
SOUTH SAN FRANCISCO, CA -- (Marketwired) -- 04/27/17 -- 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 the peer-reviewed publication of nonclinical studies of the effects of AV-101 (4-Cl-KYN), its CNS prodrug candidate, in four well-established nonclinical models of pain.

The publication, titled: "Characterization of the effects of L-4-chlorokynurenine on nociception in rodents," by lead author, Tony L. Yaksh, Ph.D., Professor in Anesthesiology at the University of California, San Diego (UCSD), and co-authors, Robert Schwarcz, Ph.D., Professor of Psychiatry and Pharmacology, University of Maryland School of Medicine, and H. Ralph Snodgrass, Ph.D., President and Chief Scientific Officer of VistaGen Therapeutics, was recently published in The Journal of Pain (DOI: 10.1016/j.jpain.2017.03.014) and is available online at http://www.jpain.org/article/S1526-5900(17)30552-7/abstract.

"In these studies, AV-101 was found to have robust anti-nociceptive effects, similar to gabapentin, but with a better side effect profile in several pre-clinical models of hyperalgesia and allodynia, results suggest AV-101's potential for treating multiple hyperpathic pain states," reported Tony L. Yaksh, Ph.D., Professor in Anesthesiology at the University of California, San Diego (UCSD).

"In comparison to gabapentin and other agents commonly used by millions of patients battling chronic neuropathic pain, we believe AV-101 has the potential to reduce debilitating pain effectively without causing burdensome side effects. Many neuropathic pain treatments on the market today have side effects, including anxiety, depression, mild cognitive impairment and sedation. The positive results published in these studies fall in line with our goal of advancing Phase 2 clinical development of AV-101 across a broad range of CNS indications, including major depressive disorder, neuropathic pain and L-DOPA-induced dyskinesia associated with Parkinson's disease. We are optimistic that we will be able to bring to market a new generation CNS medication that would help millions
of patients currently treated with therapies with inadequate efficacy and significant side
effects and safety concerns," stated H. Ralph Snodgrass, Ph.D., VistaGen's President and
Chief Scientific Officer.

**Study Summary and Key Findings:**

- AV-101 (4-Cl-KYN) prodrug was systematically administered in four rat models of
  pain to examine its analgesic and behavioral profile. There were dose-dependent
  anti-hyperalgesia effects in the four models of pain.
- Systemic delivery of AV-101 yielded brain concentrations of AV-101’s active
  metabolite, 7-Cl-KYNA. The high CNS levels of 7-Cl-KYNA were calculated to
  exceed its IC50 at the NMDA receptor GlyB site and resulted in dose-dependent
  anti-hyperplasia in the four models of facilitated processing associated with tissue
  inflammation and nerve injury.
- Contrary to the control drugs tested (gabapentin and MK-801), AV-101 had no
  discernable negative side-effects.
- Compared to the control drugs tested, AV-101 has robust anti-nociceptive effects
  with a better side effect profile, highlighting its potential for treating hyperpathic pain
  states.
- Relevance for potential additional Phase 2a clinical development:
  - Gabapentin, a commonly used drug for chronic pain, causes sedation and mild
    cognitive impairment. So, a drug that is equally effective on pain, but is better
    tolerated than gabapentin, could be quite important for the management of
    chronic neuropathic pain.
  - Study results demonstrate AV-101’s potential to counter high sensitivity to
    neuropathic pain in a manner similar to gabapentin, but without its side effects.
  - Conclusion: The study results, taken together with VistaGen's successful AV-
    101 Phase 1a and 1b clinical safety studies, support investment in an AV-101
    Phase 2a clinical study to assess efficacy and safety of AV-101 as a new
    generation treatment alternative to gabapentin for patients suffering from
    neuropathic pain.

**About AV-101**

AV-101 (4-Cl-KYN) is an oral CNS prodrug candidate in Phase 2 development in the U.S.
as a new generation treatment for major depressive disorder (MDD). AV-101 also has
broad potential utility in several other CNS disorders, including chronic 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 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, and symptoms of Parkinson's disease and Huntington's disease, where modulation of the NMDAR, AMPA pathway 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](http://www.vistagen.com) and connect with VistaGen on [Twitter](http://twitter.com), [LinkedIn](http://linkedin.com) and [Facebook](http://facebook.com).

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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