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): September 1, 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 94080
(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 1.01 Entry into a Materially Definitive Agreement.

On September 1, 2023, Vistagen Therapeutics, Inc. (the "*Company*") entered into an Exclusive Negotiation Agreement (the "*Negotiation Agreement*") by and among the Company and Fuji Pharma Co., Ltd. ("*Fuji Pharma*"), a Tokyo Stock Exchange listed, Japan-based pharmaceutical company. Pursuant to the terms and conditions of the Negotiation Agreement, the Company agreed, for a limited period of time (described below), to negotiate exclusively with Fuji Pharma a potential license to develop and commercialize the Company's PH80 product candidate in Japan, including for the acute treatment of moderate to severe vasomotor symptoms (hot flashes) due to menopause and potentially other indications. The Negotiation Agreement provides for a term of the later to occur of (i) fourteen (14) months beginning on the date of receipt of the Purchase Price (defined below) by the Company or (ii) ninety (90) days from the date that the U.S. Food and Drug Administration accepts an Investigational New Drug application for PH80 for the treatment of vasomotor symptoms (hot flashes) due to menopause ("*Exclusive Negotiation Period*").

As consideration for the Exclusive Negotiation Period provided by the Company to Fuji Pharma under the Negotiation Agreement, Fuji Pharma has agreed to make a payment to the Company of $1,500,000 ("*Purchase Price*") upon confirmation from the Company stating that a contract development and manufacturing organization has been selected by the Company for toxicity studies for PH80. The Purchase Price is not refundable, except upon a material breach of the Negotiation Agreement by the Company. Should the Company and Fuji Pharma enter into a definitive license agreement during the Exclusive Negotiation Period for the development and commercialization of PH80 in Japan (a "*Potential Definitive Agreement*"), the Purchase Price will be creditable against the signing fee for such agreement. Neither the Company nor Fuji Pharma is obligated to enter into the Potential Definitive Agreement, and if the Company and Fuji Pharma have not entered into the Potential Definitive Agreement on or before the end of the Exclusive Negotiation Period, either the Company or Fuji Pharma may terminate any further negotiations.

On September 5, 2023, the Company issued a press release announcing the Negotiation Agreement, a copy of which is attached to this Current Report on Form 8-K as Exhibit 99.1.

The foregoing description of the Negotiation Agreement is subject to and is qualified in its entirety by reference to the full text of the form of the Negotiation Agreement, a copy of which is attached hereto as Exhibit 10.1.

Item 7.01 Regulation FD Disclosure.

On September 8, 2023, the Company began utilizing a new corporate presentation, a copy of which is attached to this Current Report on Form 8-K as Exhibit 99.2.

The information in this Current Report on Form 8-K, including the information set forth in Exhibit 99.2, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "*Exchange Act*"), nor shall Exhibit 99.2 filed herewith be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

See Item 8.01 regarding the Company's issuance of a press release announcing the Negotiation Agreement.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits Index

Exhibit No.	Description
10.1	Exclusive Negotiation Agreement by and between Fuji Pharma Co., Ltd. and Vistagen Therapeutics, Inc., dated September 1, 2023.
99.1	Press Release issued by Vistagen Therapeutics, Inc., dated September 5, 2023.
99.2	Vistagen Therapeutics, Inc. Corporate Presentation, dated September 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: September 8, 2023

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

Exhibit 10.1

EXCLUSIVE NEGOTIATION AGREEMENT

This Exclusive Negotiation Agreement ("Agreement") is made and entered into on September 1, 2023 (the "Effective Date") by and between Vistagen Therapeutics, Inc., a Nevada corporation, having an address at 343 Allerton Avenue, South San Francisco, California 94080, USA ("Vistagen"), and Fuji Pharma Co., Ltd., a company organized and existing under the laws of Japan and having an address at 5-7 Sanban-cho, Chiyoda-ku, Tokyo 102-0075, Japan ("Fuji Pharma"). Vistagen and Fuji Pharma are sometimes referred to separately as a "Party" and collectively as the "Parties.

RECITALS

WHEREAS, Vistagen and Fuji Pharma wish to negotiate, on an exclusive basis, a definitive strategic development and commercialization agreement with regard to the Product (as defined below) in Japan ("Commercialization Agreement").

NOW THEREFORE, in consideration of the mutual covenants, representations, and agreements set forth herein, the Parties, intending to be legally bound, agree as follows:

AGREEMENT

1. Exclusive Negotiation Right. During the Exclusive Negotiation Period (as defined below), Fuji Pharma has the exclusive right to negotiate with Vistagen the terms of the potential Commercialization Agreement ("Exclusive Negotiation Right") in accordance with this Agreement.

2. Commercialization Agreement. If negotiated and signed by the Parties, the Commercialization Agreement will, upon its effective date, grant Fuji Pharma an exclusive license in Japan under Vistagen Technology (as defined below) to develop, use for development or commercialization, promote, sell, offer for sale and/or import for development or commercialization, and use of the Product ("Proposed Transaction"). If it is negotiated and signed, the Commercialization Agreement will include industry-standard provisions that may be agreed to by the Parties.

3. Product. Product means a pharmaceutical product containing Vistagen's investigational pherine drug candidate, PH80, as an active ingredient, whether alone or combined with other active ingredients, and indicated for the treatment of vasomotor symptoms (hot flashes) due to menopause, premenstrual disphoric disorder, migraine, and all other human therapeutic uses.

4. Vistagen Technology. For purposes of this Agreement and the Commercialization Agreement, Vistagen Technology means, to the extent applicable to Japan, the preclinical, clinical study and manufacturing data, know-how, patents, and other intellectual property, and other information owned or controlled by Vistagen that is necessary or reasonably useful for Fuji Pharma to successfully apply for an investigational new drug application ("IND") in Japan for the Product for any therapeutic indication and to conduct clinical studies. Vistagen will use its best commercial efforts to preserve, protect, and enhance Vistagen Technology in contemplation of a potential transfer of the Vistagen Technology to Fuji Pharma in the event the Parties enter into the Commercialization Agreement.

5. Payment. Upon the terms and subject to the conditions set forth herein, Vistagen hereby sells, and Fuji Pharma hereby purchases the Exclusive Negotiation Right for One Million Five Hundred Thousand U.S. Dollars (US$1,500,000) ("Purchase Price"). The Purchase Price is due upon Fuji Pharma's receipt of a confirmation letter from Vistagen stating that a contract development and manufacturing organization has been selected by Vistagen for toxicity studies for the Product ("Payment Event"). The confirmation letter shall be in writing (but not email) and accompany the contemplated timeline for such toxicity studies as agreed upon between Vistagen and such selected contract development and manufacturing organization. The Purchase Price shall be delivered to Vistagen by wire transfer of immediately available funds, net of any taxes or withholdings, no later than fifteen (15) days from the date of the Payment Event. The Purchase Price is not refundable except for the case of a material breach by Vistagen of this Agreement. However, if the Parties negotiate and enter into the Commercialization Agreement, the Purchase Price will be creditable against the signing fee for the Commercialization Agreement.

6. Exclusive Negotiation Period. The exclusive negotiation period will begin on the date of Payment Event and expire upon the later to occur of (i) fourteen (14) months from the date of Payment Event or (ii) ninety (90) days from the date that the U.S. Food and Drug Administration ("FDA") accepts an IND for the Product for the treatment of vasomotor symptoms (hot flashes) due to menopause ("Exclusive Negotiation Period"). Neither Party is obligated to enter into the Commercialization Agreement, and if the Parties have not entered into the Commercialization Agreement before the end of the Exclusive Negotiation Period, then either Party may cancel any further negotiations.

7. [Intentionally Omitted]

8. Consultations.

(a) At the written request of Fuji Pharma at any time during the Exclusive Negotiation Period, the Parties will negotiate the Proposed Transaction in good faith and attempt to agree upon the provisions of the Commercialization Agreement.

(b) During the Exclusive Negotiation Period, Vistagen shall not, and shall not permit any directors, officers, employees, agents, advisors, or representatives (collectively, "Representatives") of itself or its affiliates to, directly or indirectly, engage in any discussions or negotiations with any third party other than Fuji Pharma, or enter into any agreement (including a letter of intent, memorandum of understanding and the like, whether or not legally binding) with any third party other than the Fuji Pharma, in each case relating to (i) the Proposed Transaction or any similar arrangement or transaction in Japan or (ii) any arrangement or transaction that reasonably would be expected to prevent, impede, delay or otherwise conflict with the Exclusive Negotiation Right or attempts by Fuji Pharma to negotiate and attain the Commercialization Agreement. Without limiting the foregoing, Vistagen shall not sell, license, mortgage, or encumber in any way any rights to Vistagen Technology to the extent applicable to Japan during the Exclusive Negotiation Period.

(c) During the Exclusive Negotiation Period, Vistagen and Fuji Pharma will consult with each other periodically to evaluate development and commercialization opportunities for the Product and to facilitate obtaining favorable regulatory and prescriber perspectives regarding the Product in Japan.

(d) For the avoidance of doubt, nothing in this Agreement will prevent Vistagen, in any manner, from discussing, negotiating, or entering into one or more option, collaboration, development, commercialization, or any other kind of agreements for the Product or involving the Vistagen Technology in any territory other than Japan. For the avoidance of doubt, nothing in this Agreement grants any rights to Fuji Pharma under the Vistagen Technology.

9. Representations.

(a) Vistagen represents that no agreements between any third party and Vistagen prevent the exercise of the Exclusive Negotiation Right by Fuji Pharma in the manner contemplated by this Agreement.

(b) Vistagen and Fuji Pharma represent that they have all requisite corporate power and authority to execute and deliver this Agreement and perform its obligations hereunder. The execution and delivery by each Party of this Agreement and the consummation of the transactions contemplated hereby have been duly and validly authorized by all necessary corporate actions.

(c) Vistagen represents that it will use its best commercial efforts to submit an IND for the Product for the treatment of vasomotor symptoms (hot flashes) due to menopause; however, Fuji Pharma acknowledges that there is no guarantee that the US FDA will accept such an IND or ultimately approve the Product for marketing.

(d) Vistagen and Fuji Pharma make no other representations or warranties in connection with this Agreement other than as specified above.

10. Limitation of Liability. NEITHER PARTY WILL BE LIABLE TO THE OTHER PARTY FOR ANY INDIRECT, INCIDENTAL, CONSEQUENTIAL, SPECIAL, PUNITIVE, OR EXEMPLARY DAMAGES OR ANY LOSS OF REVENUE OR PROFITS ARISING OUT OF, IN CONNECTION WITH, THIS AGREEMENT REGARDLESS OF WHETHER SUCH PARTY HAS BEEN ADVISED OF OR IS AWARE THAT SUCH DAMAGES HAVE BEEN OR MAY BE INCURRED.

11. Miscellaneous.

(a) Governing Law. This Agreement and any dispute arising from the performance or breach hereof shall be governed by, construed, and enforced in accordance with the laws of the State of California as applied to disputes involving parties located entirely within the State and without reference to the State's conflicts of laws principles.

(b) Dispute Resolution. All disputes arising out of, or in connection with, this Agreement shall be finally settled by arbitration administered by the Singapore International Arbitration Centre ("SIAC") in accordance with the rules of the SIAC for the time being in force (the "SIAC Rules"), which rules are deemed to be incorporated by reference into this Section 11(b). Any arbitral tribunal appointed pursuant to this Section 11(b) shall consist of three arbitrators to be appointed in accordance with the SIAC Rules. The place of arbitration shall be Singapore. The language of the arbitration shall be English. The Parties undertake to keep confidential all awards in their arbitration, together with all materials in the proceedings created for the purpose of the arbitration and all other documents produced by the other Party in the proceedings not otherwise in the public domain, save and to the extent that disclosure may be required of a Party by legal duty, to protect or pursue a legal right or to enforce or challenge an award in bona fide legal proceedings before a state court or other judicial authority.

(c) Preliminary Injunctions. Notwithstanding any provision to the contrary set forth in this Agreement, in the event of an actual or threatened breach of a Party's obligations under this Agreement, a Party may seek a temporary restraining order or a preliminary injunction from any court of competent jurisdiction in order to prevent immediate and irreparable injury, loss, or damage on a provisional basis.

(d) Waiver. Neither Party may waive or release any of its rights or interests in this Agreement except in writing. The failure of either Party to assert a right hereunder or to insist upon compliance with any term or condition of this Agreement shall not constitute a waiver of that right or excuse a similar subsequent failure to perform any such term or condition.

(e) Assignability. Neither Party may assign its rights under this Agreement without the prior written consent of the other Party, such consent not to be unreasonably withheld. Notwithstanding the foregoing, either Party may assign its rights under this Agreement to a successor in connection with a merger, consolidation, spin-off, or sale of all or substantially all of its assets or that portion of its business pertaining to the Product without the prior written consent of the other Party.

(f) Notices. All notices, requests and other communications hereunder shall be in writing and shall be personally delivered or sent by courier or by registered or certified mail, return receipt requested, postage prepaid, in each case to the respective address specified below, or such other address as may be specified in writing to the other Parties hereto:

Vistagen Therapeutics, Inc.
343 Allerton Avenue
South San Francisco, CA 94080 USA
Email:
ATTN: Shawn K. Singh, J.D., Chief Executive Officer

Fuji Pharma Co., Ltd.
5-7 Sanban-cho,
Chiyoda-ku, Tokyo 102-0075, Japan
Email:
ATTN: Chaudhary Kushendra, General Manager of Business Development

(g) Force Majeure. Neither Party shall be liable to the other for failure or delay in the performance of any of its obligations under this Agreement for the time and to the extent such failure or delay is caused by riots, civil commotions, wars, hostilities between nations, embargoes, actions by a government or any agency thereof, acts of God, storms, fires, accidents, sabotage, explosions or other similar or different contingencies, the damage or harm resulting from any or all of which, in each case, shall be beyond the reasonable control of the Party invoking this Section 11(g) and not attributable to the negligence or willful misconduct of the Party invoking this Section 11(g).

(h) Disclosure of the Agreement and Use of Name. The Parties acknowledge that Vistagen may be required to disclose this Agreement pursuant to applicable rules and regulations of the U.S. Securities and Exchange Commission or the Nasdaq Capital Market, or both. Either Party may announce the existence of this Agreement, use the name of the other Party for such purpose and for regulatory compliance purposes, and as otherwise may be required by law.

(i) Severability. If any provision of this Agreement becomes or is declared by the SIAC or by a court of competent jurisdiction to be illegal, unenforceable, or void, this Agreement shall continue in full force and effect without said provision so long as this Agreement, taking into account said voided provision(s), continues to provide the Parties with the same practical economic benefits as the Agreement containing said voided provision(s) did on its Effective Date. If, after considering said voided provision(s), the Parties are unable to realize the practical economic benefit contemplated on the Effective Date, the Parties shall negotiate in good faith to amend this Agreement to reestablish the practical economic benefit provided the Parties on the Effective Date.

(j) Complete Agreement. This Agreement will constitute the entire agreement, both written and oral, between the Parties with respect to the subject matter hereof, and all prior agreements or discussions respecting the subject matter hereof, either written or oral, expressed or implied, are merged and canceled and are null and void and of no effect. No amendment or change hereof or addition hereto shall be effective or binding on either of the Parties hereto unless reduced to writing and duly executed on behalf of both Parties.

(k) Headings. The captions to the sections and articles in this Agreement are not a part of this Agreement and are included merely for the convenience of reference only and shall not affect its meaning or interpretation.

(l) Counterparts and Signatures. This Agreement may be executed in counterparts, or facsimile versions, each of which shall be deemed to be an original, and both shall be deemed one and the same agreement. Signatures to this Agreement transmitted by facsimile transmission, by electronic mail in “portable document format” (“.pdf”) form, by DocuSign, or by any other electronic means intended to preserve the original graphic and pictorial appearance of a document will have the same effect as physical delivery of the paper document bearing the original signature.

(m) Binding Effect. This Agreement shall be binding upon and shall inure to the benefit of Vistagen, Fuji Pharma, and their successors and permitted assigns.

(n) Advice of Counsel and Expenses. Vistagen and Fuji Pharma have each consulted with counsel of their choice regarding this Agreement, and each acknowledges and agrees that this Agreement shall not be deemed to have been drafted by one party or another and will be construed accordingly. Except as may otherwise expressly be provided in this Agreement, each Party shall pay the fees and expenses of its respective attorneys and all other expenses and costs incurred by such Party incidental to the negotiation, preparation, execution, and delivery of this Agreement.

(o) Intellectual Property Matters. During the Exclusive Negotiation Period, Vistagen will use its best commercial efforts to preserve, protect and enhance patents and any other intellectual property rights that are relevant to the Commercialization Agreement.

(p) Further Assurance. Each Party shall perform all further acts and execute and deliver such further documents as may be necessary or as the other Party may reasonably require to give effect to this Agreement.

IN WITNESS WHEREOF, the undersigned have caused this Agreement to be duly executed and delivered by their proper and duly authorized officers as of the date and year first written above.

Vistagen Therapeutics, Inc.

By: /s/ Shawn K. Singh
Name: Shawn K. Singh, J.D.
Title: Chief Executive Officer

Fuji Pharma Co., Ltd.

By: /s/ Takayuki Iwai
Name: Takayuki Iwai
Title: President and CEO

Exhibit 99.1

Vistagen and Fuji Enter Exclusive Negotiation Agreement for a Potential License to Develop and Commercialize Vistagen's Investigational Menopausal Hot Flash Therapy, PH80 Nasal Spray, in Japan

Vistagen to receive $1.5 million and Fuji to obtain time-limited exclusive negotiation period for the Japanese market

Recently reported exploratory Phase 2A study in women diagnosed with menopausal hot flashes demonstrated PH80's statistically significant reduction in the number of hot flashes and the severity, disruption in function, and sweating related to hot flashes as compared with placebo

SOUTH SAN FRANCISCO, Calif. & TOKYO--(BUSINESS WIRE)--Sep. 5, 2023-- Vistagen (Nasdaq: VTGN), a clinical-stage biopharmaceutical company aiming to transform the treatment landscape for individuals living with anxiety, depression, and other central nervous system (CNS) disorders, and Fuji Pharma Co., Ltd. ("Fuji") (TSE: 4554), a pharmaceutical company specializing in development, manufacture and marketing in the fields of women's healthcare and acute medical care, today announced they have entered into a time-limited (up to approximately eighteen months) agreement to negotiate exclusively with each other regarding a potential license to develop and commercialize Vistagen's PH80 in Japan, including for the acute treatment of moderate to severe vasomotor symptoms (hot flashes) due to menopause and potentially other indications. Vistagen's PH80 neuroactive nasal spray demonstrated statistically significant efficacy versus placebo in an exploratory double-blind, placebo-controlled Phase 2A study in women diagnosed with menopausal hot flashes. Fuji will make a non-refundable payment of $1.5 million to secure the time-limited exclusive negotiation rights for the Japanese market.

"As we have seen across our neuroactive pherine nasal spray pipeline, PH80 offers exciting potential to transform a significant segment of a major healthcare market, including the current treatment landscape for women's healthcare," said Shawn Singh, CEO of Vistagen. "Menopausal hot flashes affect millions of women worldwide. We share Fuji Pharma's long-standing commitment to deliver innovative treatment options with potential to enable women to improve their physical, mental and social well-being. As we continue to advance our PH80 development program in the U.S., we look forward to continuing our ongoing discussions with Fuji regarding a potential development and commercialization collaboration in Japan."

"Our core mission at Fuji Pharma centers on helping people lead healthy lives by offering excellent pharmaceutical solutions. We believe that PH80 will provide new treatment options to improve the quality of life and further strengthen our position as one of the best Japanese specialty pharmaceutical companies in women's health," said Takayuki Iwai, President & CEO of Fuji. "We will continue to engage in dialogue with Vistagen, anticipating that successful development of PH80 will contribute to women's health in Japan."

About PH80

PH80 is a rapid-onset neuroactive pherine nasal spray product candidate designed to be used in a manner analogous to a rescue inhaler for asthma, taken by patients as-needed up to multiple times daily. Several pharmacokinetic and toxicokinetic studies show that PH80 administered intranasally is below the level of detection in plasma of human subjects and laboratory animals. Based on other studies conducted by Vistagen, pherine molecules have no detectable uptake in the brain and do not absorb systemically. All these data, along with the minimal adverse events reported in all clinical studies to date, demonstrate the excellent safety profile of this new class of molecules. In a placebo-controlled exploratory Phase 2A clinical trial, PH80 demonstrated an excellent safety profile and potential as a new treatment for moderate to severe vasomotor symptoms (hot flashes) associated with menopause.

About Vasomotor Symptoms (Hot Flashes) due to Menopause

Hot flashes are vasomotor symptoms (VMS) commonly experienced by women in menopause and are accompanied by hallmark symptoms such as sudden feelings of warmth, night sweats and flushed skin. Presentation of hot flashes is directly linked to changes in hormone levels due to menopause, or to menopause induced by other medical treatments or co-existing conditions, and the causal mechanism is unclear. Hot flashes are the most common symptom of the menopausal transition, affecting about 75% of menopausal women and about 40% of women in perimenopause. Current pharmacotherapies to treat hot flashes include hormonal therapy (estrogen with or without progesterone, or a synthetic progestin), gabapentins, certain antidepressants, clonidine and fezolinetant, a neurokinin 3 (NK3) receptor antagonist, all of which are associated with certain side effects.

About Exploratory Phase 2A Study of PH80 in Vasomotor Symptoms (Hot Flashes) due to Menopause

In a randomized, double-blind, placebo-controlled exploratory Phase 2A clinical study of PH80 (n=36) designed to explore the efficacy, safety and tolerability of intranasal administration of PH80 for the acute management of menopausal hot flashes in women, PH80 induced significant reduction in the daily number of hot flashes compared to placebo at the end of the first week of treatment, and the improvement was maintained through each treatment week until the end of the treatment period. At baseline, subjects reported a mean daily number of hot flashes of 7.7 (PH80, n=18) and 8.0 (placebo, n=18). After one week of treatment, the number of hot flashes dropped to 2.8 (PH80) and 6.4 (placebo) ($p<0.001$) and after four weeks of treatment the number of hot flashes dropped to 1.5 (PH80) and 5.1 (placebo) ($p<0.001$). PH80 treatment also significantly reduced the severity, disruption in function and sweating related to hot flashes during the treatment period as compared with placebo. This exploratory Phase 2A study of PH80 was conducted in a real-world setting in Mexico and was sponsored by Pherin Pharmaceuticals (Pherin), now a wholly owned subsidiary of Vistagen, prior to Vistagen’s acquisition of Pherin in February 2023. Ellen Freeman, Ph.D. of the University of Pennsylvania served as the Principal Investigator of the study.

About Vistagen

Vistagen (Nasdaq: VTGN) is a clinical-stage biopharmaceutical company aiming to transform the treatment landscape for individuals living with anxiety, depression and other CNS disorders. Vistagen is advancing therapeutics with the potential to be faster-acting, and with fewer side effects and safety concerns, than those currently available for the treatment of anxiety, depression and multiple CNS disorders. Vistagen's pipeline includes six clinical-stage product candidates, including fasedienol (PH94B), itruvone (PH10), PH80, PH15, and PH284, with each of these being an investigational agent belonging to a new class of drugs known as pherines, as well as AV-101, which is an oral prodrug of an antagonist of the N-methyl-D-aspartate receptor (NMDAR). Pherines are neuroactive nasal sprays designed with an innovative proposed mechanism of action that activates chemosensory neurons in the nasal cavity and can beneficially impact key neural circuits in the brain without systemic absorption or direct activity on neurons in the brain. Vistagen is passionate about transforming mental health care and redefining what is possible in the treatment of anxiety, depression and several other CNS disorders. Connect at www.Vistagen.com.

About Fuji

Fuji is a Tokyo Stock Exchange (TSE) listed, Japan-based pharmaceutical company mainly engaged in the manufacture and sale of prescription based pharmaceutical products. Since our establishment in 1965, Fuji has promoted corporate philosophy that "We help people lead healthy lives by offering excellent pharmaceuticals." and "Our corporate growth is proportional to our personal growth." Fuji focuses on the field of women's health care with a wide variety of new and generic drugs for women's specific diseases such as infertility, dysmenorrhea, endometriosis, contraception, and menopausal disorders. Fuji aims to be a leading company in women's healthcare and support health of women of all ages. https://www.fujipharma.jp

Forward-looking Statements

This press release contains certain forward-looking statements within the meaning of the federal securities laws. These forward-looking statements involve known and unknown risks that are difficult to predict and include all matters that are not historical facts. 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 Vistagen and its management, are inherently uncertain. 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. Among other things, there can be no guarantee that any of the Company's drug candidates will successfully complete ongoing or future clinical trials, receive regulatory approval or be commercially successful, or that the Company will be able to successfully replicate the result of past studies of its product candidates, including PH80. Other factors that may cause such a difference include, without limitation, risks and uncertainties relating to the Company's ability to secure adequate financing for its operations, including financing or collaborative support for continued clinical development of the Company's product candidates; other risks and uncertainties related to delays in launching, conducting and/or completing ongoing and planned clinical trials; the scope and enforceability of the Company's patents, including patents related to PH80 and the Company's other pherine drug candidates; fluctuating costs of materials and other resources and services required to conduct the Company's 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, manufacture and commercialization of the Company's drug candidates. These risks are more fully discussed in the section entitled "Risk Factors" in the Company's most recent Annual Report on Form 10-K for the fiscal year ended March 31, 2023, and in the Company's most recent Quarterly Report on Form 10-Q for the quarter ended June 30, 2023, 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). The Company's SEC filings are available on the SEC's website at www.sec.gov. Additionally, you should not place undue reliance on these forward-looking statements in the future, because they apply only as of the date of this press release and should not be relied upon as representing the Company's views as of any subsequent date. The Company explicitly disclaims any obligation to update any forward-looking statements, other than as may be required by law. If the Company does update one or more forward-looking statements, no inference should be made that the Company will make additional updates with respect to those or other forward-looking statements.

Investors:
Vistagen
Mark McPartland
Senior Vice President, Investor Relations
(650) 577-3606
markmcp@vistagen.com

Fuji Pharma Co., Ltd.
Corporate Communication Section, Corporate Planning Department, Corporate Strategy Division
fsks@fujipharma.jp

Media:
Nate Hitchings
SKDK
nhitchings@skdknick.com

Source: Vistagen


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 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. Further, there can be no guarantee that any of our drug candidates will successfully complete ongoing or, if initiated, future clinical trials, receive regulatory approval or be commercially successful, or that we will successfully replicate the result of past studies of our product candidates, including fasedienol and itruvone. Other factors that may cause such a difference include, without limitation, risks and uncertainties related to our ability to secure funding that is adequate to support our development and commercialization plans and/or to secure successful strategic global and/or regional development and commercialization partnerships; other risks and uncertainties related to delays in launching, conducting and/or completing ongoing and planned clinical trials; the scope and enforceability of our patents, including patents related to our pherine drug candidates and AV-101; 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, manufacture and commercialization of our product candidates. These risks are more fully discussed in the section entitled "Risk Factors" in the Company's most recent Annual Report on Form 10-K for the fiscal year ended March 31, 2023, and in the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2023, 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. Be aware that our development and commercialization plans may change based on the kinds of risk factors described above.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates.

Mission and Investment Highlights

We are focused on delivering a new generation of CNS therapies with novel mechanisms of action targeting a broad and diverse range of CNS disorders with high unmet medical need

Six CNS clinical programs, lead candidate with recent positive Phase 3 data in social anxiety disorder

All clinical programs target novel MOAs differentiated from currently approved therapies, with potential to bring new benefits to patients, physicians, and payers

Targeting large anxiety, depression, and additional CNS markets with high unmet medical need

Experienced CNS product development team and advisors

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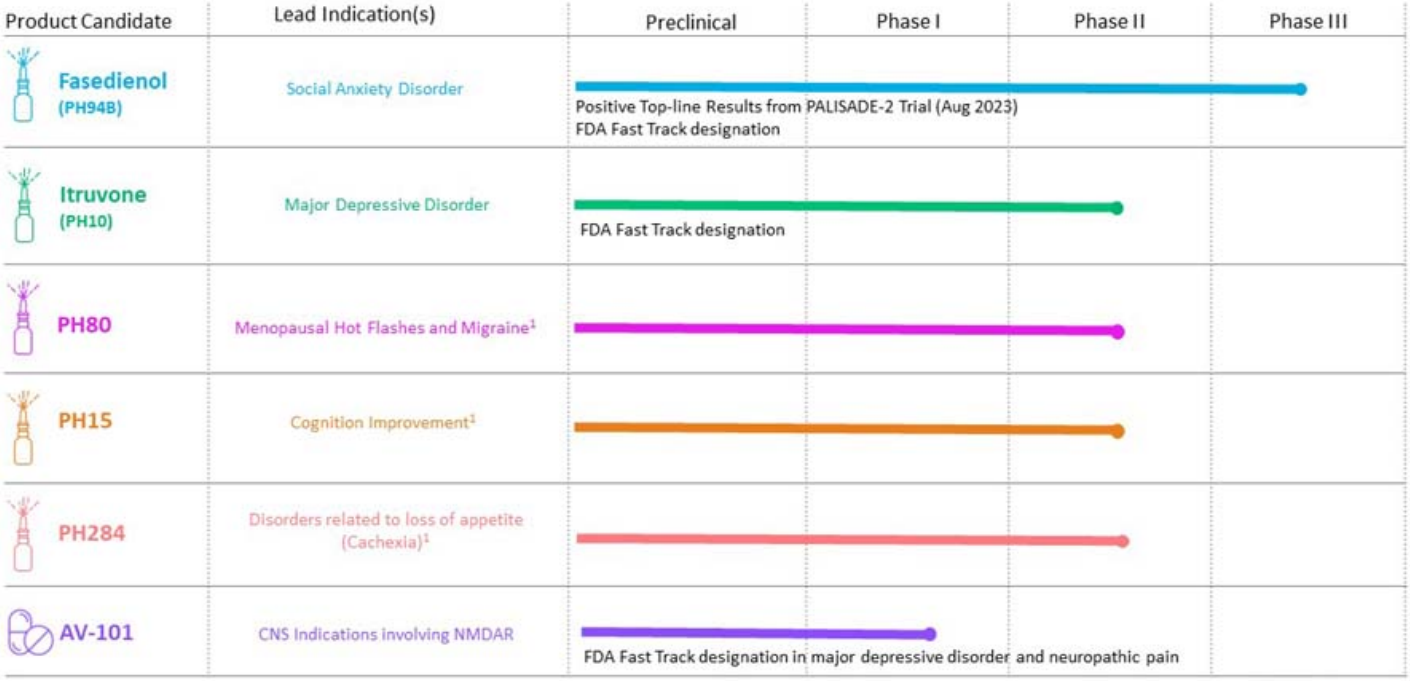
Clinical-stage Pipeline



1. Indicates US IND-enabling work necessary to facilitate further Phase 2 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 and/or sufficient support from one or more strategic collaborations, or both.

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Pherines
A new class of neuroactive
nasal sprays

Pherines

A new class of neuroactive nasal sprays

- Fast-acting, non-systemic, odorless, tasteless
- Selectively engage chemosensory receptors in the nasal passages to induce rapid-onset pharmacological and behavioral effects
- Selectively modulate brain areas, including the limbic amygdala, hypothalamus, hippocampus, locus ceruleus and prefrontal cortex, without requiring systemic absorption or binding to classic abuse liability receptors or steroidal hormone receptors
- Affect particular neuronal circuits instead of a single gene, protein, neuron or synapse
- We have consistently observed a favorable tolerability profile in all clinical trials to date


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Fasedienol Nasal Spray
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

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SAD Affects ~10% of the US Population, with only ~20% of SAD Patients Helped by Current Pharmacotherapy

Future Patients

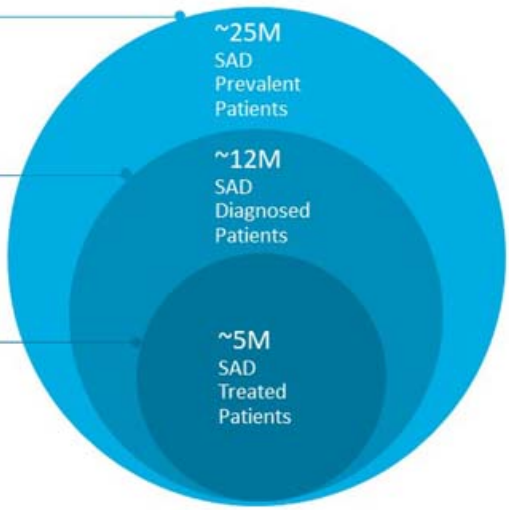
Patients suffering but unaware of SAD as a condition or not yet motivated to seek professional help.

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.

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We Believe Current Standard of Care for SAD is Inadequate

There is currently no FDA-approved, fast-acting, non-systemic treatment 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	✓	✓	✓	✓	✓	✓	✓

* Non-sedative hypnotic agents

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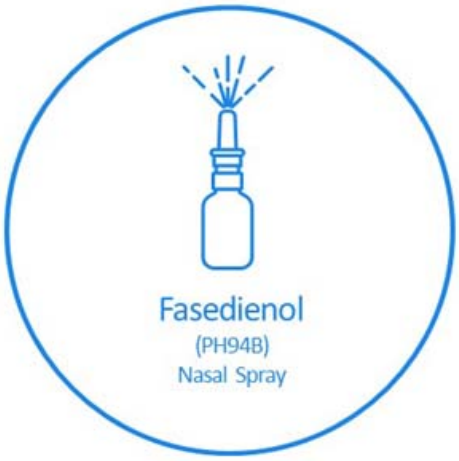
We Believe Fasedienol Brings New Optimism for SAD Treatment

- De-risked potential NDA-enabling pathway with positive results of PALISADE-2 Phase 3 trial reported in August 2023
- Novel mechanism of action, differentiated from current therapies
- Designed for patient-tailored as-needed administration, with potential use analogous to an as-needed rescue inhaler for asthma
- No observed systemic uptake or direct activity on neurons in the brain
- Does not potentiate GABA
- Favorable tolerability profile – no evidence of abuse liability potential
- As-needed use over time has potential to build confidence, resilience, and reduce fear, anxiety and avoidance of social anxiety stressors
- Target product profile expected to align with preferences of patients and providers
- FDA Fast Track Designation granted



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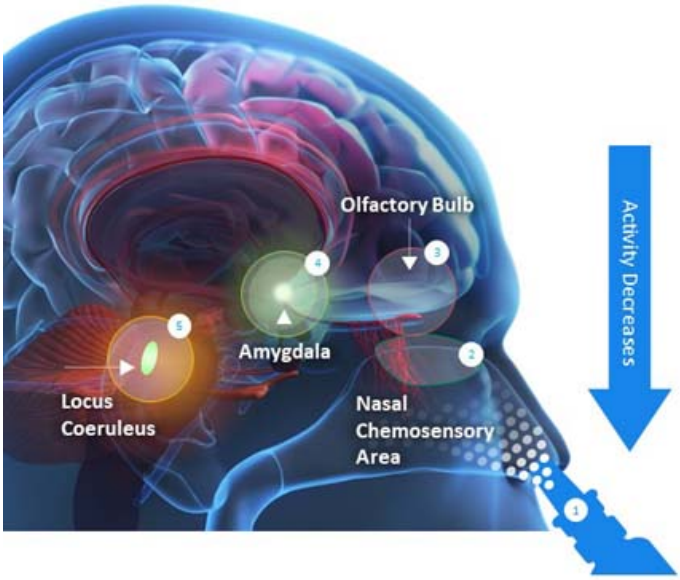
Fasedienol's Potential Mechanism of Action

Novel and differentiated from all current therapies for anxiety disorders



1. Microgram-level intranasal dose of fasedienol 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 (OBs)
4. Neurons in the OBs 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

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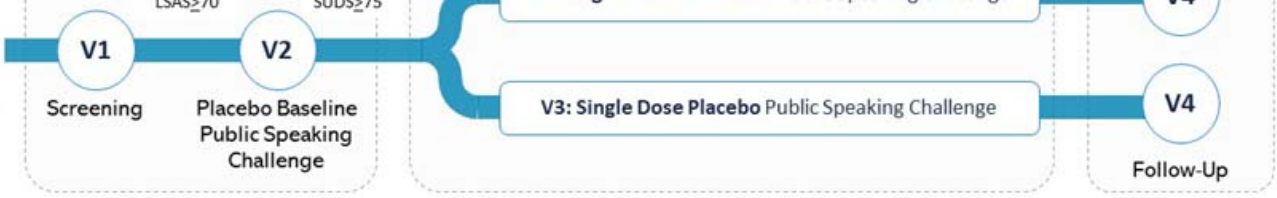
PALISADE-2 Phase 3 Trial

Study Goal

A randomized, multi-center, double-blind, placebo-controlled, single-dose administration Phase 3 trial to evaluate the efficacy, safety, and tolerability of fasedienol for the acute treatment of anxiety induced by a public speaking challenge in adult subjects with Social Anxiety Disorder in a clinical setting

Study Design



Criteria

+ SAD diagnosis: LSAS > 70
+ HAMD <18 at screening
+ Normal olfactory function, Quick Olfactory Test if needed
+ No Recent history COVID-19

− Significant psychiatric illness, use of psychotropic medication
− Suicidal Behavior
− Alcohol or substance use disorder
− Significant nasal pathology

Outcome Measures

Primary Endpoint
- Change in mean SUDS scores from baseline compared to placebo

Secondary Endpoint
- Responder Rates based on Clinical Global Impression – Improvement

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Principal Investigator: Dr. Michael Liebowitz, Columbia University

PALISADE-2 Phase 3 Trial Top-Line Efficacy Results

Positive results across primary, secondary, and exploratory endpoints

Met Primary Endpoint	**LS Mean SUDS** change from baseline vs. placebo (SUDS change from Visit 2 to Visit 3)	p=0.015
Met Secondary Endpoint	**CGI-I** proportion of responders vs. placebo (much or very much less anxious from Visit 2 to Visit 3)	p=0.033
Met Exploratory Endpoints	**PGI-C** proportion of responders vs. placebo (much or very much less anxious from Visit 2 to Visit 3)	p=0.003
	SUDS proportion of responders vs. placebo (≥20-point improvement in SUDS score from Visit 2 to Visit 3)	p=0.020

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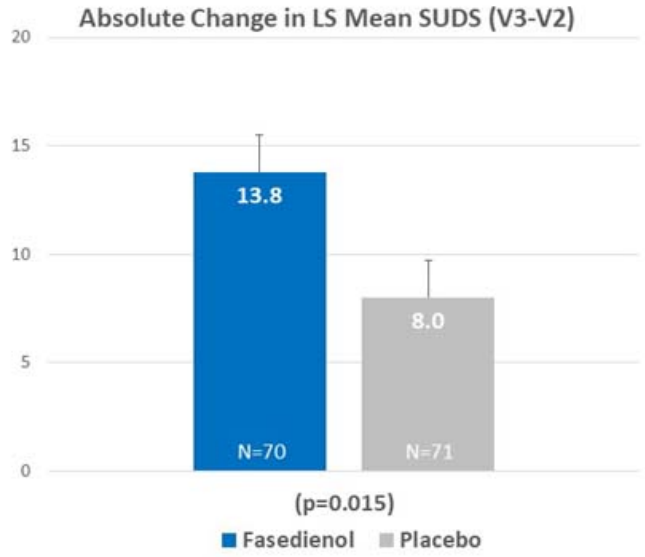
Primary Efficacy Endpoint:
Change in LS Mean* SUDS Scores from V2 to V3 vs. Placebo

Met primary endpoint with a change from Baseline in LS Mean of 5.8 points better than placebo (p=0.015)



*LS Mean = Least-squares Mean

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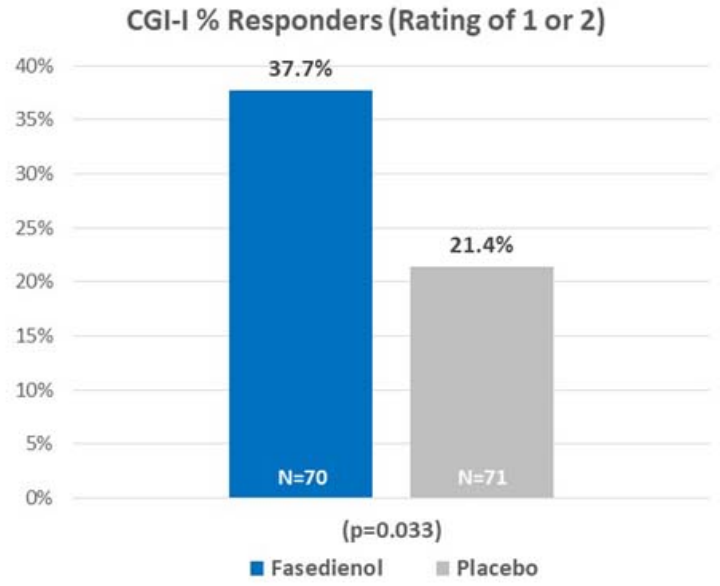
Secondary Endpoint: CGI-I responders vs. Placebo at V3

Met secondary endpoint with a proportion of responders 16.3% points greater than placebo (p=0.033)



CGI-I Score

1 = Very Much Less Anxious
2 = Much Less Anxious
3 = A Little Less Anxious
4 = No Change
5 = A Little More Anxious
6 = Much More Anxious
7 = Very Much More Anxious

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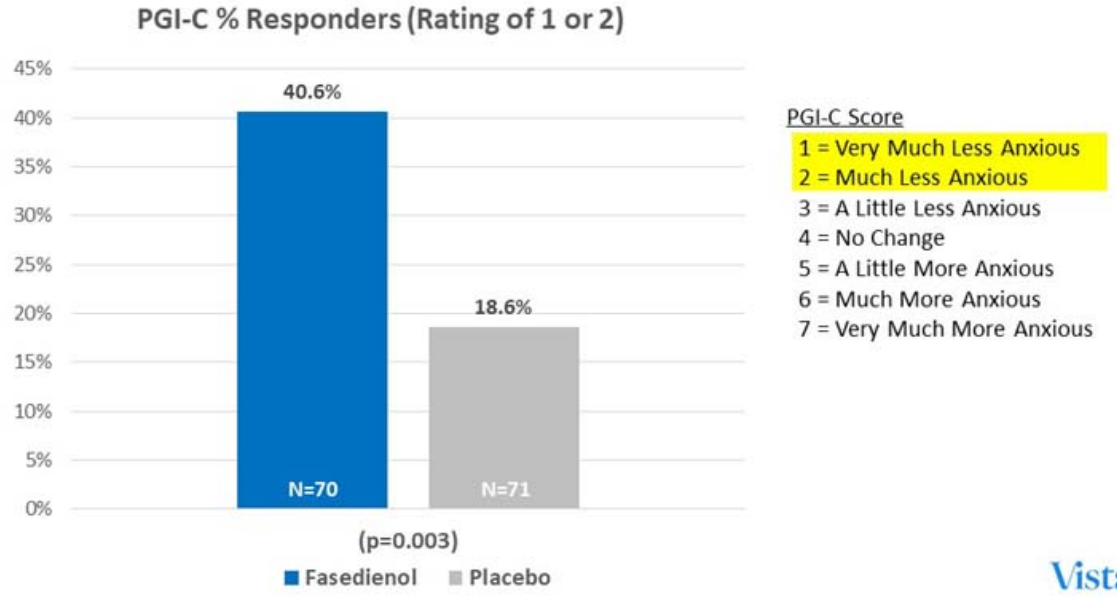
Exploratory Endpoint: PGI-C responders vs. Placebo at V3

Met exploratory endpoint with a proportion of responders 22.0% points greater than placebo (p=0.003)



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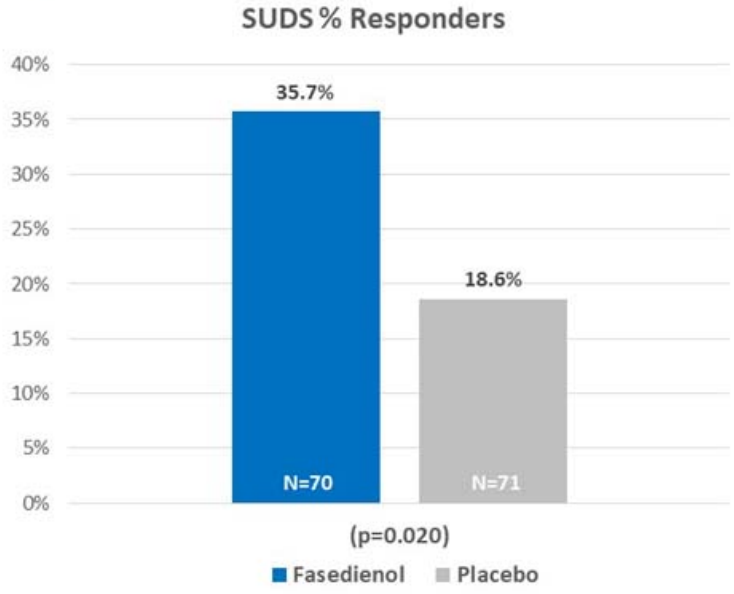
Exploratory Endpoint: SUDS responders vs. Placebo at V3

Met exploratory endpoint with a proportion of responders 17.1% points greater than placebo (p=0.020)



SUDS Responders
≥ 20-point improvement from Visit 2 baseline to Visit 3

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Tolerability Profile: Overall Summary

The tolerability profile of fasedienol was favorable and consistent with results from fasedienol trials completed to date

- No severe or serious adverse events were reported in this trial
- There were no discontinuations due to adverse events following exposure to fasedienol
- Adverse events were infrequent, and mild or moderate in severity
- There were no treatment-emergent adverse events reported above a 2% occurrence, except pyrexia in the placebo group (2.49%)

PALISADE Open Label Safety Study

Over 30,000 doses self-administered by 481 SAD patients

Design

Long-term intranasal administration of 3.2 µg of fasedienol as-needed, up to 4x/day prior to anxiety-provoking social and performance stressors in daily life, with a mean study duration of 4 months, and a maximum study duration of over 10 months

Results

- Long-term intranasal administration of 3.2 µg of fasedienol as-needed, up to 4x/day, was 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**

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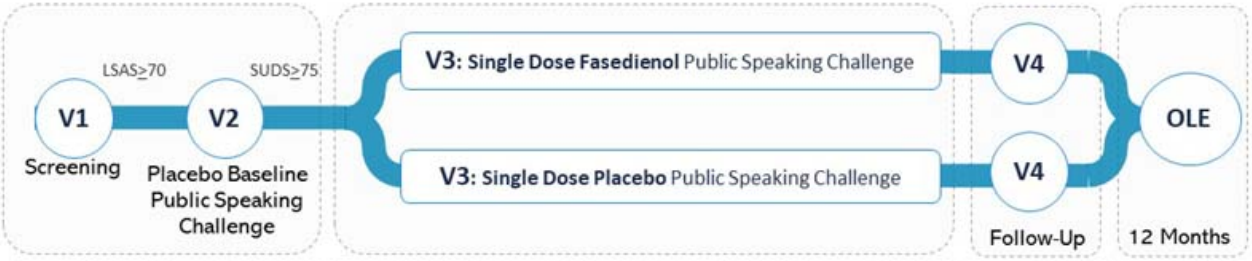
Planned Next Step: PALISADE-3 Phase 3 Trial with OLE*

Study Goal

Randomized, multi-center, double-blind, placebo-controlled, single-dose administration Phase 3 trial to evaluate the efficacy, safety, and tolerability of fasedienol for the acute treatment of anxiety induced by a public speaking challenge in adult subjects with Social Anxiety Disorder in a clinical setting

Study Design



Criteria

Inclusion Criteria

+ Female and male subjects; age 18-65
+ SAD diagnosis; LSAS ≥ 70; HAMD<18
+ Normal olfactory function determined by Quick Olfactory Test
+ Medical and psychiatric health

Exclusion Criteria

— Nasal swab within the past four weeks
— COVID-19 diagnosis + any residual symptoms within past 4 weeks
— Drug use (incl. cannabis), heavy use of alcohol, smoking, vaping
— Other primary psychiatric disorders; Receiving CNS active medications

Outcome Measures

Primary Endpoint

- Change in mean SUDS scores from V2 to V3 compared to placebo

Secondary Endpoints

Responder rates at V3 vs placebo:

- Patient Global Impression of Change
- Clinical Global Impression – Improvement

*OLE = Open Label Extension;

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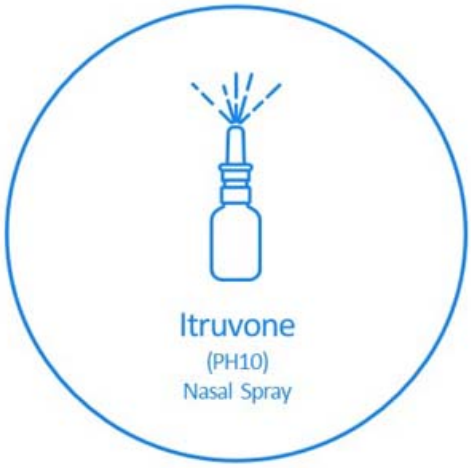
Itruvone Nasal Spray
for Major Depressive Disorder
Looking beyond the standard of care for depression disorders

Itruvone is a Potential Differentiated Monotherapy Treatment of Major Depressive Disorder

- Innovative odorless, tasteless synthetic neuroactive nasal spray
- Designed for rapid-onset antidepressant effects
- Novel and differentiated MOA from all approved antidepressants
- Designed to be non-systemic, non-sedating, non-addictive; does not potentiate GABA
- Positive exploratory Phase 2A trial completed (n=30)
- Well-tolerated in all clinical studies to date
- FDA Fast Track designation granted



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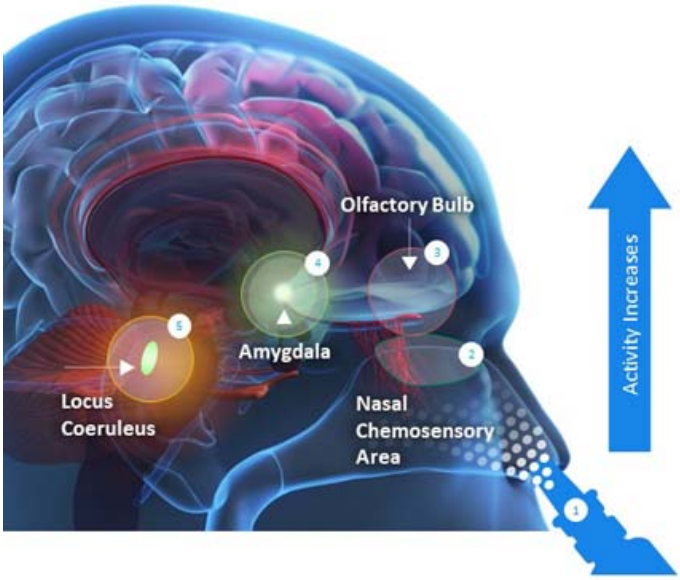
Itruvone's Potential Mechanism of Action

Novel and differentiated from all current therapies for depression disorders



1. Microgram-level intranasal dose of itruvone is administered
2. Itruvone engages peripheral receptors in nasal chemosensory neurons (NCNs)
3. Once stimulated with itruvone, NCNs then trigger subsets of interneurons in the olfactory bulbs (OBs)
4. Neurons in the OBs then stimulate GABAergic "Fear On" neurons in the limbic amygdala
5. The stimulation of the limbic amygdala INCREASES the activity of the 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

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Itruvone Antidepressant Effects in Phase 2A MDD Study

Design: Phase 2A randomized, double-blind, placebo-controlled, parallel design POC clinical study (n=30)

Dosing: 3.2 μg or 6.4 μg of itruvone or placebo i.n., 2 times per day for 8 weeks

Primary Endpoint: Change in HAMD-17 scores from baseline compared to placebo

Results:

- 6.4 μg dose significantly reduced depressive symptoms as early as one week based on HAM-D-17 scores compared to placebo (p=0.022)
- 3.2 μg dose showed a trend (p=0.101)
- Strong effect sizes for both 3.2 μg and 6.4 μg vs. placebo at 1 week and at 8 weeks

Well-tolerated, no dissociative side effects or serious adverse events observed

Results support advancement to potential 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.

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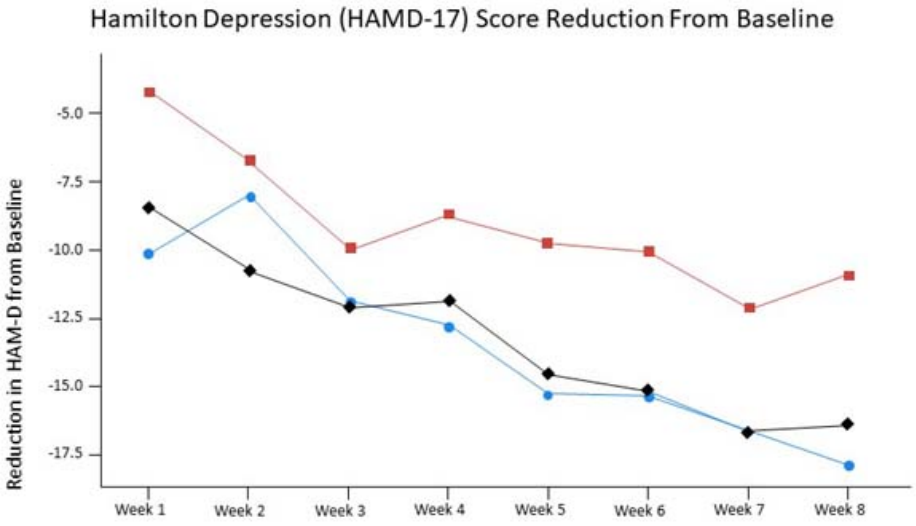
Itruvone Phase 2A MDD Study



6.4 µg 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 µg (Low Dose)	-16.3	.101	0.74
● 6.4 µg (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.

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Itruvone Potential Next Step – Phase 2B Trial*

Advanced planning for potential Phase 2B development of itruvone as a monotherapy MDD treatment is underway

- Potential Design: Double-blind, randomized, placebo-controlled, parallel study in ca. 200 total male and female subjects (18 to 65 years old) with a confirmed diagnosis of MDD, who are not currently taking any antidepressants
- Outpatient self-administration of 6.4 µg (daily) itruvone nasal spray over a 4-week period
- Potential Primary Efficacy Endpoint: Change from Baseline to Day 28 in the HAMD-17 Rating Scale

*The commencement and completion of this Phase 2B study is subject to US FDA regulatory authorization and securing sufficient capital, or sufficient support from one or more strategic partners, or both.

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PH80 Nasal Spray
for Vasomotor Symptoms
(Hot Flashes)due to Menopause
Looking beyond the standard of care
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PH80 Nasal Spray

Potential Treatment for Vasomotor Symptoms (Hot Flashes) due to Menopause

- ✓ Innovative, rapid-onset product candidate
- ✓ Novel and differentiated MOA from all approved products
- ✓ Taken as-needed for treatment of multiple menopausal hot flashes daily, use analogous to a rescue inhaler for asthma
- ✓ Expected to provide an acute effect in the moment, as well as reduce the number and severity of hot flashes over time
- ✓ No systemic uptake or direct action on CNS neurons
- ✓ We believe there are tolerability profile advantages over currently approved therapies
- ✓ Positive exploratory Phase 2A study completed (n=36)

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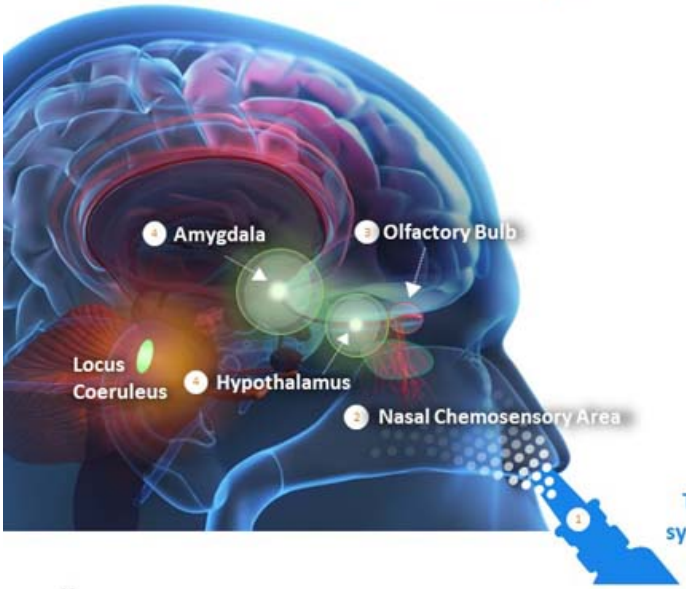
PH80's Potential Mechanism of Action

Novel and differentiated from all currently approved VMS therapies



1. Microgram-level intranasal dose of PH80 is administered
2. PH80 engages peripheral receptors in nasal chemosensory neurons (NCNs)
3. Once stimulated with PH80, NCNs then trigger subgroups of neurons in the olfactory bulbs (OBs)
4. Neurons in the OBs then stimulate neurons in the limbic amygdala and the hypothalamus

Activity Decreases

The stimulation of neurons in the limbic amygdala and the hypothalamus decreases the activity of the autonomic nervous system and decreases activation of the trigeminal-vascular neural circuits

Downstream effects potentially include:

- Decreased irritability;
- Decreased muscle tension;
- Reduced core body temperature; and
- Reduced feeling of internal heat

These changes potentially affect the neural circuits involved in vasomotor symptoms (hot flashes) due to menopause, premenstrual dysphoric disorder (PMDD), and migraine

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

PH80 Phase 2A Study in Hot Flashes: Summary

Objective: Proof-of-principle evaluation of PH80 efficacy and tolerability for the acute management of vasomotor symptoms (hot flashes) due to menopause

Study Details: Randomized, double-blind, placebo-controlled, exploratory Phase 2A study. Patients self-administered PH80 (3.2µg/dose) or placebo for 4 weeks up to 4 times daily with a dose at night if needed. Patients were followed up weekly during the treatment period

Participants: Menopausal women aged 45-60 (N=36) with ≥ 8 hot flashes of moderate to severe intensity per day on average for one week (≈ 56/week)

Outcome Measures: Daily ratings of the Number, Severity, Bother/Disruption and Sweating of daily hot flashes, PGI-C, CGI-I, Safety and Tolerability

Results: PH80 showed statistically and clinically significant improvement vs. placebo in the number of hot flashes while also significantly reducing patient-reported severity, bother/disruption, and sweating associated with hot flashes

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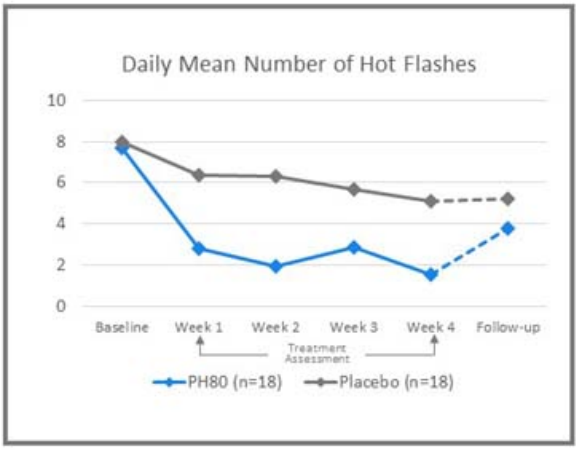
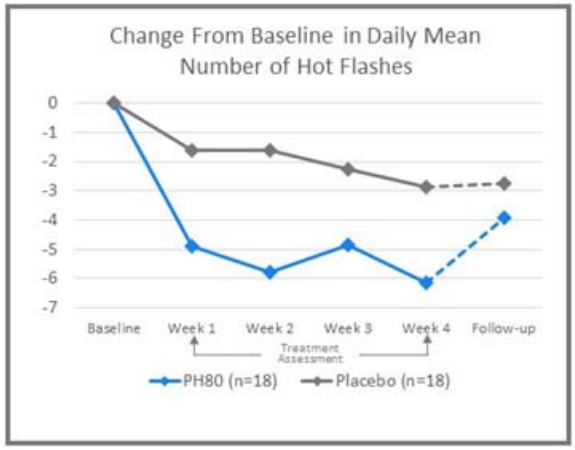
PH80 Phase 2A Study in Hot Flashes: Efficacy

Statistically and clinically significant improvement vs. placebo in the number of hot flashes at 1 week and maintained through 4 weeks of treatment ($p<0.001$)





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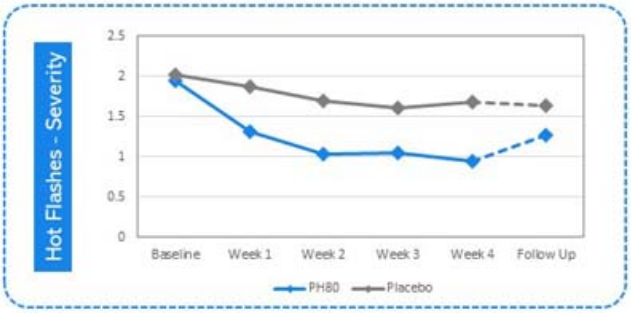
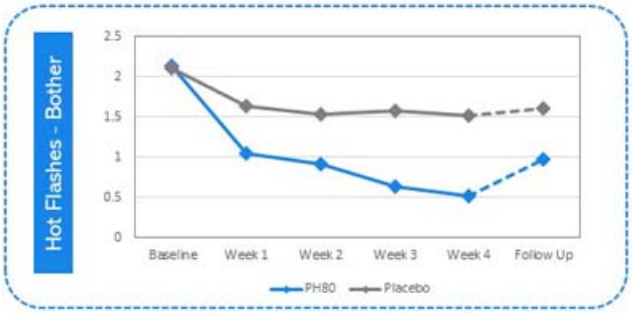
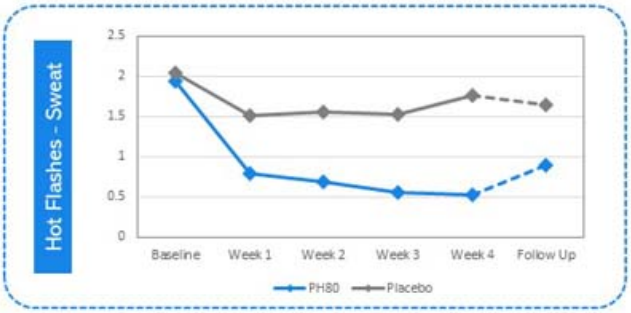
PH80 Phase 2A Study in Hot Flashes: Efficacy

PH80 also significantly reduced patient-reported severity, disruption in function, and sweating associated with hot flashes during the treatment period as compared with placebo







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PH15 Nasal Spray
for Acute Treatment of
Cognitive Impairment
caused by Mental Fatigue
Looking beyond the standard of care
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PH15 Nasal Spray

Potential for Improvement of Cognitive Impairment caused by Mental Fatigue

- ✓ Innovative, rapid-onset PRN product candidate
- ✓ User-friendly intranasal administration, taken as needed for acute improvement of cognition
- ✓ Expected to provide rapid onset and activation of brain areas
- ✓ No systemic uptake or direct action on CNS neurons
- ✓ Indirectly activates adenosine ASA receptors (ADORA2S) in the hypothalamus, similar to the MOA of caffeine
- ✓ Novel and differentiated MOA provides potential new treatment for disorders that lead to sleep deprivation and ensuing fatigue and cognitive impairment (e.g., Shift Work Disorder, Sleep Apnea, and Narcolepsy)

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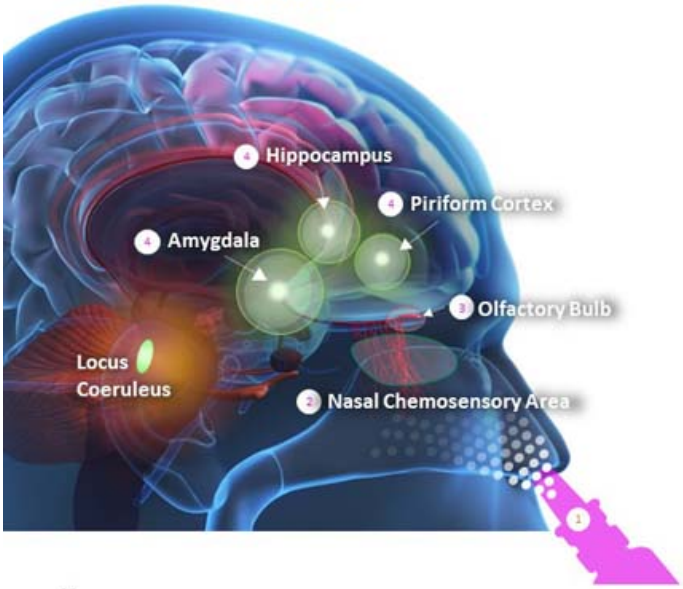
PH15 Proposed Mechanism of Action

Novel and differentiated from all currently approved therapies



1. Microgram-level intranasal dose of PH15 is administered
2. PH15 engages peripheral receptors in nasal chemosensory neurons (NCNs)
3. Once stimulated with PH15, NCNs then trigger subgroups of neurons in the olfactory bulbs (OBs)
4. Neurons in the OBs then directly stimulate neurons in several areas of the basal forebrain including the hippocampus, amygdala, and piriform cortex

Activity Increases

Increased activity in the hippocampus is responsible for improvement in cognitive function

Increased activity in the limbic amygdala in turn increases activity in the cerebral cortex, leading to improved psychomotor function

Sources: Monti L, and Liebowitz MR (2020). Neural circuits of anxiolytic and antidepressant pherine molecules. CNS Spectrums https://doi.org/10.1017/S1092852920001901X

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PH284 Nasal Spray
for Acute Treatment of
Wasting Syndrome (Cachexia)
Looking beyond the standard of care
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PH284 Nasal Spray

Potential Acute Treatment for Wasting Syndrome (Cachexia)

- ✓ Innovative, fast-acting therapy for appetite enhancement
- ✓ User-friendly intranasal administration, taken before meals
- ✓ Potential to increase subjective feelings of hunger and caloric intake in patients diagnosed with wasting syndrome, a severe consequence of many chronic diseases and advanced cancer
- ✓ Favorable tolerability and promising clinical activity
- ✓ Novel and differentiated MOA targets a neuronal circuit associated with appetite stimulation instead of a single gene, protein, neuron, or synapse, which may have therapeutic potential in wasting syndrome (cachexia)

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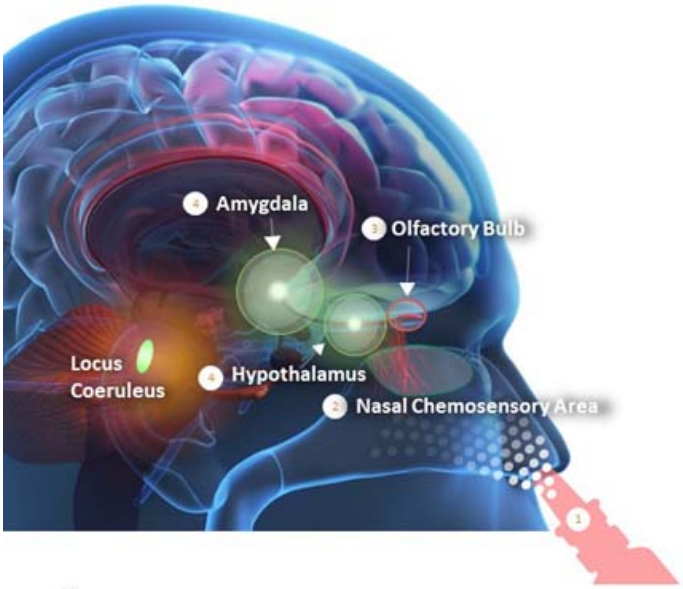
PH284 Proposed Mechanism of Action

Novel and differentiated from current treatment options



1. Microgram-level intranasal dose of PH284 is administered
2. PH284 engages peripheral receptors in nasal chemosensory neurons (NCNs)
3. Once stimulated with PH284, NCNs then trigger subsets of neurons in the olfactory bulbs (OBs)
4. Neurons in the OBs then stimulate neurons in the amygdala and the arcuate nucleus of the hypothalamus

Activity Increases

The stimulation of neurons in the arcuate nucleus of the hypothalamus increases activity of aguti-related peptide (AGRP) neurons and neuropeptide Y (NPY) neurons, which increase appetite and decrease energy expenditure

Both are key regulators of feeding, energy balance and metabolic homeostasis

Sources: Monti L, and Liebowitz MR (2020). Neural circuits of anxiolytic and antidepressant pherine molecules. CNS Spectrums https://doi.org/10.1017/S1092852920001901X

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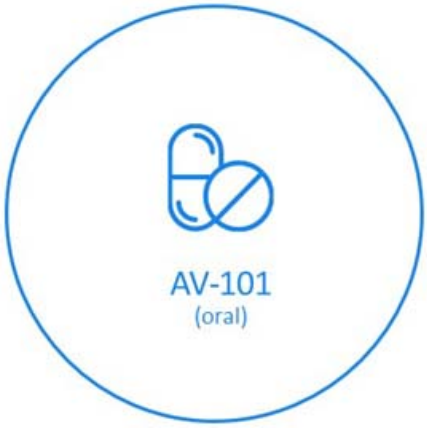
AV-101
for Potential Phase 2A Development
Looking beyond the standard of care
for disorders involving the NMDA
receptor

AV-101 for 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
- Assessing go forward potential for collaborative Phase 2A development
- FDA Fast Track designations granted for adjunctive treatment of MDD and treatment of neuropathic pain



Levodopa-Induced Dyskinesia
Associated with Parkinson's therapy

Seizures

Suicidal Ideation

Neuropathic Pain

Major Depressive Disorder

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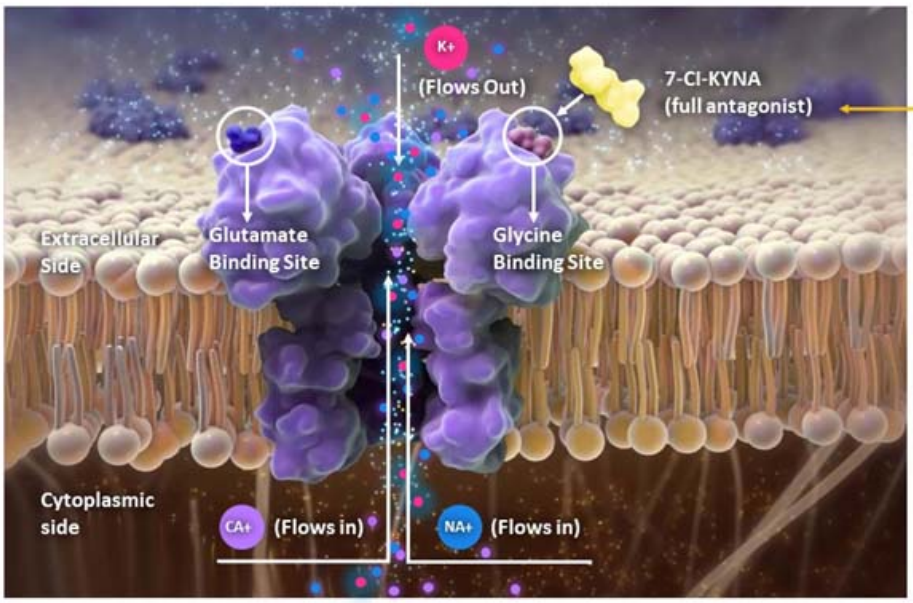
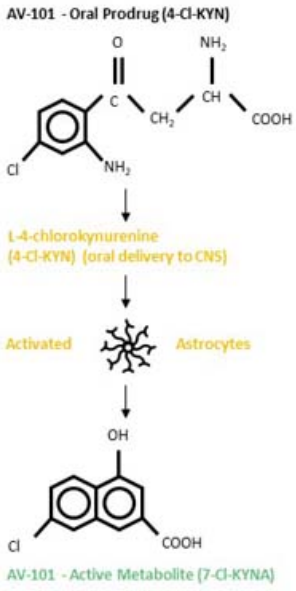
AV-101's Potential Mechanism of Action





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Distinguished Clinical and Regulatory Advisors

Representing Premier Institutions and Deep CNS and Regulatory Expertise

HARVARD UNIVERSITY

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Professor of Psychiatry, Harvard Medical School; Director, Division of Clinical Research, Massachusetts General Hospital (MGH) Research Institute; and Executive Vice Chair of the Department of Psychiatry

FDA

Thomas Laughren, M.D.

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MRN

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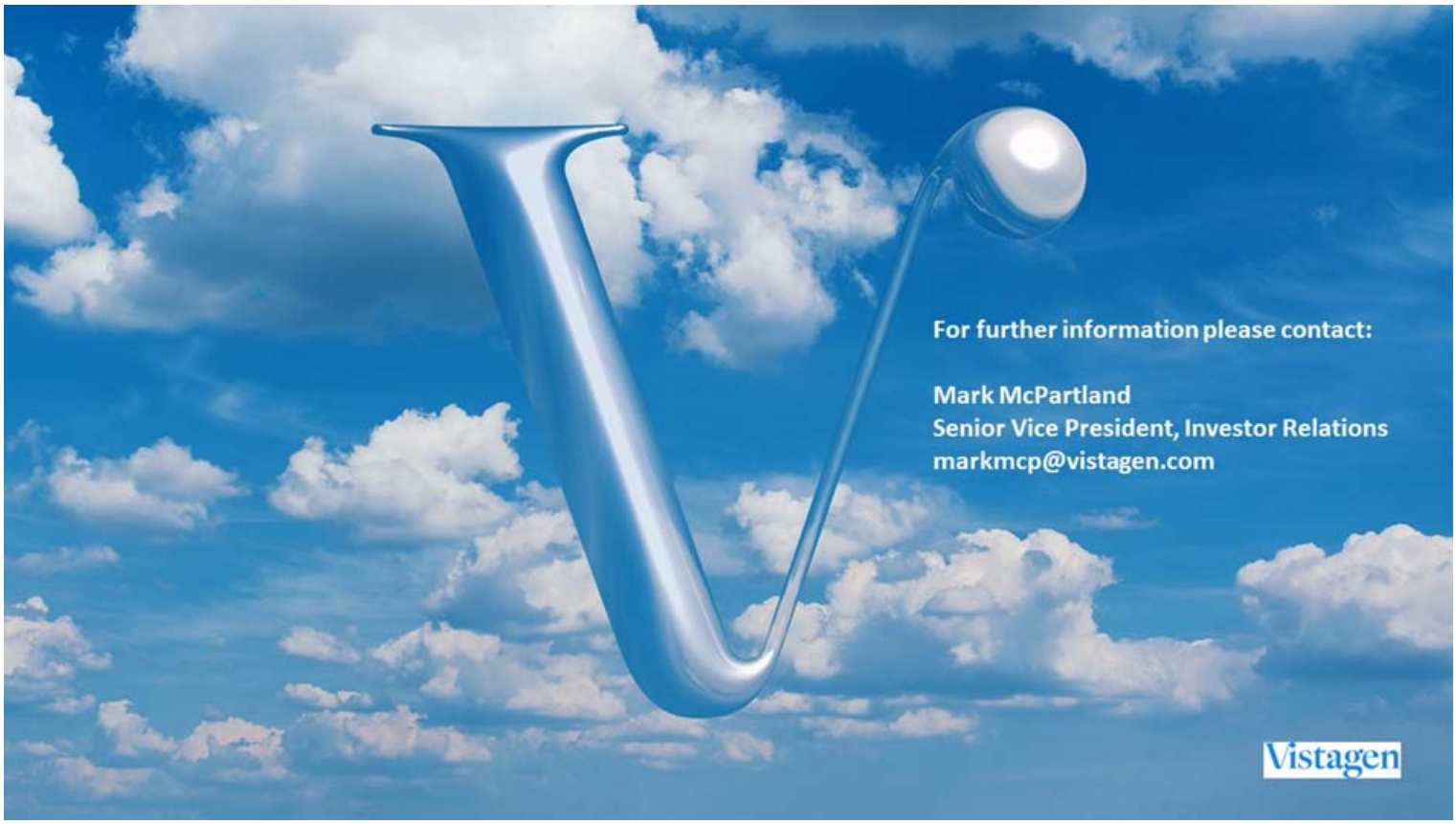
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Appendix

Fasedienol Nasal Spray for Social Anxiety Disorder (Additional Information)

Looking beyond the standard of care for anxiety disorders

Subjective Units of Distress Scale (SUDS)

Primary Efficacy Endpoint in PALISADE Phase 3 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 has become the standard for acute measurement of anxiety, now leveraged in several recent 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

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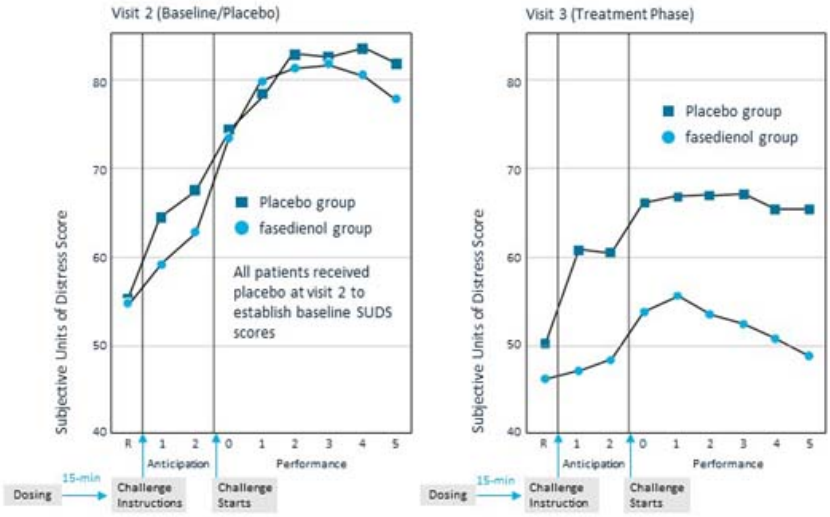
Fasedienol Efficacy in Phase 2 Public Speaking Challenge Trial

Minute-by-minute SUDS scores



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 they will have to give a 5-minute speech without notes to an audience of 3 role-players and have 2 minutes to prepare.

Source: 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.

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Liebowitz Social Anxiety Scale (LSAS)

Primary Efficacy Endpoint for Over Time Measurement

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

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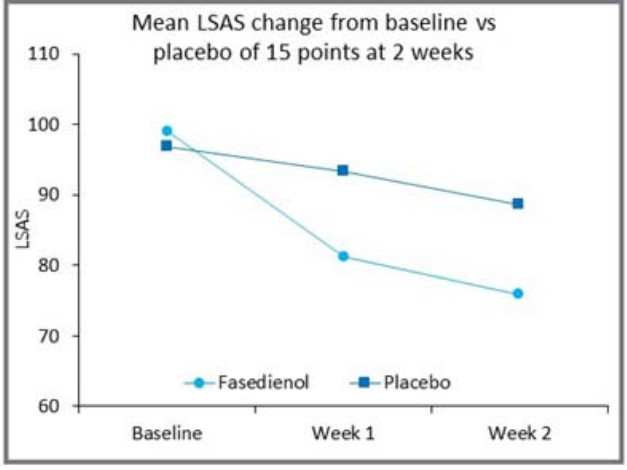
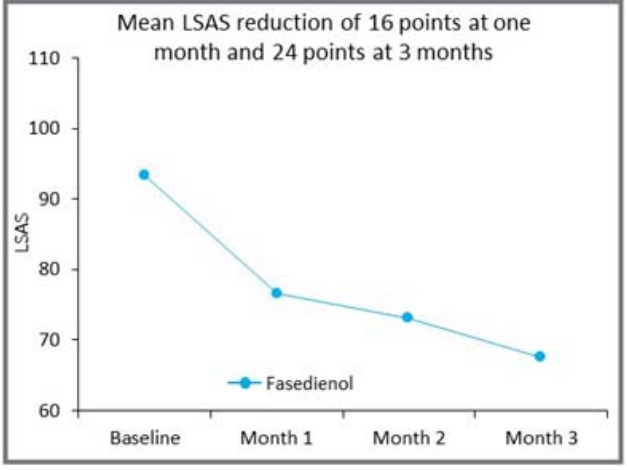
Fasedienol Efficacy Over Time as Measured by the LSAS

Fasedienol used as-needed over time has demonstrated reduction of LSAS scores in two trials

Phase 2 Crossover Study



PALISADE Open-label Safety Study



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Fasedienol Phase 1/1b Data

Well-tolerated, reduced autonomic biomarkers, increased EGNR, anxiety effects

Reduction in Autonomic Biomarkers

Statistically significant reduction in heart rate, respiratory rate, and electrodermal activity in both men and women in several studies. Intranasal 0.4 µg fasedienol also significantly increased the amplitude of the electrogram (EGNR) recorded from the nasal chemosensory epithelium in both men and women.

Increased Electrical Activity of the Nasal Chemosensory Epithelium

Dose dependent increase in electrical activity of the nasal chemosensory epithelium (EGNR) was similar in male/female healthy volunteers after ascending doses of fasedienol. Maximal EGNR amplitude was achieved at 3.2 µg dose in both men (n=10) and women (n=10). Doses higher than 6.4 µg and up to 12.8 µg did not increase EGNR amplitude and had minimal effect on the duration of the EGNR response.

Efficacy Signal in Anxiety

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

Sources:
1. Monti et al., 2014, Report CL013B; 2022, CNS Spectr 27(1):66-72; 2023, Human Psychopharmacology: Clinical and Experimental
2. 2. Liebowitz et al., 2016, Depression and Anxiety, Dec;33(12):1081-1089

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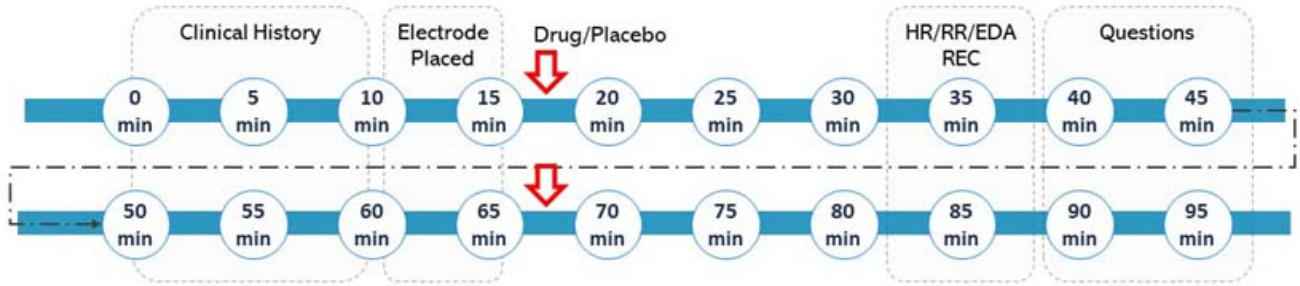
Fasedienol Reduction in Autonomic Biomarkers: Study Design

Study Goal

To study impact of fasedienol or placebo administered 30 min apart in a randomized fashion on heart rate (HR), respiratory rate (RR) and electrodermal activity (EDA) as well as electrogram of nasal receptors (EGNR)

Study Design



Criteria

Inclusion Criteria	Exclusion Criteria
+ Healthy Volunteers	— NA

Outcome Measure

- Heart rate (HR)
- Respiratory rate (RR)
- Electrodermal activity (EDA)
- Electrogram of Nasal Receptors (EGNR)

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Fasedienol Reduction in Autonomic Biomarkers: Study Results

"Physiologic biomarkers show reduced autonomic nervous system activity after intranasal administration of fasedienol in normal healthy volunteers"

- Three similarly designed Phase 1 studies were conducted in healthy volunteers (Total N=64; 32 male, 32 female) in a placebo-controlled crossover study design
- Doses ranging from 0.2 µg to 0.4 µg were administered across these studies using an experimental nasal spray device[1] that delivered low microgram doses of fasedienol or placebo locally and topically directly to the receptor area, decreasing the amount of study medication needed to activate the chemosensory receptors below the quantity administered with the metered spray pump used in clinical studies
- Physiologic biomarkers of respiratory rate, heart rate and electrodermal activity were measured in each of the 3 studies before and after administration of placebo or study medication while subjects were in a resting (no stimulation) state lying comfortably on a medical bed
- **All the physiologic measures of autonomic activity were transiently and significantly reduced in all 3 studies after intranasal administration of fasedienol, showing a reproducible sympatholytic-like effect consistent with the anxiolytic effect of fasedienol with no adverse reactions**

[1] Multifunctional Miniprobe ®; L. Monti US Patent 5,303,703

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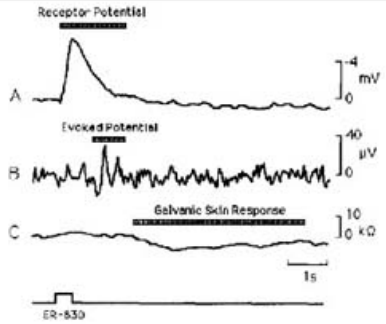
Fasedienol Electrogram of Nasal Receptors (EGNR): Study Design

Fasedienol is administered intranasally while subjects are connected to sensors



Simultaneous recordings of the receptor potential, EEG evoked potentials and galvanic skin response in a healthy human subject. Local administration of 25 pg ER-830 depolarized the receptor potential recorded from the surface nasal chemosensory mucosa while synchronizing the EEG and decreasing skin resistance.
Monti L et al. Journal of Steroid Biochemistry and Molecular Biology. 1991.

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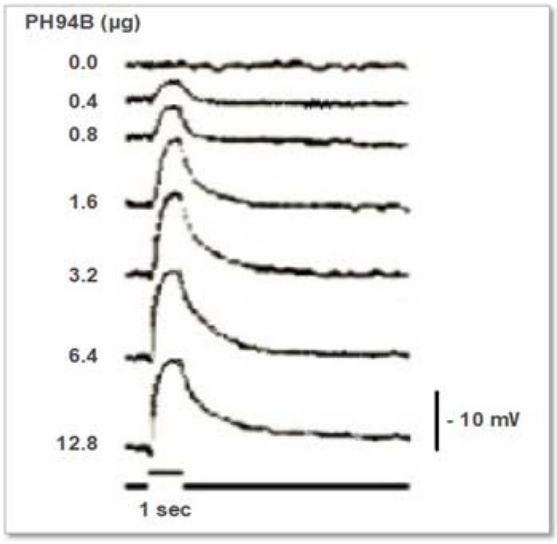
Fasedienol Electrogram of Nasal Receptors (EGNR): Study Results

Dose response led to selection of the effective dose to use in clinical trials



Dose-dependent electrical depolarization of human nasal chemosensory receptor cells in response to fasedienol

The traces show the summated response (EGNR) recorded from the nasal chemosensory receptor area in a representative human volunteer during intranasal administration of fasedienol at the quantities shown at left. Calculated 50% effective dose, ED_{50}= 1 µg.

Fasedienol 3.2 µg produced an EGNR response of maximal amplitude. Higher doses (6.4, and 12.8 µg) did not produce significant increase of EGNR amplitude and increased minimally the duration of the EGNR response.

Fasedienol 3.2 µg was selected as the effective dose to use in clinical trials.

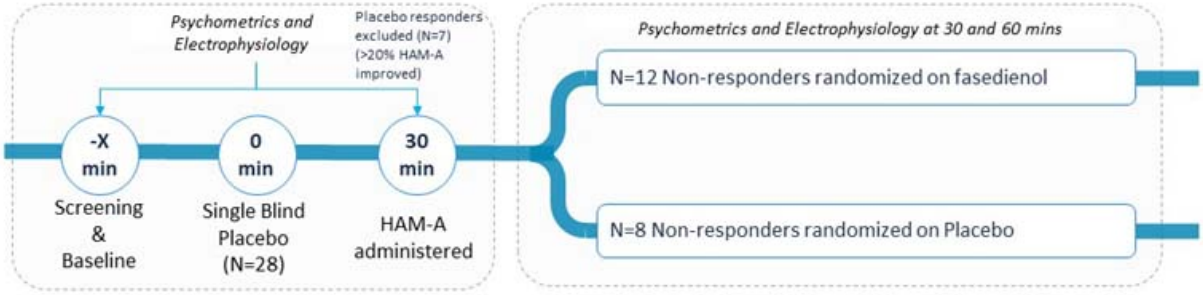
Sources: Monti et al, 2014, and 2022.

Fasedienol Generalized Anxiety Disorder: Phase 1B Study Design

Study Goal

To study the pharmacological effects of fasedienol in anxious female patients

Study Design



Criteria

Inclusion Criteria	Exclusion Criteria
+ Generalized Anxiety Disorder	— Alcohol or substance abuse
+ Females 20-45	— Any prescription meds w/in 7 days
+ HAM-A ≥ 18	— History of convulsive disorder

Outcome Measure

- Psychometrics
- Electrophysiology

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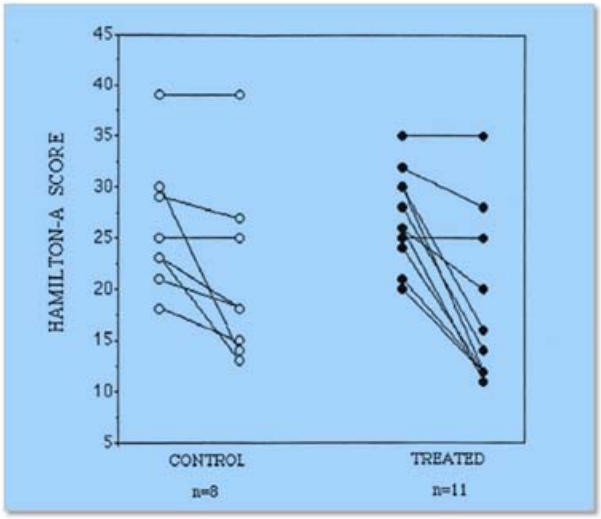
Fasedienol Generalized Anxiety Disorder: Phase 1B Study Results

Proof of concept in GAD led to the identification of SAD as the ideal indication for further clinical development



- Significant decrease in HAM-A scores within 30 min and no significant difference at 60 min
- Rapid efficacy effects without lingering effect of drug
- No adverse effects reported
- Decrease in sympathetic nervous system tone in GAD subjects similar to decrease reported in healthy volunteers

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Source: Monti L and Grosser BI, 2006