VistaGen Announces Peer-Reviewed Publication in the Scandinavian Journal of Pain Highlighting Orally-Available AV-101's Excellent Safety Profile and Potential as a Non-Opioid Treatment for Neuropathic Pain

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SOUTH SAN FRANCISCO, CA -- (Marketwired) -- 06/22/17 -- VistaGen Therapeutics Inc. (NASDAQ: VTGN), a clinical-stage biopharmaceutical company focused on developing new generation medicines for depression and other central nervous system (CNS) disorders, announced today a peer-reviewed publication in the *Scandinavian Journal of Pain* of two Phase 1 clinical studies of the effects of AV-101 (4-Cl-KYN), the Company's CNS prodrug candidate, as a potential non-opioid treatment for neuropathic pain. Safety data from both the single and multi-dose Phase 1 studies indicated that oral AV-101 was extremely safe and well tolerated, with no meaningful difference in adverse events (AEs) at any dose between AV-101 and placebo. Recently published statistically-significant positive results in four well-established preclinical models of pain associated with tissue inflammation and nerve injury, together with the excellent clinical safety profile, pharmacokinetic (PK) characteristics and consistent reductions in three pain measures (allodynia, mechanical and heat hyperalgesia) demonstrated by these studies, support future Phase 2 clinical studies of AV-101 as a potential new non-opioid treatment alternative for neuropathic pain.

The publication, titled "Randomized, Double-Blind, Placebo Controlled, Dose-Escalation Study: Investigation of the Safety, Pharmacokinetics, and Antihyperalgesic Activity of L-4 chlorokynurenine in Healthy Volunteers," by lead author, Mark Wallace, MD, and co-authors, Alexander White, MD, Kathy A Grako, PhD, Randal Lane, Allen (Jo) Cato, PhD and H. Ralph Snodgrass, PhD, was recently published in the *Scandinavian Journal of Pain* (DOI: 10.1016/j.sjpain.2017.05.004) and is available online at http://www.scandinavianjournalpain.com/article/S1877-8860(17)30128-3/fulltext.

"The excellent safety data and consistent reductions in allodynia pain and mechanical and heat hyperalgesia during the two Phase 1 clinical studies of AV-101 support our belief in its potential to treat neuropathic pain without the negative side-effects experienced with most of the drugs used today to treat pain. Additional clinical trials of AV-101 in neuropathic pain are warranted," reported Mark Wallace, MD, Distinguished Professor of Clinical Anesthesiology at the University of California, San Diego.

"The positive results published in these studies further support our belief that AV-101 has the potential to reduce pain effectively and safely, without causing burdensome side effects like gabapentin and many other neuropathic pain treatments, such as opiates, on the market today. The opioid epidemic, which stems in part from prescribing opiate analgesics for outpatient procedures, makes it imperative that we find new analgesics devoid of abuse potential. Importantly, AV-101 does not bind to opioid receptors, and yet may still have efficacy in neuropathic pain," stated Mark A. Smith, MD, PhD, Chief Medical Officer, VistaGen Therapeutics. "Additionally, a key observation from these Phase 1 studies in normal volunteers was spontaneous reports of 'feelings of well-being' in subjects exposed to AV-101, especially those in the highest dose group of 1440 mg, while none of the subjects on placebo reported any such feelings. Importantly, these feelings were *NOT* characterized as feeling intoxicated or psychotic as has been often reported by subjects taking ketamine for major depressive disorder. We are optimistic about AV-101's potential as a new treatment alternative for major depressive disorder, without ketamine-like side effects, and for neuropathic pain, without gabapentin-like side effects or opioid abuse potential."

Study Summary and Key Findings:

Two Phase 1 Clinical Studies -

- In a Phase 1A clinical study, AV-101 (4-Cl-KYN) prodrug was orally administered to healthy volunteers to examine safety and tolerability over a wide dose range.
- All doses of AV-101 were very well tolerated with no serious adverse effects; the side effects experienced were mild and indistinguishable from placebo.
- In agreement with the FDA, dose escalation in the Phase 1A study was stopped based on pharmacokinetics (PK) levels of one subject; the maximum tolerated dose was not achieved in this study.
- Excellent safety in the initial single-dose study results of six different doses of AV-101 supported the advancement into a follow-up Phase 1B multiple-dose study.
- In a Phase 1B clinical study, 50 healthy volunteers were administered either AV-101 or placebo for two consecutive weeks to examine the safety and tolerability of the orally available drug candidate in three different doses.
- Consistent with the Phase 1A study, all three doses of AV-101 were very well tolerated with no serious adverse events.
- Oral AV-101 had good PK characteristics with mean half-life of 1.7 hours.
- In the capsaicin-induced pain model, although not statistically significant, there were consistent reductions in three pain measures (allodynia, mechanical and heat hyperalgesia).
- Recently published statistically-significant positive results in four well-established preclinical models of pain associated with tissue inflammation and nerve injury, together with the excellent clinical safety profile, pharmacokinetic (PK) characteristics and consistent reductions in three pain measures (allodynia, mechanical and heat hyperalgesia) demonstrated by these studies, support future Phase 2 clinical studies of AV-101 as a potential new non-opioid treatment alternative for neuropathic pain.

About AV-101
AV-101 (4-CI-KYN) is an oral CNS prodrug candidate in Phase 2 development in the U.S., initially as a new generation treatment for major depressive disorder (MDD). AV-101 also has broad potential utility in several other CNS indications where modulation of NMDA receptors, activation of AMPA pathways and/or key active metabolites of AV-101 may achieve therapeutic benefit, including neuropathic pain and epilepsy, as well as addressing symptoms associated with neurodegenerative diseases, such as Parkinson's disease and Huntington's disease.

AV-101 is currently being evaluated in a Phase 2 monotherapy study in MDD, a study being fully funded by the U.S. National Institute of Mental Health (NIMH) and conducted by Dr. Carlos Zarate Jr., Chief, Section on the Neurobiology and Treatment of Mood Disorders and Chief of Experimental Therapeutics and Pathophysiology Branch at the NIMH, as Principal Investigator.

VistaGen is preparing to advance AV-101 into a 180-patient, U.S. multi-center, Phase 2 adjunctive treatment study in MDD patients with an inadequate response to standard FDA-approved antidepressants, with Dr. Maurizio Fava of Harvard University as Principal Investigator.

About VistaGen
VistaGen Therapeutics, Inc. (NASDAQ: VTGN), is a clinical-stage biopharmaceutical company focused on developing new generation medicines for depression and other central nervous system (CNS) disorders. VistaGen's lead CNS product candidate, AV-101, is in Phase 2 development, initially as a new generation oral antidepressant drug candidate for major depressive disorder (MDD). AV-101's mechanism of action is fundamentally differentiated from all FDA-approved antidepressants and atypical antipsychotics used adjunctively to treat MDD, with potential to drive a paradigm shift towards a new generation of safer and faster-acting antidepressants. AV-101 is currently being evaluated by the U.S. National Institute of Mental Health (NIMH) in a Phase 2 monotherapy study in MDD being fully funded by the NIMH and conducted by Dr. Carlos Zarate Jr., Chief, Section on the Neurobiology and Treatment of Mood Disorders and Chief of Experimental Therapeutics and Pathophysiology Branch at the NIMH. VistaGen is preparing to launch a 180-patient Phase 2 study of AV-101 as an adjunctive treatment for MDD patients with inadequate response to standard, FDA-approved antidepressants. Dr. Maurizio Fava of Harvard University will be the Principal Investigator of the Company's Phase 2 adjunctive treatment study. AV-101 may also have the potential to treat multiple CNS disorders and neurodegenerative diseases in addition to MDD, including chronic neuropathic pain, epilepsy, Huntington's disease, and L-Dopa-induced dyskinesias associated with Parkinson's disease and, other disorders where modulation of NMDA receptors, activation of AMPA pathways and/or key active metabolites of AV-101 may achieve therapeutic benefit.

VistaStem Therapeutics is VistaGen's wholly owned subsidiary focused on applying human pluripotent stem cell technology, internally and with collaborators, to discover, rescue, develop and commercialize proprietary new chemical entities (NCEs), including small molecule NCEs with regenerative potential, for CNS and other diseases, and cellular therapies involving stem cell-derived blood, cartilage, heart and liver cells. In December 2016, VistaGen exclusively sublicensed to BlueRock Therapeutics LP, a next generation regenerative medicine company established by Bayer AG and Versant Ventures, rights to certain proprietary technologies relating to the production of cardiac stem cells for the treatment of heart disease.

For more information, please visit www.vistagen.com and connect with VistaGen on Twitter, LinkedIn and Facebook.

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 successful launch, continuation and results of the NIMH's Phase 2 (monotherapy) and/or the Company's planned Phase 2 (adjunctive therapy) clinical studies of AV-101 in MDD, and other CNS diseases and disorders, including neuropathic pain and L-DOPA-induced dyskinesia associated with Parkinson's disease, protection of its intellectual property, and the availability of substantial additional capital to support its operations, including the Phase 2 clinical development activities described above. 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.

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