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VistaGen Announces First Patient Dosed in NIH-Sponsored Phase 2A Study of Orally Available AV-101 in Major Depressive Disorder

SAN FRANCISCO, Nov. 3, 2015 /PRNewswire/ -- VistaGen Therapeutics, Inc. (OTCQB: VSTA), a clinical-stage biopharmaceutical company committed to developing and commercializing novel medicines to treat depression, cancer and diseases and disorders involving the central nervous system (CNS), today announced that the first patient has been dosed in a Phase 2A study of its orally available AV-101 in adult patients with treatment-resistant Major Depressive Disorder (MDD). The study is being fully funded by the U.S. National Institutes of Health (NIH), and is being conducted at the U.S. National Institutes of Mental Health (NIMH), under the direction of Principal Investigator, Carlos Zarate, Jr., M.D. Dr. Zarate is Chief, Section on the Neurobiology and Treatment of Mood Disorders and Chief of Experimental Therapeutics and Pathophysiology Branch (ETPB) at the NIMH, and Clinical Professor of Psychiatry and Behavioral Sciences at The George Washington University. VistaGen received clearance from the U.S. Food and Drug Administration (FDA) and the NIH to initiate the study in July 2015, after entering into a Cooperative Research and Development Agreement (CRADA) with the NIMH in February 2015.

"We are pleased to have achieved this important milestone, notably advancing our AV-101 clinical development program, and we look forward to working closely with the esteemed leadership team at the NIMH," stated Shawn Singh, Chief Executive Officer of VistaGen. "We believe that AV-101's differentiated mechanism of action, oral availability, strong preclinical efficacy and excellent clinical safety profile support AV-101 as a potentially transformative treatment for millions of patients with MDD who are inadequately served by standard antidepressant therapies."

The single-site (NIH) Phase 2A study, expected to enroll between 24 and 28 adult patients with treatment resistant MDD, is a randomized, double-blind, placebo-controlled, crossover trial designed to evaluate the efficacy and safety of a single oral dose of AV-101 administered once daily for 14 days. Efficacy and safety will be evaluated using the standard Hamilton Depression Rating Scale (HDRS-17) and other widely-accepted measures of mood and depression. Top-line data is expected in the first half of 2017.

About AV-101

AV-101 is an orally available, prodrug candidate that readily gains access to the central

nervous system (CNS) after systemic administration and is rapidly converted in the brain by astrocytes into its active metabolite, 7-chlorokynurenic acid (7-Cl-KYNA), a well-characterized, potent, and highly-selective antagonist of the glycine-binding co-agonist (GlyB) site of the N-methyl-D-aspartate receptor (NMDAR). Current evidence suggests that AV-101's antagonism of NMDAR signaling may provide fast-acting antidepressant effects in the treatment of MDD. Preclinical peer-reviewed data published in the October 2015 *Journal of Pharmacology and Experimental Therapeutics* showed rapid, dose-dependent and persistent ketamine-like antidepressant effects, without the negative side effects seen with ketamine, and other channel-blocking NMDAR antagonists. In addition, as confirmed in two Phase 1 clinical studies, using AV-101 to target the GlyB site of the NMDAR may bypass potential adverse effects that occur with ketamine, while activating similar therapeutic pathways resulting in the "glutamate surge" that has been associated with increased neurogenesis and the rapid-acting antidepressant effects of ketamine observed in previous clinical studies.

About MDD

While most people will experience episodic depressed mood at multiple points during their life, MDD is different. MDD is the chronic, pervasive feeling of utter unhappiness, hopelessness and suffering, which impairs daily functioning. Symptoms of MDD include diminished pleasure in activities, changes in appetite that result in weight changes, insomnia or oversleeping, psychomotor agitation, loss of energy or increased fatigue, feelings of worthlessness or inappropriate guilt, difficulty thinking, concentrating or making decisions, and thoughts of death and attempts at suicide. Suicide is estimated to be the cause of death in up to 15% of individuals with MDD. MDD is one of the most common mental disorders in the United States. According to the NIMH, about 6.7% of U.S adults experience MDD each year.

About VistaGen Therapeutics

VistaGen Therapeutics, Inc. (OTCQB: VSTA) is a clinical-stage biopharmaceutical company committed to developing and commercializing novel medicines to treat depression, cancer and diseases and disorders involving the central nervous system (CNS). VistaGen's AV-101 is a new generation orally-available NMDAR GlyB antagonist in Phase 2 clinical development for the adjunctive treatment of Major Depressive Disorder in patients with an inadequate response to standard antidepressant therapies. Based on preclinical studies, AV-101 may also have potential as a treatment for other CNS-related conditions, including chronic neuropathic pain and epilepsy, as well as neurodegenerative diseases such as Parkinson's disease and Huntington's disease. VistaGen is also using its pluripotent stem cell technology platform for potential commercial applications focused on producing proprietary new chemical entities (NCEs) through drug rescue and regenerative therapies for diseases and conditions related to blood, cartilage, heart and liver cells. For additional information, please visit www.VistaGen.com.

Cautionary Statement Regarding Forward-Looking Statements

The statements in this press release that are not historical facts may constitute forward-looking statements that are based on current expectations and are subject to risks and uncertainties that could cause actual future results to differ materially from those expressed or implied by such statements. Those risks and uncertainties include, but are not limited to, risks related to the VistaGen's successful Phase 2 clinical development of AV-101 in MDD,

its drug rescue activities, protection of its intellectual property, and the availability of substantial additional capital to support its operations, including the foregoing activities. These and other risks and uncertainties are identified and described in more detail in VistaGen's filings with the Securities and Exchange Commission (SEC). These filings are available on the SEC's website at www.sec.gov. VistaGen undertakes no obligation to publicly update or revise any forward-looking statements.

To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/vistagen-announces-first-patient-dosed-in-nih-sponsored-phase-2a-study-of-orally-available-av-101-in-major-depressive-disorder-300171042.html

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