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): November 22, 2022

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 7.01 Regulation FD Disclosure.

On November 22, 2022, Vistagen Therapeutics, Inc. (the "*Company*") began utilizing a new corporate presentation, a copy of which is attached to this Current Report on Form 8-K as Exhibit 99.1.

Disclaimer.

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 November 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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: November 22, 2022

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


Vistagen
Healthy minds make healthy communities, and we are innovating to change the trajectory of global mental health care …
One Mind at a Time™
Corporate Presentation
Fall 2022

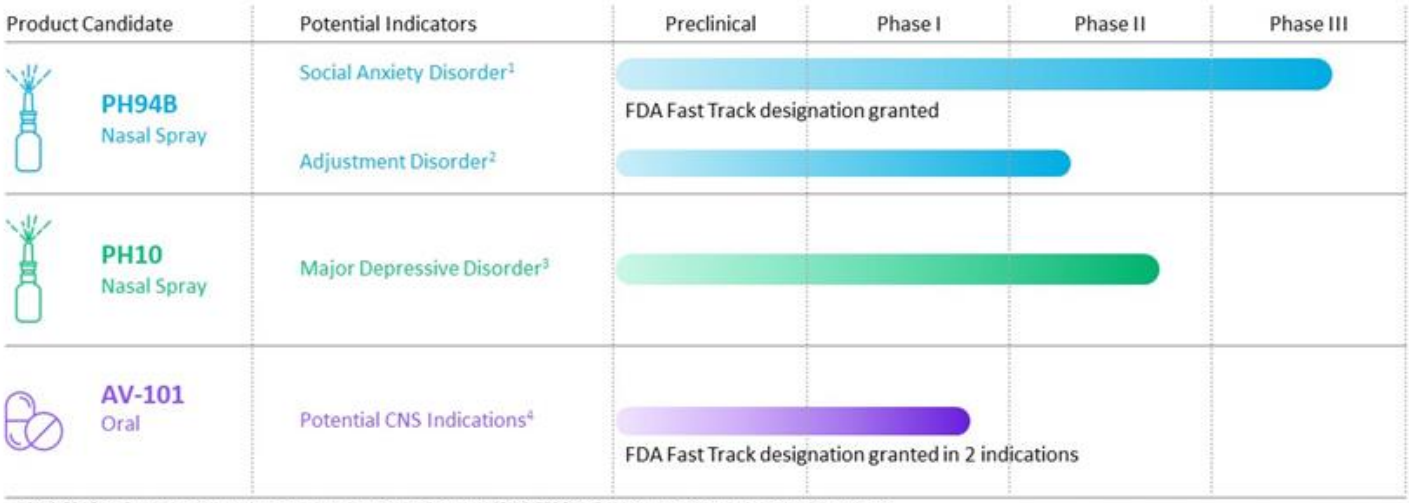
Forward Looking Statements

This presentation contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements involve known and unknown risks that are difficult to predict and include all matters that are not historical facts. These forward-looking statements include information concerning the impact of the COVID-19 pandemic, our product candidates, development efforts, collaborations, intellectual property, financial condition, plans, development programs, prospects or future events and involve known or unknown risks that are difficult to predict. In some cases, you can identify forward-looking statements by the use of words such as "may," "could," "expect," "project," "outlook," "strategy," "intend," "plan," "seek," "anticipate," "believe," "estimate," "predict," "potential," "strive," "goal," "continue," "likely," "will," "would" and variations of these terms and similar expressions, or the negative of these terms or similar expressions. Such forward-looking statements are necessarily based upon estimates and assumptions that, while considered reasonable by us and our management, are inherently uncertain.

Our actual results or developments may differ materially from those projected or implied in these forward-looking statements. Factors that may cause such a difference include, without limitation, risks and uncertainties relating to the impact of the COVID-19 pandemic; market conditions; the impact of general economic, industry or political conditions in the United States or internationally; adverse healthcare reforms and changes of laws and regulations; manufacturing and marketing risks, including risks related to the COVID-19 pandemic, which may include, but are not limited to, unavailability of or delays in delivery of raw materials for manufacture of our CNS drug candidates and difficulty in initiating or conducting clinical trials; inadequate and/or untimely supply of one or more of our CNS drug candidates to meet demand; entry of competitive products; and other technical and unexpected hurdles in the development, manufacture and commercialization of our CNS drug candidates; and the risks more fully discussed in the section entitled "Risk Factors" in our most recent Annual Report on Form 10-K for the year ended March 31, 2022, and in our most recent Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, as well as discussions of potential risks, uncertainties, and other important factors in our other filings with the U.S. Securities and Exchange Commission (SEC).

Our SEC filings are available on the SEC's website at www.sec.gov. Given these uncertainties, you should not place undue reliance on these forward-looking statements, which apply only as of the date of this presentation 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, other than as may be required by law. If we do update one or more forward-looking statements, no inference should be made that we will make additional updates with respect to those or other forward-looking statements.

Our Pipeline



1 PALISADE-1 Phase 3 trial did not achieve primary endpoint; independent interim analysis of PALISADE-2 Phase 3 trial recommended continuing study to full enrollment
2 Exploratory Phase 2A clinical trial initiated in Q4 2021
3 Successful Phase 2A clinical trial completed in Mexico; preparing US IND for potential Phase 1/2B development in the US
4 Ongoing Phase 1B DDI clinical development; assessing for potential exploratory Phase 2A clinical development

The commencement and completion of all potential studies is subject to US FDA regulatory authorization, strategic partnering and/or raising sufficient capital.


Vistagen
PH94B
for Social
Anxiety Disorder
Looking beyond the standard of care for anxiety disorders

Social Anxiety Disorder is a Serious Mental Health Condition

SAD is not simply medicalized shyness. It is a disabling disorder characterized by …

Debilitating emotional and physical symptoms

- Emotional Symptoms
  - Overwhelming fear
  - Surges of anxiety
  - Extreme self-consciousness
  - Isolation leading to depression
- Physical Symptoms
  - Blushing / Sweating
  - Trembling
  - Nausea
  - Fast Heartbeat / Chest Discomfort
  - Shortness of Breath / Dizziness

In everyday social or performance situations

Meeting new people

Presenting at work or school

Public speaking

Interviewing for a job

Eating/drinking in front of others

Going to the doctor/dentist

Source: ADAA Social Anxiety Brochure 2021

SAD affects ~10% of the US population, with only ~20% of SAD patients helped by current pharmacotherapy

Future Patients

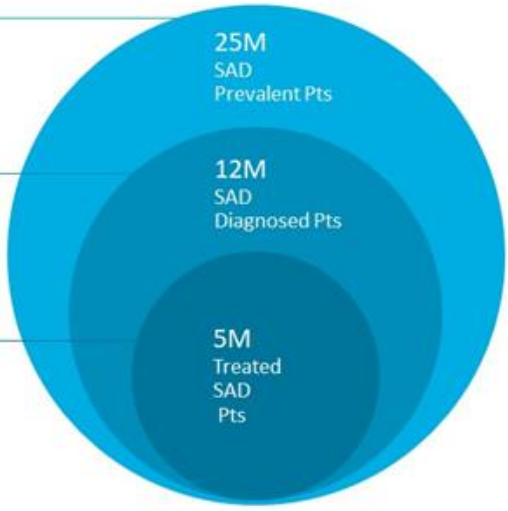
Patients suffering but unaware of SAD as a condition or not yet motivated to seek professional help.

Underserved Patients

Patients unsatisfied with or unwilling to use current treatment options due to efficacy, side effects, or addiction potential.

Existing Patients

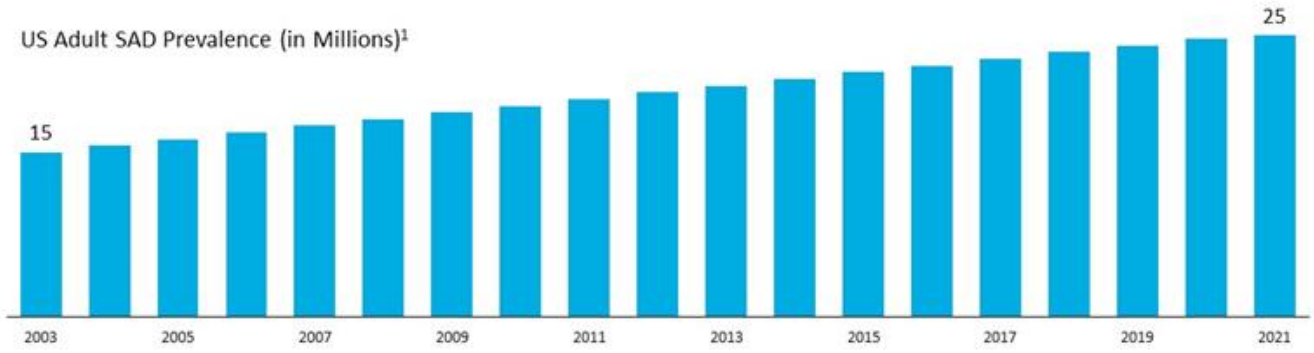
Patients cycling through treatments, often unsatisfied with their current treatment options but without alternatives.



Sources: Kantar Health. Nov 2021. National Health and Wellness Survey (NHWS), 2021. [US]. Malvern, PA.

It has been ~2 decades since a new SAD therapy was approved

SAD disease burden in the US continues to grow, but scientific innovation has been lacking



SAD is a highly prevalent condition which continues to affect increasing numbers of people each year.

Sources: 1. NCS-R Survey, 2003; Kantar NHWS 2021, Internal Projections

Current Standard of Care for SAD is Inadequate

There is no FDA-approved, fast-acting, acute treatment of anxiety for SAD

Treatments For Social Anxiety Order							
Drug	Fast- Acting	No Systemic Absorption	No Long-term Side Effects (Sexual Dysfunction Etc.)	Non-Sedating	No Cognitive/ Motor Impairment	No Withdrawal Syndrome	No Abuse Potential
FDA-approved (Sertraline, Paroxetine, Venlafaxine)	⊖	⊖	⊖	✓	✓	⊖	✓
Off-label (Benzodiazepines)	✓	⊖	⊖	⊖	⊖	⊖	⊖
Preferred SAD Therapy	✓	✓	✓	✓	✓	✓	✓

SAD Patients Desire New Treatment Options

The Ideal SAD Medication is Safe & Works Quickly
–patient survey

"If I were open to taking medication, I would like it to subside my anxiety for the day and start working within 20 minutes."

"I would want to continue on a Paxil type drug for all the time, but I'd want something like a rescue inhaler that I could use as needed."

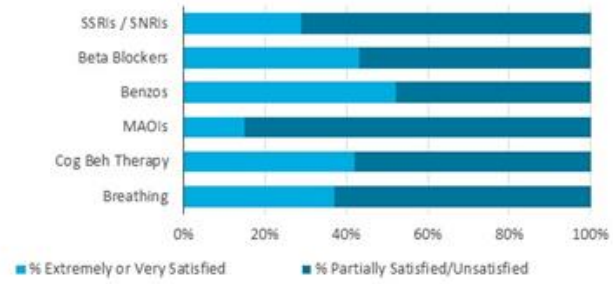
"I would want to feel calm and like I can continue to go about my day without worrying. Nothing should have to come to a screeching halt. I think expecting them to make symptoms more manageable is more realistic."

Sources: Vistagen Proprietary Market Research October 2021

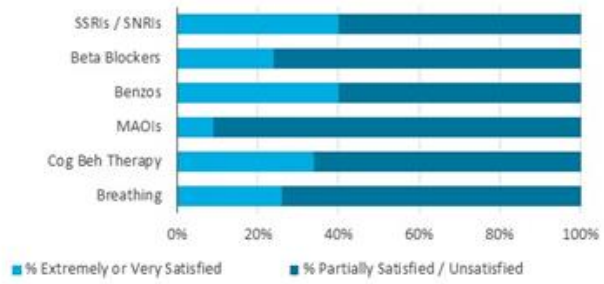
Physician Satisfaction with Current Therapies is Modest

Satisfaction with current treatments for ACUTE episodes of SAD from a large online survey

Psychiatrists (n=125)



Primary Care Physicians (n=126)



Sources: Vistagen Proprietary Market Research, Online Survey, Jan 2022

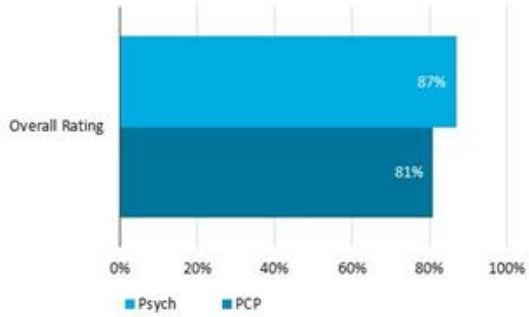
PH94B has Potential to be 1st FDA-approved Fast-acting Treatment of SAD

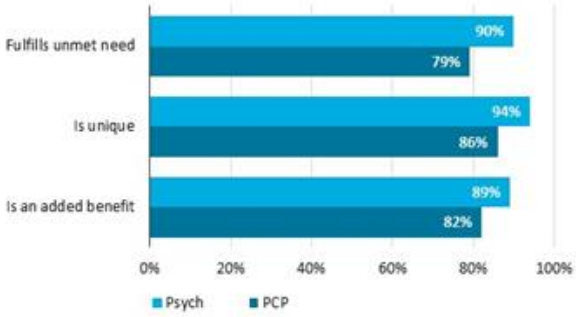
PH94B is a novel synthetic neuroactive steroid nasal spray

- Differentiated MoA from antidepressants and benzos
- Designed to be fast-acting, used as-needed and achieve functional improvement in anxiety-provoking social and performance situations in daily life
- Designed to be non-systemic, non-sedating, non-addictive (does not potentiate GABA-A or bind to typical AL receptors)
- Well-tolerated in all clinical studies to date
- In Phase 3 development in the U.S.
- FDA Fast Track designation

PH94B is rated highly by physicians and recognized as a valuable and differentiated approach to treat SAD episodes on-demand

Physician assessment of blinded PH94B product profile from large online survey

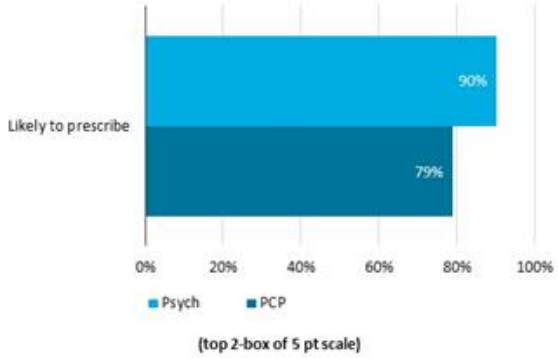


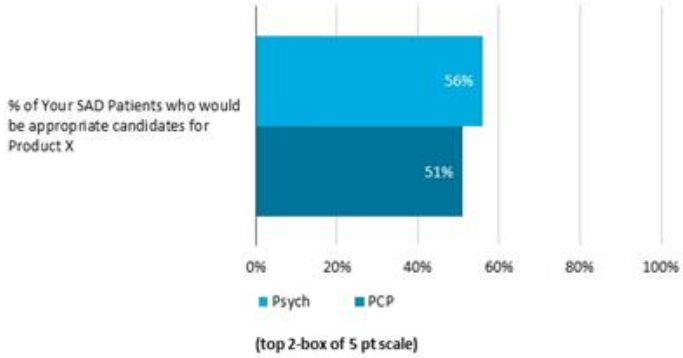


Sources: Vistagen Proprietary Market Research, Online Survey, Jan 2022 (n=251)

Physicians indicate high intent to prescribe PH94B and note it would be appropriate for the majority of their SAD patients

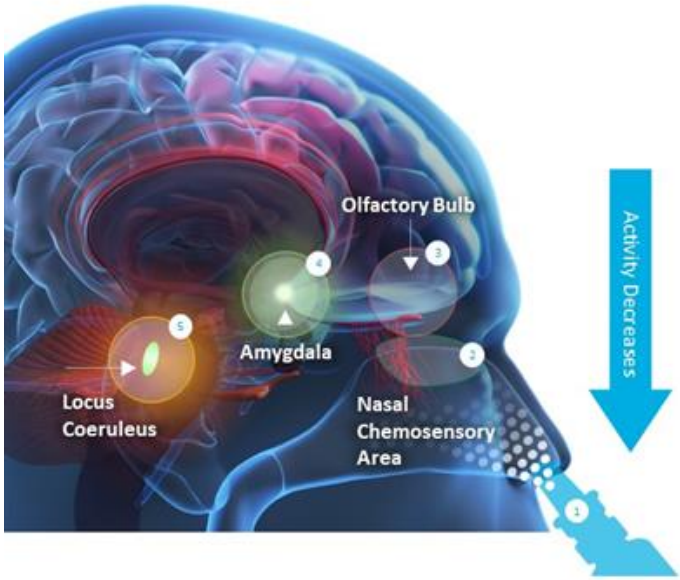
Physician assessment of a blinded PH94B product profile from large online survey





Sources: Vistagen Proprietary Market Research, Online Survey, Jan 2022 (n=251)

PH94B's Innovative MOA via Olfactory-amygdala Circuit



1. Microgram-level intranasal dose of PH94B (3.2 mcg) is administered.
2. PH94B engages peripheral receptors in nasal chemosensory neurons (NCNs).
3. Once stimulated with PH94B, NCNs then trigger subsets of interneurons in the olfactory bulbs (OB).
4. Neurons in the OB then stimulate inhibitory GABAergic "Fear Off" neurons in the limbic amygdala, the main fear and anxiety center of the brain.
5. The stimulation of the limbic amygdala DECREASES the activity of the sympathetic nervous system which facilitates fear extinction activity of the limbic-hypothalamic system as well as in other parts of the brain.

Sources: Monti L, and Liebowitz MR (2020). Neural circuits of anxiolytic and antidepressant pherine molecules. CNS Spectrums https://doi.org/10.1017/S109285292000190X

Vistagen

PH94B Phase 1 Data

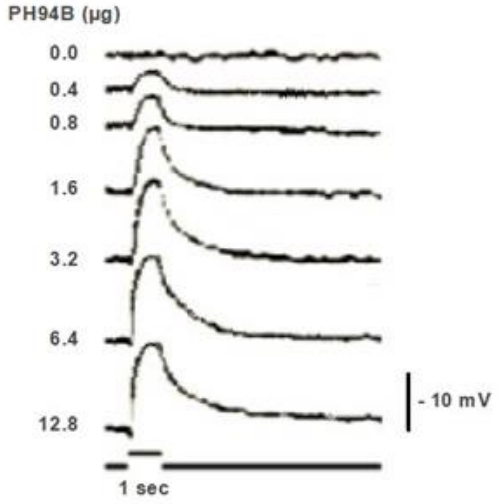
Well-tolerated, reduced autonomic biomarkers and increased EGNR

Statistically significant reduction in the autonomic biomarkers heart rate, respiratory rate, and electrodermal activity in both men (n=8) and women (n=8). Also, 0.4 mcg intranasal PH94B significantly increased the amplitude of the electrogram (EGNR) recorded from the nasal chemosensory epithelium in both men and women.

Dose dependent **increase in electrical activity of the nasal chemosensory epithelium**. EGNR was similar in male/female healthy volunteers after ascending doses of PH94B in study CL013B (Maximal EGNR amplitude was achieved at 3.2 mcg dose in both men (n=10) and women (n=10), and no significant increase was seen at higher doses (6.4 and 12.8 mcg)).

Sources: 1. Monti et al., 2022, Psych Congress; 2. Liebowitz et al., 2016, Depression and Anxiety, Dec;33(12):1081-1089

Dose-dependent electrical depolarization of human nasal chemosensory receptors in response to PH94B

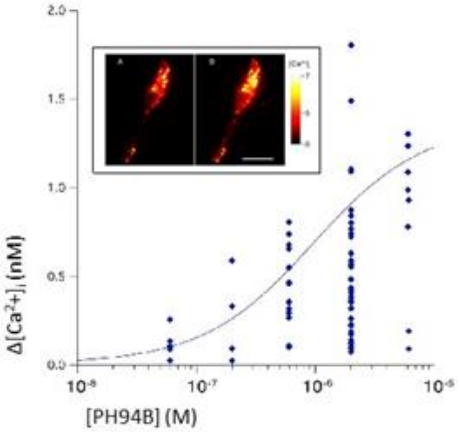


Doses between 1.6 micrograms and 3.2 micrograms expected to be efficacious

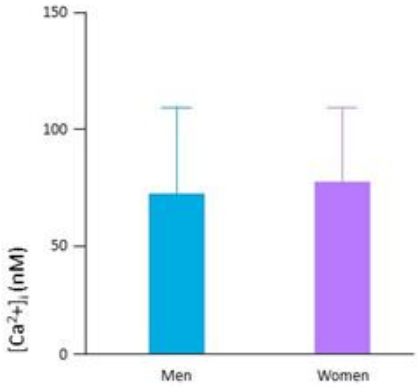
EGNR traces recorded from the nasal chemosensory receptor area in a human volunteer during intranasal administration of PH94B the quantities shown at left

Sources: Monti et al, 1994 and 2022.

Dose-dependent effect of PH94B on intracellular calcium in human nasal chemosensory cells suggests PH94B potential efficacy in both men and women



(A) Concentration dependent effect of PH94B in isolated living human nasal chemosensory cells. Half maximal effective concentration EC_{50}= 1 µM. The inset shows increased fluorescence of a chemosensory cell (right) due to increased intracellular calcium during exposure to PH94B.



(B) Similar effect of PH94B in men and women chemosensory cells

Sources: Winegar B. and Monti L. 2010.

PH94B Significant Phase 2 Data in First SAD Study

PH94B demonstrated potential to be a fast-acting, well-tolerated SAD treatment

Public speaking and social interaction challenges in clinical setting

Phase 2B randomized, double-blind, placebo-controlled multi-center study (n=91)

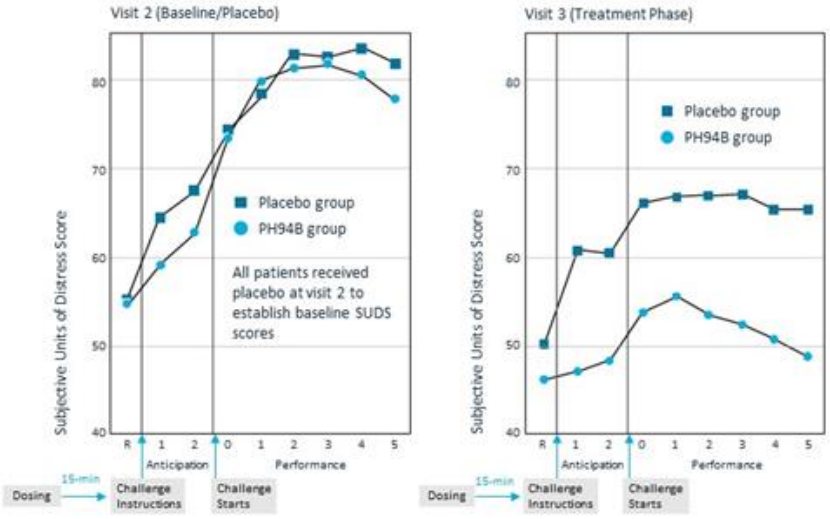
Primary efficacy endpoint

- Change in Subjective Units of Distress Scale (SUDS) scores from baseline compared to placebo
- Met primary efficacy endpoints (p=0.002 for public speaking challenge and p=0.009 for social interaction challenge)
- Very well-tolerated

Sources: 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 Phase 2 SAD Study — Public Speaking Challenge

Minute-by-minute SUDS scores



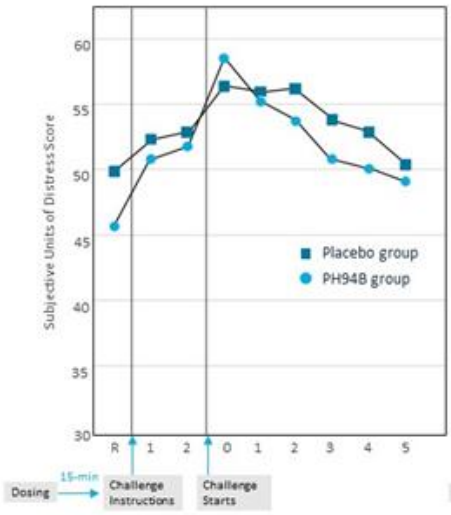
PH94B rapidly reduced anxiety in response to public speaking challenge		
	Active Group	Placebo Group
Mean Difference	26.7	14.0
Standard Deviation	21.6	16.3
Number of Subjects	45	46
t = 3.16	p = 0.002	Cohen's d (Effect Size)0.66

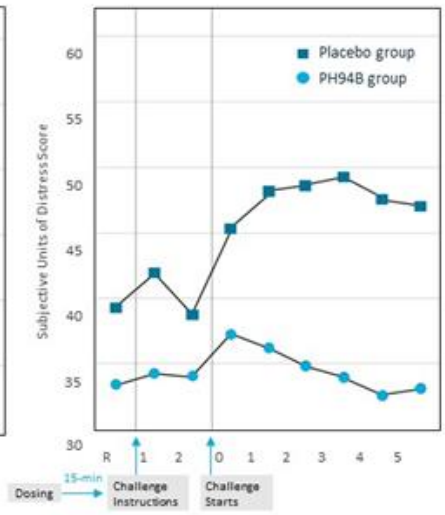
Subject is told that will have to give a 5-minute speech without notes to an audience of 3 role-players and has 2 minutes to prepare.

Sources: Liebowitz, MR, Salman, E, Nicolini, H, Rosenthal, N, Hanover, R, Morel, 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 Phase 2 SAD Study — Social Interaction Challenge

Minute-by-minute SUDS scores





PH94B rapidly reduced anxiety in response to social interaction challenge

	Active Group	Placebo Group
Mean Difference	18.3	6.6
Standard Deviation	17.4	23.6
Number of Subjects	45	46
t = 2.67	p = 0.0029	Cohen's d (Effect Size)0.56

Subject is told that will have to join a group of 3 role-players for a party-like conversation and has 2 minutes to prepare

Social interaction challenge dosing occurs ~60 minutes post public speaking challenge

Sources: 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 PALISADE-1 and PALISADE-2 Phase 3 Clinical Trials

Public speaking challenges

Principal Investigator: Dr. Michael Liebowitz, Columbia University

Objectives: Evaluate efficacy, safety, and tolerability of PH94B for the acute treatment of anxiety in adults with social anxiety disorder

Study design: US randomized, multi-center, double-blind, placebo-controlled, single-dose administration clinical trials

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

PALISADE-1: Topline results reported July 2022; primary endpoint not reached

PALISADE-2: Enrollment paused in July 2022; interim analysis of 140 subjects by independent biostatisticians completed in September 2022 recommended continuing study as planned to full enrollment; study restart expected near-term; topline results expected in 2023

PH94B Significant Phase 2 Data in Second Published SAD Study

PH94B demonstrated potential to be a novel, fast-acting treatment of anxiety in adults

Outpatient self-administration up to 4x/day as-needed prior to anxiety-provoking social and performance situations in daily life

Phase 2 randomized, double-blind, placebo-controlled multiple administration assessment, 4-week cross-over study (n=22)

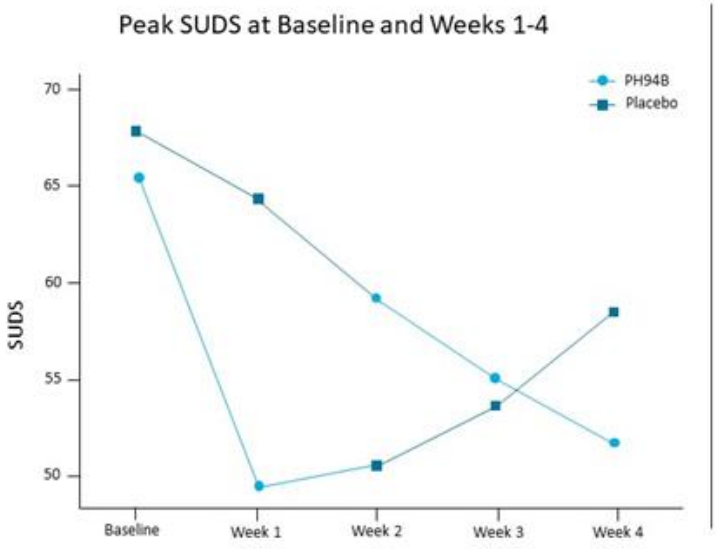
Primary efficacy endpoint

- Change in Subjective Units of Distress Scale (SUDS) scores from baseline compared to placebo
- Met primary efficacy endpoint (p=0.006, effect size = .658)
- Looking between groups at just first 2 weeks of treatment, trend superiority to placebo on the Liebowitz Social Anxiety Scale (LSAS) (p = .07) and a significant difference on the Patient Global Impression of Change (p = 0.024) and LSAS Avoidance subtotal (p = 0.02)

Sources: Liebowitz MR, Hanover R, Draine A, Lemming R, Careri J, Monti L (2016). Effect of as-needed use of intranasal PH94B on social and performance anxiety in individuals with social anxiety disorder. *Depress Anxiety* 33: 1081-1089.

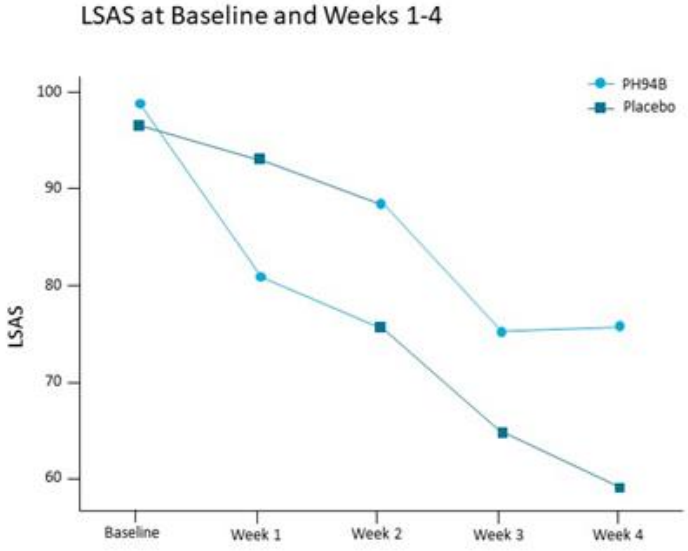
Phase 2 Outpatient Cross-over Study Results (SUDS)

Multiple administrations as-needed in anxiety-provoking social and performance situations in daily life



- Peak SUDS score for the PH94B group increased after crossover to placebo, though not back to the baseline, possibly due to increased confidence from PH94B treatment prior to crossover to placebo
- 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)

Phase 2 Outpatient Cross-over Study Results (LSAS)



- 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 trend difference (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)
- In the sample as a whole (n=22), 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

Subjective Units of Distress Scale (SUDS)

Primary efficacy endpoint in Phase 2 and Phase 3 clinical trials

The SUDS measures the self-reported intensity of anxiety and/or distress in patients with SAD

Patients are asked to rate their level of anxiety/distress on a scale of 0-100.

Physiological signs of distress such as sweating, shaking, increased heart rate or respiration, and gastrointestinal distress may be present at a score of 70, and are present at a score of 80.

SUDS is a more appropriate measure for acute anxiety during a stressor event compared to LSAS, which is used to diagnose and measure the severity of SAD and track changes over time.

SUDS has become the standard for acute measurement of anxiety, now leveraged in several ongoing clinical trials.

100	Highest anxiety/distress that you have ever felt
90	Extremely anxious/distressed
80	Very anxious/distressed; can't concentrate
70	Quite anxious/distressed; interfering with functioning
60	Moderate-to-strong anxiety or distress
50	Moderate anxiety/distress; uncomfortable, but can still function
40	Mild-to-moderate anxiety or distress
30	Mild anxiety/distress; no interference with functioning
20	Minimal anxiety/distress
10	Alert and awake, concentrating well
0	No distress; totally relaxed

Sources: Oxford Clinical Psychology. © Oxford University Press, 2014

Liebowitz Social Anxiety Scale (LSAS)

Efficacy endpoint required by the FDA for all prior SAD approvals

The LSAS is a 24-item (13 concerning performance anxiety and 11 pertaining to social situations) self-rated scale used to assess how social anxiety plays a role in a patient's life across a variety of situations

Assesses both the patient's social anxiety in situations as well as avoidance of those situations

Each item describes a situation about which the patient must answer two questions, one about fear and one about avoidance

Situation	How anxious or fearful you feel 0 = none 1 = mild 2 = moderate 3 = severe	How often you avoid the situation 0 = never 1 = occasionally 2 = often 3 = usually
1. Using a telephone in public		
2. Participating in small group activity		

The LSAS is scored by summing the item ratings. Below are the suggested interpretations for various score ranges.

Greater than 95: Very severe social phobia

80–95: Severe social phobia

65–80: Marked social phobia

55–65: Moderate social phobia

PH94B PALISADE Open Label Study

Robust functional improvement in anxiety-provoking social and performance situations in daily life, as measured by the LSAS

Design: As needed administration of PH94B prior to acute anxiety-provoking social and performance situations in daily life, up to four times per day, over a period of up to 10 months

Preliminary analysis of final data set of nearly 400 subjects demonstrates robust functional improvement in anxiety-provoking social and performance situations in daily life, as measured by the Liebowitz Social Anxiety Scale (LSAS), the efficacy endpoint required by the FDA for prior SAD approvals, as well as favorable safety and tolerability profile consistent with prior clinical studies

LSAS measurements over time may be well-suited for a Phase 3 trial to demonstrate efficacy and the true impact of PH94B on patients' lives given that it measures overall improvement in disease severity by capturing the reduction in fear and anxiety, as well as the avoidance of social and performance situations

Key Implications: Combined with the Phase 2 cross-over study, these two studies demonstrate the potential for PH94B to achieve robust overall reduction in symptoms of SAD and improvement in severity over time as measured by the LSAS.

Next Step: Planning to meet with FDA in Q1 2023 to secure clearly-defined consensus on potential study design(s) for next Phase 3 study of PH94B in SAD – PALISADE-3

PH94B Opportunities Beyond Social Anxiety Disorder

Adjustment Disorder	Prevalence: ~18M	Current treatment paradigm lacks major studies to support pharmacotherapy. A need exists for evidence based clinical interventions for adjustment disorder.
Post-Traumatic Stress Disorder	Prevalence: ~9M	A minority of PTSD patients (< 30%) achieve full remission, leaving unmet need for new effective and preventive medications.
Procedural Anxiety	Prevalence: ~9M	Current treatment options come with safety issues & variable efficacy and are not ideal for many patients and procedural situations.
Post-Partum Anxiety	Prevalence: ~0.6M	Drugs are prescribed that are approved for the general population, but none are ideal for the needs of new mothers.
Panic Disorder	Prevalence: ~7M	Treatments lack consistent symptom control, with bother-some side effects and risk of abuse. Options do not provide acute symptomatic relief.

Sources: 1. Mauro et al, 2009, 2. Reinmman et al, 2016, 3. Antonin et al, 2021, 4. Carske et al, 2005, 5. Julia et al, 2019.

PH94B Phase 2A Adjustment Disorder with Anxiety

Alarming increase in prevalence of anxiety-related disorders

Adjustment disorder with anxiety is an emotional or behavioral reaction considered excessive or disproportionate to a sudden change, stressful event or major life change, such as loss of work, divorce or health setback, occurring within three months of the stressor, and/or significantly impairing a person's social, occupational and/or other important areas of functioning.

Principal Investigator: Dr. Michael Liebowitz, Columbia University

Objectives: Evaluate efficacy, safety, and tolerability of PH94B administered 4 times per day over 4 weeks for the treatment for the treatment of anxiety in adults with adjustment disorder with anxiety

Study design: U.S. randomized, multi-center, double-blind, placebo-controlled, parallel group, multi-administration design

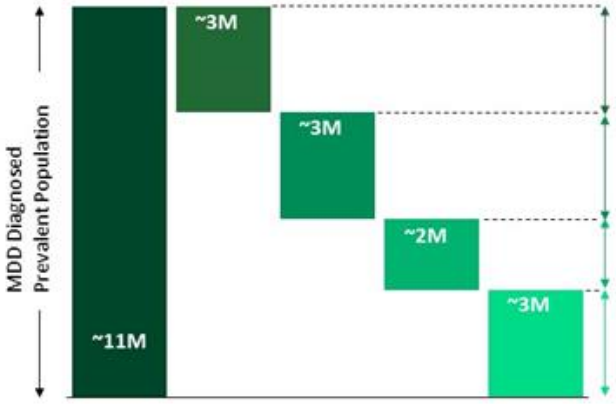
Primary Endpoint: Change from baseline in anxiety level as measured by the HAM-A at end of 4 weeks of treatment

Status: Enrollment complete; topline data expected 1Q 2023


Vistagen
PH10
for Major
Depressive Disorder
Looking beyond the standard of care
for depression disorders

Significant Unmet Need in Major Depressive Disorder (MDD)

21 million US Adults had at least one major depressive episode in 2020



Untreated Pts: A large percentage of patients remain untreated as a result of lack of options and discontinuations due to severe side effects.

First Line Treated Pts: Only 1 in 3 patients respond to first anti-depressant. May take 4 to 6 weeks or more for antidepressant effects. Significant potential side effects such as Anxiety, sexual dysfunction, insomnia, dizziness and nausea.

Second Line Treated Pts: Augmentation with anti-psychotics work in only 20% of patients. Significant potential side effects Weight gain, stomach pain, tiredness, dizziness, tardive dyskinesia, headache, nervousness, restlessness.

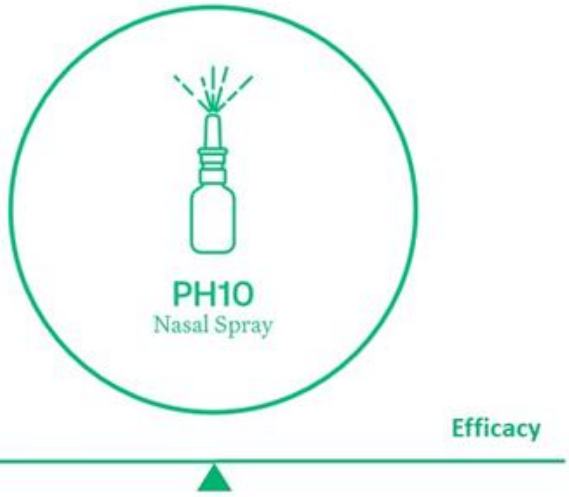
Third Line plus Pts: Huge unmet need for patients resistant to second line treatment options. Lack of safe and efficacious options for Treatment Resistant & Refractory MDD.

Sources: 1. Substance Abuse and Mental Health Services Administration. (2020). Key substance use and mental health indicators in the United States: Results from the 2019 National Survey on Drug Use and Health; 2. World Health Organization, https://www.who.int/news-room/fact-sheets/detail/depression; 3. Rush AJ, et al. Am J. Psychiatry. 2006, 163(11): 1905-1917 (STAR*D Study)

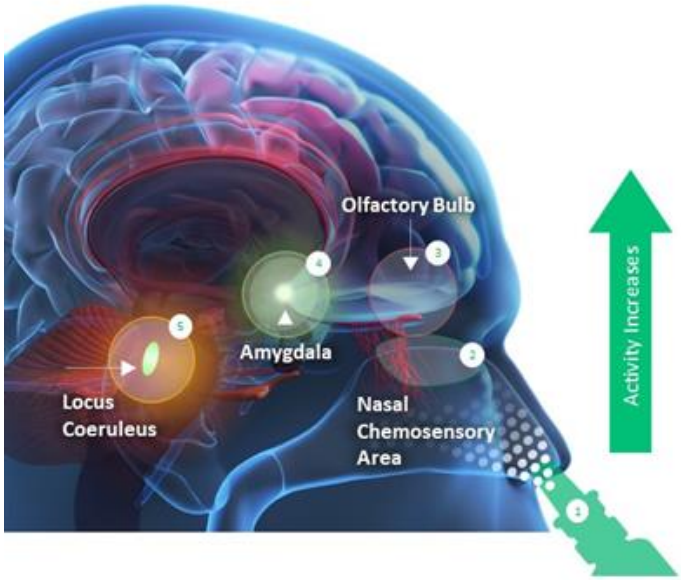
PH10 is a Potential Fast-acting Stand-alone Treatment for Major Depressive Disorder

PH10 is a novel synthetic neuroactive steroid nasal spray

- Designed for rapid onset antidepressant effects as a stand-alone monotherapy
- Differentiated MoA
- Designed to be non-systemic, non-sedating, non-addictive (doesn't potentiate GABA-A)
- Successful Phase 2A development completed
- Well-tolerated in all clinical studies to date



PH10's Mechanism of Action



1. Microgram-level intranasal dose of PH10 (3.2 mcg) engages peripheral receptors in nasal chemosensory neurons (NCNs)
2. Chemosensory receptors in nose
3. Trigger subsets of neurons in the olfactory bulbs
4. Which stimulate "Fear On" neurons in the limbic amygdala
5. Which increases activity of limbic-hypothalamic sympathetic nervous system and increases the release of catecholamines

Sources: Monti L, and Liebowitz MR (2020). Neural circuits of anxiolytic and antidepressant pherine molecules. *CNS Spectrums* https://doi.org/10.1017/S109285292000190X

Vistagen

Similarities and Differences between PH94B and PH10

PH94B and PH10 are chemically distinct, but they are designed to act on different receptors on nasal chemosensory cells, resulting in different pharmacological effects.

PH94B	Properties	PH10
Nasal Chemosensory Cells	Primary target	Nasal Chemosensory Cells
Androstane	Chemical Molecule	Pregnane
Sympatholytic	Nervous System Effect	Sympathomimetic
Anxiolytic	Pharmacological Effect	Anti-depressant

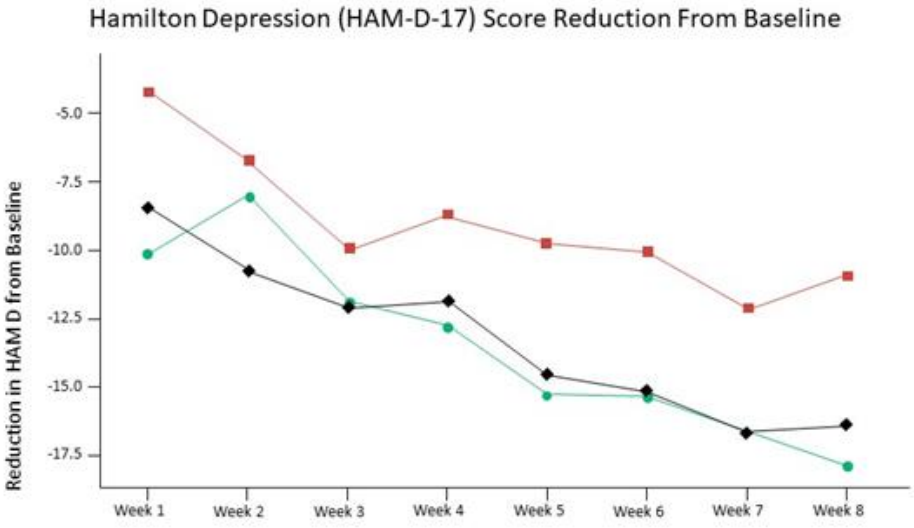
PH10 Antidepressant Effects in Published Exploratory Phase 2A Study

- Study design: Phase 2A randomized, double-blind, placebo-controlled, parallel design POC clinical study
- Dose administered: 3.2 mcg or 6.4 mcg of PH10 or placebo given intranasally 2 times per day, every day for 8 weeks
- Enrollment: n = 30
- Primary Endpoint: Change in HAM-D-17 scores from baseline compared to placebo
- **Results:** 6.4 mcg dose significantly reduced depressive symptoms as early as one week based on HAM-D-17 scores compared to placebo (p=0.022)
- Well-tolerated, no dissociative side effects or serious adverse events observed
- Results support advancement to Phase 2B clinical development

Rapid-onset antidepressant effects with PH10 observed in MDD patients with minimal side effects.

Sources: Monti, L., Nicolini, H., Liebowitz, M., & Hanover, R. (2019). "A Placebo Controlled Trial of PH10: Test of a New Rapidly Acting Intranasally Administered Antidepressant." *Br J Phar Med Res* 4(6): 2157-2168.

PH10 Phase 2A MDD Study (n=30)



6.4 mcg dose produced rapid-onset and sustained antidepressant effects in MDD patients with minimal side effects

PH10 Dose	HAM-D Score	p (PH10 vs Placebo)	Cohen's D (Effect Size)
◆ 3.2 mg (Low Dose)	16.3	.101	0.74
● 6.4 mg (High Dose)	17.8	.022	0.95
■ Placebo	10.9		

Sources: Monti, L., Nicolini, H., Liebowitz, M., & Hanover, R. (2019). "A Placebo-Controlled Trial of PH10: Test of a New Rapidly Acting Intranasally Administered Antidepressant." *Br J Phor Med Res* 4(6): 2157-2168.

PH10 Clinical Development

Stand-alone treatment for individuals with major depressive disorder

Following a successful Phase 2A study conducted in Mexico, a small Phase 1 study will be conducted prior to moving to Phase 2B development

Phase 1

- Objectives: Evaluate safety and tolerability of PH10 in healthy volunteers to confirm the previous safety, tolerability, and pharmacodynamic (PD) effects of PH10 seen in the previous two Phase 1 studies
- Study design: Double-blind, placebo-controlled study in 12 healthy volunteers
- Status: Planning enrollment to begin 4Q 2022; topline data anticipated late 1Q 2023

Phase 2B

- Plan to discuss with the FDA our go forward plan upon completion of the Phase 1 study

PH10 Opportunity Beyond Major Depressive Disorder

Treatment Resistant Depression	Prevalence: ~7M	Treatment lacks consistent symptom control, bother-some side effects and tolerance, and risk of abuse. Options do not provide acute symptomatic relief.
Post Partum Depression	Prevalence: ~0.5M	Concern of PPD treatments is high among patients; non-systemic options are needed especially for breastfeeding mothers.
Suicidal Ideation	Prevalence: ~12M	Suicidal Ideation is undertreated and lacks awareness outside of comorbid diagnosis. Overall HCPs lack understanding of suicidal antecedent validators and skills for suicide risk assessments.

Sources: 1. Results from the 2019 National Survey on Drug Use and Health; 2. Zhdanava M, et al. *J Clin Psychiatry*. 2021;82(2):20m13699; 3. Wang, Zet al, Transl Psychiatry 11, 543 (2021); 4. Cox EQ, et al. *J Clin Psychiatry*. 2016;77(9):1189-1200; 5. Piscopo K, et al, 2016 6. Bommersbach TJ, et al, *JAMA Psychiatry*. 2022;79(3):219–231.


Vistagen
AV-101
For Multiple
CNS Disorders
Looking beyond the standard of care
for CNS disorders

AV-101 + Probenecid for Multiple CNS Disorders

Designed to inhibit (but not block) NMDA receptor activity

- Oral prodrug of 7-Cl-KYNA, a potent and selective full antagonist at the glycine site of the NMDA receptor.
- Well-tolerated in all clinical studies to date.
- Two positive preclinical studies show increased brain concentrations of 7-Cl-KYNA when administered in combination with FDA-approved probenecid.
- Assessing go forward opportunities in combination with probenecid.
- FDA Fast Track designations for adjunctive treatment of MDD and treatment of neuropathic pain.

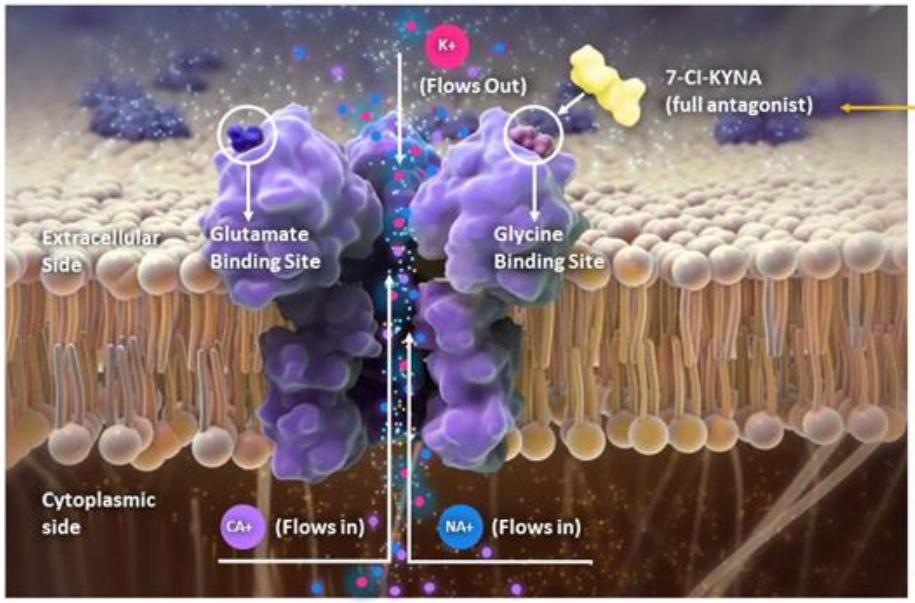
Levodopa-Induced Dyskinesia
Associated with Parkinson's therapy

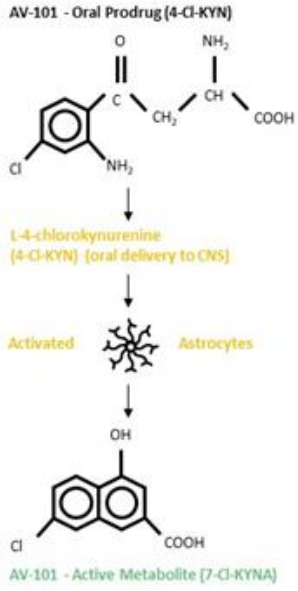
Major Depressive Disorder

Neuropathic Pain

Suicidal Ideation

AV-101's Potential MOA

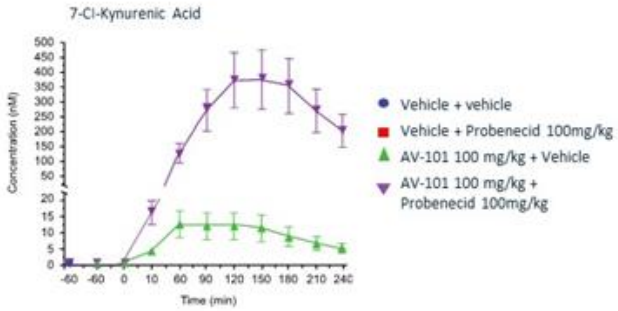




AV-101 + Probenecid

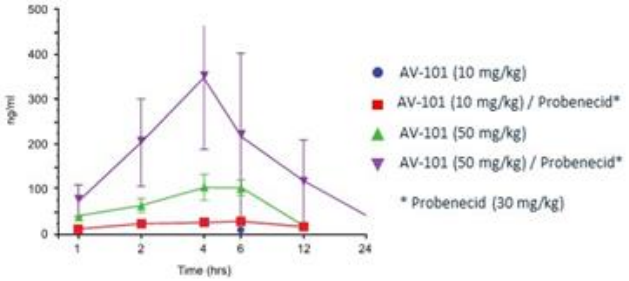
Preclinical data demonstrate substantial increases in brain concentrations of 7-Cl-KYNA

Probenecid Increases 7-Cl-KYNA Brain Levels By > 35-fold[1]



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 (100mg/kg each) Data are represented as mean ± SEM. N = 4-6/group.

Probenecid Increases 7-Cl-KYNA Brain Levels By > 3.4-fold[2]



Sources: 1. Rodent: Dickens, D., (2019, December). Drug transporters at the blood-brain barrier as targets for personalized CNS therapeutics. Speaker at British Pharmacological Society, Pharmacology 2019, Edinburgh, UK.; 2. Canine: Internal Data: there was high degree of variation in this experiment due to the limited number of animals from which suitable time-based sequential CSF samples could be drawn.

Our Mission

Radically improve mental health - **one mind at a time**™

- Multiple clinical-stage drug candidates.
- Targeting large anxiety, depression and neurology markets.
- Numerous potential catalysts in 2022, 2023 and beyond.
- Differentiated MOAs, bringing new value to patients, physicians, and payers.
- Cash to achieve multiple potential near-term catalysts.
- Experienced team to execute through commercialization.


Vistagen
Healthy minds make healthy communities, and we are innovating to change the trajectory of global mental health care …
One Mind at a Time™