January 29, 2018

Dear Fellow Stockholders:

In early-2017, I had the privilege of "Ringing the Bell" at The Nasdaq Stock Market's headquarters in Times Square on behalf of our company. That exciting and unique corporate event proved to be a symbolic prologue to the productive year for VistaGen that followed. The milestones we accomplished in 2017 have strongly positioned us to advance our AV-101 Phase 2 program to new levels throughout this year and next.

Regulatory and Clinical Development

We refer to AV-101 as a "new generation" antidepressant because its mechanism of action (the way it works in the brain) is fundamentally different from all FDA-approved antidepressants, as well as all FDA-approved atypical antipsychotics often used together with standard antidepressants. Investment, innovation, industry expertise and a lot of hard work by our focused and passionate teams, teams committed to making a game-changing impact in the treatment of multiple diseases and disorders involving the central nervous system (CNS), have advanced us to the threshold of launching our potentially transformative Phase 2 study of AV-101 for treatment of Major Depressive Disorder (MDD). Our primary goal is to develop and ultimately receive regulatory approval to commercialize AV-101 worldwide for multiple CNS diseases and disorders. Our initial regulatory and commercial strategies to accomplish that goal are focused on developing AV-101 as an oral, safe, and faster-acting new generation treatment alternative for millions of MDD patients with inadequate therapeutic results from standard antidepressants, displacing atypical antipsychotics in the current MDD drug treatment paradigm. It is a potentially game-changing goal indeed, and our teams are well-suited for the challenge.

Following a productive meeting with the U.S. Food and Drug Administration (FDA) in the Fall of 2017, we achieved two key regulatory milestones before year end. First, in October 2017, the FDA authorized us to proceed, under our Investigational New Drug (IND) application, with our U.S. multi-center Phase 2 clinical study of AV-101 as an oral new generation adjunctive treatment for MDD. This study will focus on treatment of MDD patients with an inadequate response to standard, FDA-approved antidepressants. In addition, in December 2017, the FDA granted us Fast Track Designation for development of AV-101 for treatment of MDD, providing us the opportunity for frequent FDA interactions regarding the most appropriate and efficient development pathway to bring AV-101 to MDD patients.

As a result of receiving a "green light" from the FDA, we anticipate launching our AV-101 Phase 2 MDD adjunctive treatment study during the current quarter, with topline data expected to be available during the first half of 2019.

During 2018, we expect one of our principal collaborators, the U.S. National Institute of Mental Health (NIMH), to complete its Phase 2 monotherapy study of AV-101 in treatment-resistant MDD patients. This Phase 2 study is being conducted by Dr. Carlos Zarate Jr., Chief, Section on the Neurobiology and Treatment of Mood Disorders and Chief of the Experimental Therapeutics and Pathophysiology Branch at the NIMH. AV-101

caught the attention of Dr. Zarate, widely considered a pioneer in ketamine research for MDD, and his team after head-to-head preclinical studies of AV-101 vs. ketamine, ultimately resulting in a Cooperative Research and Development Agreement (CRADA) between VistaGen and the U.S. National Institutes of Health (NIH), whereby the NIMH is fully funding and conducting the NIMH Phase 2 monotherapy MDD study of AV-101.

Manufacturing and Patents

In connection with our AV-101 Phase 2 program, as well as potential Phase 3 development and commercialization, we, together with our contract manufacturing organization, developed a novel process for the production of AV-101 drug substance. We believe our new proprietary AV-101 production process will significantly improve manufacturing efficiency.

We strengthened our intellectual property around AV-101 in 2017. In Europe, the European Patent Office (EPO) granted our patent related to methods of treating depression with AV-101 and certain other neurological indications. Additionally, the U.S. Patent and Trademark Office (USPTO) granted a patent related to certain methods of production of AV-101. These issued patents, together with the potential issuance of additional AV-101 patent applications currently under review in the US, European Union and other key pharmaceutical markets, provide VistaGen with added long-term intellectual property protection for AV-101 and enhance its commercial potential.

Additional Highlights

AV-101 for Neuropathic Pain and Parkinson's Disease Levodopa-induced Dyskinesia (PD LID)

In addition to MDD, we believe AV-101 may also have the potential to treat multiple CNS disorders and neurodegenerative diseases, including neuropathic pain, PD LID and other CNS diseases and disorders where modulation of NMDA receptors, activation of AMPA pathways and/or key active metabolites of AV-101 may achieve therapeutic benefit. In October 2017, a peer-reviewed publication of nonclinical studies of the effects of AV-101 in four well-established nonclinical models of pain was featured on the cover of *The Journal of Pain* (http://dx.doi.org/10.1016/j.jpain.2017.03.014). 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, with results suggesting AV-101's potential for treating multiple pain states. We believe the positive results published in these studies, taken together with successful AV-101 Phase 1a and 1b clinical safety studies and the epidemic abuse of prescription opioid pain medicines, support further investment in Phase 2 clinical studies to assess efficacy and safety of AV-101 as a new non-opioid treatment alternative for patients suffering from neuropathic pain. We are also excited about the opportunity to explore AV-101's potential to reduce dyskinesia associated standard levodopa, or L-DOPA, therapy for Parkinson's disease, based on results from non-clinical studies. Without diverting our priority focus on MDD, we plan to expand our AV-101 Phase 2 clinical program during the next year to include these important CNS indications with significant unmet need.

Capital Markets

2017 culminated with the closing of an underwritten public offering that generated gross proceeds of $15 million. This financing enables us to commence and advance our Phase 2 study in 2018. I want to thank, again, our underwriters and our new and existing investors for supporting our vision.

2018 J.P. Morgan Healthcare Conference and University of California, San Francisco Panel Discussion

Earlier this month, our team kicked off 2018 by hosting numerous meetings with current investors, prospective institutional investors and potential strategic partners during the 36th Annual J.P. Morgan Healthcare Conference and 10th Annual Biotech Showcase in San Francisco. Additionally, I was honored to participate on a panel with distinguished scientists and clinicians focused on the neuroscience of depression and addiction during the Healthcare Innovation Forum held at the University of California, San Francisco (UCSF) Medical Center in San Francisco. Our in-depth panel discussions were not only encouraging and motivating, but also eye-opening regarding potential advances in neuropsychiatry on the horizon at UCSF.

Reflecting on a productive week in San Francisco, it is apparent that a paradigm shift towards a new generation of faster-acting antidepressants, particularly those targeting NMDA and AMPA receptors, is emerging. The positive effects on depression and pain through the IV administration of ketamine is well documented, and significant investment has been made by big Pharma to explore its benefits. For example, Janssen Research & Development, one of the Janssen Pharmaceutical Companies of Johnson & Johnson, has made a significant investment in esketamine, an intranasally-administered NMDA receptor antagonist currently in Phase 3 development with a mechanism of action similar to ketamine treatment currently administered by injection. If approved by the FDA, esketamine would be one of the first new approaches to treat patients with MDD in the last 50 years. Similar to ketamine and esketamine, AV-101 targets the NMDA and AMPA receptors, however AV-101 is oral and it inhibits the NMDA receptor activity rather than blocking it, thereby producing ketamine-like antidepressant effects without safety concerns associated with ketamine.

I am as eager and passionate as I have ever been to see what transpires from our AV-101 Phase 2 program, especially our impending Phase 2 adjunctive treatment study in MDD patients with an inadequate response to standard antidepressants. Throughout 2018, we will remain focused on our core mission - to develop new generation medicines for depression and other CNS disorders affecting millions of people worldwide who do not currently have adequate treatment alternatives. I maintain the highest confidence in our strategy and our teams, and I anticipate that 2018 will yield even more exciting achievements intended to deliver both life-changing benefits to CNS patients and extraordinary value to our stockholders.

Very truly yours,

Shawn Singh,
Chief Executive Officer and Director
VistaGen Therapeutics, Inc.