VistaGen Therapeutics, Inc.
Form 10-K
June 24, 2016

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-K

x Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

For the fiscal year ended: March 31, 2016

or

o Transition Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Commission file number: 000-54014

VistaGen Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Nevada	20-5093315
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

343 Allerton Avenue
South San Francisco, California 94080
(650) 577-3600
(Address, including zip code, and telephone number, including area code, of registrant's principal executive office)

Securities registered pursuant to Section 12(b) of the Act

Title of each class	Name of each exchange on which registered
Common Stock, par value $0.001 per share	The NASDAQ Capital Market

Securities registered pursuant to Section 12(g) of the Act

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes o No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the

Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer o	Accelerated filer o	Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company x

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes o No x

The aggregate market value of the common stock of the registrant held by non-affiliates of the registrant on September 30, 2015, the last business day of the registrant's second fiscal quarter, was: $13,691,410.

As of June 22, 2016, there were 7,970,705 shares of the registrant's common stock, $0.001 par value per share, outstanding.

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Forward-Looking Statements

This Annual Report on Form 10-K (Annual Report) contains forward-looking statements that involve substantial risks and uncertainties. All statements contained in this Annual Report other than statements of historical facts, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “w
“should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

the availability of capital to satisfy our working capital requirements;

the accuracy of our estimates regarding expenses, future revenues and capital requirements;

our plans to develop and commercialize our lead product candidate, AV-101, initially as a treatment for Major Depressive Disorder (MDD), and subsequently as a treatment for additional diseases and disorders involving the Central Nervous System;

our ability to initiate and complete our clinical trials and to advance our product candidates into additional clinical trials, including pivotal clinical trials, and successfully complete such clinical trials;

regulatory developments in the U.S. and foreign countries;

the performance of the U.S. National Institute of Mental Health, our third-party contract manufacturer(s), contract research organization(s) and other third-party non-clinical and clinical development collaborators and regulatory service providers;

our ability to obtain and maintain intellectual property protection for our core assets;

the size of the potential markets for our product candidates and our ability to serve those markets;

the rate and degree of market acceptance of our product candidates for any indication once approved;

the success of competing products and product candidates in development by others that are or become available for the indications that we are pursuing;

the loss of key scientific, clinical and nonclinical development, and/or management personnel, internally or from one of our third-party collaborators; and

other risks and uncertainties, including those listed under Part I, Item 1A. Risk Factors.

These forward-looking statements are only predictions and we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, so you should not place undue reliance on our

forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and operating results. We have included important factors in the cautionary statements included in this Annual Report, particularly in Part I, Item 1A, titled “Risk Factors” that could cause actual future results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report and the documents that we have filed as exhibits to the Annual Report with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by applicable law.

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PART I

All brand names or trademarks appearing in this report are the property of their respective holders. Unless the context requires otherwise, references in this report to "VistaGen," the "Company," "we," "us," and "our" refer to VistaG Therapeutics, Inc., a Nevada corporation.

Item 1. Business

Company Overview

We are a clinical-stage biopharmaceutical company dedicated to developing and commercializing innovative product candidates for patients with diseases and disorders involving the central nervous system (CNS). Our lead product candidate, AV-101, is a next generation, orally available prodrug candidate in Phase 2 development, initially for the adjunctive treatment of Major Depressive Disorder (MDD) in patients with an inadequate response to standard antidepressants approved by the U.S. Food and Drug Administration (FDA). We believe AV-101 may also have potential therapeutic utility in CNS indications beyond MDD, including chronic neuropathic pain, epilepsy, Huntington's disease and Parkinson's disease.

AV-101's mechanism of action, as an N-methyl D aspartate receptor (NMDAR) antagonist binding selectively at the glycine binding (GlyB) co-agonist site of the NMDAR, is fundamentally differentiated from all FDA-approved antidepressants, as well as all atypical antipsychotics used adjunctively with standard, FDA-approved antidepressants.

Our ongoing Phase 2a clinical study of AV-101 in subjects with treatment-resistant MDD is being conducted and funded by the U.S. National Institute of Mental Health (NIMH) under our February 2015 Cooperative Research and Development Agreement (CRADA) with the NIMH. The first patient in this NIMH-sponsored Phase 2a study was dosed in November 2015. The Principal Investigator of the study is Dr. Carlos Zarate, Jr., Chief of the NIMH's Experimental Therapeutics & Pathophysiology Branch and its Section on Neurobiology and Treatment of Mood and Anxiety Disorders. Previous NIMH studies, including studies conducted by Dr. Zarate, have focused on the effects of low dose intravenous (I.V.) ketamine on treatment-resistant depression. These NIMH studies, as well as clinical research by others, have demonstrated robust antidepressant effects in patients with treatment-resistant MDD within hours of a single low dose of I.V. ketamine and stimulated research and development around a new generation of antidepressants with potential to deliver ketamine-like fast-acting antidepressant benefits without ketamine's serious side effects.

We are preparing to launch our Phase 2b clinical study of AV-101 for the adjunctive treatment of MDD in patients with an inadequate response to standard, FDA-approved antidepressants. We anticipate commencement of this multi-center, multi-dose, double blind, placebo-controlled Phase 2b efficacy and safety study at the end of the fourth quarter of 2016. Dr. Maurizio Fava, Professor of Psychiatry at Harvard Medical School and Director, Division of Clinical Research, Massachusetts General Hospital (MGH) Research Institute and Executive Director, MGH Clinical Trials Network and Institute, will be the Principal Investigator of our Phase 2b study of AV-101 in MDD. Dr. Fava was the co-Principal Investigator with Dr. A. John Rush of the largest clinical trial ever conducted in depression, the STAR*D study, whose findings were published in journals such the New England Journal of Medicine (NEJM) and the Journal of the American Medical Association (JAMA). We anticipate top line results in this Phase 2b study in the second quarter of 2018.

In addition to clinical development of AV-101, we are focused on advancing potential commercial applications of our human pluripotent stem cell (hPSC) technology platform with respect to drug rescue programs aimed at developing proprietary small molecule new chemical entities (NCEs) for our drug candidate pipeline. We are also focused on potential regenerative medicine (RM) applications using blood, cartilage, heart and/or liver cells derived from hPSCs,

and may pursue these applications in collaboration with third-parties.

AV-101 and Major Depressive Disorder

Background

The World Health Organization (WHO) estimates that 350 million people worldwide are affected by depression. According to the U.S. National Institutes of Health (NIH) major depression is one of the most common mental disorders in the U.S. The NIMH reports that, in 2014, an estimated 15.7 million adults aged 18 or older in the U.S. had at least one major depressive episode in the past year. This represented 6.7 percent of all U.S. adults. According to the U.S. Centers for Disease Control and Prevention (CDC) one in 10 Americans over the age of 12 takes an antidepressant medication.

Most standard, FDA-approved antidepressants target neurotransmitter reuptake inhibition – either serotonin (SSRIs) or serotonin/norepinephrine (SNRIs). Even when effective, these standard depression medications take many weeks to achieve adequate antidepressant effects. Nearly two out of every three drug-treated depression patients, including an estimated 6.9 million drug-treated MDD patients in the U.S., obtain inadequate therapeutic benefit from initial treatment with a standard antidepressant. Unfortunately, even after treatment with as many as four different standard antidepressants, nearly one out of every three drug-treated depression patients do not achieve adequate therapeutic benefits. Such treatment-resistant depression patients often seek to treat their depression with non-drug-related approaches, such as Electroconvulsive Therapy (ECT), or to augment their inadequate response to standard antidepressants by adding an atypical antipsychotic (such as, for example, aripiprazole) to their treatment regimen, despite the only modest potential therapeutic benefit and significant risk of additional side effects.

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All standard antidepressants have risks of significant side effects, including, among others, potentially anxiety, metabolic syndrome, sleep disturbance and sexual dysfunction. They also have a "Black Box" warning due to risks of worsening depression and suicide in certain groups. Use of atypical antipsychotics to augment inadequately performing standard antidepressants increases the risk of serious side effects, including, potentially, tardive dyskinesia, significant weight gain, diabetes and heart disease, while offering only a modest potential increase in therapeutic benefit. Use of ECT increases the risk of serious side effects, including, headaches, tiredness, disorientation, intense sleepiness, hallucinations and long-term memory loss.

AV-101

AV-101, our orally available prodrug candidate, is in Phase 2 clinical development for the adjunctive treatment of MDD patients with an inadequate response to standard antidepressants. As published in the October 2015 issue of the peer-reviewed, Journal of Pharmacology and Experimental Therapeutics, in an article entitled, The prodrug 4-chlorokynurenine causes ketamine-like antidepressant effects, but not side effects, by NMDA/glycineB-site inhibition, using well-established preclinical models of depression, AV-101 was shown to induce fast-acting, dose-dependent, persistent and statistically significant antidepressant-like responses, following a single treatment. These responses were equivalent to those seen with a single, sub-anesthetic control dose of the NMDAR antagonist ketamine. In the same preclinical studies, a standard antidepressant, the SSRI fluoxetine, did not induce rapid onset antidepressant-like responses. In addition, these studies confirmed that the fast-acting antidepressive effects of AV-101 were mediated through the GlyB site and involved the activation of a key neurological pathway, the alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor pathway. Activation of the AMPA receptor pathway is a common feature of fast-acting antidepressants.

Following the completion of our NIH-funded, randomized, double blind, placebo-controlled Phase 1a and Phase 1b safety studies, we are now collaborating with the NIMH in Phase 2a. Under our February 2015 CRADA, the NIMH is sponsoring, and Dr. Carlos Zarate Jr. of the NIMH as Principal Investigator is conducting, our ongoing Phase 2a efficacy and safety study of AV-101 in subjects with treatment-resistant MDD. The trial is expected to enroll 20 to 28 patients. The first patient was dosed in November 2015, and we currently anticipate receiving topline results in the second quarter of 2017.

We are preparing to launch our Phase 2b clinical study of AV-101 for the adjunctive treatment of MDD in patients with an inadequate response to standard, FDA-approved antidepressants. We anticipate the launch of this Phase 2b study, with Dr. Maurizio Fava of Harvard Medical School serving as Principal Investigator, at the end of the fourth quarter of 2016. We anticipate top line results from this Phase 2b study in the second quarter of 2018. Although no assurances can be given, we currently estimate that AV-101 may be ready for commercialization in 2021.

Several preclinical studies support the hypothesis that AV-101 also has the potential to treat multiple additional CNS disorders and neurodegenerative diseases beyond MDD, including chronic neuropathic pain, epilepsy, Parkinson's disease and Huntington's disease, where modulation of the NMDAR, AMPA pathway and/or active metabolites of AV-101 may achieve therapeutic benefit.

CardioSafe 3D™; NCE Drug Rescue and Regenerative Medicine

CardioSafe 3D™ is our customized in vitro cardiac bioassay system capable of predicting potential human heart toxicity of small molecule NCEs in vitro, long before they are ever tested in animal and human studies. Our current strategic interests involving our stem cell technology platform include (i) advancing current internal efforts focused on CardioSafe 3D drug rescue to expand our drug candidate pipeline with selected proprietary small molecule NCEs, leveraging substantial prior research and development investments by pharmaceutical companies and others related to public domain NCEs terminated before FDA approval due to heart toxicity risks and (ii) establishing collaborative

arrangements with qualified third-parties focused on regenerative medicine (RM) applications, including (A) cell-based therapy (injection of stem cell-derived mature organ-specific cells obtained through directed differentiation), (B) cell repair therapy (induction of regeneration by biologically active molecules administered alone or produced by infused genetically engineered cells), or (C) tissue engineering (transplantation of in vitro grown complex tissues), involving hPSC-derived blood, bone, cartilage, heart and/or liver cells.

Our Strategy

Our core strategy is to develop, and commercialize innovative small molecule CNS drugs that address significant unmet medical needs. We have assembled a management team and a team of scientific, clinical, and regulatory advisors, including recognized experts in the fields of depression, multiple other CNS diseases and disorders, and stem cell biology, with significant industry and regulatory experience to lead and execute the development and commercialization of AV-101 and any additional CNS or other product candidates we may develop internally or acquire from third-parties.

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Key elements of our strategy are to:

Develop and commercialize AV-101 for depression, including, initially, as an adjunctive treatment for MDD patients with an inadequate response to standard, FDA-approved antidepressants. Under our 2015 CRADA with the NIMH, in collaboration with Dr. Carlos Zarate of the NIMH, we launched our ongoing NIMH-sponsored AV-101 MDD Phase 2a clinical study in patients with treatment resistant MDD. The first patient in this study was dosed in November 2015. We are currently preparing to launch our multi-center Phase 2b clinical study of AV-101 for the adjunctive treatment of MDD in patients with an inadequate response to standard, FDA-approved, antidepressants. We are developing AV-101 internally, and may either continue to do so through our submission of a New Drug Application (NDA) to the FDA or, prior to submitting an AV-101 NDA, collaborate with a pharmaceutical company with a strong commercial presence in depression and other CNS markets. If AV-101 is approved by the FDA and other regulatory agencies, we may collaborate with one or more pharmaceutical companies with extensive commercial capabilities in multiple depression and other CNS markets and/or contract with a specialty sales force focused primarily on psychiatrists and long-term care physicians who are high prescribers of standard antidepressants and atypical antipsychotics.

Leverage the commercial potential of AV-101 by expanding our development and commercialization programs to additional CNS-related diseases and disorders. We believe AV-101 has broad therapeutic potential. Accordingly, we may pursue clinical development and commercialization opportunities for AV-101 across a range of CNS-related indications that are underserved by currently available CNS medicines and represent significant unmet medical needs. Based on AV-101 preclinical studies, and by leveraging our successful NIH-funded AV-101 Phase 1a and 1b clinical safety studies, we may now have opportunities to expand Phase 2 development of AV-101 beyond MDD to include, among other CNS-related indications, chronic neuropathic pain, epilepsy, Huntington's disease and Parkinson's disease.

Capitalize on our drug rescue and RM opportunities using our stem cell technology. CardioSafe 3D enables us to screen NCEs in drug rescue programs intended to produce proprietary NCEs for our internal drug candidate pipeline, without incurring many of the substantial costs and risks typically inherent in new drug discovery and nonclinical drug development. We are also focused on establishing new strategic collaborations, including potential license and/or spin-off opportunities, involving potential RM applications of our stem cell platform. As most of our resources are currently focused on the clinical development of AV-101, we believe one or more strategic licensing or development collaborations and/or spin-off transactions involving RM applications of our stem cell technology platform could allow us to realize potential value from our stem cell technology platform while focusing primarily on clinical development of AV-101, other CNS drug candidates we may acquire and/or drug candidates we may develop through internal drug rescue.

Pursue in-licensing and acquisition of other product candidates for treatment of CNS-related disorders. While our resources are currently focused primarily on clinical development of AV-101 for MDD, we anticipate pursuing license or acquisition of additional CNS-related product candidates. These may be developed independently or in partnerships. We believe a diversified CNS product candidate portfolio will mitigate risks inherent in drug development and increase the likelihood of our success.

Grow our internal development pipeline through drug rescue using our stem cell technology platform. We have developed our cardiac bioassay system, CardioSafe 3D, for drug rescue applications intended to produce proprietary small molecule NCEs for our internal drug development pipeline, without incurring many of the substantial costs and risks typically inherent in new drug discovery and nonclinical drug development.

Our Product Opportunities

AV-101 (L-4-chlorokynurenine or 4-Cl-KYN)

Overview and Mechanism of Action

AV-101 is an orally available, clinical-stage prodrug candidate that readily gains access to the CNS after systemic administration and is rapidly converted in the brain into its active metabolite, 7-chlorokynurenic acid (7-Cl-KYNA), a well-characterized, potent and highly selective antagonist of the NMDAR at the GlyB co-agonist site.

Current evidence suggests that AV-101's modulation of NMDAR signaling may provide fast-acting antidepressant effects in the treatment of MDD. In addition, as confirmed in our AV-101 Phase 1 clinical studies, targeting the GlyB site of the NMDAR does not have the adverse effects typically associated with classic NMDAR antagonists, such as ketamine, and other NMDA channel blockers.

Major Depressive Disorder