope and enforceability of Vistagen's patents, including patents related to its pherine product candidates, and other technical and unexpected hurdles in the development, manufacture and/or potential commercialization of Vistagen's product candidates. These risks and others are more fully discussed in the section entitled "Risk Factors" in Vistagen's most recent Quarterly Report on Form 10-Q for the period ended June 30, 2026, as well as discussions of potential risks, uncertainties, and other important factors in Vistagen's other filings with the U.S. Securities and Exchange Commission (SEC). Vistagen'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 Vistagen's views as of any subsequent date. Vistagen explicitly disclaims any obligation to update any forward-looking statements other than as may be required by law. If Vistagen does update one or more forward-looking statements, no inference should be made that Vistagen will make additional updates with respect to those or other forward-looking statements.

[1] As previously reported, the Company believes its clinical program for fasedienol nasal spray for the acute treatment of social anxiety disorder has achieved the minimum patient exposures as recommended under ICH E1, the international regulatory standard governing safety database exposure recommendations for drugs intended for long-term treatment (chronic or repeated intermittent use for longer than 6 months) of non-life-threatening conditions. As a result, for business reasons, the Company closed the OLE portion of PALISADE-4 in July 2026, prior to the data cut. Accordingly, at the time of study closure, not all participants in the study had the opportunity to reach the four-month observation point.

[2] Liebowitz MR. Social Phobia. In Klein DF, (Ed). Anxiety: S.Karger AG 1987:141–173.

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