

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): May 27, 2020

VistaGen Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

NEVADA
(State or other jurisdiction of incorporation)

000-54014
(Commission File Number)

20-5093315
(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:

<u>Title of each class</u>	<u>Trading Symbol(s)</u>	<u>Name of each exchange on which registered</u>
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 7.01 Regulation FD Disclosure.

On May 27, 2020, VistaGen Therapeutics, Inc. (the “Company”) announced its agreement with Nuformix plc to develop new crystalline forms of AV-101 that may have superior delivery, an enhanced therapeutic profile and additional intellectual property protection. A copy of the Company’s press release is attached hereto as Exhibit 99.1.

On June 1, 2020, the Company began utilizing a new corporate presentation, a copy of which is attached to this Current Report on Form 8-K as Exhibit 99.2.

The information in Item 7.01 of this Current Report on Form 8-K, including the information set forth in Exhibit 99.1 and 99.2, 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 and 99.2 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	Press Release issued by VistaGen Therapeutics, Inc., dated May 27, 2020.
99.2	VistaGen Therapeutics, Inc. Corporate Presentation, dated Summer 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: June 1, 2020

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



VistaGen and Nuformix Announce Agreement to Develop Novel Patentable Cocrystalline Forms of AV-101 for Treatment of Multiple CNS Conditions

*Novel Cocrystal Form of AV-101 Administered with Probenecid
May Have Superior Delivery, an Enhanced Therapeutic Profile
and Additional Intellectual Property Protection*

SOUTH SAN FRANCISCO, Calif., May 27, 2020 – VistaGen Therapeutics (NASDAQ: VTGN), a clinical-stage biopharmaceutical company developing new generation medicines for anxiety, depression and other central nervous system (CNS) diseases and disorders with high unmet need, and Nuformix plc (LSE: NFX.L), a pharmaceutical development company focused on unlocking the therapeutic potential and value of known drugs, today announced their agreement to develop novel cocrystal-based formulations of VistaGen's CNS product candidates. Under the terms of the agreement, VistaGen and Nuformix initially will apply Nuformix's proprietary technology platform to develop patentable new crystalline forms of AV-101 that may have superior delivery, an enhanced therapeutic profile and additional intellectual property protection. If successful, VistaGen and Nuformix will consider opportunities to extend the collaboration to other CNS therapeutic candidates with a view to unlocking additional therapeutic and commercial opportunities.

"Nuformix has a successful track record of using cocrystal technology to re-engineer the crystalline form of small molecule drugs for their own development and for select partners," said H. Ralph Snodgrass, PhD, VistaGen President and Chief Scientific Officer. "Their team is not only highly experienced, but also scientifically creative. We look forward to a productive collaboration."

"We're very pleased to announce this collaboration with VistaGen and the opportunity to collaborate in CNS therapeutics," said Dan Gooding, PhD, Nuformix Chief Executive Officer. "VistaGen and Nuformix share similar objectives in the development of new therapies and we look forward to making an important contribution to VistaGen's comprehensive AV-101 programme and developing the relationship further."

AV-101 is VistaGen's oral NMDAR (N-methyl-D-aspartate receptor) glycine site antagonist, in development in combination with probenecid, a safe and well-known oral drug used to treat gout and to increase the therapeutic benefit of numerous antibacterial, anticancer and antiviral drugs. Recently reported preclinical data suggest that there is a substantially increased brain concentration of AV-101 prodrug (4-Cl-KYN) and its active metabolite, 7-chlorokynurenic acid (7-Cl-KYNA), when given together with probenecid. With its exceptionally few side effects and excellent safety profile in all clinical studies to date, AV-101, together with probenecid, has potential to be a new generation oral treatment for chronic neuropathic pain, epilepsy, levodopa-induced dyskinesia associated with Parkinson's disease therapy, major depressive disorder, and suicidal ideation.

About AV-101

AV-101 (4-Cl-KYN) targets the NMDAR (N-methyl-D-aspartate receptor), an ionotropic glutamate receptor in the brain. Abnormal NMDAR function is associated with numerous CNS diseases and disorders. AV-101 is an oral prodrug of 7-chlorokynurenic acid (7-Cl-KYNA), which is a potent and selective full antagonist of the glycine co-agonist site of the NMDAR that inhibits the function of the NMDAR. Unlike ketamine and many other NMDAR antagonists, 7-Cl-KYNA is not an ion channel blocker. In all studies to date, AV-101 has exhibited no dissociative or hallucinogenic psychological side effects or safety concerns similar to those that may be caused by amantadine, esketamine and ketamine. With its exceptionally few side effects and excellent safety profile, AV-101 has potential to be an oral new generation treatment for multiple large-market CNS indications where current treatments are inadequate to meet high unmet patient needs. The 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 Cocrystals

Pharmaceutical cocrystals are materials composed of two or more different molecules, usually an active pharmaceutical ingredient together with a “co-former” molecule. Cocrystals can be engineered to enhance the bioavailability, pharmacokinetics, stability and manufacturing of drug products.

About VistaGen

VistaGen Therapeutics is a multi-asset, clinical-stage biopharmaceutical company developing new generation medicines for anxiety, depression and certain CNS diseases and disorders where current treatments are inadequate, resulting in high unmet need. VistaGen's [pipeline](#) is focused on three clinical-stage CNS drug candidates, each with a differentiated mechanism of action, an exceptional safety profile, and therapeutic potential in multiple large and growing CNS markets. For more information, please visit www.vistagen.com and connect with VistaGen on [Twitter](#), [LinkedIn](#) and [Facebook](#).

About Nuformix

Nuformix is a pharmaceutical development company focused on unlocking the therapeutic potential and value of known drugs. Nuformix risk-mitigated development strategy has resulted in a pipeline of discoveries through which it has developed and patented novel forms of approved small molecules. Nuformix is targeting high-value unmet needs via drug repurposing with a lead programme in fibrosis (NXP002). Nuformix plc shares are traded on the London Stock Exchange's Official List under the ticker: NFX. For more information please visit www.nuformix.com.

VistaGen Forward-Looking Statements

This release contains various statements concerning VistaGen's future expectations, plans and prospects, including without limitation, our expectations regarding discovery, development and commercialization of patentable cocrystalline forms of AV-101, either alone or in combination with probenecid, for treatment of CNS diseases and disorders with high unmet need, including chronic neuropathic pain, epilepsy, levodopa-induced dyskinesia associated with Parkinson's disease therapy, major depressive disorder, and suicidal ideation. In addition, statements concerning the Company's future expectations may include statements regarding intellectual property and commercial protection of our drug candidates. Each of these statements 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. Those risks include the following: (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 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; (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 the substantial additional capital necessary to support our operations, including our ongoing and/or planned preclinical and/or clinical development studies; and (vii) we may encounter technical and other unexpected hurdles and delays 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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VistaGen®
Therapeutics

www.vistagen.com

 Nasdaq: VTGN

Summer 2020

LOOKING BEYOND CURRENT TREATMENTS FOR 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, development efforts, collaborations, intellectual property, financial condition, plans and development programs. These statements involve risks, uncertainties and assumptions, and are based on the current estimates and assumptions of the management of VistaGen Therapeutics, (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.

COVID-19 Pandemic is Causing a Mental Health Pandemic

The Washington Post

“A third of Americans now show signs of clinical anxiety or depression, Census Bureau finds amid coronavirus pandemic”

TIME

“Anti-anxiety medication prescriptions up 34 percent since coronavirus”

CNN Health

“The coronavirus pandemic is causing a mental health crisis, the UN warns”

TIME THE AGE OF ANXIETY

Beyond Stress • Lessons and Treatments • You Are Not Alone



“The Coronavirus Pandemic May Be Causing an Anxiety Pandemic”



Social Media is Damaging Mental Health



“How ‘Keeping Up With The Joneses’ On Social Media is Damaging Everyone’s Mental Health”

Forbes



“Why Instagram is the Worst Social Media for Mental Health”

TIME

“How Removing ‘Likes’ from Instagram Could Affect Our Mental Health”



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



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



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



The “Benzo Epidemic” is Upon Us

“Benzodiazepines: Primary Care’s New Drug Problem”

PsychiatryAdvisor



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

CNN health

“Use of Opioids, Benzodiazepines at Same Time is Skyrocketing.”

FORTUNE

VistaGen is committed to developing and commercializing new generation medicine for large and growing anxiety, depression and neurology markets worldwide where current treatments are inadequate to meet the needs of millions of patients.

www.vistagen.com



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

Our CNS Pipeline



Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3
PH94B Neuroactive Nasal Spray*	Social Anxiety Disorder ^{†1}	[Progress bar: Preclinical to Phase 3]			
	Generalized Anxiety Disorder ⁴	[Progress bar: Preclinical to Phase 2]			
	Adjustment Disorder with Anxiety ³	[Progress bar: Preclinical to Phase 2]			
	Peripartum Anxiety ⁴	[Progress bar: Preclinical to Phase 2]			
	Perioperative Anxiety ⁴	[Progress bar: Preclinical to Phase 2]			
	Panic Disorder ⁴	[Progress bar: Preclinical to Phase 2]			
	PTSD ⁴	[Progress bar: Preclinical to Phase 2]			
PH10 Neuroactive Nasal Spray*	Major Depressive Disorder ²	[Progress bar: Preclinical to Phase 2]			
	Postpartum Depression ⁴	[Progress bar: Preclinical to Phase 2]			
	Treatment-resistant Depression ⁴	[Progress bar: Preclinical to Phase 2]			
	Suicidal Ideation ⁴	[Progress bar: Preclinical to Phase 2]			
AV-101 (oral)*	Major Depressive Disorder ^{†5}	[Progress bar: Preclinical to Phase 2]			
	Neuropathic Pain ^{†5}	[Progress bar: Preclinical to Phase 2]			
	LID associated with Parkinson's Therapy ⁵	[Progress bar: Preclinical to Phase 2]			
	Suicidal Ideation ⁵	[Progress bar: Preclinical to Phase 2]			
	Epilepsy ⁵	[Progress bar: Preclinical to Phase 2]			

* The commencement of all potential studies noted above with dashed arrow bars is subject to U.S. FDA regulatory approval and the availability of sufficient funding.
† FDA Fast Track designation granted

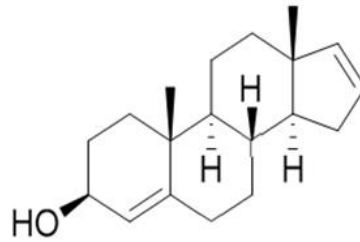
- | | |
|--|--|
| 1. Successful Phase 2 program completed; preparing for Phase 3 program | 4. Assessing for potential Phase 2A program |
| 2. Successful Phase 2A program completed; preparing for Phase 2B program | 5. Assessing for potential Phase 1B/2A study with probenecid |
| 3. Preparing for U.S. Phase 2A program | |

PH94B neuroactive nasal spray

(3 β)-androsta-4,16-dien-3-ol

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

- Social Anxiety Disorder
- Adjustment Disorder with Anxiety
- Postpartum Anxiety
- PTSD
- Generalized Anxiety Disorder
- Preoperative/Pre-testing Anxiety
- Panic Disorder

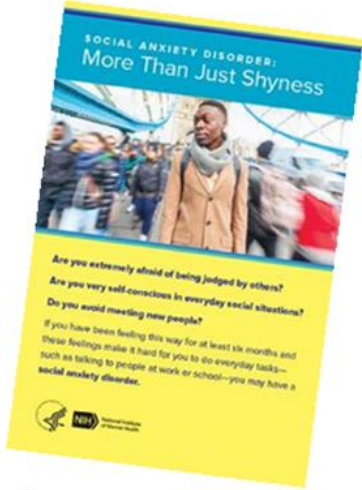


VistaGen[®]
Therapeutics



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

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



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 million¹

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



¹Harvard 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



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

Antidepressants

- ✘ 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, as needed treatment for SAD

PH94B for Social Anxiety Disorder

- First-in-class
- Successful Phase 2 completed; preparing for Phase 3
- Fast acting (15 minutes), exceptional safety
- Non-systemic (microgram dosing)
- Non-sedating and non-addictive
- FDA Fast Track designation; first ever granted by FDA

Potential to be the first FDA-approved, fast-acting, as needed treatment for SAD



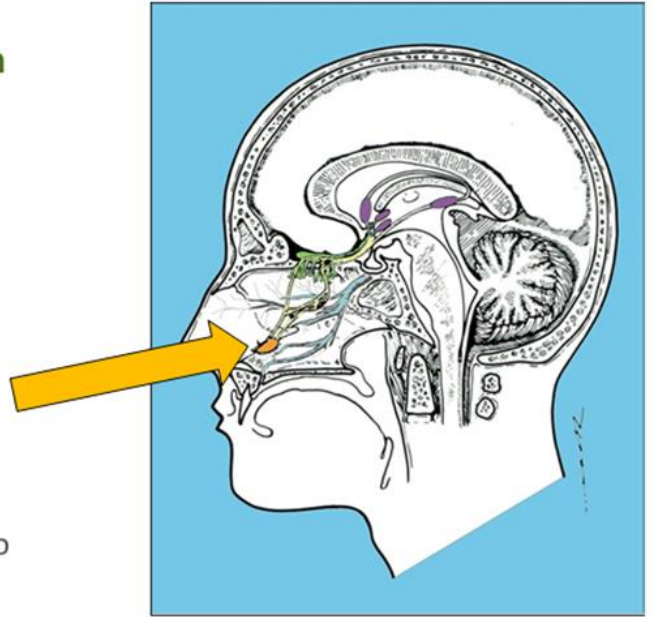
**VistaGen®
Therapeutics**



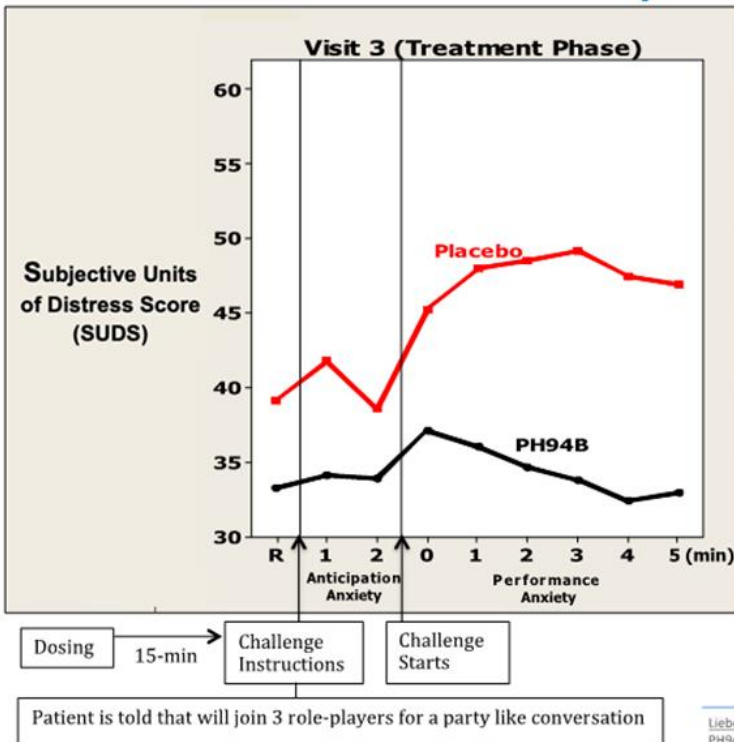
LOOKING BEYOND CURRENT TREATMENTS FOR CNS DISEASES AND DISORDERS WITH HIGH UNMET NEED

PH94B's 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 in nasal passages 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 anti-anxiety effects



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



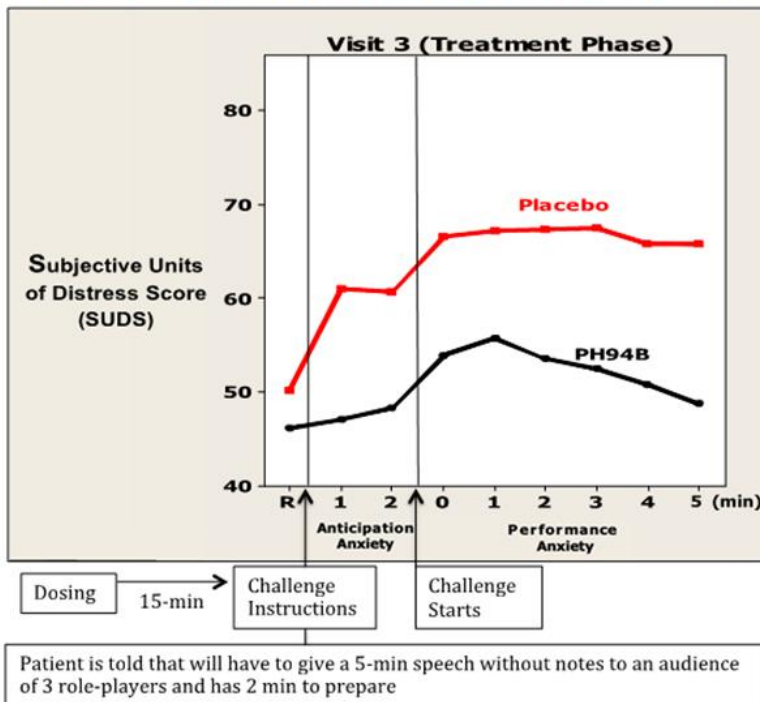
PH94B Rapidly Reduced Anxiety in Response to Social Interaction Challenge

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, Nicollini, H, Rosenthal, N, Hanover, R, Monti, L (2014). Effect of an acute intranasal aerosol dose of PH948 on social and performance anxiety in women with social anxiety disorder. *Am. J. Psychiatry* 171:675-682.

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



PH94B Rapidly Reduced Anxiety in Response to Public Speaking Challenge

Active Group:

Mean Difference = 26.7

Standard Deviation = 21.6

Number of Subjects = 45

Placebo Group:

Mean Difference = 14.0

Standard Deviation = 16.3

Number of subjects = 46

t = 3.16

p = 0.002

**Cohen's d
(Effect Size)
.72**

PH94B Initial Phase 3 Study for Social Anxiety Disorder

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
- 15 sites in North America
- Proposed primary endpoint, change in Subjective Units of Distress Scale (SUDS) from baseline compared to placebo
- Target enrollment, n = ca. 250
- Target start, 1H 2021

Proposed Primary Endpoint: Change in SUDS from baseline compared to placebo

PH94B Commercial Opportunity – U.S. SAD Market

SUBSTANTIAL UNMET NEED

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 as needed use, most clinicians intend to offer PH94B to a majority of their patients with SAD. 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 non-systemic, non-addictive, non-sedating nasal spray over an oral benzodiazepine.

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

Adjustment Disorder with Anxiety Related to COVID-19

Adjustment Disorder

- An emotional or behavioral reaction considered excessive or out of proportion to a stressful event or major life change
- Occurs within three months of the stressor
- Significantly impairs a person's social, occupational and/or other important areas of functioning



Adjustment Disorder and COVID-19

- COVID-19 pandemic has created fear, anxiety and uncertainty about health, economy, unemployment, and new social norms
- Constant changes and inconsistencies of standards and guidelines and ever-evolving knowledge of effects of COVID-19 are resulting in increased anxiety and individuals are uncertain when there will be relief
- Current anti-anxiety medicines have significant limitations and problematic side effects and safety concerns

PH94B Phase 2 Program for Adjustment Disorder

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

- Treatment of Adjustment Disorder with Anxiety related to the COVID-19 Pandemic

PART A

- Pilot, open-label Phase 2A single site study in NYC
- 3.2 µg of PH94B up to 4 times a day for 4 weeks
- Target enrollment, ca. n = 30
- Target start, Q4 2020/Q1 2021

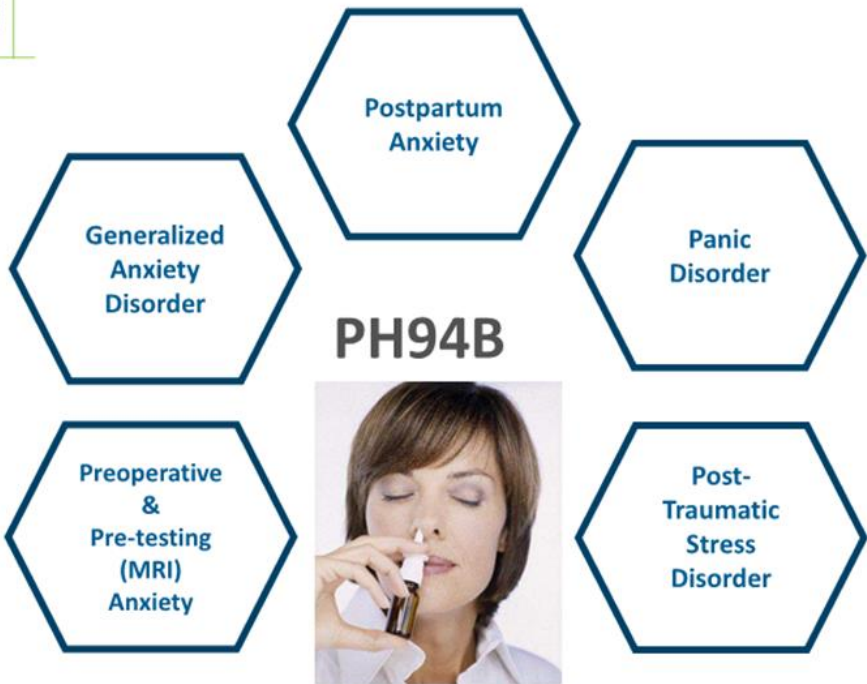
Primary Endpoint: Change in Hamilton Anxiety Scale (HAM-A) from baseline

PART B

- Randomized, double-blind, placebo-controlled study
- 3.2 µg of PH94B up to 4 times a day for 4 weeks
- Multi-center, ca. 15 sites
- Target enrollment, n = 150

Primary Endpoint: Change in Hamilton Anxiety Scale (HAM-A) from baseline compared to placebo

PH94B: Additional Indications Beyond SAD & Adjustment Disorder



**Potential Next Steps:
Phase 2A POC studies**

PH10 neuroactive nasal spray

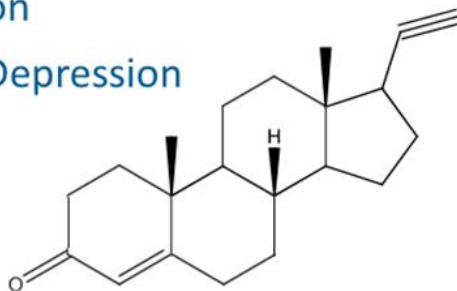
Pregn-4-en-20-yne-3-one



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Novel, safe, fast-acting therapy for:

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



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

Major Depressive Disorder in the U.S.

1 in 4 women



diagnosed with depressive disorders

1 in 6 men



1 in 8



age 12 and over takes an antidepressant¹

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.

FDA-Approved Oral MDD Treatments Fall Short

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

Oral 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

PH10 for MDD

- First-in-class
- Successful Phase 2A completed
- Rapid-onset antidepressant effects
- Microgram dosing, non-systemic
- Well-tolerated, minimal side effects
- Preparing for U.S. Phase 2B in 2021

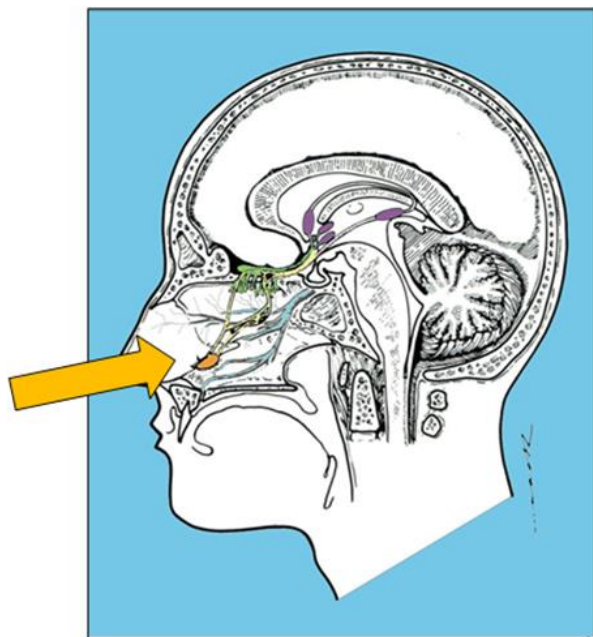
Potential stand-alone and adjunctive at-home therapy with fast-acting, esketamine-like antidepressant effects, without side effects and safety concerns of ketamine-based therapy



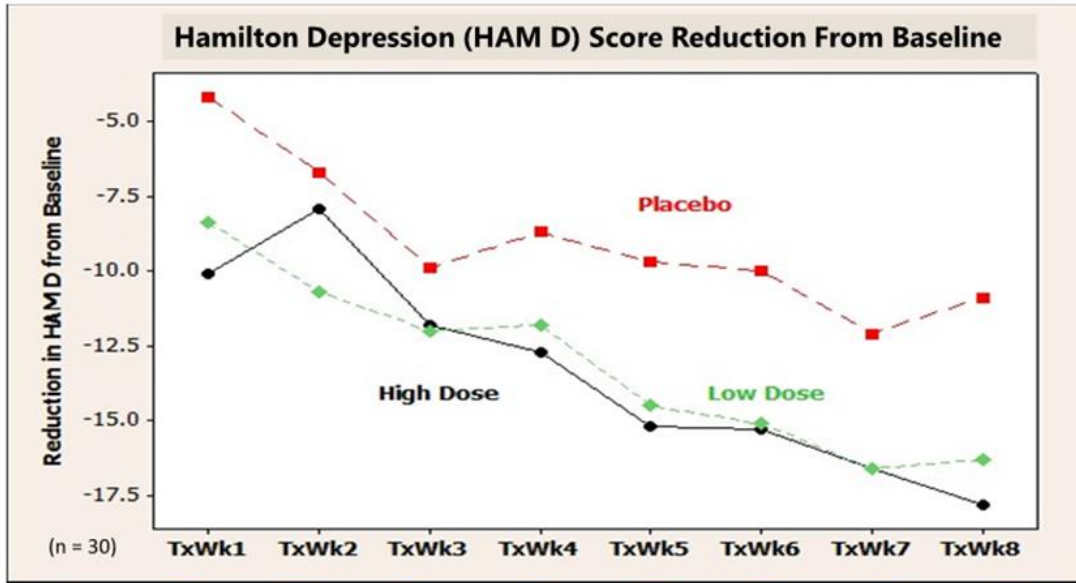
LOOKING BEYOND CURRENT TREATMENTS FOR CNS DISEASES AND DISORDERS WITH HIGH UNMET NEED

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 in the nasal passages 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 Published Phase 2A MDD Monotherapy Study (n = 30)



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

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		

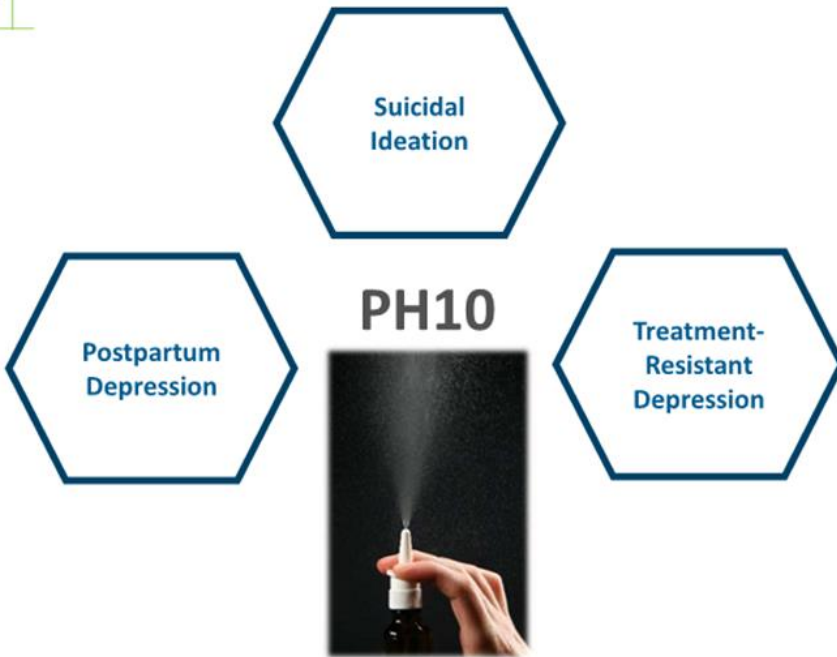
PH10 U.S. Phase 2B Development Plan for MDD

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 or less
- Target enrollment, n= ca. 150 patients
- Target start, 1H 2021

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

PH10: Additional Indications Beyond MDD



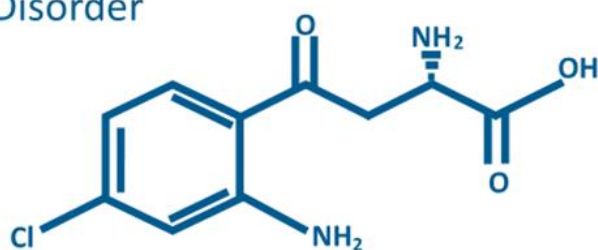
**Potential Next Steps:
Phase 2A studies**

AV-101

L-4-chlorokynurenine

Novel oral NMDA receptor GlyB antagonist for:

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



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Therapeutics



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



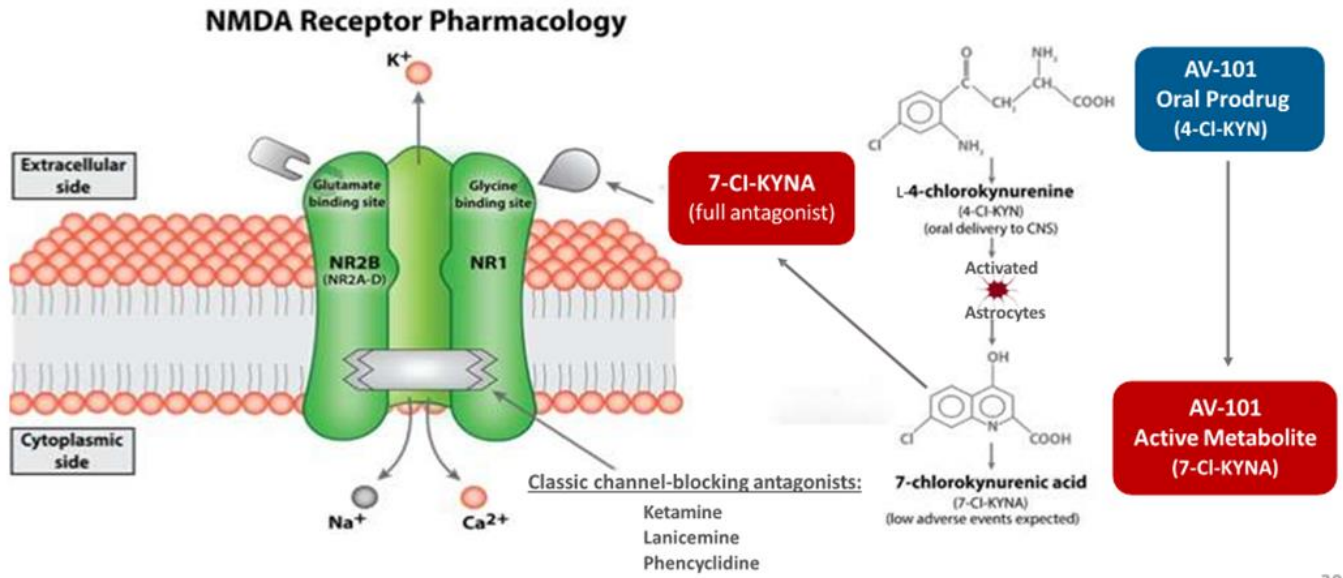
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AV-101's Mechanism of Action

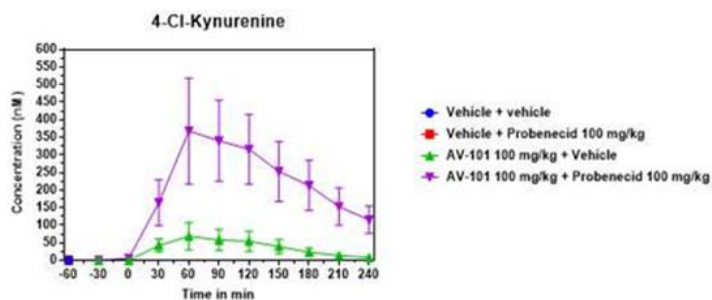
4-Cl-KYN (prodrug) → 7-Cl-KYNA (active metabolite)



AV-101 and Probenecid Synergy

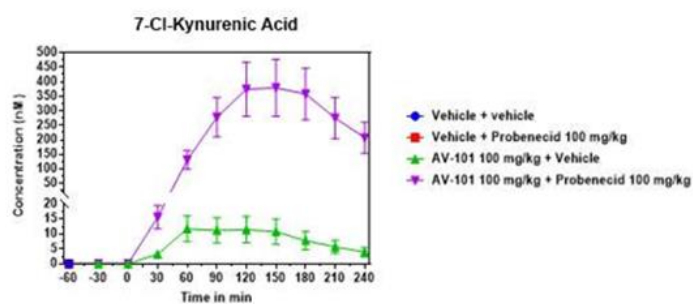
Recent preclinical studies demonstrate substantial increases in rodent brain concentrations of both AV-101 (4-Cl-KYN) and 7-Cl-KYNA

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. ¶

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,

AV-101 with Probenecid for Multiple CNS Indications



**Potential Next Steps:
Phase 1B/2A POC studies
with adjunctive probenecid**

Distinguished Clinical and Regulatory Advisors



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Experienced Team Leading Execution



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
- Calypso Biomedical; Discovery Foods; California & Hawaiian Sugar; Clorox



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Chief Medical Officer

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Vice President, Corporate Development

- 20 years of experience in corporate development, capital markets and management consulting
- Stellar Biotechnologies; MZ Group; Hayden Communications; Alliance Advisors

3 Differentiated, Clinical-Stage CNS Drug Candidates

- Novel mechanisms of action
- Rapid-onset potential
- Exceptional safety profiles
- Multiple large global markets



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