VistaGen Therapeutics Initiates Phase 2 Study of AV-101 for Major Depressive Disorder

April 5, 2018

SOUTH SAN FRANCISCO, CA -- (Marketwired) -- 04/05/18 -- VistaGen Therapeutics, Inc. (NASDAQ: VTGN), a clinical-stage biopharmaceutical company developing new generation medicines for depression and other central nervous system (CNS) disorders, today announced the initiation of ELEVATE, the Company's double-blind, placebo-controlled Phase 2 clinical study to evaluate the efficacy and safety of AV-101 (L-4-chlorokynurenine) as an adjunctive treatment of Major Depressive Disorder (MDD) in patients with an inadequate response to current antidepressants approved by the U.S. Food and Drug Administration (FDA).

AV-101, an oral N-methyl-D-aspartate (NMDA) receptor glycine B (GlyB) antagonist, belongs to a new generation of investigational medicines in neuropsychiatry known as glutamate receptor modulators having the potential to treat MDD faster than current FDA-approved antidepressants commonly known as SSRIs and SNRIs, which target the neurotransmitters serotonin and/or norepinephrine, respectively.

"Major Depressive Disorder is one of the most common diseases affecting the U.S. population and many patients who suffer from it do not respond adequately to currently available treatments," said Professor Maurizio Fava, M.D., Executive Vice Chair, Department of Psychiatry, Massachusetts General Hospital (MGH) and Associate Dean for Clinical & Translational Research, Harvard Medical School. "This is an important clinical study given the properties of AV-101. By studying AV-101, with its ability to be orally available and to inhibit glutamatergic NMDA receptor activity through GlyB site binding, we hope to improve clinical outcomes in depressed patients with an inadequate response to standard antidepressant therapies."

"AV-101 has shown very promising results in preclinical antidepressant models, with ketamine-like efficacy, but none of ketamine's side effects," [1] said Mark A. Smith, M.D., Ph.D., Chief Medical Officer of VistaGen Therapeutics. "Building on excellent safety data from our Phase 1 clinical program in which AV-101 was well-tolerated, with no psychotomimetic or hallucinogenic side effects observed, we now have the opportunity in our ELEVATE study to determine whether the exciting preclinical efficacy will translate into beneficial effects for patients with MDD and provide a safe and effective alternative to existing adjunctive treatments for MDD, including atypical antipsychotics, which have numerous potential side effects and safety concerns."

About ELEVATE

ELEVATEis a Phase 2, randomized, double-blind, multi-center, placebo-controlled clinical trial designed to examine the efficacy and safety of adjunctive use of oral AV-101 for MDD in patients with an inadequate response to standard antidepressant therapy with either an FDA-approved selective serotonin reuptake inhibitor (SSRI) or serotonin norepinephrine reuptake inhibitor (SNRI). Approximately 180 patients will be randomized to receive either AV-101 or placebo, orally, once daily, in conjunction with their ongoing antidepressant, for fourteen days. The primary endpoint of the study is the change from baseline as measured by the Montgomery-Asberg Depression Rating Scale (MADRS). Dr. Maurizio Fava of Massachusetts General Hospital and Harvard Medical School is the Principal Investigator of the study. Top-line results are expected in the first half of 2019.

About Major Depressive Disorder (MDD)

MDD is a serious biologically-based mood disorder, affecting approximately 16 million adults in the United States.[2] Individuals with MDD exhibit depressive symptoms, such as a depressed mood or a loss of interest or pleasure in daily activities, for more than a two-week period, as well as impaired social, occupational, educational or other important functioning which has a negative impact on their quality of life. About one in eight Americans aged 12 and over takes an FDA-approved antidepressant.[3] While current FDA-approved antidepressants are widely used, about two-thirds of patients with MDD do not respond to their initial antidepressant treatment.[4] Inadequate response to current antidepressants is among the key reasons MDD is one of the leading public health concerns in the United States, creating a significant unmet medical need for new agents with fundamentally different mechanisms of action.

About AV-101

AV-101 is an oral N-methyl-D-aspartate (NMDA) receptor glycine B (GlyB) antagonist in Phase 2 clinical development in the United States, initially as a new adjunctive treatment of MDD in patients with an inadequate response to current FDA-approved antidepressants. AV-101 has a novel mechanism of action (MOA), meaning its MOA is fundamentally different from all current FDA-approved treatments for depression. Most current FDA-approved antidepressants, commonly known as SSRIs and SNRIs, target the neurotransmitters serotonin and/or norepinephrine, respectively. If effective, SSRIs and SNRIs take many weeks to achieve therapeutic benefits. AV-101 targets glutamate, the most prevalent neurotransmitter in the brain. Similar to intravenous ketamine, an NMDA receptor antagonist which blocks activity of the NMDA receptor causing psychotomimetic side effects and safety concerns, AV-101 inhibits NMDA receptor activity and has the potential to achieve ketamine-like antidepressant effects, but with oral administration and without ketamine's side effects and safety concerns. AV-101 may also have the potential to treat neuropathic pain, epilepsy, Parkinson's disease levodopa-induced dyskinesia, suicidal ideation and other CNS diseases and disorders where modulation of the NMDA receptors and activation of AMPA pathways may achieve therapeutic benefits.

About VistaGen

VistaGen Therapeutics, Inc. (NASDAQ: VTGN) is a clinical-stage biopharmaceutical company developing new generation medicines for depression and other CNS disorders. VistaGen's lead CNS product candidate, AV-101, is an oral NMDA receptor GlyB antagonist in Phase 2 clinical development in the United States, initially as a new adjunctive treatment of MDD in patients with an inadequate response to current FDA-approved antidepressants. The FDA has granted Fast Track designation to AV-101 for development as a potential adjunctive treatment of MDD.

[1] Zanos, P., et al. (2015) "The Prodrug 4-Chlorokynurenine Causes Ketamine-Like Antidepressant Effects, but Not Side Effects, by NMDA/GlycineB-Site Inhibition." J Pharmacol Exp Ther 355:76-85

[2] Nat. Inst. of Mental Health website, 2017; Available at https://www.nimh.nih.gov/health/statistics/major-depression.shtml.

[3] Pratt LA, Brody DJ, Gu Q. Antidepressant use among persons aged 12 and over: United States, 2011-2014. NCHS data brief, no 283 (2017). www.cdc.gov/nchs/products/databriefs/db283.htm

[4] Rush AJ, et al. Am J. Psychiatry. 2006, 163(11): 1905-1917 (STAR*D Study)

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 concerning VistaGen's future expectations, plans and prospects, including without limitation, our expectations regarding development of AV-101, the potential of AV-101 for the treatment of MDD and various other CNS diseases and disorders and the expected timing of data from the ELEVATE study constitute forward-looking statements for the purposes of the safe harbor provisions under the Private Securities Litigation Reform Act of 1995. These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those contemplated in these forward-looking statements. Among these risks is the possibility that we may encounter unexpected adverse events in patients in the ELEVATE study that cause us to discontinue further development of AV-101; we may not be able to successfully demonstrate the safety and efficacy of AV-101 at each stage of clinical development; success in preclinical studies or in early-stage clinical trials may not be repeated or observed in ongoing or future AV-101 studies, and ongoing or future preclinical and clinical results may not support further development of AV-101 or be sufficient to gain regulatory approval to market AV-101; decisions or actions of regulatory agencies may negatively affect the progress of the ELEVATE study or the initiation, timing and progress of future AV-101 clinical trials, and our ability to proceed with further clinical studies or to obtain marketing approval; we may not be able to obtain or maintain adequate intellectual property protection and other forms of marketing and data exclusivity for AV-101; we may not have access or be able to secure substantial additional capital to support our operations, including clinical development of AV-101 activities described above; and we may encounter technical and other unexpected hurdles in the manufacturing and development of AV-101 or other product candidates, as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent annual report on Form 10-K, and subsequent quarterly reports on Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in our filings with the Securities and Exchange Commission (SEC), including the availability of substantial additional capital to support our operations, including the AV-101 clinical development activities described above. Our SEC filings are available on the SEC's website at www.sec.gov. In addition, any forward-looking statements represent our views only as of today, and should not be relied upon as representing our views as of any subsequent date. We explicitly disclaim any obligation to update any forward-looking statements.

Company Contact
Mark A. McPartland
VistaGen Therapeutics Inc.
Phone: +1 (650) 577-3600
Email: IR@vistagen.com

Investor Contact:
Valter Pinto / Allison Soss
KCSA Strategic Communications
Phone: +1 (212) 896-1254/+1 (212) 896-1267
Email: VistaGen@KCSA.com

Source: VistaGen Therapeutics, Inc.

Released April 5, 2018