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 30, 2020

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

NEVADA	**000-54014**	**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))

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	VTGN	Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR 230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR 240.12b-2)

Emerging Growth Company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act ☐

Item 3.01 Notice of Delisting or Failure to Satisfy a Continued Listing Rule or Standard; Transfer of Listing.

On March 30, 2020, VistaGen Therapeutics, Inc. (the "*Company*") received a letter (the "*Letter*") from the Listing Qualifications Staff of The Nasdaq Stock Market, LLC ("*Nasdaq*") notifying the Company that the listing of its shares of common stock, par value $0.001 per share ("*Common Stock*"), was not in compliance with Nasdaq Listing Rule 5550(b)(2) (the "*MVLS Rule*") for continued listing on the Nasdaq Capital Market, as the market value of the Company's listed securities was less than $35 million for the previous 30 consecutive business days. Under Nasdaq Listing Rule 5810(c)(3)(C), the Company has a period of 180 calendar days, or until September 28, 2020, to regain compliance with the MVLS Rule. To regain compliance, during this 180-day compliance period, the market value of the Company's listed securities must be $35 million or more for a minimum of 10 consecutive business days.

The Letter has no immediate effect on the continued listing status of the Company's Common Stock on the Nasdaq Capital Market, and, therefore, the Company's listing remains fully effective.

There can be no assurance that the Company will regain compliance with the MVLS Rule during the 180-day period in which to regain compliance or maintain compliance with the other Nasdaq listing requirements. Regardless of any outcome in connection with the MVLS Rule, as disclosed in the Company's Current Report on Form 8-K, filed on January 31, 2020, if the Company fails to regain compliance with the minimum bid price requirement set forth in Nasdaq Listing Rule 5550(a)(2) for at least ten consecutive business days prior to July 29, 2020, its Common Stock will continue to be subject to delisting by Nasdaq, provided, however, that, if such requirement is not met by July 29, 2020, Nasdaq may grant the Company a second 180 calendar day period to regain compliance if, by such date, the Company (i) is in compliance with the MVLS Rule and all other initial listing standards for the Nasdaq Capital Market, other than the minimum closing bid price requirement and (ii) notifies Nasdaq of its intent to cure the deficiency.

Item 8.01 Other Items.

On April 3, 2020, the Company began utilizing a new corporate presentation. A copy of the updated corporate presentation is attached to this Current Report on Form 8-K as Exhibit 99.1.

The information in 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 9.01 Financial Statements and Exhibits.

(d) Exhibits Index

Exhibit No.	Description
99.1	VistaGen Therapeutics, Inc. Corporate Presentation, dated April 2020.

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: April 3, 2020

By: */s/ Shawn K. Singh*
Shawn K. Singh
Chief Executive Officer


VistaGen®
Therapeutics
www.vistagen.com
Nasdaq: VTGN
Spring 2020
LOOKING BEYOND CURRENT TREATMENTS FOR CNS DISEASES AND DISORDERS WITH HIGH UNMET NEED

www.vistagen.com

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, 2019, filed with the Securities and Exchange Commission (SEC) on June 25, 2019, as well as any updates to those risk factors filed with the SEC from time to time in our current and periodic reports on Forms 8-K and 10-Q, respectively. 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.


Looking Beyond Current Treatments for
CNS Diseases and Disorders with High Unmet Need
VistaGen is developing differentiated new generation medications for large and growing mental health and neurology markets where current treatments are inadequate to meet the needs of millions of patients worldwide.
VistaGen®
Therapeutics

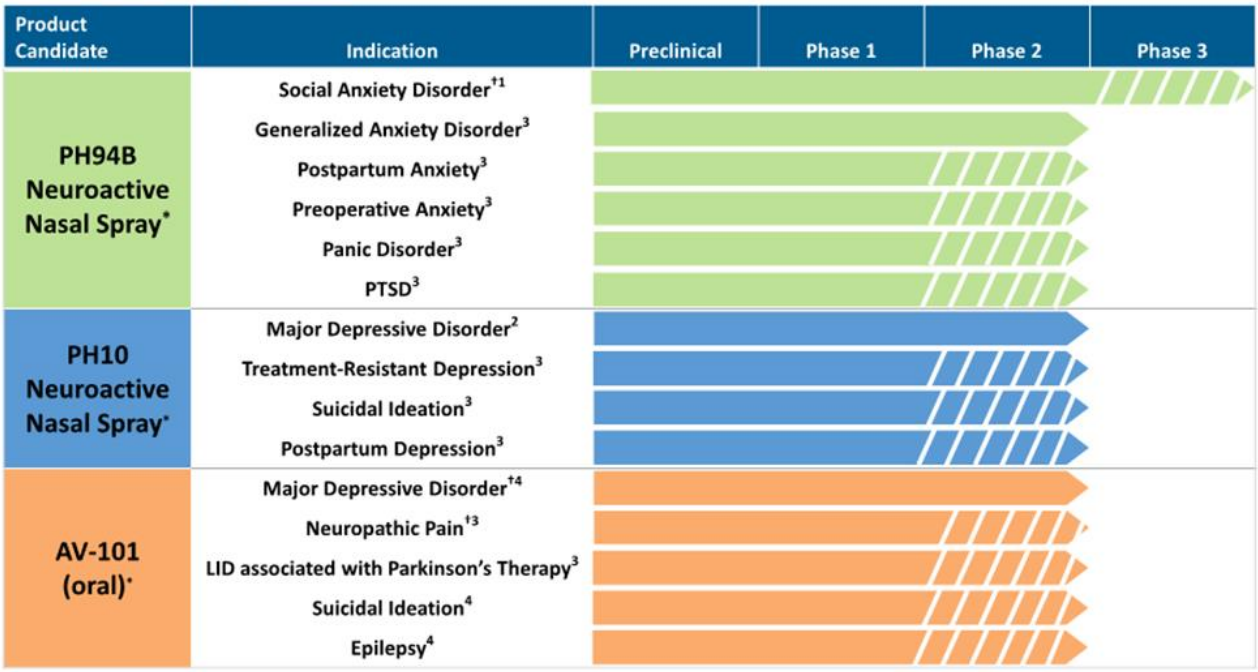
www.vistagen.com

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

VistaGen Therapeutics

- 3 differentiated clinical-stage product candidates
- Novel mechanisms of action
- Rapid-onset
- Exceptional safety
- Each candidate has potential in multiple markets

Our CNS Pipeline



* All potential future studies are subject to securing sufficient internal and/or collaborative third-party funding

† FDA Fast Track designation granted

1. Preparing for initial U.S. Phase 3 clinical study
2. Preparing for initial U.S. Phase 2b clinical study
3. Assessing for potential Phase 2a POC study
4. Assessing for potential Phase 2a POC study with adjunctive probenecid

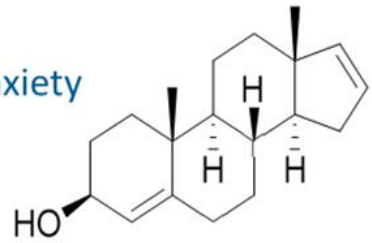
PH94B neuroactive nasal spray

(3β)-androsta-4,16-dien-3-ol

VistaGen® Therapeutics

Novel, fast-acting, non-systemic therapy for:

- Social Anxiety Disorder
- Generalized Anxiety Disorder
- Postpartum Anxiety
- Preoperative/Pre-testing (MRI) Anxiety
- Panic Disorder
- PTSD



LOOKING BEYOND CURRENT TREATMENTS FOR CNS DISEASES AND DISORDERS WITH HIGH UNMET NEED

Social Anxiety Disorder (SAD) in the U.S.

VistaGen® Therapeutics

National Institutes of Health

More than Just Shyness

One of the most prevalent mental health conditions in the U.S.

Affects as many as

20 million[1]

Americans

Anxiety and fear in everyday social and performance situations

- meeting new people
- making a work presentation
- giving a speech
- interviewing for a job
- eating/drinking in front of others

[1]Harvard Medical School, 2007. National Comorbidity Survey (NCS). (Update - 2017, August 21); Kessler, et al, US National Comorbidity Survey Replication, 2005
https://www.nimh.nih.gov/health/publications/social-anxiety-disorder-more-than-just-shyness/index.shtml

Current SAD Drug Treatments Fall Short

VistaGen Therapeutics

FDA APPROVED

Not FDA-Approved
*** Prescribed Off-label ***

Antidepressants (2 SSRIs, 1 SNRI)

- Slow onset, chronic administration
- May worsen anxiety initially
- Significant potential side effects
  - Nausea and vomiting
  - Weight gain
  - Sleepiness
  - Sexual problems
- Potential drug-drug interaction

Benzodiazepines & Beta Blockers

- Addiction risk
- Significant potential side effects
  - Nausea and vomiting
  - Blurred vision
  - Dizziness
  - Sedation
  - Confusion and cognitive impairment

There is no FDA-approved, fast-acting PRN treatment for SAD

PH94B for SAD

- First-in-class; different from all SAD therapies
- Successful Phase 2 completed
- U.S. Phase 3 launch in 2H 2020
- Rapid onset efficacy (10-15 minutes), exceptional safety
- Microgram dosing (3.2 µg), non-systemic
- Well-tolerated, non-sedating, non-addictive
- FDA Fast Track designation; first granted by FDA for SAD

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

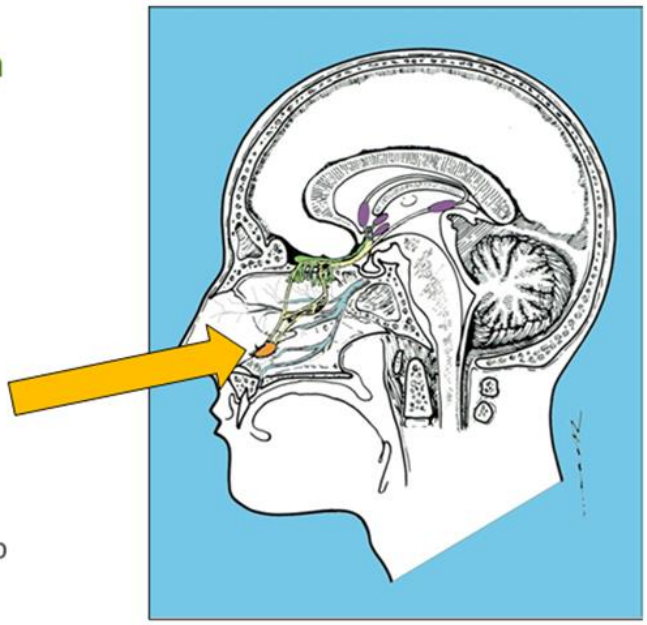
VistaGen® Therapeutics

LOOKING BEYOND CURRENT TREATMENTS FOR CNS DISEASES AND DISORDERS WITH HIGH UNMET NEED

VistaGen Therapeutics

PH94B Mechanism of Action

- **Engages nasal chemosensory receptors, which activate neural circuits in the brain that suppress fear and anxiety**
  - Nasal chemosensory receptors activate olfactory bulb (OB) neurons that project to the limbic amygdala
  - Modulates activity of the limbic-hypothalamic autonomic nervous system, which is involved in the pathophysiology of SAD and multiple other anxiety and mood disorders
  - Does not require systemic uptake and distribution to produce rapid onset pharmacological effects



PH94B Reduced Social Anxiety Produced by Public Speaking and Social Interaction Challenges in Published Phase 2 Study

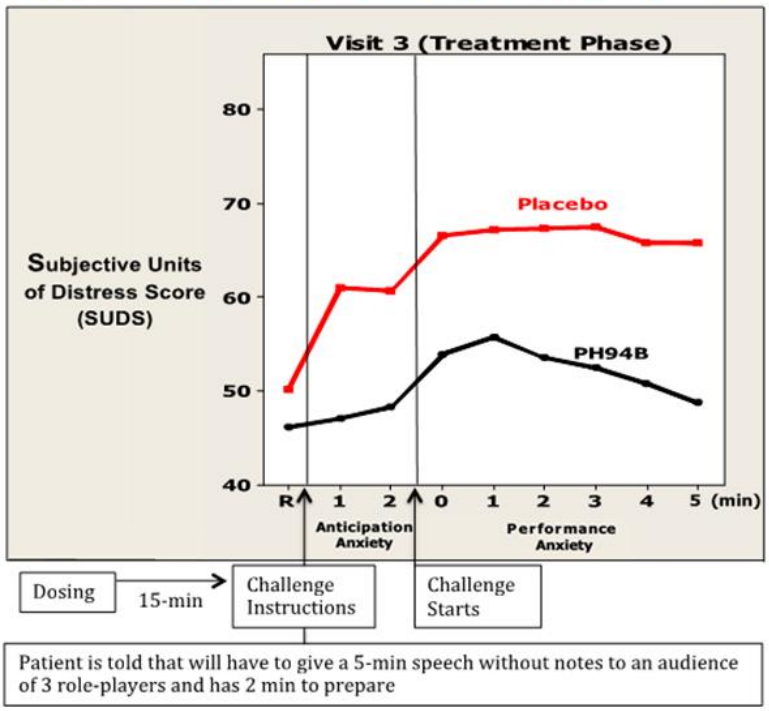
VistaGen Therapeutics

- Phase 2 multi-center, randomized, double-blind, placebo-controlled, parallel design laboratory study
- 91 female patients with SAD, ages 19-60
- 1.6 µg of PH94B or placebo given intranasally 15 min before each challenge
- Rapid onset efficacy; placebo-like safety and tolerability
- Primary endpoint: Change in Subjective Units of Distress Scale (SUDS) from baseline compared to placebo
- PH94B significantly reduced anxiety using the SUDS compared to placebo ($p<0.01$)

PH94B reduced anxiety in SAD patients in 10-15 minutes

MR Liebowitz et al, Am J Psychiatry (2014) 171:675-682

Published PH94B Phase 2 Study – Public Speaking (n = 91)



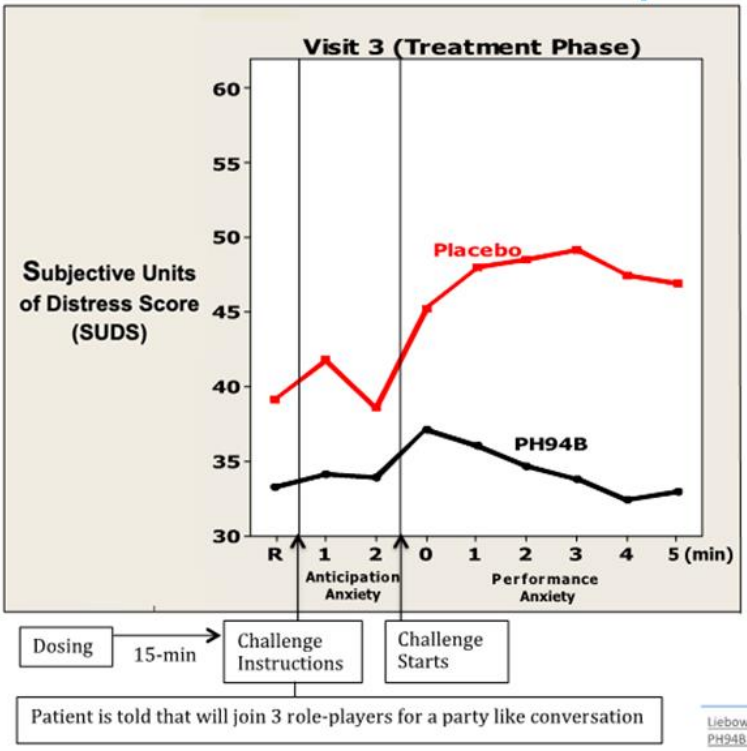
PH94B Rapidly Reduced Anxiety in Response to Public Speaking Challenge

Active Group:	Placebo Group:
Mean Difference = 26.7	Mean Difference = 14.0
Standard Deviation = 21.6	Standard Deviation = 16.3
Number of Subjects = 45	Number of subjects = 46

t = 3.16	p = 0.002	Cohen's d (Effect Size) .72

Liebowitz, MR, Salman, E, Nicolini, H, Rosenthal, N, Hanover, R, Monti. L (2014). Effect of an acute intranasal aerosol dose of PH94B on social and performance anxiety in women with social anxiety disorder. *Am. J. Psychiatry* 171:675-682.

Published PH94B Phase 2 Study – Social Interaction (n = 91)



PH94B Rapidly Reduced Anxiety in Response to Social Interaction Challenge

Active Group:	Placebo Group:
Mean Difference = 18.3	Mean Difference = 6.6
Standard Deviation = 17.4	Standard Deviation = 23.6
Number of Subjects = 45	Number of Subjects = 46

t = 2.67	p = 0.009	Cohen's d (Effect size) .56

Liebowitz, MR, Salman, E, Nicolini, H, Rosenthal, N, Hanover, R, Monti. L (2014). Effect of an acute intranasal aerosol dose of PH94B on social and performance anxiety in women with social anxiety disorder. *Am. J. Psychiatry* 171:675-682.

PH94B Reduced Anxiety in a Pilot Phase 3 "Real World" SAD Cross-over Study

VistaGen Therapeutics

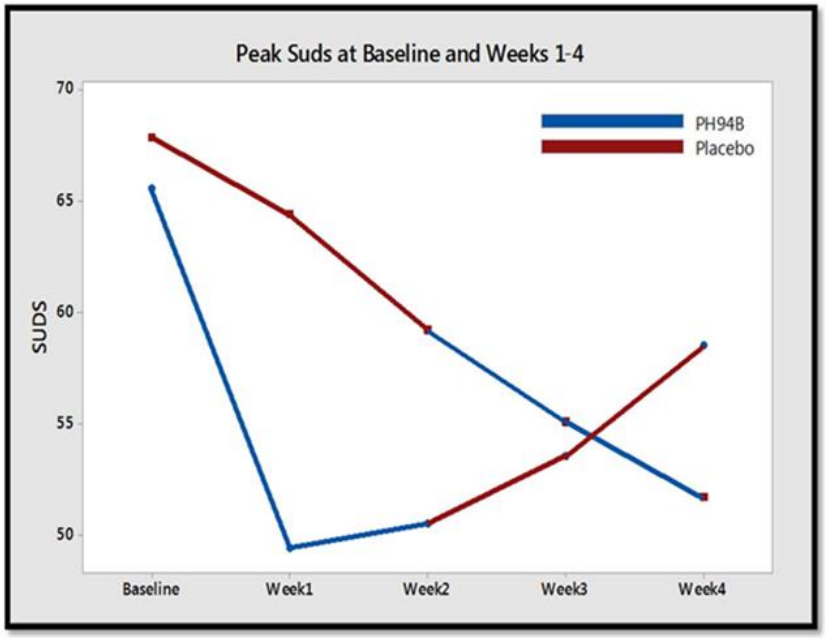
- Randomized, double-blind, 4 week (two 2-week periods), cross-over study
- 22 male and female patients ages 18-65 with social anxiety disorder (SAD)
- Before a potentially stressful social situation, females self-administered 1.6 µg of PH94B or placebo and males self-administered 3.2 µg of PH94B or placebo, up to 4X/day
- PH94B significantly reduced anxiety on SUDS compared to placebo ($p<0.01$)
- Strong trend for improvement on LSAS during first period before cross-over
- Carryover effects of PH94B after cross-over support using a parallel design in Phase 3

PH94B reduced anxiety in SAD patients in the "real world"
Phase 3 will employ a standard parallel design

MR Liebowitz et al, Depression and Anxiety (2016) 33:1081-1089

PH94B Pilot Phase 3 Cross-over Study

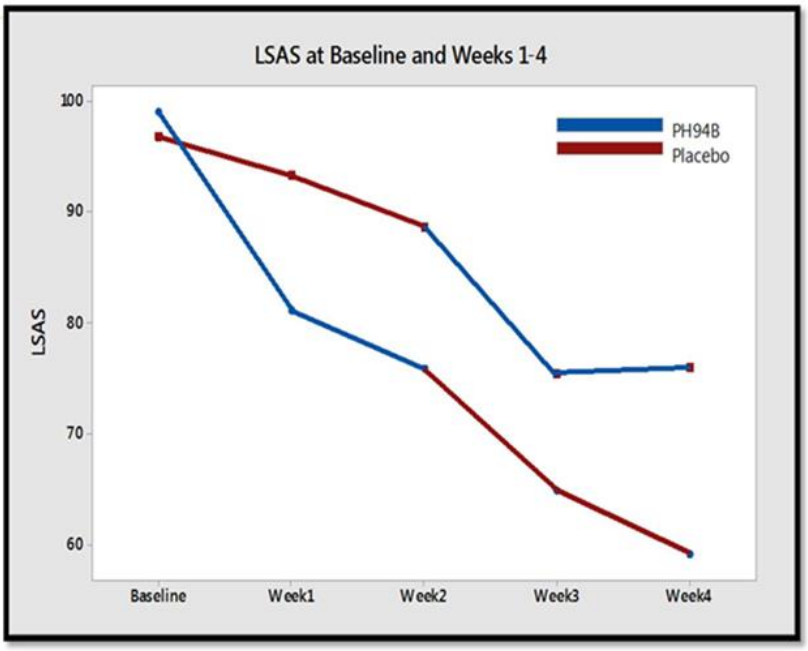
VistaGen Therapeutics



- Early suggestions of drug/placebo differences were seen in week 1 and week 2 SUDS scores: average change in SUDS at week 1 was 16.1 for PH94B vs. 3.4 for placebo (t=1.86, p=.078, ES .79); at week 2, the average change was 15.9 for PH94B and 6.9 for placebo (t= 1.35, p=0.192, ES .576)
- Peak SUDS score for the PH94B group increased after cross-over to placebo, though not back to the baseline, due to increased confidence from PH94B treatment prior to the cross-over to placebo

PH94B Pilot Phase 3 Cross-over Study

VistaGen Therapeutics



- In the sample as a whole, drop in LSAS scores after treatment did not differ between groups because subjects receiving PH94B before receiving placebo continued to improve when crossed over to placebo
- After the first 2 weeks of treatment, subjects who received PH94B dropped an average of 23.2 points on the LSAS, while those who received placebo dropped only 8.2 points, showing a strong trend for improvement on LSAS (t=1.9, p=.07) with a large effect size of .812
- Similar trend differences on total LSAS scores were seen after 1 week of treatment, where the PH94B group showed a 17.8 point drop compared to a 3.5 point drop with placebo (t=2.02, p=.057, ES .86)

VistaGen Therapeutics

PH94B U.S. Phase 3 Study for SAD

Principal Investigator: Dr. Michael Liebowitz, Columbia University, New York

- Randomized, double-blind, placebo-controlled, parallel design monotherapy study
- 3.2 μg of PH94B or placebo for 4 weeks
- Multi-center, ca. 15 sites in North America
- Target enrollment, n = ca. 250
- Target start, 1H 2021

Primary Endpoints: Change in LSAS and SUDS from baseline compared to placebo

PH94B Commercial Opportunity – U.S. SAD Market

VistaGen Therapeutics

SUBSTANTIAL UNMET NEED

Though SAD is highly prevalent with a significant impact on quality of life recognition, diagnosis and treatment remain low. There are few novel medications in development. PH94B promotion, SAD disease education and DTC efforts will drive physician urgency to diagnose and treat.

UNIQUE MOA

While some clinicians are skeptical, most are cautiously optimistic that PH94B is not habit-forming due to its novel, differentiated MOA and non-systemic administration.

STRONG INTENT TO PRESCRIBE

Motivated by safety/tolerability, efficacy and convenient PRN use, most clinicians intend to offer PH94B to a majority of their patients with SAD. Additionally, most patients are interested in trying PH94B and would be motivated to discuss with an HCP after seeing an advertisement.

EASE OF USE

Given similar efficacy, patients and clinicians will likely prefer PH94B's faster onset vs. antidepressants and may prefer a convenient, non-systemic, non-addictive as-needed nasal spray administration over a daily pill.

*Includes Pediatric indication, peak year sales; excludes all other anxiety-related disorders; market research and commercial assessment prepared by i3 Strategy, Winter 2019

VistaGen Therapeutics

The "Benzo Epidemic"

"It's not just opioids: What doctors want you to know about benzos"

CNN health

"Benzodiazepines: Primary Care's New Drug Problem"

PsychiatryAdvisor

"Use of Opioids, Benzodiazepines at Same Time is Skyrocketing."

FORTUNE

www.vistagen.com

Impact of Social Media on Mental Health

VistaGen Therapeutics

"Why Instagram is the Worst Social Media for Mental Health"

TIME

"Association between Social Media Use and Depression among U.S. Young Adults"

NIH National Institutes of Health

"How 'Keeping Up With The Joneses' On Social Media is Damaging Everyone's Mental Health"

Forbes

"How Removing 'Likes' from Instagram Could Affect Our Mental Health"

PBS

"Lots of Time on Social Media Linked to Anxiety, Depression in Teens"

U.S. News & World Report

"A Rise in Depression Among Teens and Young Adults Could be Linked to Social Media Use"

npr

PH94B: Additional Indications Beyond SAD

VistaGen Therapeutics

Potential Next Steps: Phase 2a POC studies

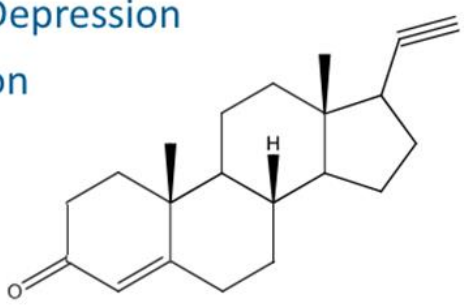
PH10 neuroactive nasal spray

Pregn-4-en-20-yne-3-one

VistaGen® Therapeutics

Novel, safe, fast-acting therapy for:

- Major Depressive Disorder
- Treatment-Resistant Depression
- Postpartum Depression
- Suicidal Ideation



LOOKING BEYOND CURRENT TREATMENTS FOR CNS DISEASES AND DISORDERS WITH HIGH UNMET NEED

www.vistagen.com

Major Depressive Disorder in the U.S.

VistaGen Therapeutics

LARGE ADDRESSABLE MARKET WITH HIGH UNMET NEED[2,3]

11.6M
Drug-treated patients with Major Depressive Disorder

7.3M
Inadequate response to 1st antidepressant

5.1M
Treatment-resistant after 2nd antidepressant

1. CDC – NCHS – 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.

VistaGen® Therapeutics

FDA-Approved MDD Treatments Fall Short

Current Oral 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 potential side effects**
  - Anxiety, sexual dysfunction, insomnia, dizziness, nausea and vomiting, headache, sweating

Atypical Antipsychotics

- **Often do not work**
  - Only ca. 20% of patients respond to augmentation
- **Significant potential side effects**
  - Weight gain, stomach pain, tiredness, dizziness, tardive dyskinesia, headache, nervousness, restlessness

VistaGen Therapeutics

Ketamine-based therapy offers new hope to millions with TRD, but is it a long-term solution?

"Ketamine Depression Treatment Passes Another Trial, But Isn't For Everyone"

Forbes

Janssen Global Services

"In the clinical trials, the most common side effects of SPRAVATO™ when used along with an antidepressant taken by mouth included: dissociation, dizziness, nausea, sedation, spinning sensation, reduced sense of touch and sensation, anxiety, lack of energy, increased blood pressure, vomiting, and feeling drunk."[1]

Janssen Pharmaceuticals, Inc.
Press Release, March 5, 2019

1. Johnson & Johnson Press Release. Janssen Announces U.S. FDA Approval of SPRAVATO™ (esketamine) CIII Nasal Spray for Adults with Treatment-Resistant Depression (TRD) Who Have Cycled Through Multiple Treatments Without Relief. Available at: https://www.jnj.com/janssen-announces-u-s-fda-approval-of-spravatotm-esketamine-ciii-nasal-spray-for-adults-with-treatment-resistant-depression-trd-who-have-cycled-through-multiple-treatments-without-relief

PH10 for MDD

VistaGen® Therapeutics

- First-in-class; different from all antidepressants
- Successful Phase 2a completed
- Rapid-onset antidepressant effects
- Microgram dosing, non-systemic
- Well-tolerated, minimal side effects
- Preparing for U.S. Phase 2b in 1H 2021

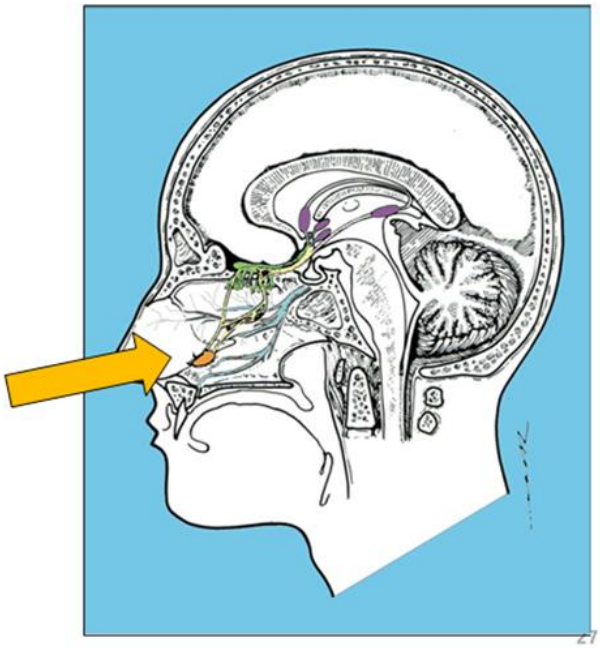
Potential stand-alone and adjunctive at-home therapy with fast-acting, esketamine-like antidepressant effects, without side effects and safety concerns of ketamine-based therapy

LOOKING BEYOND CURRENT TREATMENTS FOR CNS DISEASES AND DISORDERS WITH HIGH UNMET NEED

VistaGen Therapeutics

PH10 Mechanism of Action

- **Engages nasal chemosensory receptors, which activate neural circuits in the brain leading to antidepressant effects**
  - Nasal chemosensory receptors activate olfactory bulb (OB) neurons that project to the limbic amygdala
  - OB neurons stimulate neurons in the limbic amygdala that release norepinephrine and increase activity of the limbic-hypothalamic sympathetic nervous system
  - Does not require systemic uptake and distribution to produce pharmacological effects



PH10 Demonstrated Antidepressant Effects in MDD Patients in Published Exploratory Phase 2a Study

VistaGen® Therapeutics

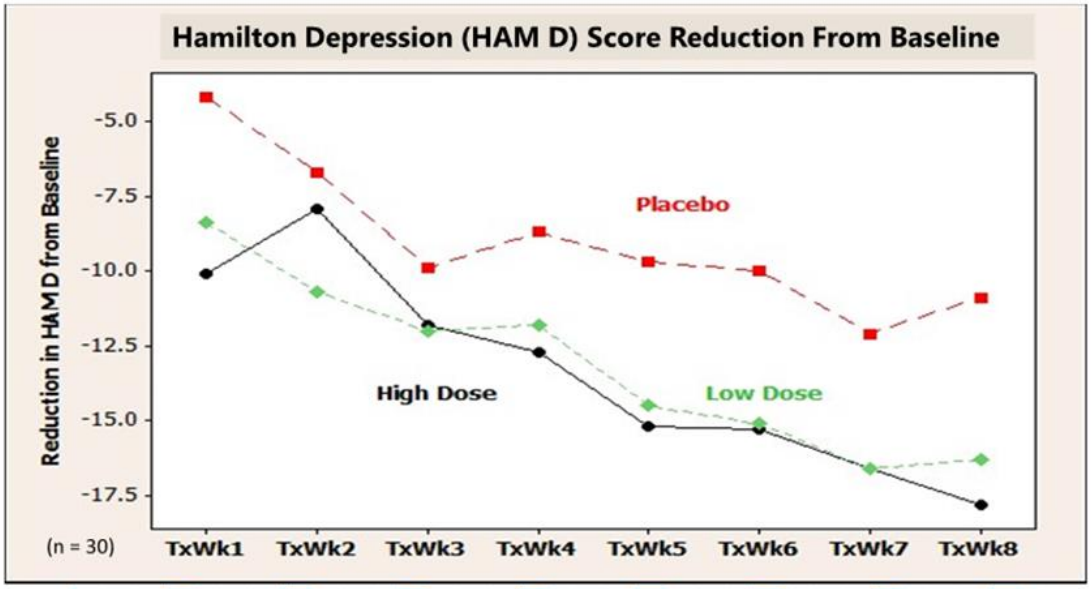
- Phase 2 randomized, double-blind, placebo-controlled, 8-week, parallel design POC study conducted in Mexico City
- 30 male and female MDD patients, ages 18-65
- 3.2 µg or 6.4 µg of PH10 or placebo given intranasally 2 times per day, every day for 8 weeks
- Primary endpoint: Change in HAM-D-17 scores from baseline compared to placebo
- 6.4 µg dose significantly reduced depressive symptoms as early as one week based on the Hamilton Depression Scale (HAM-D17) compared to placebo (p=0.022)
- Very well tolerated, no dissociative side effects or serious adverse events

Rapid onset antidepressant effects in MDD patients with minimal side effects

Monti, L., Nicolini, H., Liebowitz, M., & Hanover, R. (2019). "A Placebo Controlled Trial of PH20: Test of a New Rapidly Acting Intranasally Administered Antidepressant." Br J Phar Med Res 4(6): 2157-2168.

PH10 Exploratory Phase 2a MDD Monotherapy Study (n = 30)

VistaGen Therapeutics



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		

Microgram doses of PH10 neuroactive nasal spray improved MDD symptoms with rapid-onset efficacy

PH10 U.S. Phase 2b Development Plan for MDD

VistaGen Therapeutics

Principal Investigator: Dr. Michael Liebowitz, Columbia University, New York

- Randomized, double-blind, placebo-controlled, multi-center monotherapy study
- MDD patients with zero or 1 prior failure on a standard antidepressant
- Twice a day administration of PH10 (3.2 μg or 6.4 μg) or placebo for 4 weeks
- Rapid onset potential within one week
- Target enrollment, n= ca. 150-200 patients
- Target start, 1H 2021

Primary Endpoint: Change in HAM-D-17 from baseline compared to placebo

PH10: Additional Indications Beyond MDD

VistaGen Therapeutics

Suicidal Ideation

Postpartum Depression

PH10

Treatment-Resistant Depression

Potential Next Steps: Phase 2a studies

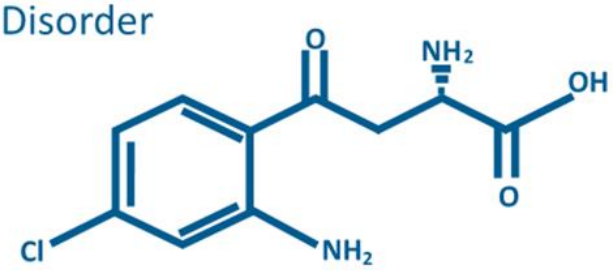
AV-101

L-4-chlorokynurenine

VistaGen® Therapeutics

Novel oral NMDA receptor GlyB antagonist for:

- Major Depressive Disorder
- Suicidal Ideation
- Neuropathic Pain
- Epilepsy
- Levodopa-Induced Dyskinesia associated with Parkinson's Therapy



Dickens, D., (2019, December). Drug transporters at the blood-brain barrier as targets for personalised CNS therapeutics. Speaker at British Pharmacological Society, Pharmacology 2019, Edinburgh, UK,

LOOKING BEYOND CURRENT TREATMENTS FOR CNS DISEASES AND DISORDERS WITH HIGH UNMET NEED

AV-101

- Oral prodrug of 7-Cl-KYNA
- Selective NMDA receptor glycine site antagonist
- Well-tolerated in all clinical studies to date
- No dissociative side effects or treatment-related SAEs
- Non-addictive, non-sedating
- FDA Fast Track designations in MDD and pain

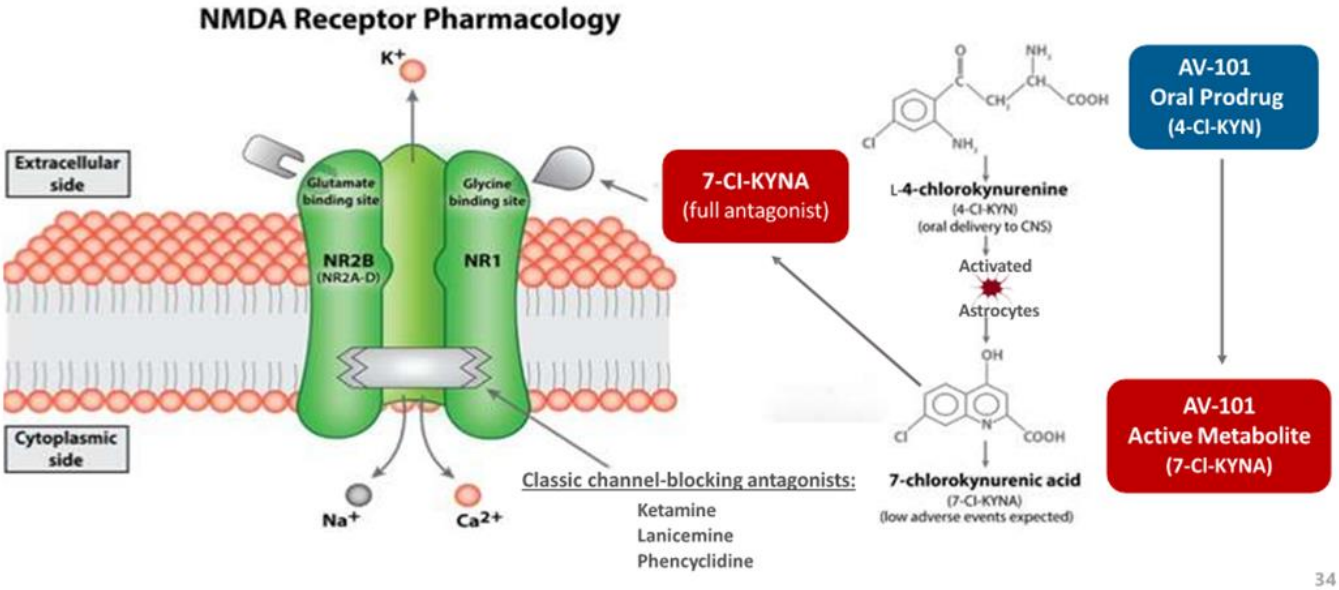
VistaGen® Therapeutics

Nasdaq: VTGN

www.vistagen.com

AV-101's Mechanism of Action

4-Cl-KYN (prodrug) → 7-Cl-KYNA (active metabolite)



AV-101 in Published Phase 1 Clinical Trials

AV-101 is very well-tolerated and orally bioavailable

- Plasma half-life is about 2 hr
- Dosed up to 1440 mg daily for 2 weeks
- Adverse events were placebo-like, except for some feelings of euphoria ("well-being")
- No ketamine-like psychosis
- No QT prolongation
- No abnormalities in clinical chemistry or hematology

Contents lists available at ScienceDirect

Scandinavian Journal of Pain

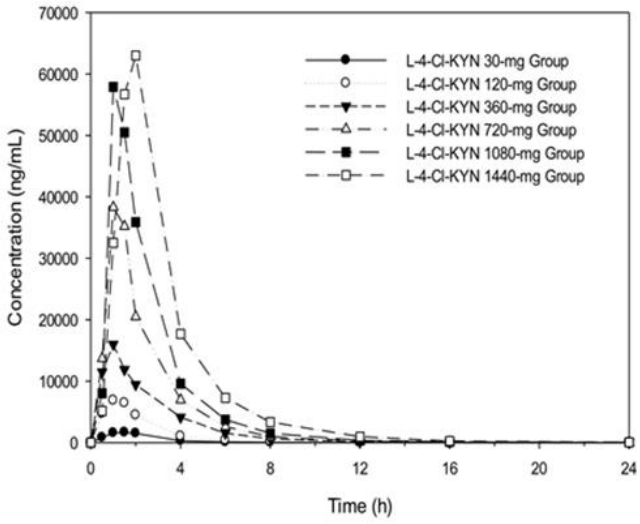
journal homepage: www.ScandinavianJournalPain.com

Clinical pain research

Randomized, double-blind, placebo-controlled, dose-escalation study: Investigation of the safety, pharmacokinetics, and antihyperalgesic activity of L-4-chlorokynurenine in healthy volunteers

Mark Wallace[a,*], Alexander White[b], Kathy A. Grako[c], Randal Lane[c], Allen (Jo) Cato[c], H. Ralph Snodgrass[d]

Plasma levels of AV-101 in normal volunteers following single oral dosing



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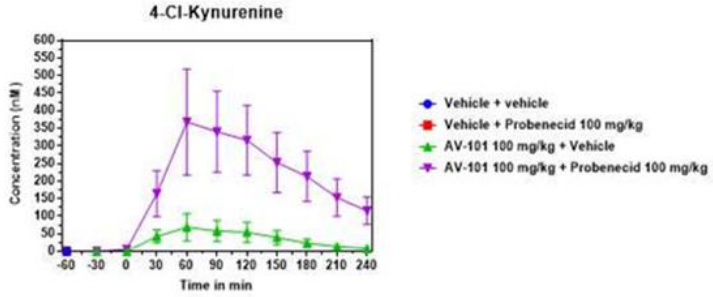
AV-101 and Adjunctive Probenecid

Recent preclinical studies demonstrate substantial increases in rodent brain concentrations of both AV-101 (4-Cl-KYN) and 7-Cl-KYNA

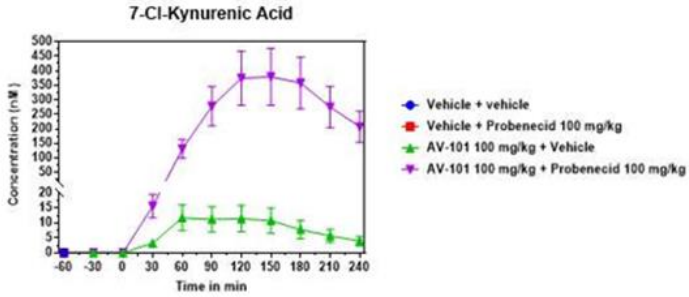
VistaGen Therapeutics

Probenecid increases AV-101 (4-Cl-KYN) brain levels by ~ 7 fold



• Figure 1 → Levels of 4-Cl-KYN in PFC of adult male Sprague-Dawley rats following IP administration (T=0) of AV-101 and probenecid alone or in combination (100 mg/kg, each).
Data are represented as mean ± SEM. N = 4-6/group.

Probenecid increases 7-Cl-KYNA brain levels by > 35 fold



• Figure 2 → Levels of 7-Cl-KYNA in PFC of adult male Sprague-Dawley rats following IP administration (T=0) of AV-101 and probenecid alone or in combination (100 mg/kg, each).
Data are represented as mean ± SEM. N = 4-6/group.

AV-101 with Adjunctive Probenecid for Multiple Indications

VistaGen Therapeutics

Major Depressive Disorder

Suicidal Ideation

Neuropathic Pain

AV-101

Levodopa-Induced Dyskinesia associated with Parkinson's Therapy

Epilepsy

Potential Next Steps: Phase 2a POC studies with adjunctive probenecid

AV-101 for Major Depressive Disorder

VistaGen Therapeutics

- Ketamine-like antidepressant effects, no ketamine-like side effects in published preclinical studies[1]
- No differentiation in initial Phase 2 MDD study (1440 mg with adjunctive ADT)
- Well-tolerated, no psychotomimetic side effects or serious adverse events
- Recent preclinical studies with adjunctive probenecid suggest path forward
- AV-101/probenecid preclinical studies in 2020
- FDA Fast Track designation granted

Potential Next Step: Phase 1b/2a study with adjunctive probenecid

1. Zanos, P., et al. (2015) "The Prodrug 4-Chlorokynurenine Causes Ketamine-Like Antidepressant Effects, but Not Side Effects, by NMDA/GlycineB-Site Inhibition." *J Pharmacol Exp Ther* 355:76-85

AV-101 for Suicidal Ideation

U.S. Department of Veterans Affairs

Baylor College of Medicine

VistaGen Therapeutics

Baylor / VA Phase 1b NMDAR Target Engagement Study (n=10)

- Successful target engagement relevant to NMDAR antagonism and suicidal ideation
- Double-blind, placebo-controlled, cross-over study sponsored by U.S. Department of Veterans Affairs (VA) and conducted at Baylor College of Medicine
- Two single doses of AV-101 (720 mg and 1440 mg) and placebo
- Focused on dose-response relationship between AV-101 and EEG biomarkers related to NMDAR function and blood biomarkers associated with suicidality
- High dose (1440 mg) of AV-101 associated with dose-related increase in 40 Hz ASSR
- Well-tolerated, no dissociative AE's or SAE's

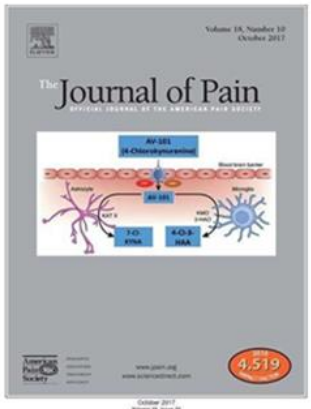
Potential Next Step: Phase 2a study with adjunctive probenecid

AV-101 for Neuropathic Pain in Preclinical Studies

VistaGen Therapeutics

- Significant dose-response with similar efficacy in a rat model of a mononeuropathy as compared to gabapentin (Neurontin) and pregabalin (Lyrica)[1]
- Robust analgesic effects, similar to gabapentin and pregabalin, but fewer side effects as measured in the rotarod assay
- Potential oral non-opioid treatment option for neuropathic pain
- Non-addictive and non-sedating
- FDA Fast Track designation granted

Potential Next Step: Phase 2a study with adjunctive probenecid



1 - Yaksh, T.L., et al. (2017). "Characterization of the Effects of L-4-Chlorokynurenine on Nociception in Rodents." The Journal of Pain 18: 1184-1196

AV-101 for Seizures in Preclinical Studies

VistaGen Therapeutics

- Multiple published reports demonstrate that, if delivered by injection into brain, 7-Cl-KYNA substantially reduces the frequency of seizures in animal models
- AV-101 dramatically reduced seizures in two rodent models of seizures[1]
  - Seizure data obtained from spontaneously seizing CLE rats (n = 6)
    - Test Period per trial: 6 hours
    - Baseline: 8.3 ± 1 seizures
    - AV-101: 4.8 ± 1 seizures
  - 43% reduction in seizures, $p<0.02$ (two-tailed t-test)

Potential Next Step: Phase 2a study with adjunctive probenecid

1. Collaboration with E. Bertram, University of Virginia

VistaGen Therapeutics

AV-101 for Levodopa-induced Dyskinesia associated with Parkinson's Therapy in Preclinical Studies

- Antidyskinetic effects in the MPTP primate model similar to those generally observed with amantadine therapy, but without adverse effects experienced with amantadine
- Significantly (p = 0.01) reduced LID without affecting timing, extent, or duration of anti-Parkinsonian therapeutic benefits of levodopa[1]
- Potential to replace oral amantadine for LID associated with Parkinson's therapy

Sun Pharma

Potential Next Step: Phase 2a study with adjunctive probenecid

1. Collaboration with Dr. Thérèse Di Paolo, CHU de Québec – Université Laval Research Center

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VistaGen Therapeutics

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Experienced Team Leading Execution

VistaGen Therapeutics

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

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. 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

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

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

VistaGen® Therapeutics

- 3 differentiated clinical-stage product candidates
- Novel mechanisms of action
- Rapid-onset
- Exceptional safety
- Each candidate has potential in multiple markets

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