VistaGen Reports Positive Preclinical Data Differentiating Mechanism of Action of PH94B from Risk-Ridden Benzodiazepines

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New electrophysiological data demonstrate that PH94B does not directly modulate GABA (gamma aminobutyric acid) receptors

SOUTH SAN FRANCISCO, Calif., Nov. 12, 2020 /PRNewswire/ -- VistaGen Therapeutics (NASDAQ: VTGN), a biopharmaceutical company developing new generation medicines for anxiety, depression and other central nervous system (CNS) disorders, today announced new *in vitro* electrophysiology data demonstrating that the mechanism of action of PH94B, the intranasal neuroactive steroid the Company is preparing for Phase 3 development as a potential acute rapid-onset treatment of anxiety in adults with social anxiety disorder, does not involve direct activation of GABA-A receptors, in distinct contrast to the mechanism of action of benzodiazepines ("benzos"), which act as direct positive modulators of GABA-A receptors.

"We are very pleased with the results of these studies that suggest PH94B's mechanism of action may not have benzodiazepine-like side effects, such as sedation and cognitive impairment, or abuse liability," stated Shawn K. Singh, Chief Executive Officer of VistaGen. "While benzodiazepines provide relief for many Americans struggling with anxiety, their extremely risky safety profile does not lend itself to long term use. The mechanism of action contributes to the safety profile. As we have seen in Phase 2 clinical studies, while PH94B is able to produce rapid-onset benzo-like, anti-anxiety effects, this study demonstrates that PH94B does not have a benzo-like mechanism of action. As we approach Phase 3 development of PH94B, especially given the FDA's recent public announcement about safety concerns associated with benzo use, these new data make us even more excited about PH94B's potential to change lives without the risky side effects and safety concerns of benzos."

Recently, the U.S. Food and Drug Administration (FDA) released a Drug Safety Communication (DSC) detailing the risks associated with use of benzodiazepines, a class of drugs commonly prescribed for treatment of anxiety disorders and other conditions. According to the FDA communication, 92 million benzodiazepine prescriptions were filled in 2019. The FDA's DSC detailed safety concerns regarding the serious risks of abuse, addiction, physical dependence, and withdrawal reactions linked to long-term use of benzodiazepines, and the FDA announced that it is requiring an updated Boxed Warning, the FDA's most prominent type of safety warning, for all benzodiazepine medications.

"We thought it was important to conduct a study to help differentiate the mechanism of action of PH94B from that of benzodiazepines, therefore, we contracted with EuroFins Discovery to determine whether PH94B has positive modulatory effects on GABA receptors using *in vitro* patch clamp electrophysiology," noted Mark A. Smith, M.D., Ph.D., Chief Medical Officer of VistaGen. "Benzodiazepines such as alprazolam and diazepam mediate their anti-anxiety effects by acting as positive modulators at GABA receptors to make them more responsive to GABA and thereby increase inhibitory neuronal activity in the brain. PH94B had no agonist or antagonist effects on GABA receptors. While PH94B may regulate endogenous GABA circuits in the brain, it does not appear to directly bind to or modulate GABA receptors at concentrations <10mM, which differentiates its mechanism of action from benzodiazepines."

These studies are significant because they indicate that PH94B has no relevant benzodiazepine-like activity. With widespread anxiety-provoking stressors related to the COVID-19 pandemic, civil unrest, election results, the economy, and distance learning during 2020, the number of individuals facing anxiety disorders is rising and a safer treatment alternative to benzodiazepines is imperative. PH94B may have the potential to displace benzodiazepines and become the safer alternative in the drug treatment paradigm for anxiety disorders.

About PH94B

PH94B is an innovative odorless synthetic neuroactive steroid nasal spray with therapeutic potential in a wide range of mental health disorders involving anxiety or phobia. Self-administered in microgram-level doses, PH94B produces rapid onset (within approximately 15 minutes) anti-anxiety effects and does not require systemic uptake and distribution to generate these effects.

VistaGen is currently preparing PH94B for pivotal Phase 3 development as a potential acute treatment of anxiety in adults with Social Anxiety Disorder (SAD). The FDA has granted Fast Track designation for development of PH94B for this indication, believed to be the first such designation by the FDA for a drug candidate for SAD.

With its rapid-onset pharmacology, lack of systemic exposure and sedation, and its excellent safety profile in all studies to date, we believe PH94B has potential to provide a safe alternative to benzodiazepines and other pharmacological alternatives in the drug treatment paradigm for anxiety disorders. View more background information on SAD and a video on PH94B's mechanism of action.

About VistaGen
VistaGen Therapeutics is a clinical-stage biopharmaceutical company developing and commercializing differentiated new generation medicines that go beyond the current standard of care for anxiety, depression and other CNS disorders. Each of VistaGen's three drug candidates has a differentiated mechanism of action, an exceptional safety profile in all studies to date, and therapeutic potential in multiple CNS markets. For more information, please visit www.vistagen.com and connect with VistaGen on Twitter, LinkedIn and Facebook.

Forward Looking Statements

Various statements in this release are "forward-looking statements" concerning VistaGen's future expectations, plans and prospects, including the potential for successful Phase 3 development of PH94B. These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties which could cause actual results to differ materially from those contemplated in these forward-looking statements, including the risks that: development and approval of PH94B may not be achieved in any market; the FDA may decide that the results of the Company's PH94B Phase 3 clinical program are not sufficient for regulatory approval for acute treatment of anxiety in adult patients with SAD or any other anxiety-related disorder; development of PH94B may not be successful in any indication; success in nonclinical studies or in earlier-stage clinical trials may not be repeated or observed in future studies which may not support further development or be sufficient to gain regulatory approval to market PH94B; adverse events may be encountered at any stage of development that negatively impact further development. Other risks and uncertainties include, but are not limited to, issues related to: adverse healthcare reforms and changes of laws and regulations; general industry and market conditions; manufacturing and marketing risks, which may include, but are not limited to, unavailability of or delays in delivery of raw materials for manufacture of PH94B; inadequate and/or untimely supply of PH94B to meet demand; entry of competitive products; and other technical and unexpected hurdles in the development, manufacture and commercialization of PH94B, as well as those risks more fully discussed in the section entitled "Risk Factors" in VistaGen's most recent Annual Report on Form 10-K for the year ended March 31, 2020, as well as discussions of potential risks, uncertainties, and other important factors in either company's other filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent the Company's views only as of today and should not be relied upon as representing its views as of any subsequent date. The Company explicitly disclaims any obligation to update any forward-looking statements.

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