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

#### FORM 8-K

# CURRENT REPORT PURSUANT TO SECTION 13 OR 15(d) of the SECURITIES EXCHANGE ACT OF 1934

Date of Report (Date of earliest event reported): March 13, 2019

## VistaGen Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

**NEVADA** 

001-37761

20-5093315

(State or other jurisdiction of incorporation)

(Commission File Number)

(IRS Employer Identification Number)

343 Allerton Ave.
South San Francisco, California 94090
(Address of principal executive offices)

(650) 577-3600

(Registrant's telephone number, including area code)

### **Not Applicable**

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:
□ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425) □ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a -12) □ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d -2(b)) □ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e -4(c))

#### Item 7.01 Regulation FD Disclosure.

On March 13, 2019, VistaGen Therapeutics, Inc. (the "Company") began utilizing a new corporate presentation. A copy of the Corporate Presentation is attached hereto as Exhibit 99.1.

The information in this Item 7.01 of this Current Report on Form 8-K, including the information set forth in Exhibit 99.1, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), nor shall Exhibit 99.1 filed herewith be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

#### Item 8.01 Other Events.

On March 13, 2019, the Company announced that the U.S. Patent and Trademark Office has issued a Notice of Allowance for U.S. Patent Application 15/812,599 related to certain methods of production for AV-101, the Company's oral NMDA receptor glycine site antagonist in Phase 2 development for major depressive disorder. A copy of this press release is attached to this Current Report on Form 8-K as Exhibit 99.2.

#### Item 9.01 Financial Statements and Exhibits.

See Exhibit Index.

# Signatures

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

VistaGen Therapeutics, Inc.

Date: March 14, 2019 By: <u>/s/ Shawn K. Singh</u>

Shawn K. Singh

Chief Executive Officer

# EXHIBIT INDEX

Exhibit No.	Description				
<u>99.1</u>	Corporate Presentation, dated March 13, 2019				
99.1 99.2	Press Release issued by VistaGen Therapeutics, Inc., dated March 13, 2019				



LOOKING BEYOND CURRENT
TREATMENTS FOR
CENTRAL NERVOUS SYSTEM (CNS)
DISEASES AND DISORDERS WITH
HIGH UNMET NEED





Forward-looking Statements



This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements concern our product candidates, our development efforts, our collaborations, our intellectual property, our financial condition, our plans and our development programs. These statements involve risks, uncertainties and assumptions, and are based on the current estimates and assumptions of the management of VistaGen Therapeutics, Inc. (Company) as of the date of this presentation and are subject to uncertainty and changes. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements include, among others, those set forth in our Annual Report on Form 10-K for the year ended March 31, 2018, filed with the Securities and Exchange Commission (SEC) on June 26, 2018, as well as any updates to those risk factors filed with the SEC from time to time in our periodic and current reports on Forms 8-K and 10-Q. All statements contained in this presentation are made only as of the date of this presentation, and the Company undertakes no duty to update this information unless required by law.

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# Looking beyond current therapies for CNS diseases and disorders with high unmet need





# Emphasis: at-home use, rapid-onset, exceptional safety



3 late-stage product candidates with new generation MOAs

2 with Phase 2 POC efficacy and safety, 3rd with potential in 2019

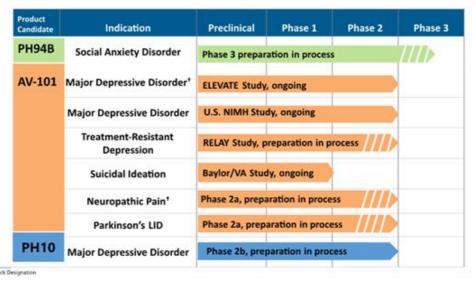


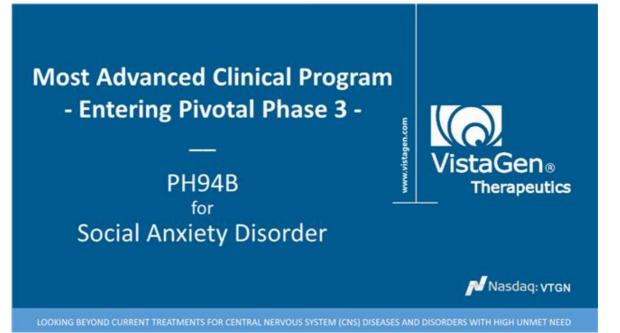
3 clinical readouts during 2019

At least **1** pivotal Phase 3 study launch in 2020

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# **Current SAD Treatment Options Fall Short**





# Not FDA-Approved Prescribed Off-label

### Antidepressants

- ★ Slow onset, chronic administration
- \* May worsen anxiety initially
- Significant side effects
- ➤ Potential drug-drug interaction

### Benzodiazepines & Beta Blockers

- × Addiction risk
- × Sedation
- ★ Cognitive impairment
- × Cardiac concerns

# There is no FDA-approved PRN treatment for SAD

# **PH94B**

# Novel PRN Treatment, Rapid-Onset Efficacy, Exceptional Safety





- Novel CNS neuroactive steroid nasal spray
- Activates nasal chemosensory receptors that trigger neural circuits in the brain that suppress fear and anxiety
- PRN treatment prior to a fear- or anxiety-producing social event
- Rapid-onset efficacy (10 to 15 minutes)
- Microgram dose, no systemic exposure
- Well-tolerated through Pilot Phase 3
- Non-sedating, non-addictive

Phase 2 and Pilot Phase 3 Complete
Preparing for Pivotal Phase 3 launch in 2020

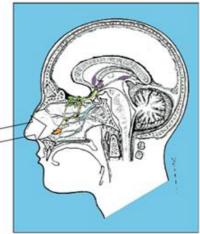
Potential to be the first FDA-approved PRN treatment for SAD

### PH94B Mechanism of Action

**Activates Neural Circuits that Suppress Fear and Anxiety** 

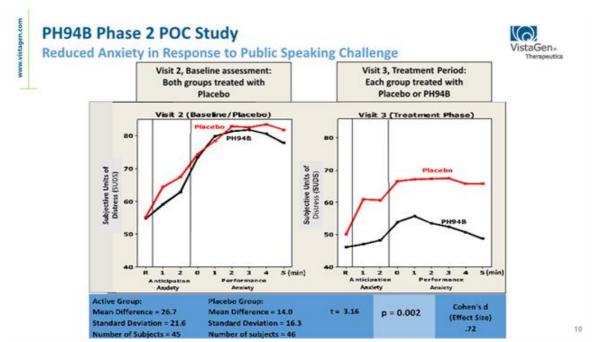


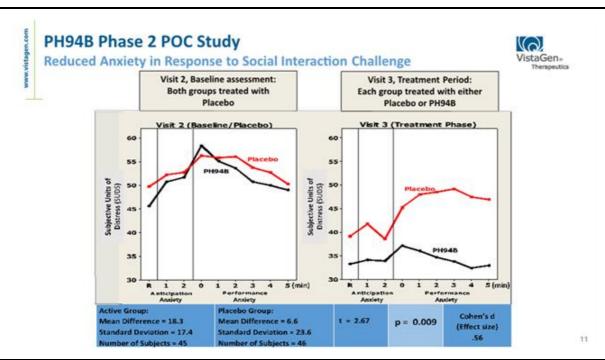
- Fundamentally different from all current treatments
- Activates nasal chemosensory receptors that trigger neural circuits in the brain that suppress fear and anxiety
  - Engages nasal chemosensory receptors that trigger a subset of neurons in the main olfactory bulbs (OB)
  - OB neurons stimulate inhibitory GABAergic neurons in the amygdala, releasing anxiolytic neuropeptide S, decreasing release of norepinephrine, and facilitating fear extinction and activity of the limbic-hypothalamic parasympathetic system

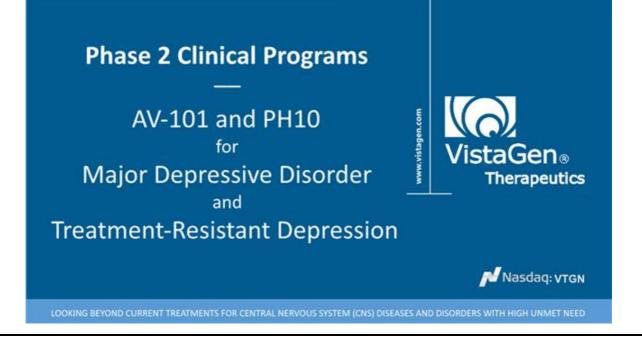


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1 in 4 women



1 in 6 men



1 in 8



diagnosed with depressive disorders

age 12 and over takes an antidepressant'

#### LARGE ADDRESSABLE MARKET WITH HIGH UNMET NEED2,3

11.6M

Drug-treated patients with Major Depressive Disorder 7.3M

Inadequate response to 1st antidepressant

5.1M

Treatment-resistant after 2nd antidepressant

L CDC - NCH5 - National Center for Health Statistics, August 2017; 2. Rush AJ, et al. Am J. Psychiatry. 2006, 163(11): 1905-1917 (STAR\*D Study); 3. Decision Resources. 2016

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# **Current Drug Treatments Fall Short**



# **Antidepressants**

- · Often do not work; slow to work
  - Initial ADT effective in 1 of 3 patients
  - May take 4 to 6 weeks or more for antidepressant effects
- · Significant side effects
  - Anxiety, sexual dysfunction, insomnia

# **Atypical Antipsychotics**

- · Often do not work
  - Only ca. 20% of patients respond to augmentation
- Significant side effects
  - Weight gain, akathisia, insomnia, dizziness, tardive dyskinesia

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# Ketamine-based therapies offer new hope to millions, but are they long-term solutions?



"Club Drug Ketamine Provides Hope in Fight Against Depression"

TIME

The New Hork Times

Fast-Acting Depression Drug, Newly Approved, Could Help Millions

- · Safety?
- · Durability?
- Side Effects?

- Convenience?
- · Compliance?
- Cost?

# AV-101 for MDD and TRD: Transformative Potential



**Rapid-onset Potential with Exceptional Safety** 

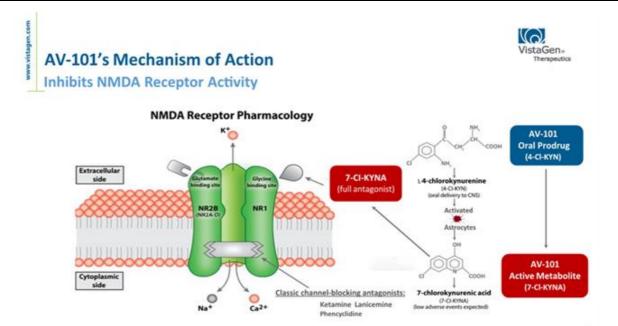


- Oral prodrug of 7-Cl-KYNA
- NMDA receptor glycine site antagonist (a full antagonist)
- Rapid-onset antidepressant effects and neurogenesis in preclinical studies
- Well-tolerated in all clinical studies to date
- No psychological side effects

Intended for chronic at-home use

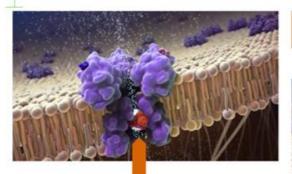
**FDA Fast Track designation** 

Phase 2 studies ongoing Clinical readouts in 2019



# AV-101's Mechanism of Action Inhibits NMDA Receptor Activity





Ketamine completely blocks the ion channel of the NMDA receptor

AV-101's active metabolite (7-CI-KYNA) does not block NMDA receptor activity; it inhibits it



# AV-101 vs. Ketamine in Published Preclinical Studies



Rapid-acting, Antidepressant-like Effects	AV-101	Ketamine
Forced-swim	COMPARABLE  COMPARABLE  COMPARABLE  COMPARABLE	
Tail-suspension		
Learned-helplessness		
lovelty-suppressed feeding		
Side Effects	AV-101	Ketamine
Psychotomimetic and rewarding	No	Yes
Hyper movement	No	Yes
Movement sensitization	No	Yes
Circling and rearing	No	Yes
Sensory-motor gating	No	Yes

Zanos, P., et al. (2015). "The Prodrug 4-Chlorokynurenine Causes Ketamine-Like Antidepressant Effects, but Not Side Effects, by NMOA/Glycine8-Site Inhibition." J Pharmacol Exp Ther 19

AV-101 Published Phase 1A and 1B Safety Studies



Excellent safety profile, similar to placebo



- Two NIH-funded Phase 1 safety studies conducted in 86 normal volunteers
- · Phase 1A: Single ascending dose: 30 to 1440 mg administered once
- Phase 1B: Multiple ascending dose: 360, 1080 and 1440 mg administered daily for
- Well-tolerated, AE's similar to placebo

Multiple subjects on AV-101 (none on placebo) reported positive feelings of well-being similar to antidepressant effects reported with ketamine, but without ketamine's psychological side-effects

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.

# AV-101 NIMH Phase 2 Study for MDD





### Principal Investigator: Dr. Carlos Zarate, Jr., National Institute of Mental Health

- · NIH-sponsored, ongoing at NIMH
- · Monotherapy for TRD, cross-over study, once per day for 14 days
- Blinded AEs suggest AV-101 continues to be exceptionally well-tolerated
- CSF measurements of AV-101, 7-CI-KYNA and quinolinic acid will be taken
- Glutamate levels in brain measured by MR spectroscopy in response to AV-101
- · Target enrollment, ca. 20 adults
- Target topline results, end of Q2 2019

Primary Endpoint: Change in HAM-D from baseline compared to placebo

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# AV-101 ELEVATE Phase 2 Study for MDD



### Principal Investigator: Dr. Maurizio Fava, Harvard Medical School

- Company-sponsored
- Adjunctive treatment for inadequate response to current SSRI/SNRI therapy
- · Oral dose, once per day for 14 days
- Blinded AEs suggest AV-101 continues to be exceptionally well-tolerated
- · Target enrollment, ca. 180 patients
- Target topline results, end of Q3 2019

Primary Endpoint: Change in MADRS-10 from baseline compared to placebo

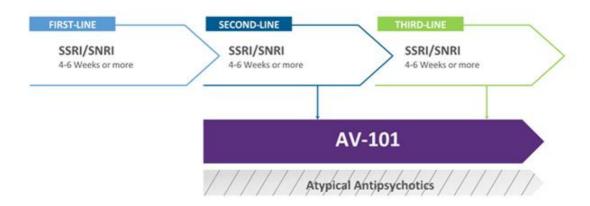
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# Initial Regulatory and Commercial Objectives for AV-101



**Displace Adjunctive Atypical Antipsychotics** 



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# **Next Step: The RELAY Study**

**Prevent TRD Relapse following Ketamine-based Therapy** 



- Phase 2 study preparation in process
- Relapse prevention post-ketamine-based therapy, AV-101 vs. placebo
- Multi-center, double blind, placebo-controlled (ca. 200 subjects)
- TRD patients who have responded to IV ketamine or intranasal esketamine
- Oral dose, once per day for 12 weeks
- Potential target launch: mid-2020

Primary Endpoint: Kaplan-Maier survival analysis for time to relapse following response to IV ketamine or intranasal esketamine

# PH10 for MDD

# Rapid-Onset, Exceptional Safety



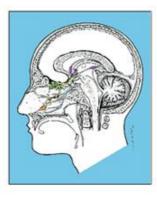


- Novel CNS neuroactive steroid nasal spray
- Activates nasal chemosensory receptors that trigger neural circuits in the brain leading to antidepressant effects
- Rapid-onset antidepressant efficacy in Phase 2a
- Microgram dose, no systemic exposure
- Well-tolerated, minimal side effects

Phase 2a POC Completed
Preparing to Launch Phase 2b in

2020

Potential First-Line Take-Home ADT without Psychological Side Effects



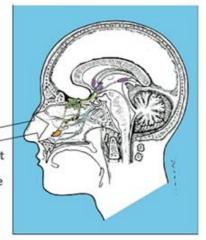
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# PH10 Mechanism of Action

**Activates Neural Circuits Leading to Antidepressant Effects** 

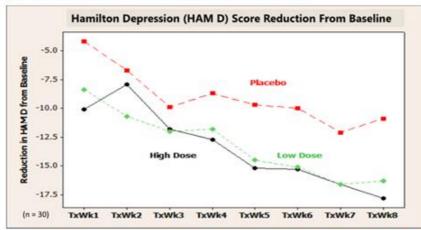


- Fundamentally different from all current treatments
- Activates nasal chemosensory receptors that trigger neural circuits in the brain leading to antidepressant effects
  - Engages nasal chemosensory receptors that trigger a subset of neurons in the main olfactory bulbs (OB)
  - OB neurons stimulate neurons in the limbic amygdala that release CRH, glutamate and norepinephrine, increasing release of norepinephrine, serotonin and dopamine in the CNS, and increasing activity of the limbic-hypothalamic sympathetic nervous system



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# PH10 Phase 2a MDD Study (Monotherapy)



PH10 Dose	HAM D Score	P (PH10 vs Placebo)	Cohen's D (Effect Size)
3.2 µg (Low Dose)	16.3	.101	0.74
6.4 μg (High Dose)	17.8	.022	0.95
Placebo	10.9		



Ultra low doses of intranasal PH10 improve MDD symptoms with rapidonset efficacy.

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# Summary: AV-101 and PH10 for MDD and TRD Multiple Shots on Goal



Augmentation for inadequate response to SSRIs/SNRIs

AV-101 ELEVATE Study (ongoing)

Relapse prevention after successful ketamine-based therapy

AV-101 RELAY Study (preparing for launch in 2020)

# First-line monotherapy

PH10 Phase 2b Study (preparing for launch in 2020)





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# **Phase 1 Clinical Program**

AV-101 for Suicidal Ideation





LOOKING REYOND CURRENT TREATMENTS FOR CENTRAL NERVOUS SYSTEM (CNS) DISEASES AND DISORDERS WITH HIGH LINMET NEED

# **AV-101 for Suicidal Ideation**







# Baylor / VA Phase 1b Clinical Study

- · Sponsored by U.S. Department of Veteran's Affairs (VA)
- · Ongoing at Baylor University
- · First-step study testing for potential anti-suicidal effects of AV-101
- · Double-blind, placebo-controlled, crossover design
- Two single doses of AV-101 (720 mg and 1440 mg) and placebo over three weeks
- · Target enrollment: 12 healthy U.S. Veterans
- Topline results anticipated in Q4 2019

Primary Objective: Target engagement relevant to NMDA antagonism and suicidal ideation

# **Additional Programs**

**AV-101** Neuropathic Pain Parkinson's LID





VistaGen=

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# **AV-101 for Neuropathic Pain**

- Potential oral non-opioid treatment option
- Non-addictive and non-sedating in published preclinical studies
- · FDA Fast Track designation



"[W]e've undertaken ... steps to advance the development of nonaddictive treatments for pain."1 Scott Gottlieb, M.D.,

FDA Commissioner

AV-101 for Parkinson's LID

- Levodopa-induced dyskinesia (LID)
- · Reduced mean dyskinesia scores in Parkinsonian monkeys with L without worsening Parkinson's symptoms
- · Potential to replace oral amantadine for PD LID



Next Step: Phase 2a study launch in 2020

Next Step: Phase 2a study launch in 2020

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# **Experienced Team Leading Execution**



- 25 years of experience with biopharmaceutical companies, a healthcare venture capital firm and a profitable CRO
- Artemis Neuroscience; SciClone Pharmaceuticals; Cato BioVentures; Cato Research: Morrison & Foerster



- senior biotechnology management
- · Progenitor; Lineberger Comprehensive Cancer Center



# Mark A. McPartland

20 years of experience in corporate development, capital markets and management consulting

Jerrold D. Dotson, CPA

Chief Financial Officer, Secretary

California & Hawaiian Sugar; Clorox

management finance and administration Calypte Biomedical: Discovery Foods:

20 years of experience in senior

Stellar Biotechnologies; MZ Group; Hayden Communications: Alliance Advisors

# Mark A. Smith, M.D.,

#### Chief Medical Officer

- · 20 years of large Pharma CNS drug development experience
- · Teva Pharmaceuticals; Shire Pharmaceuticals; AstraZeneca Pharmaceuticals; DuPont Pharmaceutical Company; U.S. National Institute of Mental Health



Vice President, Corporate Development

# **Distinguished Clinical and Regulatory Advisors**





#### Maurizio Fava, M.D.

Professor of Psychiatry, Harvard Medical School; Director, Division of Clinical Research, Massachusetts General Hospital (MGH) Research Institute; Executive Director, MGH Clinical Trials Network and Institute



#### Sanjay Mathew, M.D.

Associate Professor of Psychiatry and Behavioral Sciences, Marjorie Bintilif Johnson and Raleigh White Johnson; Jr. Chair for Research in Psychiatry and Menninger Department of Psychiatry & Behavioral Sciences, Baylor College of Medicine



#### Michael Liebowitz, M.D.

Professor of Clinical Psychiatry, Columbia University, Managing Director and Founder, The Medical Research Network, LLC; Director (retired), Anxiety Disorders Clinic at the New York State Psychiatric Institute



#### Gerard Sanacora, Ph.D., M.D.

Professor of Psychiatry, Yale School of Medicine; Director, Yale Depression Research Program; Scientific Director, Yale-New Haven Hospital Interventional Psychiatry Service



#### Thomas Laughren, M.D.

Director (retired), U.S. Food and Drug Administration (FDA) Division of Psychiatry Products, Office of New Drugs, Center for Drug Evaluation and Research (CDER)



#### Mark Wallace, M.D.

Professor of Clinical Anesthesiology, Chair of the Division of Pain Medicine, Medical Director and Director at the University of California, San Diego

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# Looking beyond current therapies for CNS diseases and disorders with high unmet need





Emphasis: at-home use, rapid-onset, exceptional safety



3 late-stage product candidates with new generation MOAs

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2 with Phase 2 POC efficacy and safety, 3rd with potential in 2019



3 clinical readouts during 2019

At least **1** pivotal Phase 3 study launch in 2020

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LOOKING BEYOND CURRENT
TREATMENTS FOR
CENTRAL NERVOUS SYSTEM (CNS)
DISEASES AND DISORDERS WITH
HIGH UNMET NEED







### VistaGen Therapeutics Receives Notice of Allowance for Additional U.S. Patent Regarding Methods of Production for AV-101

**SOUTH SAN FRANCISCO, Calif., March 13, 2019** - <u>VistaGen Therapeutics</u> (NASDAQ: VTGN), a clinical-stage biopharmaceutical company developing new generation medicines for depression and other central nervous system (CNS) diseases and disorders with high unmet need, today announced that the U.S. Patent and Trademark Office (USPTO) has issued a Notice of Allowance for <u>U.S. Patent Application 15/812,599</u> related to certain methods of production for AV-101, VistaGen's oral NMDA receptor glycine site antagonist in Phase 2 development for major depressive disorder (MDD). The patent, once issued, will expand upon the related claims obtained in <u>U.S. Patent No. 9,834,801</u> granted to VistaGen by the USPTO in December 2017 and will not expire until at least 2034.

#### About AV-101

VistaGen's AV-101 (4-Cl-KYN) is an investigational, oral NMDA receptor glycine site antagonist with potential to be a treatment for multiple CNS indications with high unmet need. AV-101 is currently in Phase 2 clinical development in the U.S. for MDD and in a first-step target engagement study in healthy volunteer U.S. military Veterans for suicidal ideation. The U.S. Food and Drug Administration (FDA) has granted Fast Track designation for development of AV-101 as both a potential adjunctive treatment for MDD and as a non-opioid treatment for neuropathic pain.

#### About VistaGen

VistaGen Therapeutics is a clinical-stage biopharmaceutical company developing new generation medicines with for multiple CNS diseases and disorders with high unmet need. Each of VistaGen's CNS pipeline candidates, AV-101, PH10 and PH94B, has potential for convenient, at-home use, rapid-onset therapeutic benefits, and exceptional safety. As noted above, AV-101 is an oral NMDA receptor glycine site antagonist (a full antagonist) in Phase 2 development in the U.S. for treatment of MDD and in a first-step target engagement study in healthy volunteer U.S. military Veterans for suicidal ideation. PH10 nasal spray is a potential first-in-class CNS neuroactive steroid with rapid-onset antidepressant effects observed at microgram doses and without systemic exposure. PH10 is in Phase 2 development for MDD. PH94B nasal spray is a potential first-in-class CNS neuroactive steroid with rapid-onset effects observed at microgram doses and without systemic exposure. Phase 2 development for PH94B for social anxiety disorder (SAD) has been completed successfully, and PH94B is now being prepared for Phase 3 development as an on-demand PRN treatment of SAD.

For more information, please visit www.vistagen.com and connect with VistaGen on Twitter, LinkedIn and Facebook.

#### **Forward-Looking Statements**

This release contains various statements concerning VistaGen's future expectations, plans and prospects, including without limitation, our expectations regarding development and commercialization of our CNS pipeline, including AV-101 for MDD, neuropathic pain and suicidal ideation, PH94B for SAD, and PH10 for MDD, as well as our intellectual property and commercial protection of our drug candidates, all of which constitute forward-looking statements for the purposes of the safe harbor provisions under the Private Securities Litigation Reform Act of 1995. These forward-looking statements are neither promises nor guarantees of future performance and are subject to a variety of risks and uncertainties, many of which are beyond our control, and may cause actual results to differ materially from those contemplated in these forward-looking statements. Among these risks is the possibility that (i) we may encounter unexpected adverse events in patients during our clinical development of any product candidate that cause us to discontinue further development, (ii) we may not be able to successfully demonstrate the safety and efficacy of our product candidates at each stage of clinical development, (iii) success in preclinical studies or in early-stage clinical trials may not be repeated or observed in ongoing or future studies, and ongoing or future preclinical and clinical results may not support further development of, or be sufficient to gain regulatory approval to market AV-101, PH94B, and/or PH10, (iv) decisions or actions of regulatory agencies may negatively affect the progress of, and our ability to proceed with, further clinical studies or to obtain marketing approval for our drug candidates, (v) we may not be able to obtain or maintain adequate intellectual property protection and other forms of marketing and data exclusivity for our product candidates, (vi) we may not have access to or be able to secure substantial additional capital to support our operations, including our ongoing clinical development activities; and (vii) we may encounter technical and other unexpected hurdles in the manufacturing and development of any of our product candidates. Certain other risks are more fully discussed in the section entitled "Risk Factors" in our most recent annual report on Form 10-K, and subsequent quarterly reports on Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in our other filings with the Securities and Exchange Commission (SEC). Our SEC filings are available on the SEC's website at www.sec.gov. In addition, any forward-looking statements represent our views only as of the issuance of this release and should not be relied upon as representing our views as of any subsequent date. We explicitly disclaim any obligation to update any forward-looking statements.

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