Vistagen Receives U.S. Patent for AV-101 to Treat Neuropathic Pain

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SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Feb. 5, 2025-- Vistagen (Nasdaq: VTGN), a clinical-stage biopharmaceutical company pioneering neuroscience to deliver groundbreaking therapies for individuals affected by psychiatric and neurological disorders, today announced that the U.S. Patent and Trademark Office (USPTO) granted a patent to the Company for its oral non-opioid product candidate, AV-101, for the treatment of neuropathic pain. The patent will not expire until at least 2034 and is part of Vistagen's global patent portfolio on manufacturing methods and therapeutic uses for AV-101 to treat various disorders involving the NMDA receptor.

"This new patent advances our AV-101 portfolio and significantly strengthens our position for potential collaborative development and commercialization of this clinical-stage product candidate," stated Shawn Singh, President and Chief Executive Officer of Vistagen. "We look forward to identifying potential partnering opportunities for AV-101 as a non-opioid alternative for pain, as well as dyskinesias and other neurological disorders."

Preclinical data previously published in the peer-reviewed journal, *The Journal of Pain,*[1] demonstrate robust antinociceptive effects of AV-101, similar to gabapentin, but with a better side effect profile in several preclinical models of hyperalgesia and allodynia. Compared to the control drugs tested (gabapentin and MK-801), AV-101 has similar robust anti-nociceptive effects, but contrary to the control drugs tested, non-opioid AV-101 had no discernable negative side effects. The preclinical study was conducted by Tony L. Yaksh, Ph.D., Professor of Anesthesiology and Pharmacology at the University of California, San Diego.

Further preclinical research conducted by Dr. Yaksh comparing AV-101 to pregabalin in the Chung ligation model of pain, an accepted gold standard preclinical model for chronic neuropathic pain caused by nerve damage, demonstrated that AV-101 had a significant dose response with similar efficacy in this rat model of a mononeuropathy as compared to pregabalin, which was used as an active comparator. The statistically significant positive preclinical results suggest AV-101's potential to treat multiple hyperpathic pain states. [2]

Additionally, clinical data from both the single and multi-dose Phase 1 studies previously published in the peer-reviewed publication, *Scandinavian Journal of Pain*,[3] indicated that oral AV-101 was well-tolerated, with no meaningful difference in adverse events at any dose between AV-101 and placebo. While the AV-101 study was not designed to achieve statistical significance in reducing pain in healthy volunteers, there were consistent reductions for allodynia pain and mechanical and heat hyperalgesia. The study was conducted by Mark S. Wallace, M.D., Professor of Anesthesiology and Pain Management Specialist at the University of California, San Diego.[4]

Vistagen plans to seek potential strategic collaborations to further advance the potential clinical development and commercialization of AV-101 for disorders involving the NMDA receptor, particularly pain and dyskinesias.

About AV-101

AV-101 (4-Cl-KYN) is an investigational non-opioid oral prodrug that targets the NMDA receptor, an ionotropic glutamate receptor in the brain. AV-101's active metabolite, 7-Cl-KYNA, is not an ion channel blocker, unlike classic channel-blocking NMDA receptor antagonists such as ketamine and amantadine, which the Company believes is the reason for the compound's comparatively improved safety and tolerability profile. In clinical and nonclinical testing completed to date, AV-101 has demonstrated high oral bioavailability, efficient transport across the blood-brain barrier, a postulated preferential conversion to 7-Cl-KYNA in brain areas most affected by Parkinson's disease, and an excellent pharmacokinetic (PK) profile.

No binding of AV-101 or 7-Cl-KYNA to off-site targets was identified by an extensive receptor screening study. Moreover, in all clinical trials completed to date, AV-101 has been well-tolerated with no serious adverse psychological side effects or other safety concerns that are often observed with classic channel-blocking NMDA receptor antagonists. Clinical studies to date also suggest an improved side effect profile vs. other non-opioid drugs approved to treat conditions associated with pain, such as gabapentin (approved to treat post-herpetic neuralgia and adjunctively to treat partial onset epileptic seizures) and pregabalin (approved to treat neuropathic pain associated with diabetic peripheral neuropathy and post-herpetic neuralgia), both of which produce sedation in some patients.

A range of preclinical and Phase 1 clinical studies suggest AV-101's therapeutic potential in multiple CNS indications, including levodopa-induced dyskinesia, neuropathic pain, and seizures. The U.S. FDA has granted Fast Track designation for development of AV-101 as a potential non-opioid treatment for neuropathic pain and adjunctive treatment of major depressive disorder. Vistagen plans to seek strategic partnering support to further advance the potential clinical development and commercialization of AV-101.

About Vistagen

Headquartered in South San Francisco, CA, Vistagen (Nasdaq: VTGN) is a clinical-stage biopharmaceutical company pioneering neuroscience with nose-to-brain neurocircuitry to develop and commercialize a new class of intranasal product candidates called pherines. Pherines specifically and selectively bind to peripheral receptors in human nasal chemosensory neurons, which activate olfactory bulb-to-brain neurocircuits without requiring systemic absorption or uptake into the brain to achieve desired therapeutic benefits and differentiated safety. Vistagen's neuroscience pipeline also includes an oral prodrug with potential to impact certain neurological conditions involving the NMDA receptor. Vistagen is passionate about developing transformative treatment options to improve the lives of individuals underserved by the current standard of care for multiple highly prevalent disorders, including social anxiety disorder, major depressive disorder, and vasomotor symptoms (hot flashes) associated with menopause. Connect at www.Vistagen.com.

[1] Yaksh, T.L., et al. (2017). “Characterization of the Effects of L-4-Chlorokynurenine on Nociception in Rodents.” The Journal of Pain 18:1184-1196. https://doi.org/10.1016/j.jpain.2017.03.014

[2] Vistagen, data on file

[3]Wallace, M. et. al. (2017). “Randomized, double-blind, placebo-controlled, dose-escalation study: Investigation of the safety, pharmacokinetics, and antihyperalgesic activity of L-4-chlorokynurenine in healthy volunteers.” Scandinavian Journal of Pain 17(1): 243-251. https://doi.org/10.1016/j.sjpain.2017.05.004

[4] Dr. Mark S. Wallace serves as an advisor to Vistagen

Forward-looking Statements

This press release contains certain forward-looking statements within the meaning of the federal securities laws. These forward-looking statements involve known and unknown risks that are difficult to predict and include all matters that are not historical facts. In some cases, you can identify forward-looking statements by the use of words such as “may,” “could,” “expect,” “project,” “outlook,” “strategy,” “intend,” “plan,” “seek,” “anticipate,” “believe,” “estimate,” “predict,” “potential,” “strive,” “goal,” “continue,” “likely,” “will,” “would” and variations of these terms and similar expressions, or the negative of these terms or similar expressions. Such forward-looking statements are necessarily based upon estimates and assumptions that, while considered reasonable by Vistagen and its management, are inherently uncertain. As with all pharmaceutical products, there are substantial risks and uncertainties in the process of development and commercialization and actual results or development may differ materially from those projected or implied in these forward-looking statements. There can be no guarantee that the scope of protection and enforceability provided by any patents issued for any of Vistagen’s product candidates, including AV-101, will be sufficient to deter competition, or that any of Vistagen’s product candidates, including AV-101, will successfully replicate past preclinical studies and/or clinical trials, complete ongoing or future clinical trials in part or at all, receive regulatory approval or be commercially successful. Other factors that may cause such a difference include, without limitation, risks and uncertainties relating to Vistagen’s ability to pursue and/or secure collaborative support for continued clinical development of AV-101; other risks and uncertainties related to delays in launching, conducting and/or completing ongoing and planned clinical trials; fluctuating costs of materials and other resources and services required to conduct Vistagen’s ongoing and/or planned clinical and nonclinical trials; current and potential future healthcare reforms; market conditions; the impact of general economic, industry or political conditions in the United States or internationally; and other technical and unexpected hurdles in the development, manufacture and commercialization of Vistagen’s product candidates. These risks are more fully discussed in the section entitled "Risk Factors" in Vistagen’s most recent Annual Report on Form 10-K for the fiscal year ended March 31, 2024, and in its most recent Quarterly Report on Form 10-Q for the period ended September 30, 2024, as well as discussions of potential risks, uncertainties, and other important factors in our other filings with the U.S. Securities and Exchange Commission (SEC). Vistagen’s SEC filings are available on the SEC’s website at www.sec.gov. Additionally, you should not place undue reliance on these forward-looking statements in the future, because they apply only as of the date of this press release and should not be relied upon as representing Vistagen’s views as of any subsequent date. Vistagen explicitly disclaims any obligation to update any forward-looking statements, other than as may be required by law. If Vistagen does update one or more forward-looking statements, no inference should be made that Vistagen will make additional updates with respect to those or other forward-looking statements.

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