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, 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

Clinical-stage, CNS-focused

AV-101, oral prodrug, new generation NMDAR GlyB antagonist

Depression, neuropathic pain, Parkinson’s disease LID, suicidal ideation

Multiple potential clinical catalysts in 2018 and 2019
Major Depressive Disorder (MDD) in U.S.

1 in 8

age 12 and over takes an antidepressant

Over 7 Million

with inadequate response to current antidepressants

U.S. DRUG-TREATED MARKET IS LARGE AND UNDERSERVED

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

Shortcomings of Current MDD Drug Treatment Options

Antidepressants

• Often do not work
  – Only 1 of 3 respond to initial treatment

• Numerous side effects
  – Anxiety, agitation, irritability, sexual problems, nausea, insomnia, dizziness, fatigue, drowsiness

• Slow to work
  – May take at least 4 weeks to work

Adjunctive Atypical Antipsychotics

• Often do not work
  – Only 10% to 20% of MDD patients respond

• Numerous side effects
  – Weight gain, metabolic syndrome, tardive dyskinesia, sedation, fidgeting, restlessness, fatigue, insomnia

• Safety concerns
  – “Black Box” warnings, mortality in elderly, cardiovascular complications, stroke
Current MDD Drug Treatment Paradigm: “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
The Ketamine Story – A Paradigm Shift in MDD Treatment

DIFFERENT MOA

- FDA-approved anesthetic
- Commonly used
- Injection only
- NMDAR antagonist

MOA is fundamentally different from all current antidepressants and atypical antipsychotics

SAFETY CONCERNS

- Dissociation
- Hallucinations
- Confusion
- Dizziness
- Increased BP
- Schedule III for Abuse Potential (“Special K”)

FAST-ACTING ANTIDEPRESSANT

“[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

1
NIMH Breakthrough Ketamine Study in Treatment-resistant MDD

ROBUST ANTIDEPRESSANT EFFECTS WITHIN 1 DAY OF A SINGLE IV INFUSION

Responder\(^x\) Rates at 1 Day with IV Ketamine in Treatment-resistant MDD

\(^x\) Proportion of patients with treatment-resistant MDD with at least 50% improvement in depression rating

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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, but is it a long-term solution?

CAN KETAMINE’S ANTIDEPRESSANT BENEFITS BE MAINTAINED SAFELY?

“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
ORAL, KETAMINE-LIKE ANTIDEPRESSANT EFFECTS, WITHOUT KETAMINE-LIKE SIDE EFFECTS

- Prodrug, rapidly absorbed through the gut
- Transported into the brain
- Converted in the brain into its active metabolite
- Inhibits NMDAR activity through Gly\textsubscript{B} site binding
- Does not block NMDAR ion channel, as ketamine does
- Activates AMPA receptors and synaptogenic signaling
- Fast-acting antidepressant effects in rodent models
- Well-tolerated in NIH-funded Phase 1 safety studies
AV-101’s Mechanism of Action

NMDAR INHIBITION, AMPAR ACTIVATION, SYNAPTOGENIC SIGNALING

Prodrug

AV-101

7-CI-KYNA (full antagonist)

Active metabolite

NMDA Receptor Pharmacology

Extracellular side

Glutamate binding site

Glycine binding site

NR2B (NR2A-D)

NR1

Cytoplasmic side

K^+

Na^+

Ca^{2+}

Classic channel-blocking antagonist:

Ketamine

Lanicemine

Phencyclidine

4-chlorokynurenine (4-CI-KYN)

(oral delivery to CNS)

Activated

Astrocytes

7-chlorokynurenine acid (7-CI-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>EQUIVALENT</td>
</tr>
<tr>
<td>Tail-suspension</td>
<td>EQUIVALENT</td>
<td>EQUIVALENT</td>
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<tr>
<td>Learned-helplessness</td>
<td>EQUIVALENT</td>
<td>EQUIVALENT</td>
</tr>
<tr>
<td>Novelty-suppressed feeding</td>
<td>EQUIVALENT</td>
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</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>

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### Phase 1a
- Randomized, double-blind, placebo-controlled
- Single oral dose, with sequential dose-escalation
- 6 single dose levels: 30, 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), with 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, even at maximum dose; good bioavailability; no serious adverse events
- At higher doses, some subjects on AV-101 (none on placebo) reported positive feelings of well-being similar to antidepressant effects reported with ketamine, without ketamine’s side effects

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NIMH CRADA-Sponsored Phase 2 Study
AV-101 MONOTHERAPY IN TREATMENT-RESISTANT MDD PATIENTS

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

- Ongoing at NIMH
- Double-blind, placebo-controlled, crossover design
- Oral monotherapy in treatment-resistant MDD patients, once per day for 14 days
- Multiple biomarkers
- Target enrollment: ca. 20
- Completion expected in H2 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

MDD Monotherapy
H2 2017
H1 2018
H2 2018

NIMH completion expected
First Goal for AV-101: Displace Atypical Antipsychotics in MDD 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

AV-101
Adjunctive Atypical Antipsychotics
**AV-101 Phase 2 Adjunctive Treatment Study**

**ORAL ADJUNCTIVE TREATMENT FOR INADEQUATE SSRI/SNRI MONOTHERAPY**

**Principal Investigator:**
Maurizio Fava, MD, Harvard

- Projected enrollment = ca. 180 adult MDD patients with an inadequate response to current antidepressants
- Double-blind, placebo-controlled, Sequential Parallel Comparison Design
- Efficacy and safety of AV-101 in conjunction with current antidepressants
- Single oral dose, once per day for 14 days
- Topline results H1 2019

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

**Secondary Endpoints:**
Additional widely-accepted measures of mood, depression and cognition
Second Goal for AV-101:
Post-Ketamine Maintenance for MDD and Suicidal Ideation

Prevent relapse in MDD and suicidal ideation post-ketamine infusion

Phase 2 study of AV-101 vs. placebo, post-ketamine infusion, in MDD patients with suicidal ideation
Third Goal for AV-101: Treat Neuropathic Pain (NP)

Oral, Non-Opioid, Non-Sedating NP Treatment Option

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

Fourth Goal for AV-101:
Parkinson’s disease levodopa-induced dyskinesia (PD LID)

Reduce PD LID, without amantadine-like side effects and safety concerns

Phase 2 study of AV-101 vs placebo in Parkinson’s patients
Multiple Potential AV-101 Phase 2 Catalysts in 2018 and 2019

2H
FDA green light for MDD adjunctive treatment study
✓ Completed

1H
Launch MDD adjunctive treatment study

1H
Complete MDD adjunctive treatment study

1H
Topline results of MDD adjunctive treatment study

2H
FDA Fast Track designation for MDD program
✓ Completed

1H
NIMH completion of MDD monotherapy study

2H
NIMH completion of MDD monotherapy study

2H
Potential launch of studies for pain, PD LID and/or post-ketamine MDD and suicidal ideation
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
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- Artemis Neuroscience; SciClone Pharmaceuticals; Cato BioVentures; Cato Research: Morrison & Foerster

**Jerrold D. Dotson, CPA**
Chief Financial Officer, Secretary
- 20 years of experience in senior management finance and administration
- Calyppe 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
Preeminent 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
Clinical-stage, CNS-focused

AV-101, oral, new generation CNS drug candidate with multiple shots on goal

Depression, neuropathic pain, Parkinson’s disease LID, suicidal ideation

Multiple potential clinical catalysts in 2018 and 2019