DEVELOPING NEW GENERATION MEDICINES FOR DEPRESSION AND OTHER CNS DISORDERS
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, 2017, filed with the Securities and Exchange Commission (SEC) on June 29, 2017, 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.
VistaGen Overview

NASDAQ: VTGN

Focused on Central Nervous System (CNS) disorders with high unmet need

AV-101 has game-changing potential in depression and pain

Long-term support from U.S. National Institutes of Health (NIH)

Multiple potentially transformative clinical and corporate catalysts in 2018/2019
Past 6 Months – Most Productive in Company History

December 2017
$15 million underwritten public offering

December 2017
USPTO granted AV-101 US patent

November 2017
EPO granted AV-101 EU patent

October 2017
AV-101 on cover of *Journal of Pain*

October 2017
FDA green light for ELEVATE Phase 2 MDD study

January 2018
FDA Fast Track designation for AV-101 for MDD

March 2018
USPTO NOA for AV-101 US patent

March 2018
USPTO NOA for AV-101 US patent

March 2018
ELEVATE Study Launch

April 2018
EPO NOI for AV-101 EU patent

Solid Foundation
Depression in the U.S.

1 in 4 women 1 in 6 men diagnosed with depressive disorders

1 in 8 age 12 and over takes an antidepressant\(^1\)

U.S. DRUG-TREATED DEPRESSION MARKET IS LARGE WITH HIGH UNMET NEED\(^2,3\)

11.6M U.S. Drug-Treated MDD Patients

7.3M Inadequate response to 1st Line antidepressant

63% treated with 2nd Line antidepressant

5.1M Treatment-resistant after 2nd line antidepressant

44% treatment-resistant after 2nd Line antidepressant

Current Drug Treatment Options for Depression Fall Short

Current Antidepressants

- Often do not work
  - Initial treatment effective in 1 of 3 patients
- Slow to work
  - May take 4 to 6 weeks or more to achieve antidepressant effects
- Numerous side effects
  - Agitation, irritability, sexual dysfunction, nausea, insomnia, dizziness, fatigue

Current Adjunctive Atypical Antipsychotics

- Often do not work
  - Only 10 to 20% of MDD patients respond
- Safety concerns
  - “Black Box” warnings, mortality in elderly, cardiovascular complications, stroke
- Numerous side effects
  - Weight gain, metabolic syndrome, akathisia, tardive dyskinesia, anxiety
Current Depression Drug Treatment Paradigm: “Wait and See, Rinse and Repeat …”

FIRST LINE
SSRI/SNRI
4-6 Weeks or more

SECOND LINE
SSRI/SNRI
4-6 Weeks or more

THIRD LINE
SSRI/SNRI
4-6 Weeks or more

Adjunctive Atypical Antipsychotics

- ABILIFY (aripiprazole)
- REXulti (loxapine)
- Seroquel (ziprasidone)
The Ketamine Story: A Breakthrough Shift in the Depression Treatment Paradigm

FUNDAMENTALLY DIFFERENT MOA

- FDA-approved anesthetic
- NMDAR antagonist
- Works on a different neurotransmitter than antidepressants
- IV only (intranasal spray in Phase 3)
- Must be given in a medical setting

FASTER-ACTING THAN ALL CURRENT DRUGS

“[K]etamine, given intravenously, might be the most important breakthrough in antidepressant treatment in decades.”

Thomas Insel
Former Director, U.S. National Institute of Mental Health

HAS SIDE EFFECTS & SAFETY CONCERNS

- DEA Schedule III Drug
- Risk of Abuse
- Dissociation
- Hallucinations
- Confusion
- Dizziness
- Increased BP
NIMH Ketamine Study in Treatment-Resistant Depression

BREAKTHROUGH RESULTS WITHIN 1 DAY OF A SINGLE TREATMENT

Ketamine Responder\(^\text{\textregistered}\) Rates at 1 Day in Patients with Treatment-resistant Depression

\[^{\text{\textregistered}}\text{Proportion of patients with treatment-resistant depression with at least 50% improvement in depression rating.}\]

\[^{2}\text{Zarate, C. A., Jr., et al. (2006) "A randomized trial of an N-methyl-D-aspartate antagonist in treatment-resistant major depression." Arch Gen Psychiatry 63:856-864.}\]
Ketamine offers new hope for patients with depression, but is it a convenient and safe long-term solution?

“Club Drug Ketamine Provides Hope in Fight Against Depression”

“Drugs to Lift Depression in Hours Rather Than Weeks”

1: http://www.nimh.nih.gov/about/director/2014/ketamine.shtml
AV-101: A New Generation Antidepressant Candidate

- ORAL NMDAR GLYB ANTAGONIST
- MOA FUNDAMENTALLY DIFFERENT FROM ALL CURRENT FDA-APPROVED ANTIDEPRESSANTS
- MODULATES NMDAR; ACTIVATES AMPAR
- KETAMINE-LIKE ANTIDEPRESSANT EFFECTS
- NO KETAMINE-LIKE SIDE EFFECTS OR SAFETY CONCERNS

- Very well-tolerated in two NIH-funded Phase 1 safety studies
- ELEVATE, Phase 2 depression study, results expected in 1H 2019
AV-101’s Mechanism of Action

INHIBITS NMDA RECEPTORS, ACTIVATES AMPA RECEPTORS

AV-101 Prodrug (4-Cl-KYN)

AV-101 Active Metabolite (7-Cl-KYNA)
# AV-101 vs. Ketamine in Published Preclinical Studies

## KETAMINE-LIKE ANTIDEPRESSANT EFFECTS, NO KETAMINE-LIKE SIDE EFFECTS

<table>
<thead>
<tr>
<th>Benefits</th>
<th>AV-101</th>
<th>Ketamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forced-swim</td>
<td>EQUIVALENT</td>
<td></td>
</tr>
<tr>
<td>Tail-suspension</td>
<td>EQUIVALENT</td>
<td></td>
</tr>
<tr>
<td>Learned-helplessness</td>
<td>EQUIVALENT</td>
<td></td>
</tr>
<tr>
<td>Novelty-suppressed feeding</td>
<td>EQUIVALENT</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Negative Behavioral Effects</th>
<th>AV-101</th>
<th>Ketamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abusive potential</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Hyper movement</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Movement sensitization</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Circling and rearing</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Sensory-motor gating</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### Phase 1a
- Randomized, double-blind, placebo-controlled
- Single oral dose, with sequential dose-escalation
- 6 single dose levels: 120, 360, 720, 1,080 & 1,440 mg
- 36 subjects: 18 treatment, 18 placebo; 6 per cohort

### Phase 1b
- Randomized, double-blind, placebo-controlled
- Daily oral dose (14 days), sequential dose-escalation
- 3 dose levels: 360, 1,080 and 1,440 mg
- 48 subjects: 36 treatment, 12 placebo; 16 per cohort

### RESULTS
- Well-tolerated, good bioavailability; no SAEs
- At higher doses, some subjects on AV-101 (none on placebo) reported positive feelings of well-being similar to antidepressant effects reported with ketamine, but without ketamine’s side-effects

NIMH-Sponsored Phase 2 Study

Principal Investigator: Dr. Carlos Zarate, Jr., NIMH

Study Design

- Ongoing at NIMH clinic in Maryland
- Double-blind, placebo-controlled, crossover design
- Single oral dose monotherapy in patients with treatment-resistant depression, once per day/14 days
- Emphasis on key biomarkers – CSF analysis, neuroimaging
- Target enrollment: ca. 20 adults
- Completion anticipated by end of 2018

Primary Endpoint:
Safety and efficacy using standard Hamilton Rating Scale (HDRS)

Secondary Endpoints:
Change from baseline in widely-accepted measures of mood, depression and cognition
First Goal for AV-101

Displace Atypical Antipsychotics in the Depression Drug Treatment Paradigm

**FIRST LINE**

SSRI/SNRI
4-6 Weeks or more

**SECOND LINE**

SSRI/SNRI
4-6 Weeks or more

**THIRD LINE**

SSRI/SNRI
4-6 Weeks or more

Adjunctive AV-101

Adjunctive Atypical Antipsychotics
ELEVATE Phase 2 Study for Depression

Adjunctive Treatment for Inadequate Response to Current Antidepressants

Principal Investigator:
Maurizio Fava, MD, Harvard

- Projected enrollment = ca. 180 patients
- Double-blind, placebo-controlled, 2-Stage Sequential Parallel Comparison Design
- **Objective:** assess efficacy and safety of AV-101 plus current antidepressants in patients with an inadequate response to current antidepressants
- Single oral dose, once per day for 14 days
- Results expected in 1H 2019

**Primary Endpoint:**
Efficacy demonstrated by decrease on Montgomery-Asberg Depression Rating Scale

**Secondary Endpoints:**
Additional widely-accepted measures of mood, depression and cognition

**Timeline:**
- **MDD Adjunctive Therapy**
  - 2H 2017
  - 1H 2018
  - 2H 2018
  - 1H 2019

- **Clinical Site Preparation and FDA Approval to Launch**
- **Study Initiation**
- **Topline Results**
Second Goal for AV-101

Prevent relapse of depression following ketamine therapy

NEXT STEP in 2019

Phase 2 study of AV-101 vs. placebo following ketamine therapy in patients with Major Depressive Disorder
Neuropathic Pain in the U.S.

6% - 10% of U.S. population suffers from neuropathic pain\(^1\)

Current treatments fall short
- Prescription opioids (oxycodone)
- Anticonvulsants (pregabalin)
- Antidepressants (SSRIs)

Side effects and Safety Concerns
- Addiction
- Sleepiness, drowsiness, dizziness
- Suicidal thoughts or behavior
- Drug-drug interactions

Overuse of addictive prescription opioids is at epidemic levels

---

Third Goal for AV-101

New Oral, Non-Addictive, Non-Sedating Treatment for Pain

Phase 2 study of AV-101 vs placebo in patients with neuropathic pain

NEXT STEP in 2019

Fourth Goal for AV-101
Reduce Parkinson’s disease levodopa-induced dyskinesia

Levodopa-induced dyskinesia occurs in most patients with PD after 5-10 years

NEXT STEP in 2019
Phase 2 study of AV-101 vs placebo in Parkinson’s patients
High-Value Peer M&A Underscores Upside Potential

After Rapastininel Phase 2, Allergan paid Naurex $571 million in cash, and agreed to over $1 billion for potential future milestones

Rapastininel

- Similar MOA to AV-101 (NMDAR/AMPA)
- Ketamine-like antidepressant effects
- No ketamine-like side effects
- IV ONLY – NOT ORAL

Acquired by Allergan after Phase 2

- $571 million in cash at closing
- Over $1.0 billion in potential milestones
- Currently in Phase 3 development
Experienced Team Leading Execution

Ralph Snodgrass, Ph.D.
President, Chief Scientific Officer
• 23 years of experience in senior biotechnology management
• Progenitor; Lineberger Comprehensive Cancer Center

Mark A. Smith, M.D., Ph.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

Shawn K. Singh
Chief Executive Officer
• 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

Ralph Snodgrass, Ph.D.
President, Chief Scientific Officer
• 23 years of experience in senior biotechnology management
• Progenitor; Lineberger Comprehensive Cancer Center

Mark A. Smith, M.D., Ph.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

Jerrold D. Dotson, CPA
Chief Financial Officer, Secretary
• 20 years of experience in senior management finance and administration
• Calypte Biomedical; Discovery Foods; California & Hawaiian Sugar; Clorox

Mark A. McPartland
Vice President, Corporate Development
• 20 years of experience in corporate development, capital markets and management consulting
• Stellar Biotechnologies; MZ Group; Hayden Communications: Alliance Advisors
Leading CNS 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

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)

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

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

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
## AV-101 Pipeline

<table>
<thead>
<tr>
<th>Compound</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>(AV-101)</td>
<td>Major Depressive Disorder</td>
<td></td>
<td>E L E V A T E</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(4-CI-KYN)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AV-101</td>
<td>Neuropathic Pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(4-CI-KYN)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AV-101</td>
<td>Post-Ketamine MDD/Suicidal Ideation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(4-CI-KYN)</td>
<td>Relapse</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AV-101</td>
<td>Parkinson’s Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(4-CI-KYN)</td>
<td>Levodopa-Induced Dyskinesia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AV-101</td>
<td>Epilepsy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(4-CI-KYN)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
VistaGen Summary

NASDAQ: VTGN

Clinical stage, focused on multiple major CNS markets with high unmet need

AV-101, oral new generation CNS drug candidate with game-changing potential as a non-addictive, non-sedating, at-home treatment for depression and pain

Highly-experienced team leading execution

Potentially transformative clinical and corporate catalysts in 2018/2019
Supplemental Information
# Capitalization
**NASDAQ: VTGN**

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common Stock</td>
<td>22,957,615</td>
</tr>
<tr>
<td>Preferred Stock (fixed conversion)(^{(1)})</td>
<td>4,228,252</td>
</tr>
<tr>
<td><strong>Total Common and Preferred</strong></td>
<td><strong>27,160,867</strong></td>
</tr>
<tr>
<td>Stock Plan Options</td>
<td>5,300,338</td>
</tr>
<tr>
<td>Common Stock Warrants(^{(2)})</td>
<td>16,603,516</td>
</tr>
<tr>
<td><strong>Total Options and Warrants</strong></td>
<td><strong>21,903,854</strong></td>
</tr>
<tr>
<td><strong>Total Common, Preferred, Options and Warrants</strong></td>
<td><strong>49,089,721</strong></td>
</tr>
</tbody>
</table>

As of May 2, 2018

1. Shown on an as converted basis; no voting rights
2. WAEP = $2.85 per share
# AV-101 Advantages vs. NR2B Specific

**NMDA RECEPTOR ANTAGONISTS**

There are 9 different variants of the NMDAR

<table>
<thead>
<tr>
<th></th>
<th>Di-heteromeric NMDARs</th>
<th>Tri-heteromeric NMDARs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1/2A</td>
<td>1/2B</td>
</tr>
<tr>
<td>AV-101 Gly_B NMDA receptor antagonist regulates</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>NR2B specific NMDA receptor antagonist regulates</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

- In addition to neuronal cell-specific expression, within individual neurons, several NMDA receptor subtypes can be expressed.
- NR2B-selective compounds can only modulate 4 of the 9 NMDA receptor variants.
- AV-101 decreases NMDA receptor function on all 9 NMDA receptor variants.

---

Publications

- Li, C., et. al. (2016) “Activation of hippocampal BDNF signaling is involved in the antidepressant-like effect of the NMDA receptor antagonist 7-chlorokynurenic acid.” Brain Research 1630:73-82.