Vistagen Receives Notice of Allowance for AV-101 Canadian Patent for Treatment of Dyskinesia Related to Levodopa Therapy for Parkinson's Disease

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Oral levodopa is the gold standard treatment for motor symptoms in individuals diagnosed with Parkinson's disease, despite the risk of dyskinesia (sudden uncontrolled movements) related to long-term use of levodopa

Published preclinical data in widely used MPTP non-human primate model of Parkinson's disease show AV-101 reduced levodopa-induced dyskinesias without adverse side effects often observed with amantadine therapy, while also maintaining antiparkinsonian activity of levodopa

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jul. 13, 2023-- Vistagen (Nasdaq: VTGN), a late clinical-stage biopharmaceutical company aiming to transform the treatment landscape for individuals living with anxiety, depression, and other central nervous system (CNS) disorders, today announced that the Canadian Intellectual Property Office (CIPO) issued a Notice of Allowance for a patent related to the use of AV-101 for reduction of dyskinesia (sudden uncontrolled movements) induced by the administration of levodopa (L-Dopa), the most commonly prescribed medication for treatment of Parkinson's disease (PD). AV-101 is the Company's oral prodrug antagonist at the NMDAR (N-methyl-D-aspartate receptor) glycine site. The patent, once granted, will not expire until at least 2034. The U.S. Patent and Trademark Office (USPTO) granted a related U.S. patent for Vistagen's AV-101 and similar patents have been granted or are pending in several additional major pharmaceutical markets.

Preclinical data previously published in the international, peer-reviewed journal, *Cells*, demonstrate the effects of AV-101 in a widely-used MPTP non-human primate model for reproducing motor complications of PD, including dyskinesia observed in many PD patients treated with L-Dopa. In this study, AV-101's efficacy against L-Dopa induced dyskinesia (LID) was measured through behavioral scores on a dyskinesia scale, and a Parkinsonian disability scale was used to measure L-Dopa antiparkinsonian efficacy. The study demonstrated that AV-101 significantly ($p = 0.01$) reduced LID without affecting the timing, extent, or duration of the therapeutic benefits of L-Dopa. No adverse events attributable to the drug were observed during the study. The preclinical study was conducted by Dr. Thérèse Di Paolo, Emeritus Professor in the Faculty of Pharmacy at Laval University in Canada and among the world's leading researchers focused on PD and LID, pursuant to Vistagen's research agreement with CHU de Québec – Université Laval Research Center in Québec, Canada.

About AV-101

AV-101 is an oral prodrug of 7-chloro-kynurenic acid (7-Cl-KYNA), a potent and selective full antagonist of the glycine binding site of the NMDAR that inhibits the function of the NMDAR. Unlike ketamine, amantadine and other NMDAR antagonists, 7-Cl-KYNA is not an ion channel blocker. In clinical and nonclinical testing completed to date, AV-101 has demonstrated good oral bioavailability 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 NMDAR antagonists such as ketamine and amantadine. Nonclinical results also indicate that long-term administration of AV-101 induces hippocampal neurogenesis, a hallmark of drugs that have antidepressive effects, and increases endogenous levels of KYNA, which also is a functional NMDAR glycine site antagonist. A range of preclinical and clinical studies suggest therapeutic potential in multiple indications, including levodopa-induced dyskinesia, neuropathic pain, seizures, major depressive disorder, and suicidal ideation. Vistagen is preparing for Phase 2A development of AV-101, on its own or with collaborators, as a treatment for one or more neurological disorders involving the NMDAR.

About Vistagen

Vistagen (Nasdaq: VTGN) is a late clinical-stage biopharmaceutical company aiming to transform the treatment landscape for individuals living with anxiety, depression and other CNS disorders. Vistagen is advancing therapeutics with the potential to be faster-acting, and with fewer side effects and safety concerns, than those currently available for treatment of anxiety, depression and multiple CNS disorders. Vistagen's pipeline includes six clinical-stage product candidates, including fasedienol (PH94B), ituvone (PH10), PH15, PH80, and PH284, each an investigational agent belonging to a new class of drugs known as pherines, as well as AV-101, which is an oral prodrug antagonist of the N-methyl-D-aspartate receptor (NMDAR). Pherines, which are administered as low-dose nasal sprays, are designed with a novel rapid-onset mechanism of action that activates chemosensory neurons in the nasal cavity and can beneficially impact key neural circuits in the brain without systemic uptake or direct activity on CNS neurons in the brain. Vistagen is passionate about transforming mental health care and redefining what is possible in the treatment of anxiety, depression and several other CNS disorders. Connect at www.vistagen.com.

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. Among other things, there can be no guarantee that the scope of protection and enforceability provided by any patents issued for any of the Company's drug candidates, including AV-101, will be sufficient to deter competition, or that any of the Company's drug candidates, including AV-101, will successfully complete ongoing or future clinical trials, receive regulatory approval or

be commercially successful. Other factors that may cause such a difference include, without limitation, risks and uncertainties relating to the Company's ability to secure adequate financing for its operations, including financing or collaborative support for continued clinical development of any of the Company's product candidates; 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 the Company's ongoing and/or planned clinical and non-clinical trials; 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 the Company's drug candidates. These risks are more fully discussed in the section entitled "Risk Factors" in the Company's most recent Annual Report on Form 10-K for the fiscal year ended March 31, 2023, 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). The Company'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 the Company's views as of any subsequent date. The Company explicitly disclaims any obligation to update any forward-looking statements, other than as may be required by law. If the Company does update one or more forward-looking statements, no inference should be made that the Company will make additional updates with respect to those or other forward-looking statements.

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Investors:
Mark McPartland
Senior Vice President, Investor Relations
(650) 577-3606
markmcp@vistagen.com

Media:
Nate Hitchings
SKDK
nhitchings@skdknick.com

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