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): April 27, 2023

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 April 27, 2023, 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 April 2023
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: April 27, 2023

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
Spring 2023

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 our product candidates, development efforts, collaborations and/or potential strategic partnerships, 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, and there can be no assurance that any estimate and assumption contained within these forward looking statements will materialize. As with all pharmaceutical products, there are substantial risks and uncertainties in the process of development and commercialization and actual results or development may differ materially from those projected or implied in these forward-looking statements. Other factors that may cause such a difference include, without limitation, risks and uncertainties relating to our ability to secure adequate financing for our operations and development of our drug candidates, including financing, collaborative support and/or strategic partnership for continued clinical development of our product candidates; the completion and results of our ongoing and/or future clinical studies; the scope and enforceability of our patents; other risks and uncertainties related to delays in launching, conducting and/or completing ongoing and planned clinical trials, including delays or other adverse effects due to the COVID-19 pandemic; fluctuating costs of materials and other resources and services required to conduct our ongoing and/or planned clinical and non-clinical trials; market conditions; the impact of general economic, industry or political conditions in the United States or internationally; and other technical and unexpected hurdles in the development our drug candidates. These risks are 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 December 31, 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.

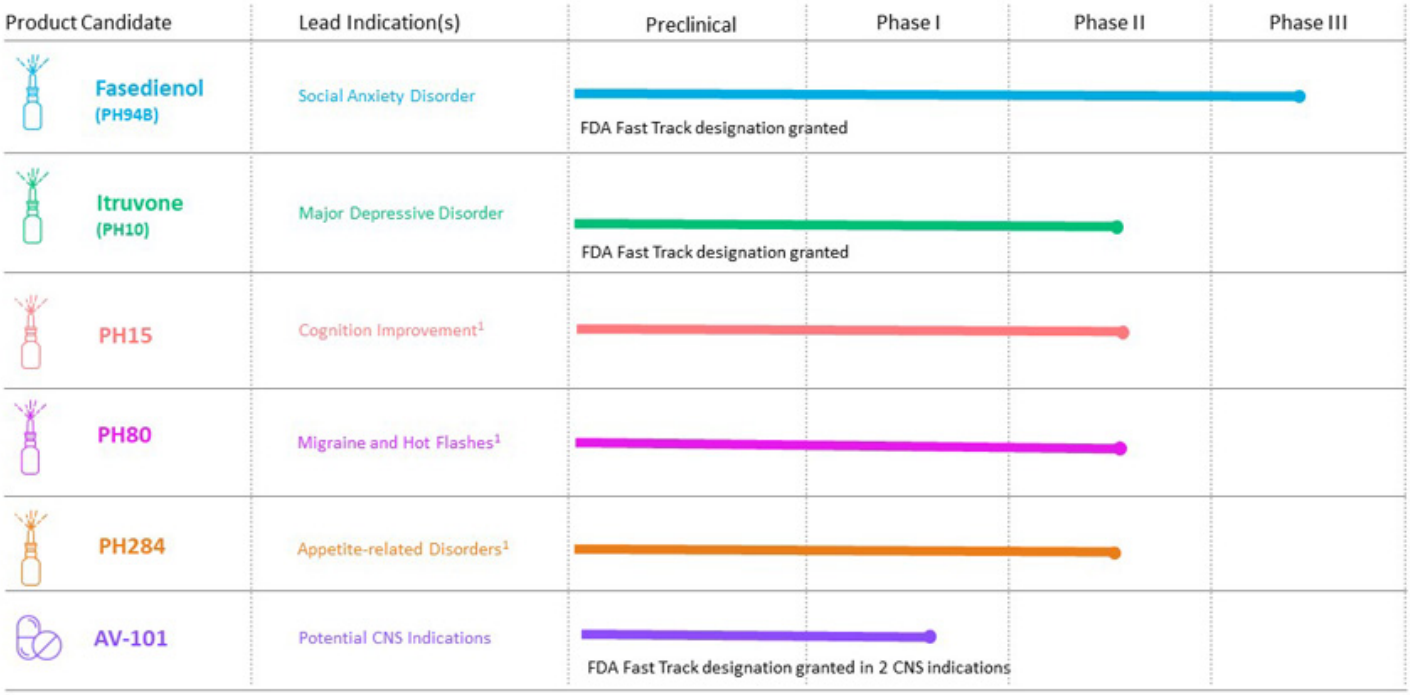
We explicitly disclaim any obligation to update any forward-looking statements, other than as may be required by law. If we do update one or more forward-looking statements, no inference should be made that we will make additional updates with respect to those or other forward-looking statements.

Our Mission

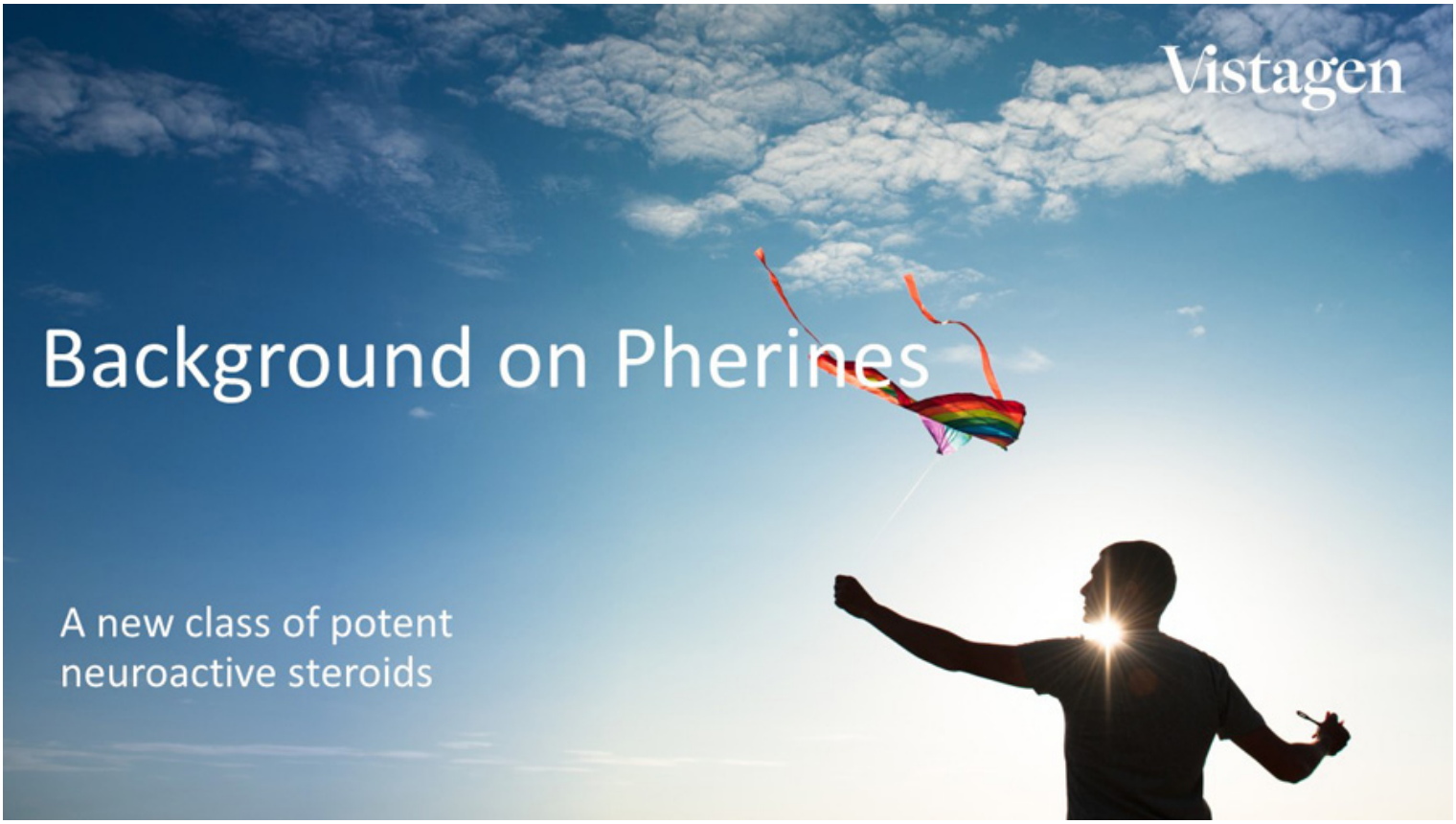
Radically improve mental health - **One Mind at a Time**™

- Six clinical-stage drug candidates
- Differentiated MOAs, bringing new value to patients, physicians, and payers
- Five pherine assets with positive Phase 2 data
- Targeting large anxiety, depression and neurology markets
- Experienced CNS team and advisors

Our Pipeline



1. Indicates US IND-enabling work necessary to facilitate further clinical development in the US
The commencement and completion of all potential studies is subject to US FDA regulatory authorization and/or securing sufficient capital, or strategic collaborations, or both.


Vistagen
Background on Pherines
A new class of potent
neuroactive steroids

What are Pherines?

Odorless, Tasteless, Non-systemic, Rapid-onset, Favorable Safety Profile

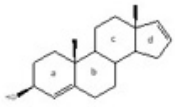
- Pherines are a new class of potent neuroactive steroids that are thought to selectively engage chemosensory receptors in the nasal passages and induce rapid-onset pharmacological and behavioral effects.
- Pherines are thought to selectively modulate brain areas, including the limbic amygdala, hypothalamus, hippocampus, locus ceruleus and prefrontal cortex, without systemic uptake and without binding to classic abuse liability receptors or to steroidal hormone receptors.
- Pherines have shown a consistently favorable safety profile in all clinical to date.

Vistagen's Pherine Assets

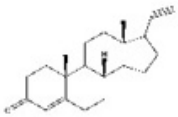
Vistagen owns all intellectual property rights to five clinical-stage pherines, as well as an extensive steroidal molecule database

There are six pherine families: androstane, estrene, estrane, pregnane, norpregnane and cholane.

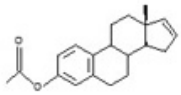
- **Fasedienol (PH94B)** or 3β-hydroxy-androsta-4,16-dien-ol
  - Hydrocarbon Core: Androstane
  - Social Anxiety Disorder (SAD)



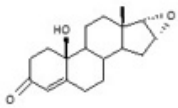
- **Ituruvone (PH10)** or Pregn-4-en-20-yne-3-one
  - Hydrocarbon Core: Pregnane
  - Major Depressive Disorder



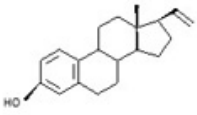
- **PH15** or estra-1,3,5(10),16-tetraen-3-yl-acetate
  - Hydrocarbon Core: Estrane
  - Cognition Improvement



- **PH80** or 16a,17a-epoxyestr-4-en-10-ol-3-one
  - Hydrocarbon Core: Estrane
  - Migraine
  - Hot Flashes



- **PH284** or (17β)19-norpregna-1,3,5(10)-trien-3-ol
  - Hydrocarbon Core: Norpregnane
  - Appetite-related Disorders



Vistagen


Vistagen
Fasedienol
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 chronic 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

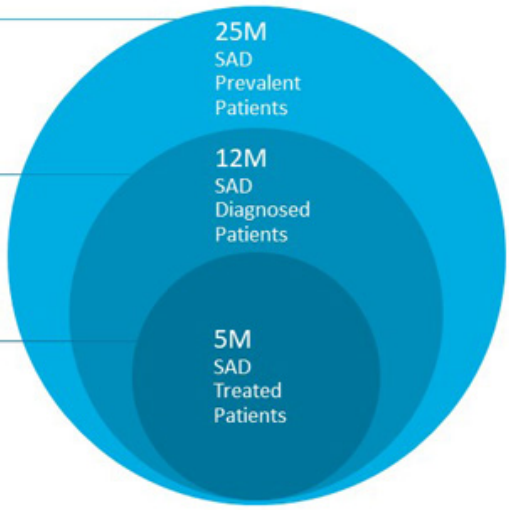
Patients suffering but unaware of SAD as a condition or not yet motivated to seek professional help.

Underserved Patients

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

Existing Patients

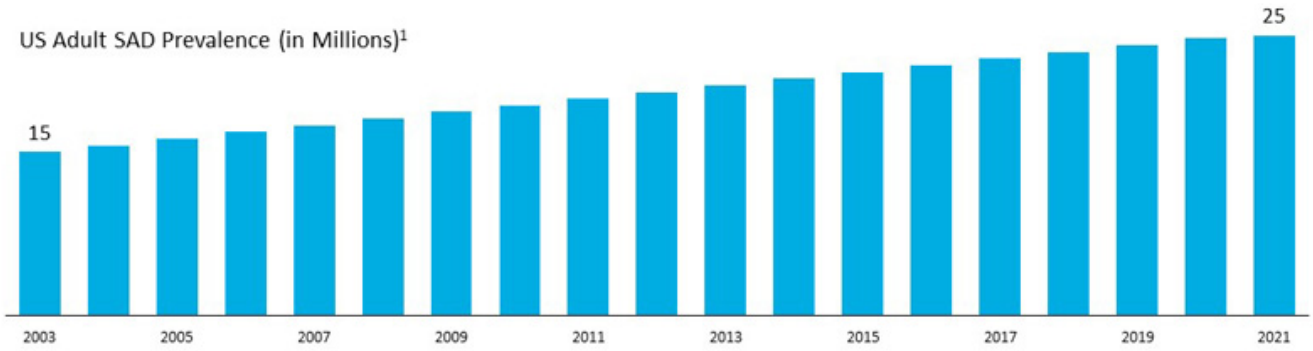
Patients cycling through treatments, often unsatisfied with their current treatment options but without alternatives.



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

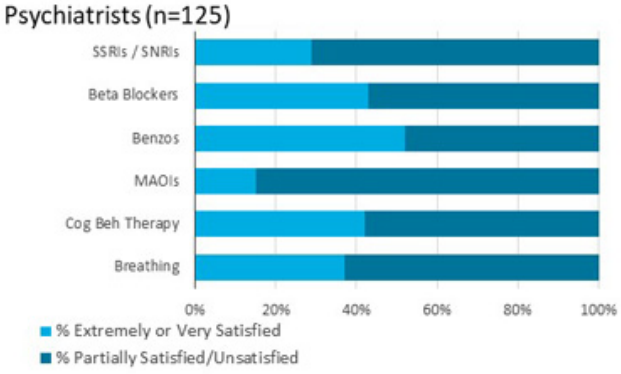
There is no FDA-approved, fast-acting, acute treatment of anxiety for SAD

Desired Product Profile of Treatments For Social Anxiety Disorder							
Drug	Fast- acting	Non-systemic	No Long-term Side Effects	Non-sedating	No Cognitive/ Motor Impairment	No Withdrawal Syndrome	No Abuse Potential
FDA-approved **(Sertraline, Paroxetine, Venlafaxine)**	⊖	⊖	⊖	✓	✓	⊖	✓
Off-label (Benzodiazepines)	✓	⊖	⊖	⊖	⊖	⊖	⊖
Preferred SAD Therapy	✓	✓	✓	✓	✓	✓	✓

Physician Satisfaction with Current Therapies is Modest

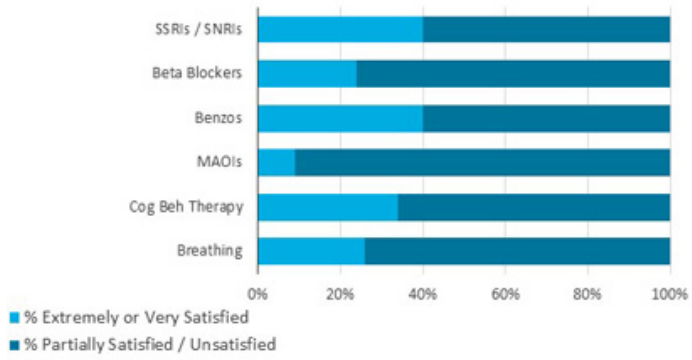
Satisfaction with current treatments for acute episodes of SAD from a large online survey

Psychiatrists (n=125)



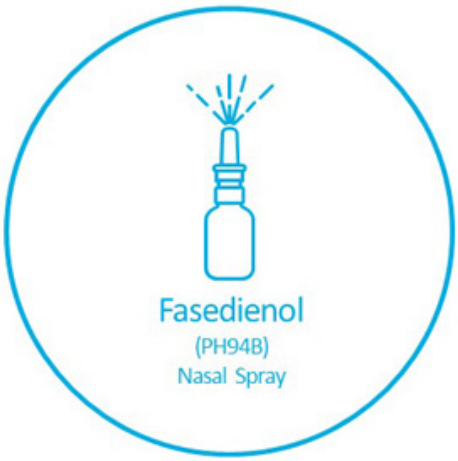
Sources: Vistagen Proprietary Market Research, Online Survey, Jan 2022

Primary Care Physicians (n=126)



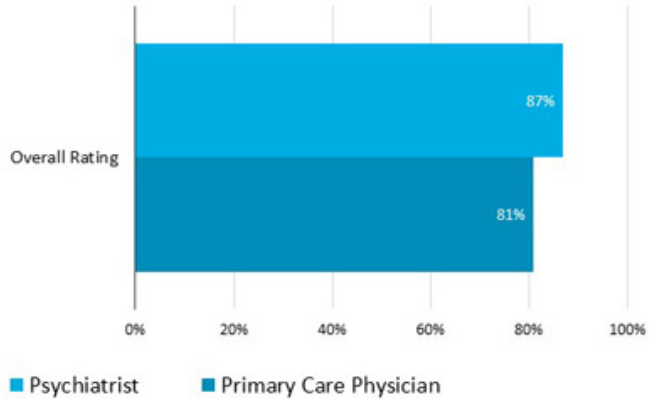
Fasedienol Brings New Optimism for SAD Treatment

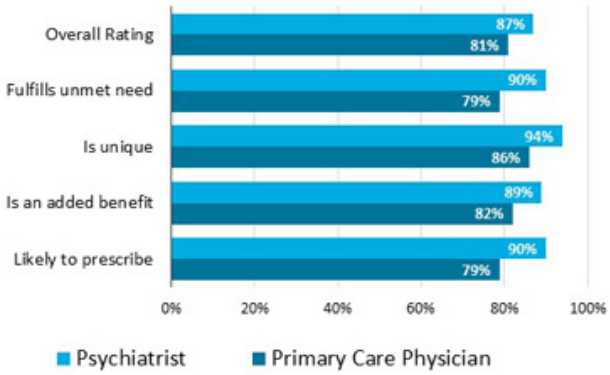
- First-in-class PRN neuropsychiatric product candidate, use analogous to a rescue inhaler for asthma
- User-friendly intranasal administration, as needed
- No systemic uptake or direct activity on neurons in the brain
- Exceptional safety profile – no evidence of abuse liability potential
- PRN use over time builds confidence, resilience, and reduces fear, anxiety and avoidance of social and performance stressors
- FDA has confirmed that the LSAS is the appropriate efficacy endpoint to measure reductions in fear/anxiety and avoidance
- Target Product Profile matches the wish list of patients and providers
- De-risked late-stage development pathway
- FDA Fast Track Designation



Fasedienol Profile is Rated Highly by Physicians and Recognized as a Valuable and Individualized Approach to Treat SAD Episodes On-demand

Physician assessment of blinded fasedienol product profile from large online survey





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

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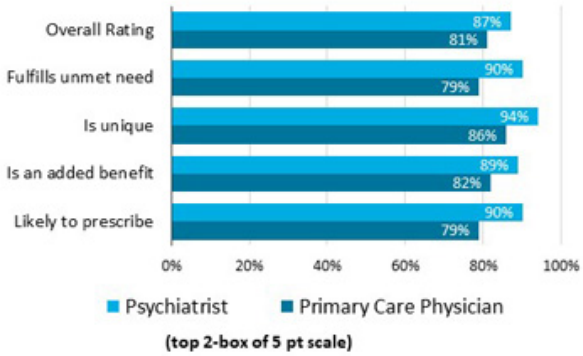
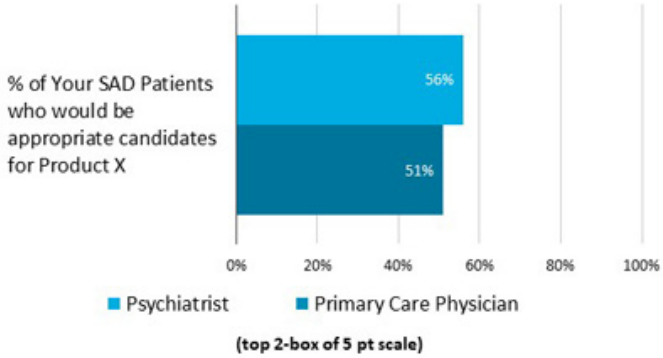
Physicians Indicate High Intent to Prescribe Fasedienol and Note it would be Appropriate for the Majority of their SAD Patients

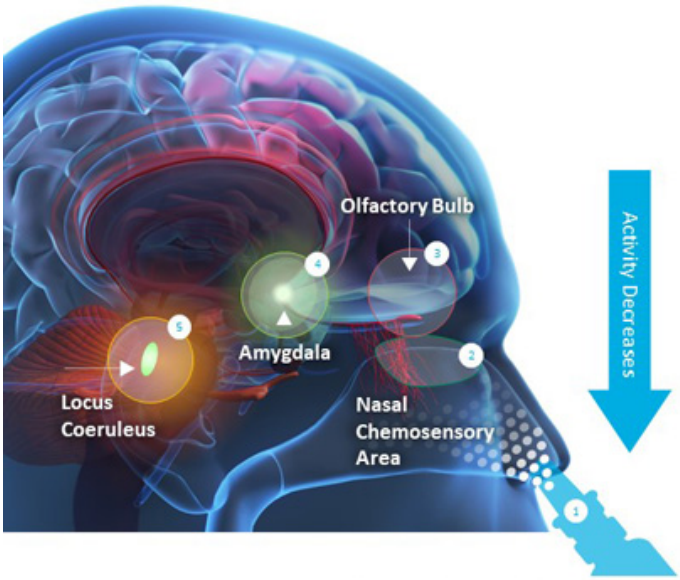
Physician assessment of a blinded fasedienol product profile from large online survey





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

Fasedienol's Innovative MOA via Olfactory-amygdala Circuit



1. Microgram-level intranasal dose of fasedienol (3.2 mcg) is administered.
2. Fasedienol engages peripheral receptors in nasal chemosensory neurons (NCNs).
3. Once stimulated with fasedienol, 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

Fasedienol Phase 1/1B Data

Well-tolerated, reduced autonomic biomarkers, increased EGNR, and showed anxiolytic effects

Reduction in Autonomic Biomarkers

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 fasedienol significantly increased the amplitude of the electrogram (EGNR) recorded from the nasal chemosensory epithelium in both men and women.

Increased Nasal Chemosensory Electrical Activity

Dose dependent increase in electrical activity of the nasal chemosensory epithelium. EGNR was similar in male/female healthy volunteers after ascending doses of fasedienol 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)).

Efficacy Signal in Anxiety

Rapid decrease in anxiety 30 min after intranasal fasedienol administration in generalized anxiety. Lead to the identification of SAD as the ideal clinical path forward based on input from Dr Michael Liebowitz.

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

Subjective Units of Distress Scale (SUDS)

Primary efficacy endpoint in Phase 2 and Phase 3 clinical trials for acute measurement

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 for measurement over time

The LSAS is a 24-item clinician-rated scale used to assess how SAD impacts a patient's life across a variety of situations
13 situations pertain to performance (P) and 11 pertain to social situations (S)

- 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	Fear or Anxiety 0 = none 1 = mild 2 = moderate 3 = severe	Avoidance 0 = never 1 = occasionally 2 = often 3 = usually
1. Telephoning in public (P)		
2. Participating in small groups (P)		
⋮	⋮	⋮
23. Giving a party (S)		
24. Resisting a high pressure sales person (S)		

- Scored by summing the item ratings. Below are the suggested interpretations for various score ranges.

Greater than 110: Very severe social anxiety

90–110: Severe social anxiety

70–90: Marked social anxiety

50–70: Moderate social anxiety

Fasedienol Significant Phase 2 Data in Clinic-based SAD Study

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

Public speaking and social interaction challenges in clinical setting

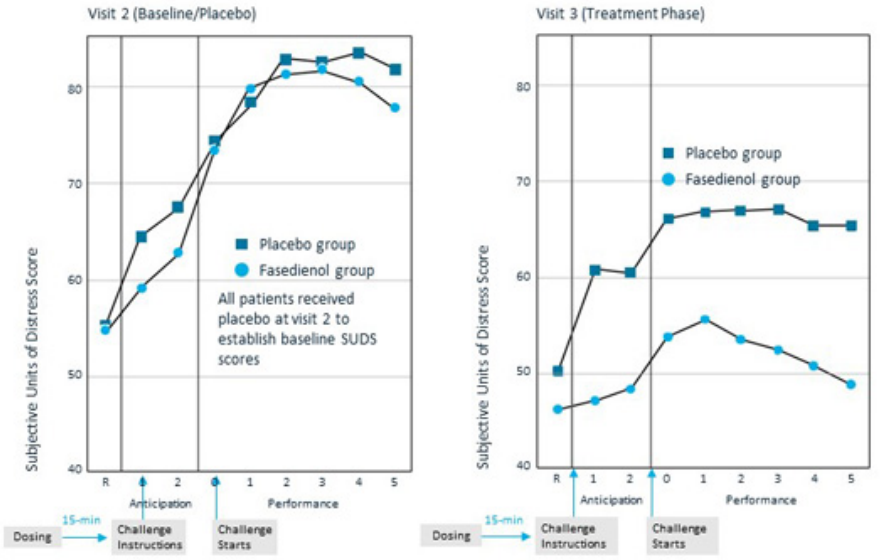
Phase 2B randomized, double-blind, placebo-controlled multi-center study (n=91)

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.

Phase 2 Study – Public Speaking Challenge (SUDS)

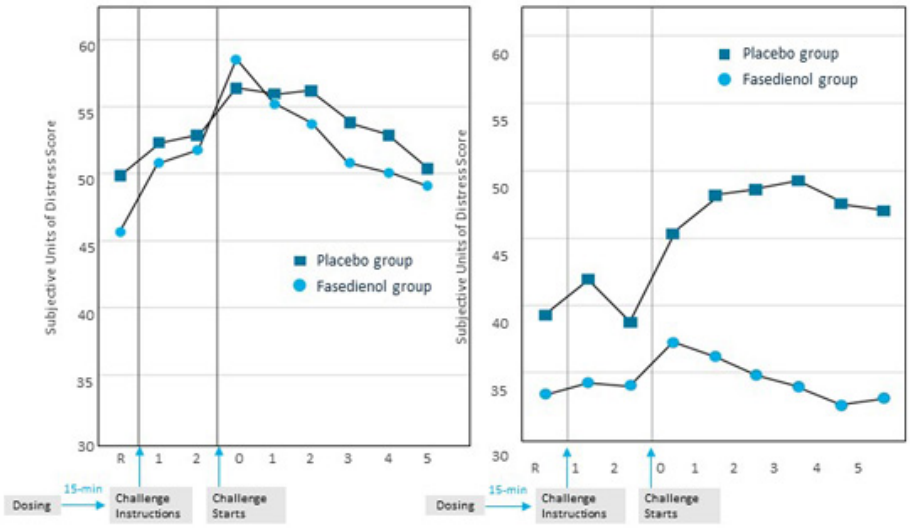


Fasedienol rapidly reduced anxiety in response to public speaking challenge		
	Active Group	Placebo Group
Mean Difference	26.7	14.0
Standard Deviation	21.6	16.3
Number of Subjects	45	46
t = 3.16	p = 0.002	Cohen's d (Effect Size)0.66

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, 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.

Phase 2 Study – Social Interaction Challenge (SUDS)



Fasedienol 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.

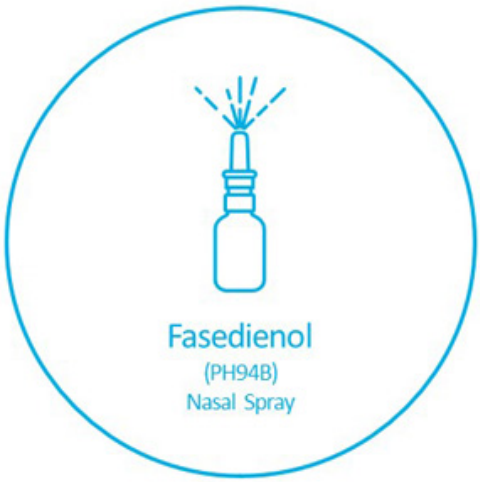
Fasedienol Phase 2 Real-World SAD Crossover Study

Fasedienol 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 crossover study (n=22)

- Primary efficacy endpoint was 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 the first 2 weeks of treatment, trend superiority over placebo on the Liebowitz Social Anxiety Scale (LSAS) (p=0.07) and a significant difference on the Patient Global Impression of Change (p=0.024) and LSAS Avoidance subtotal (p=0.02)

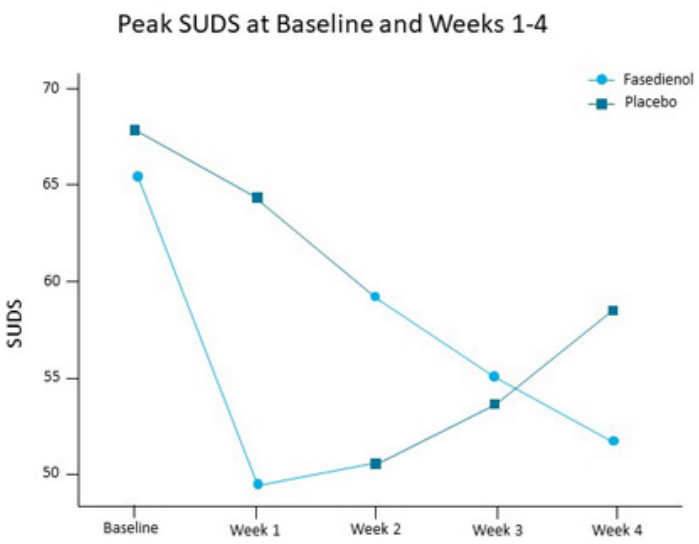


Sources: Liebowitz MR, Hanover R, Draine A, Lemming R, Careri J, Monti L (2016). Effect of as-needed use of intranasal PH94B on social and performance anxiety in individuals with social anxiety disorder. *Depress Anxiety* 33: 1081-1089.

Vistagen

Phase 2 Real-World Crossover Study Results (SUDS)

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

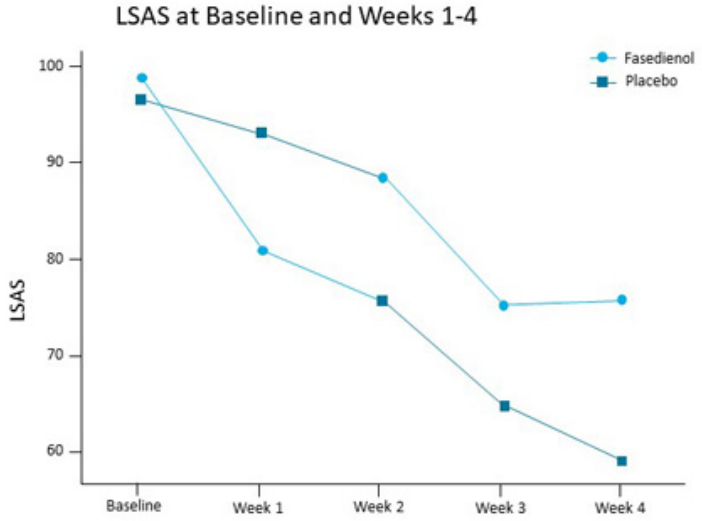


- Peak SUDS score for the fasedienol group increased after crossover to placebo, though not back to the baseline, possibly due to increased confidence from fasedienol treatment prior to crossover to placebo
- Early suggestions of drug/placebo differences were seen in Week 1 and Week 2 SUDS scores: average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

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 Real-World Crossover Study Results (LSAS)

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



- After the first 2 weeks of treatment, subjects who received fasedienol 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=0.07), with a large effect size of .812
- Similar trend differences on total LSAS scores were seen after 1 week of treatment, where the fasedienol group showed a 17.8-point drop compared to a 3.5-point drop with placebo (t=2.02, p=0.057, ES .86)
- In the sample as a whole (n=22), drop in LSAS scores after treatment did not differ between groups because subjects receiving fasedienol before receiving placebo continued to improve when crossed over to placebo

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.

PALISADE Phase 3 Clinical Program Summary

Phase 3 clinic-based, single–administration public speaking challenge studies (SUDS)

PALISADE Phase 3 public speaking challenge studies modeled after Phase 2 study public speaking challenge study due to COVID-related constraints – US randomized, multi-center, double-blind, placebo-controlled, single dose administration clinical trials

Primary endpoint: Change in Subjective Units of Distress Scale (SUDS) scores from baseline compared to placebo

Topline results from PALISADE-1 did not meet the primary endpoint. Certain potential explanations for the unexpected outcome were related to:

- single-dose assessment study
- methodological complexities in scaling the study design during multiple surges in the COVID-19 pandemic introduced significant systemic variability, including subject stress, personnel turnover, mask wearing, and monitoring challenges
- potentially reduced response to fasedienol due to impaired olfactory cell function due to COVID-19

After pausing PALISADE-2 in the summer of 2022 and securing an independent interim analysis (IA) of data from 140 subjects who completed the study, which IA recommend proceeding with the study as planned, Vistagen determined that PALISADE-2 should not be resumed due to expense, time, and methodological complexities involved in restarting, as well as learnings from PALISADE-1 results and results from two single-administrations public speaking challenge studies indicated that each missed their primary endpoint

Fasedienol Real-world Open Label Study (Safety)

Favorable safety and tolerability data in nearly 500 patients

Long-term intranasal administration of 3.2 µg fasedienol prior to acute anxiety-provoking social and performance situations in daily life, as-needed, up to four times per day, over a period of up to 10 months

Patients self-administered over 30,000 doses of fasedienol in real-world settings, with a mean study duration of 4 months, and a maximum study duration of over 10 months

Safety results:

- The long-term intranasal administration of 3.2 µg of fasedienol, up to four times a day, as-needed, was safe and well-tolerated in adult SAD patients (n=481)
- Of the 481 SAD patients in the study who received at least one dose of fasedienol, at least one treatment-emergent adverse event (TEAE) was reported by 56.8% of subjects, with 54.9% of the 481 patients reporting mild or moderate TEAEs and only 1.9% of patients reporting severe TEAEs
- Headache was the most common TEAE (17.0%); COVID-19 infection was reported by 11.4% of patients
- No other TEAE occurred in more than 5.0% of subjects

Fasedienol Real-World Open Label Study (LSAS)

Efficacy demonstrated by continued reductions in LSAS scores, from as early as 1 month of treatment

Fasedienol demonstrated clinically meaningful reductions in fear, anxiety and avoidance of anxiety-provoking social and performance situations in daily life, as measured by the LSAS, building on LSAS data from a previous placebo-controlled Phase 2 study of fasedienol in SAD

Exploratory efficacy results:

- At 1 month, mean reduction on the LSAS was 16 points, with 36% experiencing a 20-point or greater reduction (n=385)
- At 2 months, mean reduction on the LSAS was 20 points, with 44% experiencing a 20-point or greater reduction (n=324)
- At 3 months, mean reduction on the LSAS was 24 points, with 55% experiencing a 20-point or greater reduction, and with 36% experiencing a 30-point or greater reduction (n=218)
- Clinician Global Impression of Improvement (CGI-I) indicated 28.6% of 385 patients at one month were “much” or “very much” improved
- For subjects who continued in the study, total LSAS scores continued to decline from baseline, with improvements observed each month on the LSAS through 9 months. The continued improvement in LSAS scores is indicative of the value of multiple, as-needed administrations of fasedienol over time.


Vistagen
Phase 3 Path Forward
Social Anxiety Disorder
FEARLESS Clinical Program

From PALISADE to FEARLESS

Pursuing multi-administration, real-world Phase 3 study design, using the LSAS as the primary efficacy endpoint

PALISADE	FEARLESS	Rationale
▪ Single dose administration	▪ Dosing over time	▪ Removes variability and single-dose efficacy assessment of the PSC study design
▪ Complex, clinic-based public speaking challenge (PSC) studies	▪ Real-world setting dosed as-needed in anxiety-provoking situations	▪ PRN dosing over time may be the preferred treatment mode
▪ SUDS as the primary efficacy endpoint	▪ LSAS as the primary efficacy endpoint	▪ Use of LSAS as the primary efficacy endpoint supported by fasedienol results from placebo-controlled Phase 2 crossover study and real-world open-label study
▪ Three industry single-dose PSC studies in SAD conducted during COVID and reported from July 2022 to December 2022 missed their primary SUDS endpoint	▪ Phase 1 studies show fasedienol modulates autonomic arousal; taking fasedienol during or before anxiety-provoking situations or heightened anxiety may be the best way to demonstrate efficacy over time	▪ All prior registration studies for the three currently FDA approved treatments were positive, and all studies used the LSAS as the primary efficacy endpoint
▪ Difficult to successfully scale up the PSC study design for large Phase 3 clinical trials	▪ PRN dosing over time, in response to individualized anxiety-provoking situations in real-world settings, may be a better way for patients to use the drug	

FEARLESS Phase 3 Program

Next potential Phase 3 study of fasedienol for treatment of SAD

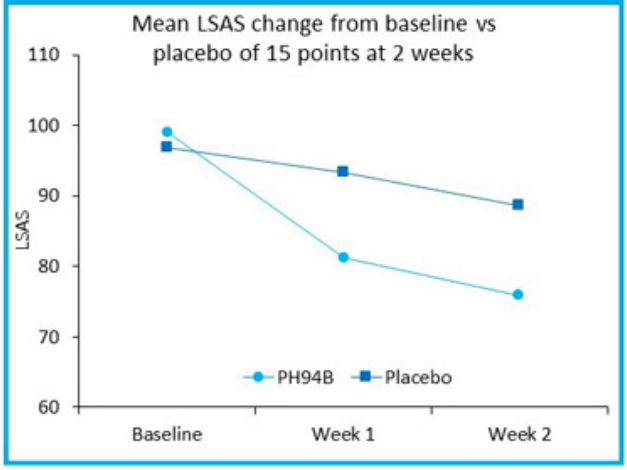
- The combined placebo-controlled Phase 2 and open label safety study data demonstrate favorable safety and tolerability and the potential for fasedienol to achieve robust overall reduction in symptoms of SAD and improvement in severity over time as measured by the LSAS
- LSAS measurements over time are well-suited for Phase 3 studies to demonstrate efficacy and the true impact of fasedienol on patients' lives, measuring overall improvement in disease severity by capturing the reduction in fear and anxiety, as well as avoidance of social and performance situations
- Based on all clinical studies to date, the LSAS study design best fits the pharmacological properties of fasedienol when used in patients with SAD and supports the way fasedienol would be used by SAD patients, if approved
- Positive meeting with FDA confirmed use of the LSAS as the primary efficacy endpoint support using the LSAS as the primary endpoint in the next potential Phase 3 study of fasedienol in SAD –

FEARLESS-1

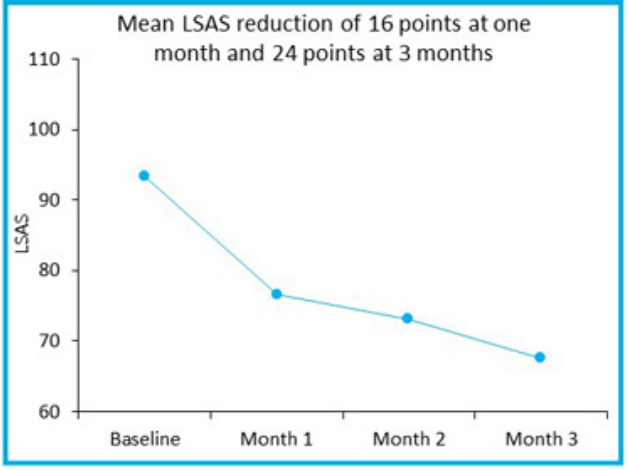
Fasedienol Efficacy Summary (LSAS)

Fasedienol used PRN over time has demonstrated reduction of LSAS scores in two trials

Phase 2 Crossover Study



PALISADE Open-Label Safety Study



Real-World Use with LSAS as Primary Efficacy Endpoint

Recent positive FDA feedback confirms acceptable use of LSAS in future Phase 3

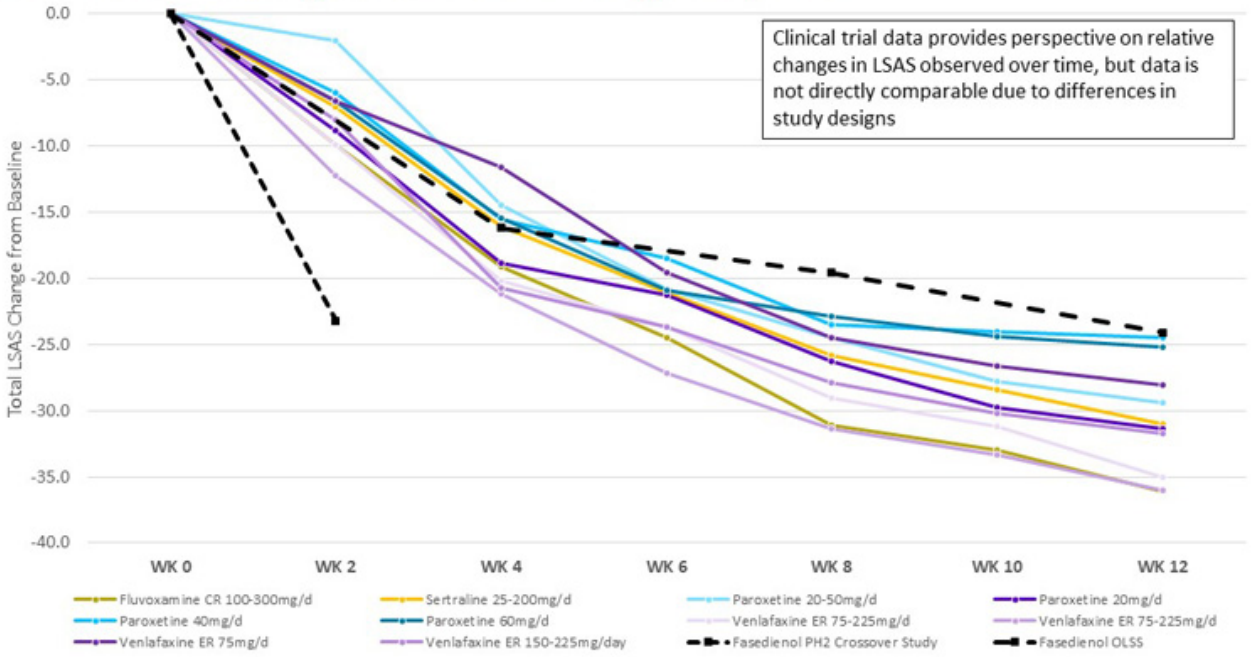
LSAS data from Phase 2 placebo-controlled crossover study and large Phase 3 open label study suggest that studies involving multiple administrations of fasedienol over time, on an as-needed basis, when subjects experience socially stressful situations in their daily life, may most accurately demonstrate the safety and efficacy potential of fasedienol in patients with SAD and the way fasedienol would be used by SAD patients, if approved.

All prior registration studies for the three medications, two SSRIs and one SNRI, currently approved by the FDA for treatment of SAD were positive, and all studies used the LSAS as the primary efficacy endpoint.

In placebo-controlled Phase 2 study of fasedienol, the amount of separation between fasedienol and placebo at the end of the first 2 weeks on the LSAS was comparable to what was observed after 12 weeks in the consistently positive registration trials for the three medications currently approved by the FDA for the treatment of SAD.

Cross Study Comparison of LSAS Scores (Change from Baseline)

Fasedienol reduction in LSAS seen in the Phase 2 Crossover Study and Open-Label Study are comparable to reductions seen in the registration studies of the approved products



Sources:
1. Liebowitz et al.,
2. Baldwin et al,
3. Liebowitz et al.,
4. Allgulander et al.,
5. Stein MB et al.,
6. Liebowitz MR et al.,
7. CL028; IND 061332; Module 5.3.5.1,
8. CL030; Data presented in briefing document

Vistagen

Note: LSAS values estimated from charts and tables in publications; fasedienol Open-Label Study captured only monthly data

Fasedienol Opportunities Beyond Social Anxiety 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. Reismnan et al, 2016, 3. Antonin et al, 2021, 4. Carske et al, 2005, 5. Julia et al, 2019.

Fasedienol's Differentiated Profile Provides Robust Commercial Opportunity

Substantial Unmet Need

Fasedienol promotion, SAD disease education and U.S. DTC advertising efforts will drive physician urgency to diagnose and treat given two decades with no innovation and few novel anti-anxiety medications in development.

Unique MOA

Clinicians are relieved that fasedienol is not habit-forming due to its novel, differentiated MOA, non-systemic administration and lack of benzodiazepine-like side effects

Strong Intent to Prescribe

Clinicians intend to offer fasedienol to a majority of their SAD patients given its safety/tolerability, efficacy and on-demand use. Patients are interested in trying fasedienol and would discuss with an HCP after seeing an advertisement.

Ease of Use

Patients and clinicians will likely prefer fasedienol's on-demand, rapid-onset activity, much like a rescue inhaler for an acute asthma attack, and its exceptional side effect profile vs. antidepressants, benzodiazepines and beta blockers.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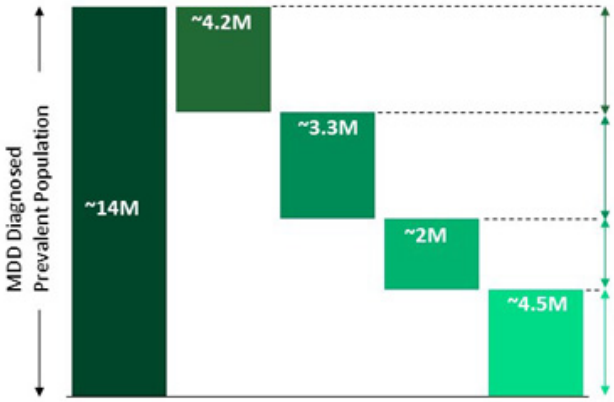
Itruvone
for
Major Depressive Disorder
Looking beyond the standard of care
for depression disorders

Significant Unmet Need in Major Depressive Disorder

21 million US Adults had at least one major depressive episode in 2021



Untreated Pts: A large percentage of patients remain untreated due to stigma, perceived lack of effective treatment 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, weight gain, insomnia, dizziness and nausea.

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

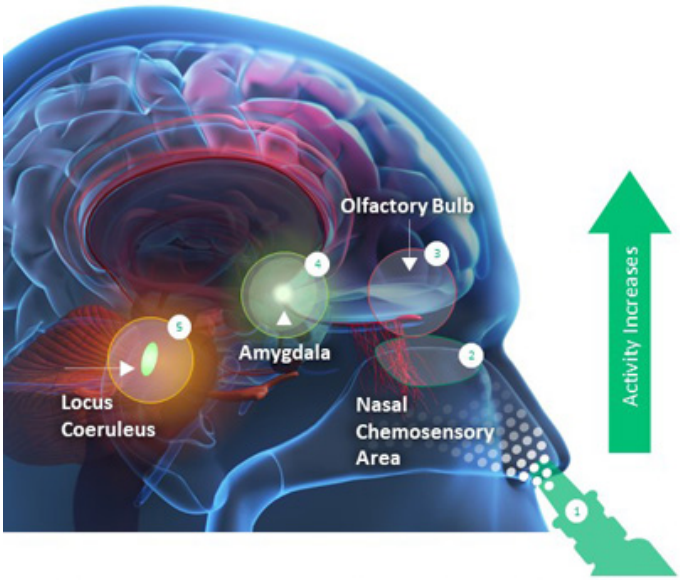
Third Line plus Pts: Huge unmet need for patients resistant to second line treatment options. Lack of safe and efficacious options for Treatment Resistant & Refractory MDD.

Sources: 1. Substance Abuse and Mental Health Services Administration. (2023). Key Substance Use and Mental Health Indicators in the United States: Results from the 2021 National Survey on Drug Use and Health; 2. 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; 3. World Health Organization, https://www.who.int/news-room/fact-sheets/detail/depression; 4. Rush AJ, et al. Am J. Psychiatry. 2006, 163(11): 1905-1917 (STAR*D Study)

Itruvone is a potential fast-acting, stand-alone treatment for Major Depressive Disorder

- Itruvone is an odorless, tasteless synthetic neuroactive 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
- FDA Fast Track Designation

Itruvone's Mechanism of Action



1. Microgram-level intranasal dose of itruvone (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

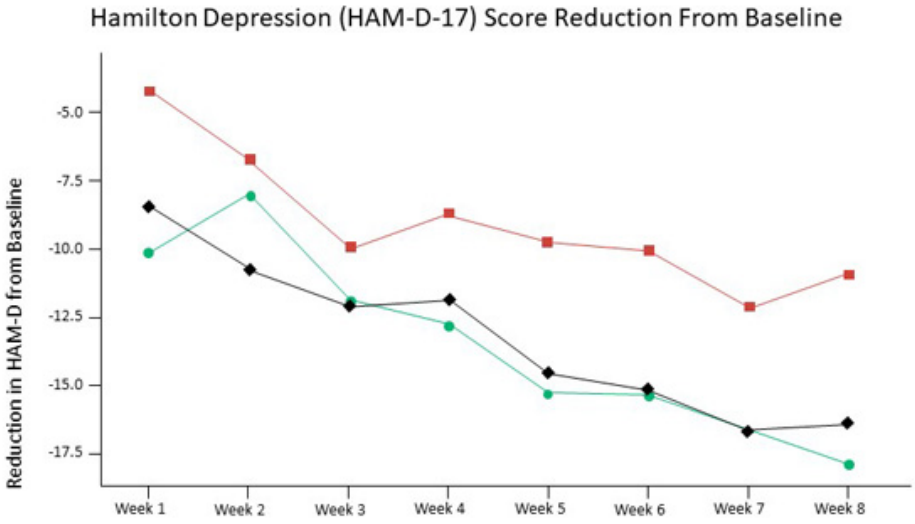
Itruvone Antidepressant Effects in Phase 2A Study

- Study Design: Phase 2A randomized, double-blind, placebo-controlled, parallel design POC clinical study
- Dose Administered: 3.2 mcg or 6.4 mcg of itruvone 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 itruvone 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.

Itruvone Phase 2A MDD Study (n=30)



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

Itruvone Dose	HAM-D Score	p (itruvone 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 Phar Med Res* 4(6): 2157-2168.

Itruvone Clinical Development

Stand-alone treatment for individuals with MDD

Following a successful Phase 2A study conducted in Mexico, a small US Phase 1 study was recently completed in Q1 2023 to facilitate advancing to Phase 2B development in the US

Phase 1

Objectives: Evaluate safety and tolerability of itruvone in healthy volunteers to confirm the previous safety, tolerability, and pharmacodynamic (PD) effects of itruvone seen in the previous two Phase 1 studies

Study Design: Double-blind, placebo-controlled study in 12 healthy volunteers

Status: Study completed in March 2023; topline results anticipated in Q2 2023

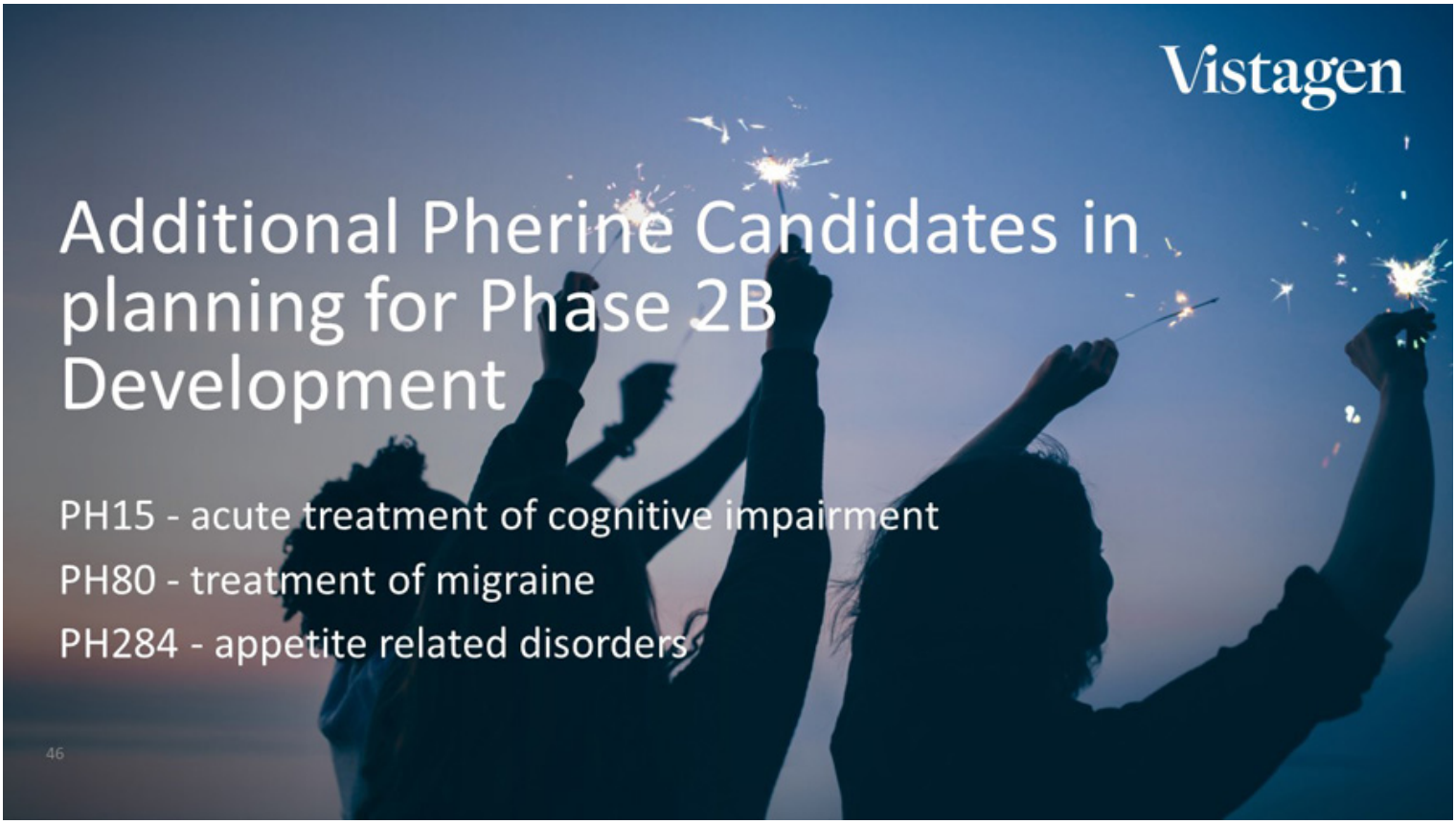
Phase 2B

Advanced planning of Phase 2B clinical development underway

Itruvone Opportunities 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.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Additional Pherine Candidates in planning for Phase 2B Development
PH15 - acute treatment of cognitive impairment
PH80 - treatment of migraine
PH284 - appetite related disorders
46

PH15 Nasal Spray

Early-stage investigational synthetic neuroactive steroid

Alzheimer's Disease is the most common cause of progressive mental failure (dementia) in the aging population. In the U.S., approximately 5.5 million people are affected, and the prevalence worldwide is estimated to be as high as 24 million[1].

Acute Treatment of Cognitive Impairment

- Cognitive deficits are characterized by progressive loss of memory, cognition, reasoning and emotional stability that can gradually lead to an impact in the quality of life.
- Early functional MRI studies in human volunteers at Stanford University revealed that intranasal administration of PH15 induced rapid activation of brain areas related to cognition
- In double blind, placebo-controlled study in human subjects conducted at National Institute of Psychiatry, Sleep Disorders Clinic. INNSZ. Mexico City, Mexico, intranasal PH15 showed rapid and significant improvement in cognitive and psychomotor performance and improvement of reaction time that was better than the effect of a placebo and 2 mg of oral caffeine

Next steps: US IND-enabling CMC and toxicology studies to facilitate potential US Phase 2B development

Sources: 1. Alzheimer's and Dementia, Elsevier, 2017

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PH80 Nasal Spray

Early-stage investigational synthetic neuroactive steroid with potential to engage nasal chemosensory receptor cells which in turn modulate neural circuits in the basal forebrain associated with the control of body temperature, as well as premonitory and aura symptoms of migraines

Acute Management of Menopausal Hot Flash

- In a small exploratory double blind, placebo-controlled Phase 2A study (n=40) in women diagnosed with menopausal hot flashes conducted at Hospital Angeles, Mexico City Mexico, PH80 showed clinically significant improvement in the number and severity of hot flashes and other symptoms of menopause in the subjects treated with PH80

Acute Treatment of Migraine Headache

- In an exploratory Phase 2A clinical study conducted at Hospital Angeles, Mexico City, Mexico, PH80 showed a profile compatible with the relief of the premonitory and aura symptoms of migraines

Next steps: US IND-enabling CMC and toxicology studies to facilitate potential US Phase 2B development

PH284 Nasal Spray

Early-stage investigational synthetic neuroactive steroid

Cachexia is a serious but under recognized consequence of many chronic diseases with body mass loss of >10% and a prevalence of 5% to 15% in end–stage chronic heart failure and 50% to 80% in advanced cancer.

Acute Management of Appetite-related Disorders

Brief exploratory Phase 2A randomized, double blind, placebo controlled clinical study (n=40) in patients diagnosed with cachexia due to terminal cancer conducted at the National Institute of Cancerology and National Institute of Nutrition. INNSZ. Mexico City, Mexico.

Patients were dosed 4 times per day, 30 minutes before each major meal

At the end of the 7-day treatment period with intranasal PH284 or placebo, PH284-treated patients showed a significant increase in the subjective feeling of hunger (appetite), an increase in body weight and an improved quality of life, as compared with the placebo-treated group

Next steps: US IND-enabling CMC and toxicology studies to facilitate potential US Phase 2B development

Sources: 1. Alzheimer's and Dementia, Elsevier, 2017

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

AV-101 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
- Potential to inhibit the function of the NMDA receptor, without fully blocking NMDA receptor function like ketamine and other NMDAR antagonists
- 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 Phase 2A clinical development options with or without probenecid
- FDA Fast Track designations for adjunctive treatment of MDD and treatment of neuropathic pain

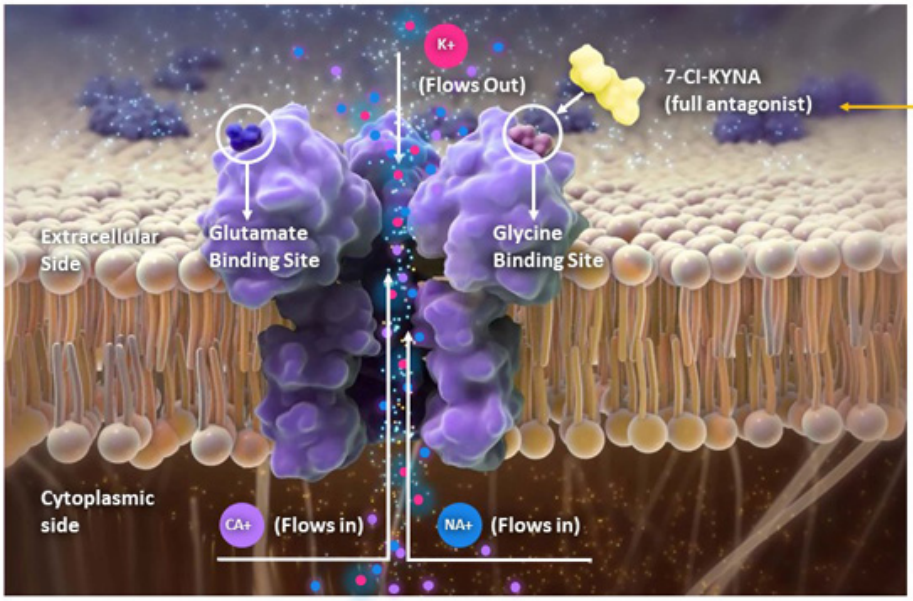
Levodopa-Induced Dyskinesia
Associated with Parkinson's therapy

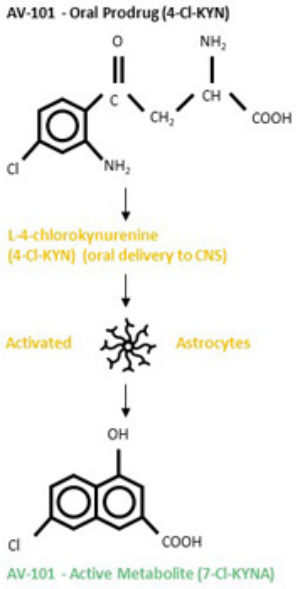
Major Depressive Disorder

Neuropathic Pain

Suicidal Ideation

AV-101's Potential MOA





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Thomas Laughren, M.D.

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MRN

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Sanjay Mathew, M.D.

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

Yale University

Gerard Sanacora, Ph.D., M.D.

Professor of Psychiatry, Yale School of Medicine; Director, Yale Depression Research Program; Scientific Director, Yale-New Haven Hospital Interventional Psychiatry Service

UC San Diego SCHOOL OF MEDICINE

Mark Wallace, M.D.

Professor of Clinical Anesthesiology, Chair of the Division of Pain Medicine, Medical Director and Director at the University of California, San Diego

Vistagen

Investment Highlights

Vistagen's mission is to radically improve mental health – One Mind at a Time™

- Six clinical-stage drug candidates
- Five pherine assets with positive phase 2 data
- Targeting large anxiety, depression and neurology markets
- Differentiated MOAs, bringing new value to patients, physicians, and payers
- Multiple potential partnership opportunities
- Experienced CNS team and advisors


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