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 10, 2023

Crinetics Pharmaceuticals, Inc.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-38583**	**26-3744114**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

10222 Barnes Canyon Road, Bldg. #2	
San Diego, California	**92121**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (858) 450-6464

(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	CRNX	Nasdaq Global Select Market

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

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 September 10, 2023, Crinetics Pharmaceuticals, Inc. (the "Company" or "Crinetics") issued a press release and made available a corporate presentation announcing topline results from its Phase 3 PATHFNDR-1 study (NCT04837040). Copies of the press release and corporate presentation are attached as Exhibits 99.1 and 99.2, respectively, to this report. The corporate presentation will also be available under the "Investors" section of the Company's website. The Company intends to deliver the corporate presentation during a conference call and live webcast with the investment community on September 11, 2023, at 8:00 a.m. Eastern Time.

The information contained in this Item 7.01, including in Exhibits 99.1 and 99.2 hereto, is being "furnished" and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, is not subject to the liabilities of that section and is not deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except as shall be expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

On September 10, 2023, Crinetics announced that paltusotine, an oral, once-daily investigational compound, achieved positive results by meeting the primary endpoint and all secondary endpoints of the Phase 3 PATHFNDR-1 study (NCT04837040). PATHFNDR-1 was a randomized, double-blind, placebo-controlled 36-week treatment period followed by an optional open label extension study evaluating paltusotine in participants with acromegaly switching from standard-of-care injected depot somatostatin analogs. The study enrolled participants with acromegaly who were biochemically controlled on octreotide or lanreotide depot monotherapy. PATHFNDR-1 is one of two ongoing, placebo-controlled Phase 3 studies of once-daily, oral paltusotine.

The study met statistical significance ($p<0.0001$) on the primary endpoint, based on the proportion of participants taking paltusotine (83%) who maintained an insulin-like growth factor 1 (IGF-1) level ≤ 1.0 times the upper limit of normal (xULN) compared to those taking placebo (4%). All secondary endpoints also met statistical significance: change from baseline in IGF-1 level (xULN) ($p<0.0001$), change from baseline in Acromegaly Symptoms Diary (ASD) total score ($p=0.02$) and proportion of participants who maintained a growth hormone (GH) level of <1.0ng/mL ($p=0.0003$).

In PATHFNDR-1, paltusotine was well tolerated and no serious or severe adverse events were reported in participants treated with paltusotine. The frequency of participants with at least one treatment emergent adverse event (TEAE) was comparable in the paltusotine (PAL) treatment arm vs. placebo (PBO) arm (80% vs. 100% respectively). The most commonly reported TEAEs in paltusotine included: arthralgia (27% PAL vs. 57% PBO), headache (20% PAL vs. 36% PBO), diarrhea (23% PAL vs. 14% PBO), abdominal pain (17% PAL vs. 11% PBO) and nausea (10% PAL vs. 7% PBO). The frequency of adverse events considered related to acromegaly was notably lower in paltusotine treated participants compared to placebo treated participants (30% vs. 86% respectively).

A full analysis of the PATHFNDR-1 results is underway, which the Company expects to present at upcoming scientific conferences. PATHFNDR-2, a Phase 3 study of oral paltusotine in participants with acromegaly who are treatment-naïve or not currently receiving medical therapy, is fully enrolled and topline data are expected in the first quarter of 2024. Pending successful findings from the PATHFNDR-2 study, Crinetics plans to submit a new drug application to the U.S. Food and Drug Administration in 2024 seeking regulatory approval for all acromegaly patients who require pharmacotherapy, including newly diagnosed patients and those switching from other therapies.

The Company is also conducting an open-label Phase 2 study to evaluate paltusotine in patients with carcinoid syndrome and expects to report interim results later this year.

The PATHFNDR Program consists of two Phase 3 double-blind, placebo-controlled studies. PATHFNDR-1 (NCT04837040) enrolled a total of 58 adults with acromegaly who entered with an IGF-1 level ≤ 1.0 xULN on octreotide or lanreotide depot monotherapy. They were randomized to receive once-daily, oral paltusotine for 36 weeks or placebo. PATHFNDR-2 (NCT05192382) enrolled 112 adults with acromegaly who had elevated IGF-1 levels but were medication naïve or were not being treated with pharmacotherapy (untreated patients).

The primary endpoint for both studies is the proportion of patients achieving IGF-1 ≤1.0 xULN compared to placebo. If successful, Crinetics believes these studies could support registration of paltusotine in the United States and Europe for all acromegaly patients who require pharmacotherapy, including untreated patients and those switching from standard of care.

Forward-Looking Statements

This report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical facts contained in this report are forward-looking statements, including statements regarding the plans and timelines for the clinical development of paltusotine, including the therapeutic potential and clinical benefits or safety profile thereof; the expected timing of topline data from

the ongoing Phase 3 clinical study of paltusotine in acromegaly and Phase 2 study of paltusotine in carcinoid syndrome; plans to submit data from the ongoing Phase 3 clinical studies of paltusotine in acromegaly to regulators in support of applications seeking approval for the use of paltusotine in acromegaly patients and the expected timing of an NDA submission for paltusotine for the treatment for all acromegaly patients who require pharmacotherapy; and the potential for any of our ongoing clinical studies to show safety or efficacy. These forward-looking statements speak only as of the date of this report and are subject to a number of risks, uncertainties and assumptions, including, without limitation, topline data that we report may change following a more comprehensive review of the data related to the clinical studies and such data may not accurately reflect the complete results of a clinical study, and the FDA and other regulatory authorities may not agree with our interpretation of such results; we may not be able to obtain, maintain and enforce our patents and other intellectual property rights, and it may be prohibitively difficult or costly to protect such rights; the COVID-19 pandemic and other geopolitical events may disrupt Crinetics' business and that of the third parties on which it depends, including delaying or otherwise disrupting its clinical studies and preclinical studies, manufacturing and supply chain, or impairing employee productivity; unexpected adverse side effects or inadequate efficacy of the company's product candidates that may limit their development, regulatory approval and/or commercialization; the company's dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the success of Crinetics' clinical studies and nonclinical studies; regulatory developments in the United States and foreign countries; clinical studies and preclinical studies may not proceed at the time or in the manner expected, or at all; the timing and outcome of research, development and regulatory review is uncertain, and Crinetics' drug candidates may not advance in development or be approved for marketing; Crinetics may use its capital resources sooner than expected; any future impacts to our business resulting from geopolitical developments outside our control; and the other risks and uncertainties described in the company's periodic filings with the SEC. The events and circumstances reflected in the company's forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Additional information on risks facing Crinetics can be found under the heading "Risk Factors" in Crinetics' periodic reports, including its annual report on Form 10-K for the year ended December 31, 2022. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by applicable law, Crinetics does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release dated September 10, 2023
99.2	Corporate Presentation
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 hereunto duly authorized.

Crinetics Pharmaceuticals, Inc.

Date: September 11, 2023

By: /s/ R. Scott Struthers, Ph. D.
R. Scott Struthers, Ph. D.
President and Chief Executive Officer

Crinetics' Once-Daily Oral Paltusotine Achieved the Primary and All Secondary Endpoints in the Phase 3 PATHFNDR-1 Study Evaluating Treatment of Patients with Acromegaly

83% of Participants on Paltusotine Maintained IGF-1 ≤1.0 xULN vs. 4% on placebo (p<0.0001)

Mean IGF-1 Levels Were Maintained on Paltusotine vs. an Increase on Placebo (p<0.0001) After Switching from Injected Depot Standard of Care

Mean Acromegaly Symptom Diary Scores Were Maintained on Paltusotine vs. an Increase on Placebo (p=0.02) After Switching from Injected Depot Standard of Care

Paltusotine Was Well-Tolerated with No Severe or Serious Adverse Events

Management Will Host a Conference Call Monday, September 11, 2023 at 8:00 a.m. Eastern Time

SAN DIEGO – September 10, 2023 – Crinetics Pharmaceuticals, Inc. (Nasdaq: CRNX) today announced that paltusotine, an oral, once-daily investigational compound, achieved positive results by meeting the primary endpoint and all secondary endpoints of the Phase 3 PATHFNDR-1 study (NCT04837040). PATHFNDR-1 was a randomized, double-blind, placebo-controlled 36-week treatment period followed by an optional open-label extension study evaluating paltusotine in participants with acromegaly switching from standard-of-care injected depot somatostatin analogs. The study enrolled participants with acromegaly who were biochemically controlled on octreotide or lanreotide depot monotherapy. PATHFNDR-1 is one of two ongoing, placebo-controlled Phase 3 studies of once-daily, oral paltusotine.

The study met statistical significance (p<0.0001) on the primary endpoint, based on the proportion of participants taking paltusotine (83%) who maintained an insulin-like growth factor 1 (IGF-1) level ≤ 1.0 times the upper limit of normal (xULN) compared to those taking placebo (4%). All secondary endpoints also met statistical significance:

	Paltusotine (n=30)	Placebo (n=28)	p-value
Primary Endpoint:			
Proportion of participants who maintained an IGF-1 level ≤ 1.0 xULN, % (n)	83% (25/30)	4% (1/28)	<0.0001
Secondary Endpoints:			
Change from baseline in IGF-1 level (xULN)*	0.04 ± 0.09	0.83 ± 0.10	<0.0001
Change from baseline in Acromegaly Symptoms Diary (ASD) total score*	-0.6 ± 1.5	4.6 ± 1.6	0.02
Proportion of participants who maintained a growth hormone (GH) level of <1.0ng/mL, % (n)**	87% (20/23)	28% (5/18)	0.0003

* Least Squares Mean ± standard error
** In participants with baseline GH <1.0 ng/mL

"The results of PATHFNDR-1 are relevant to the patients we see every day in clinical practice who are biochemically controlled on standard-of-care injections. My colleagues and I are increasingly convinced many patients would appreciate an oral alternative which confers similar benefits without the burden and discomfort of the injections," stated Monica R. Gadelha, M.D., Ph.D., professor of endocrinology at the Medical School of the Universidade Federal do Rio de Janeiro and a principal investigator in the PATHFNDR program. "This

study demonstrated that the transition to paltusotine was done seamlessly and the results showed once-daily, oral paltusotine maintained both symptom control as well as biochemical control when switching from monthly injections."

In PATHFNDR-1, paltusotine was well tolerated and no serious or severe adverse events were reported in participants treated with paltusotine. The frequency of participants with at least one treatment emergent adverse event (TEAE) was comparable in the paltusotine (PAL) treatment arm vs placebo (PBO) arm (80% vs. 100% respectively). The most commonly reported TEAEs in paltusotine included: arthralgia (27% PAL vs. 57% PBO), headache (20% PAL vs. 36% PBO), diarrhea (23% PAL vs. 14% PBO), abdominal pain (17% PAL vs. 11% PBO) and nausea (10% PAL vs. 7% PBO). The frequency of adverse events considered related to acromegaly was notably lower in paltusotine treated participants compared to placebo treated participants (30% vs. 86% respectively).

"We designed paltusotine to be the preferred therapeutic option for people living with acromegaly. We could not be more excited by the results from PATHFNDR-1, which further reinforce our conviction that, if approved, paltusotine could address patients' unmet need for a simple, oral, once-daily therapy. These data showed that upon switching from injected standard of care, paltusotine provided reliable, durable control of their disease. We intend to seek regulatory approval as quickly as possible once we complete the PATHFNDR-2 study early next year," said Scott Struthers, Ph.D., founder and chief executive officer of Crinetics. "I would like to express my deep gratitude to the study participants, clinical staff, and Crinetics' employees around the world who contributed to the success of this high-quality clinical study and who have worked so hard to bring this potential medicine for people living with acromegaly one major step closer to fruition."

"These robust results for paltusotine reaffirm the strength of Crinetics' core platform for creating high quality, small molecule, oral drugs that act at G-protein coupled receptors," added Stephen Betz, Ph.D., founder and chief scientific officer of Crinetics. "I am extremely excited to continue to explore the utility of paltusotine for the treatment of carcinoid syndrome, as well as advance the rest of our innovative pipeline of internally discovered investigational compounds for people who live with other endocrine diseases including congenital adrenal hyperplasia, Cushing's disease, hyperparathyroidism, Graves' disease, hyperinsulinism, diabetes, and obesity. Paltusotine is an important lead program, and we're just getting started."

A full analysis of the PATHFNDR-1 results is underway, which the Company expects to present at upcoming scientific conferences. PATHFNDR-2, a Phase 3 study of oral paltusotine in participants with acromegaly who are treatment-naïve or not currently receiving medical therapy, is fully enrolled and topline data are expected in the first quarter of 2024. Pending successful findings from the PATHFNDR-2 study, Crinetics plans to submit a new drug application to the U.S. Food and Drug Administration in 2024 seeking regulatory approval for all acromegaly patients who require pharmacotherapy, including newly diagnosed patients and those switching from other therapies.

The Company is also conducting an open-label Phase 2 study to evaluate paltusotine in patients with carcinoid syndrome and intends to report preliminary results later this year.

Data Review Conference Call

Crinetics will hold a conference call and live webcast on Monday, September 11, 2023 at 8:00 a.m. Eastern Time to discuss topline results from the PATHFNDR-1 study. To participate, please dial 1-877-451-6152 (domestic) or 1-201-389-0879 (international) and refer to conference ID 13740941. To access the webcast, click here. Following the live event, a replay will be available on the of the Company's website.

About the PATHFNDR Program

The PATHFNDR Program consists of two Phase 3 double-blind, placebo-controlled studies. PATHFNDR-1 (NCT04837040) enrolled a total of 58 adults with acromegaly who entered with an IGF-1 level ≤ 1.0 xULN on octreotide or lanreotide depot monotherapy. They were randomized to receive once-daily, oral paltusotine for 36 weeks or placebo. PATHFNDR-2 (NCT05192382) enrolled 112 adults with acromegaly who had elevated IGF-1 levels but were medication naïve or were not being treated with pharmacotherapy (untreated patients).

The primary endpoint for both studies is the proportion of patients achieving IGF-1 ≤1.0 xULN compared to placebo. If successful, Crinetics believes these studies could support registration of paltusotine in the United States and Europe for all acromegaly patients who require pharmacotherapy, including untreated patients and those switching from standard of care.

About Acromegaly

Acromegaly is a serious rare disease generally caused by a pituitary adenoma, a benign tumor in the pituitary that secretes growth hormone (GH). Excess GH secretion causes excess secretion of IGF-1 from the liver. Prolonged exposure to increased levels of IGF-1 and GH leads to progressive and serious systemic complications, often resulting in bone, joint, cardiovascular, metabolic, cerebrovascular, or respiratory disease. Acromegaly symptoms include headache, joint aches, fatigue, sleep apnea, severe sweating, hyperhidrosis/oily skin, bone and cartilage overgrowth, abnormal growth of hands and feet, enlargement of heart, liver, and other organs and alteration of facial features. Uncontrolled acromegaly results in increased mortality and has a debilitating impact on daily functioning and quality of life.

Surgical removal of pituitary adenomas, if possible, is the preferred initial treatment for most acromegaly patients. Pharmacotherapy is used for patients who are not candidates for surgery, or when surgery is unsuccessful in achieving treatment goals. Approximately 50% of patients with acromegaly prove to be candidates for pharmacotherapy. Injectable depot somatostatin analogues are the most common initial pharmacologic treatment; however, these drugs require monthly depot injections with large gauge needles that are commonly associated with pain, injection site reactions, and an increased burden on the lives of patients.

About Paltusotine

Paltusotine is the first oral, once-daily selectively targeted somatostatin receptor type 2 (SST2) agonist and is currently in Phase 3 investigational studies. It was designed by the Crinetics discovery team to provide an efficacious and convenient once-daily option for people living with acromegaly and neuroendocrine tumors. In Phase 2 studies and the recently completed PATHFNDR-1 Phase 3 study, paltusotine maintained IGF-1 levels in acromegaly patients who switched from monthly injectable medications to paltusotine. IGF-1 is the primary biomarker endocrinologists use to manage their acromegaly patients.

About Crinetics Pharmaceuticals

Crinetics Pharmaceuticals is a clinical stage pharmaceutical company focused on the discovery, development, and commercialization of novel therapeutics for endocrine diseases and endocrine-related tumors. Paltusotine, an investigational, first-in-class, oral somatostatin receptor type 2 (SST2) agonist, is in Phase 3 clinical development for acromegaly and Phase 2 clinical development for carcinoid syndrome associated with neuroendocrine tumors. Crinetics has demonstrated pharmacologic proof-of-concept in a Phase 1 clinical study for CRN04894 a first-in-class, investigational, oral ACTH antagonist, that is currently in Phase 2 clinical studies for the treatment of Cushing's disease and congenital adrenal hyperplasia. All of the Company's drug candidates are orally delivered, small molecule new chemical entities resulting from in-house drug discovery efforts, including additional discovery programs addressing a variety of endocrine conditions such as hyperparathyroidism, polycystic kidney disease, Graves' disease, thyroid eye disease, hyperinsulinism, diabetes and obesity.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical facts contained in this press release are forward-looking statements, including statements regarding the plans and timelines for the clinical development of paltusotine, including the therapeutic potential and clinical benefits or safety profile thereof; the expected timing of topline data from the ongoing Phase 3 clinical study of paltusotine in acromegaly and Phase 2 and Phase 3 studies of paltusotine in carcinoid syndrome; plans to submit data from the ongoing Phase 3 clinical studies of paltusotine in acromegaly to regulators in support of applications seeking approval for the use of paltusotine in acromegaly patients and the expected timing of an NDA submission for paltusotine for the treatment for all acromegaly patients who require pharmacotherapy; our product candidates for patients who live with endocrine diseases including congenital adrenal hyperplasia, Cushing's disease, hyperparathyroidism, Graves' disease, hyperinsulinism, diabetes and obesity; the potential for any of our ongoing clinical studies to show safety or efficacy; and our plans to identify and create new drug candidates for additional diseases. These forward-looking statements speak only as of the date of this press release and are subject to a number of risks, uncertainties and assumptions, including, without limitation, topline data that we report may change following a more comprehensive review of the data related to the clinical studies and such data may not accurately reflect the complete results of a clinical study, and the FDA and other regulatory authorities may not agree with our interpretation of such results; we may not be able to obtain, maintain and enforce our patents and other intellectual property rights, and it may be prohibitively difficult or costly to protect such rights; the COVID-19 pandemic and other geopolitical events may disrupt Crinetics' business and that of the third parties on which it depends, including delaying or otherwise disrupting its clinical studies and preclinical studies, manufacturing and supply chain, or impairing employee productivity; unexpected adverse side effects or inadequate efficacy of the company's product candidates that may limit their development, regulatory approval and/or commercialization; the company's dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the success of Crinetics' clinical studies and nonclinical studies; regulatory developments in the United States and foreign countries; clinical studies and preclinical studies may not proceed at the time or in the manner expected, or at all; the timing and outcome of research, development and regulatory review is uncertain, and Crinetics' drug candidates may not advance in development or be approved for marketing; Crinetics may use its capital resources sooner than expected; any future impacts to our business resulting from geopolitical developments outside our control; and the other risks and uncertainties described in the company's periodic filings with the SEC. The events and circumstances reflected in the company's forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Additional information on risks facing Crinetics can be found under the heading "Risk Factors" in Crinetics' periodic reports, including its annual report on Form 10-K for the year ended December 31, 2022. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by applicable law, Crinetics does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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Exhibit 99.2

Crinetics Pharmaceuticals

PATHFNDR-1

Paltusotine Acromegaly Therapy Featuring a Non-Invasive Daily Regimen

TOPLINE RESULTS FROM PALTUSOTINE PHASE 3 PATHFNDR-1 STUDY

A Randomized, Placebo-Controlled, Multi-Center Study to Evaluate the Safety and Efficacy of Paltusotine in Subjects with Acromegaly Treated with Long-acting Somatostatin Receptor Ligands

SAFE HARBOR STATEMENT

This presentation contains forward-looking statements. Crinetics Pharmaceuticals, Inc. ("Crinetics") cautions you that statements contained in this presentation regarding matters that are not historical facts are forward-looking statements. These statements are based on the company's current beliefs and expectations. Such forward-looking statements include, but are not limited to, statements regarding: the potential benefits of paltusotine for acromegaly patients and patients with carcinoid syndrome; the potential for the PATHFNDR program to support registration of paltusotine for all acromegaly patients who require pharmacotherapy; the expected timing of topline data from the PATHFNDR-2 study and the Phase 2 and Phase 3 studies in patients with carcinoid syndrome and the expected timing of the submission of a new drug application for paltusotine for the treatment of acromegaly and related open label extension studies. In some cases, you can identify forward-looking statements by terms such as "may," "believe," "anticipate," "could," "should," "estimate," "expect," "intend," "plan," "project," "will," "forecast," "laying the foundation," "aspiring," "target" and similar terms.

These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, without limitation: topline data that we report may change following a more comprehensive review of the data related to the clinical studies and such data may not accurately reflect the complete results of a clinical study, and the FDA and other regulatory authorities may not agree with our interpretation of such results; the risk that preliminary results of preclinical studies or clinical studies do not necessarily predict final results and that one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data, and as more patient data become available; potential delays in the commencement, enrollment and completion of clinical studies and the reporting of data therefrom; the FDA or other regulatory agencies may require additional clinical studies of paltusotine or suggest changes to our planned Phase 3 clinical studies prior to and in support of the approval of a New Drug Application or applicable foreign regulatory approval; the COVID-19 pandemic may disrupt our business and that of the third parties on which we depend, including delaying or otherwise disrupting our clinical studies and preclinical studies, manufacturing and supply chain, or impairing employee productivity; our dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the success of our clinical studies, nonclinical studies and preclinical studies for paltusotine; regulatory developments or price restrictions in the United States and foreign countries; unexpected adverse side effects or inadequate efficacy of our product candidates that may limit their development, regulatory approval and/or commercialization; our ability to obtain and maintain intellectual property protection for our product candidates; we may use our capital resources sooner than we expect; and other risks described under the heading "Risk Factors" in documents we file from time to time with the Securities and Exchange Commission ("SEC"). Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and, except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

PATHFNDR-1 Met the Primary and All Secondary Endpoints and Paltusotine Was Well-Tolerated

PRIMARY ENDPOINT

- ☑ **83% of participants on paltusotine maintained IGF-1 ≤ 1.0xULN vs 4% on placebo (p<0.0001)**

SECONDARY ENDPOINTS (paltusotine arm vs. placebo)

- ☑ **Change from baseline in IGF-1 (p<0.0001)**
- ☑ **Change from baseline in Acromegaly Symptoms Diary score (p=0.02)**
- ☑ **Proportion of participants who maintained GH <1.0 ng/mL (p=0.0003)**

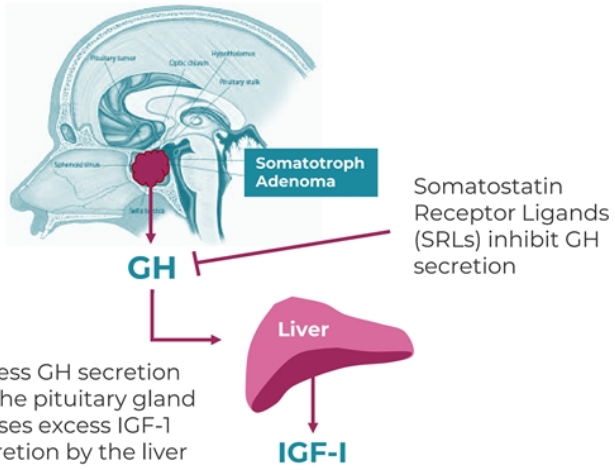
SAFETY

- ☑ **Paltusotine was well-tolerated with no severe or serious adverse events**
- ☑ **Paltusotine demonstrated no new safety signals**

Paltusotine is an investigational drug in clinical studies for the treatment of acromegaly and carcinoid syndrome

What is Acromegaly?

Acromegaly is caused by a benign pituitary tumor secreting excess growth hormone (GH)
Uncontrolled acromegaly is debilitating and increases risk of early death



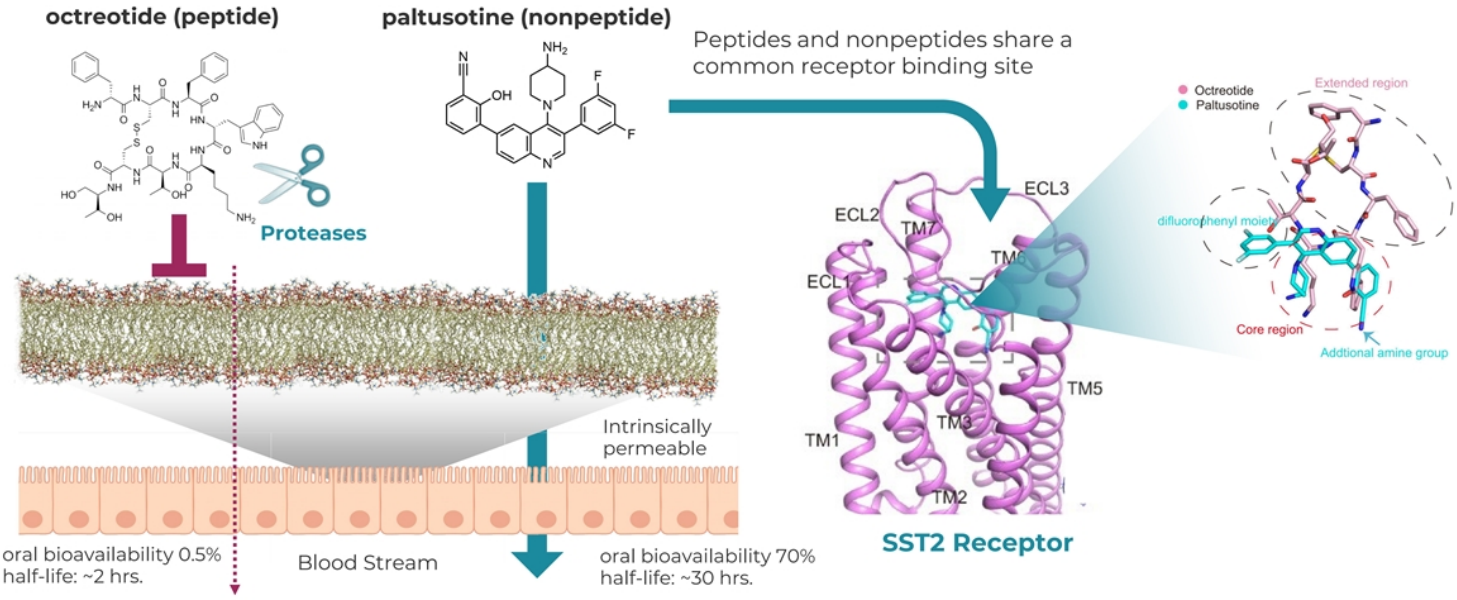
- Changed Facial Features
- Prognathism
- Enlarged Hands
- Carpel Tunnel
- Arthritis

- Hypertension
- Hypopituitarism
- Hepatomegaly
- Impaired Glucose
- Thyroid Hypertrophy

- Headache
- Vision Defects
- Perspiration
- Joint Pain
- Swelling
- Respiratory Issues

Sources: http://www.fipapatients.org; Bex M, Abs R, T'Sjoen G, et al. Eur J Endocrinol. 2007;157(4):399-409

Paltusotine Was Designed as the First Once-Daily, Oral, Selectively Targeted SST2 Agonist



Sources: Madan et al. Pituitary, (2022) 25:328-339; Heo, Yoon et al. eLife (2022);0:e76823; Zhao et al. Nature Commun, (2023) 14, 962

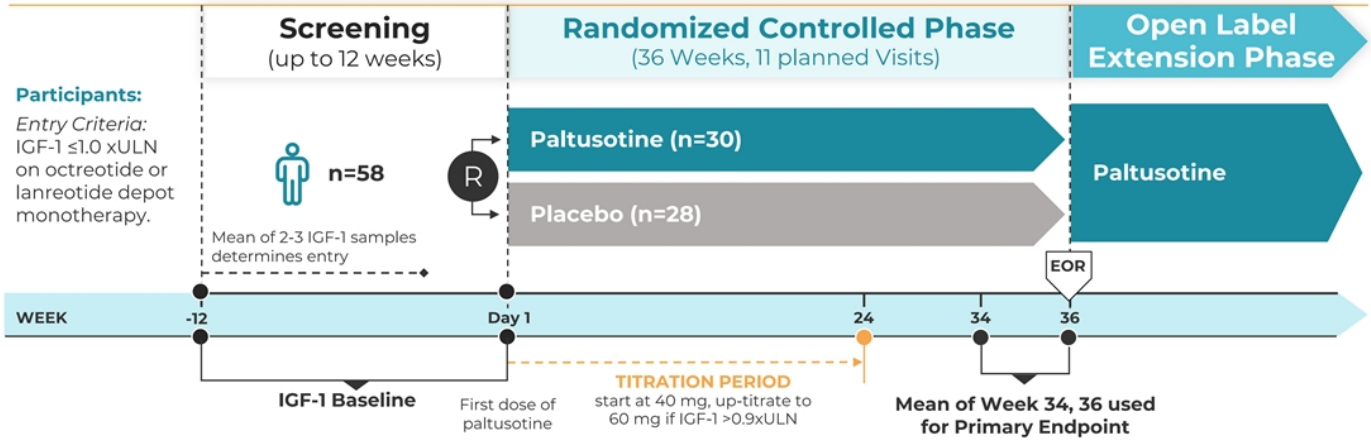
Goal for Paltusotine:
Help People to Focus on Living Life

Current Standard of Care	Disease Control	Tolerability	Patient Experience
	**Poor symptom control:** worsening of symptoms at the end of each injection cycle[1,2]	**Treatment-related injection site reactions** reported by 77% of patients on monthly SRLs[3]	Depot SRL injections are **painful and often need to be administered in a doctor's office**
Potential Benefits of Paltusotine* 	**Reliable, consistent and durable IGF-1 control**	**No injections** **Well tolerated** with no severe or serious adverse events	**Once daily oral tablet** has potential to reduce strain on daily routine and healthcare system

* If paltusotine receives regulatory approval. Clinical studies to support applications for regulatory approval are ongoing.

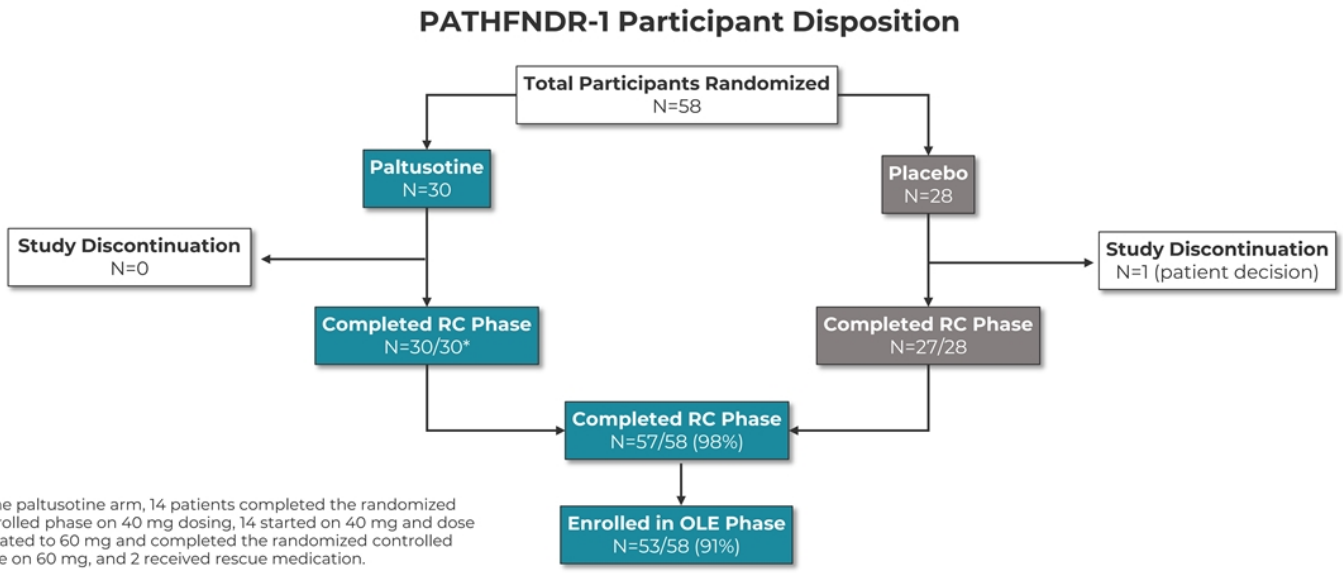
SRL: Somatostatin receptor ligand; Sources: 1. Geer et al. BMC Endocrine Disorders, (2020) 20:117; 2. Strasburger et al. European Journal of Endocrinology, (2016) 174; 3. Fleseriu et al. Frontiers in Endocrinology; March 2021, Vol.12

Evaluated Participants Switching from Standard of Care Depots to Once Daily Oral Paltusotine



Primary Endpoint: Proportion of patients with IGF-1 ≤1.0 xULN (mean of samples from weeks 34 and 36)
IGF-1 Baseline: Mean of 3-4 IGF-1 samples (including Day 1 sample) prior to start of study drug dosing.
EOR: End of Randomized Controlled Phase. If participant is rescued, then last observation prior to rescue is used for EOR value.
Rescue: Participant received injected SRL and was classified as a non-responder if there were two consecutive IGF-1 ≥ 1.3 xULN on 60 mg *AND* exacerbation of acromegaly clinical signs/symptoms as determined by the investigator.

98% of Participants Completed the Randomized Controlled Phase of PATHFNDR-1 and 91% Enrolled in the Open Label Extension (OLE) Phase



*In the paltusotine arm, 14 patients completed the randomized controlled phase on 40 mg dosing, 14 started on 40 mg and dose escalated to 60 mg and completed the randomized controlled phase on 60 mg, and 2 received rescue medication.

Participant Characteristics

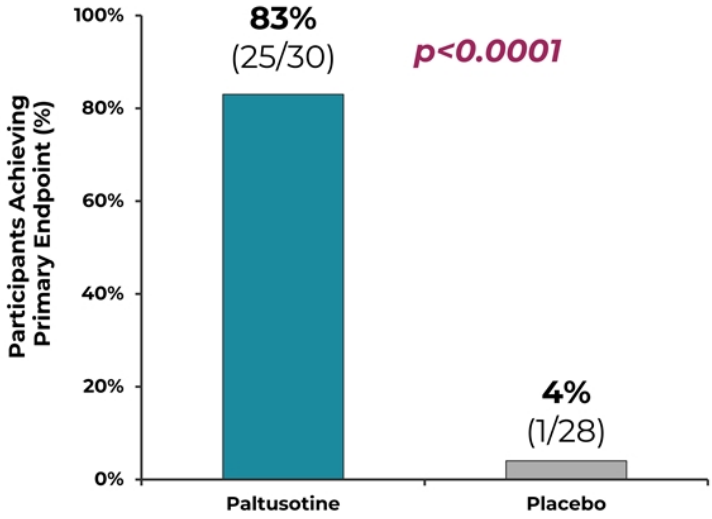
Participant Characteristics	Paltusotine N=30	Placebo N=28	Overall N=58
Female, n (%)	**15 (50%)**	**17 (61%)**	**32 (55%)**
Age at informed consent - Mean (SD), years	**55.9 (14.6)**	**53.9 (12.9)**	**54.9 (13.7)**
Weight - Mean (SD), kg	**83.7 (18.6)**	**73.2 (16.0)**	**78.6 (18.1)**
BMI - Mean (SD), kg/m²	**29.9 (5.6)**	**27.6 (5.9)**	**28.8 (5.8)**
Geography, n (%)			
United States	6 (20%)	5 (18%)	11 (19%)
Europe and Israel	13 (43%)	12 (43%)	25 (43%)
Latin America	11 (37%)	11 (39%)	22 (38%)

Disease Characteristics

Disease Characteristics and Previous Treatment	Paltusotine N=30	Placebo N=28	Overall N=58
Duration since acromegaly diagnosis - Mean (SD), months	**187 (88)**	**121 (82)**	**155 (91)**
Pituitary surgery performed - n (%)	**26 (87%)**	**24 (86%)**	**50 (86%)**
Duration since pituitary surgery - Mean (SD), months	**172 (89)**	**102 (65)**	**138 (85)**
Baseline IGF-1 xULN - Mean (SD)	**0.83 (0.14)**	**0.82 (0.16)**	**0.83 (0.15)**
Baseline GH - Mean (SD), ng/mL	**0.92 (1.02)**	**0.89 (0.83)**	**0.90 (0.93)**
Prior SRL at time of screening			
Octreotide, n (%)	18 (60%)	16 (57%)	34 (59%)
Monthly Dose: 10 mg / 20 mg / ≥30 mg (n)	1 / 7 / 10	2 / 11 / 3	3 / 18 / 13
Lanreotide, n (%)	12 (40%)	12 (43%)	24 (41%)
Monthly Dose: 60 mg / 90 mg* / 120 mg (n)	2 / 4 / 6	1 / 5 / 6	3 / 9 / 12

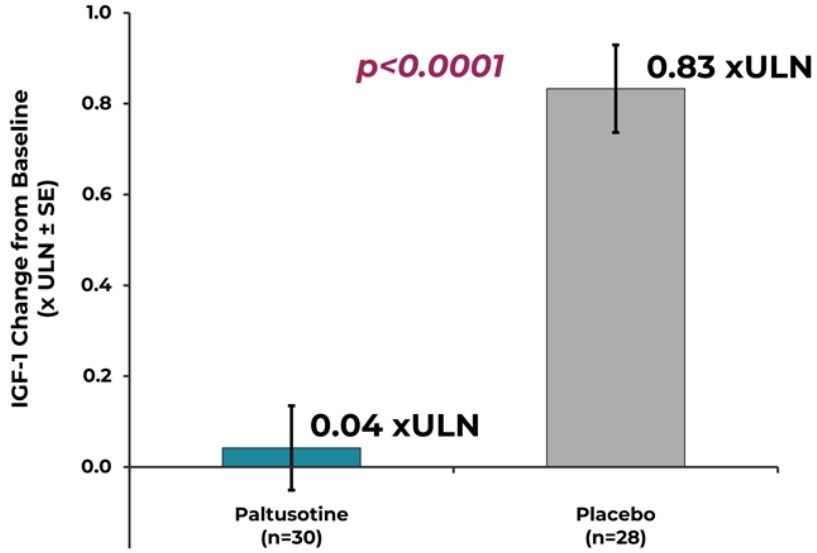
* 1 participant received 120 mg every 6 weeks and was considered part of the 90 mg group.

Primary Endpoint Achieved: 83% of Participants on Paltusotine Maintained IGF-1 ≤1.0 xULN



Participants who were rescued or stopped the assigned treatment before week 34 did not meet the protocol-defined primary endpoint.

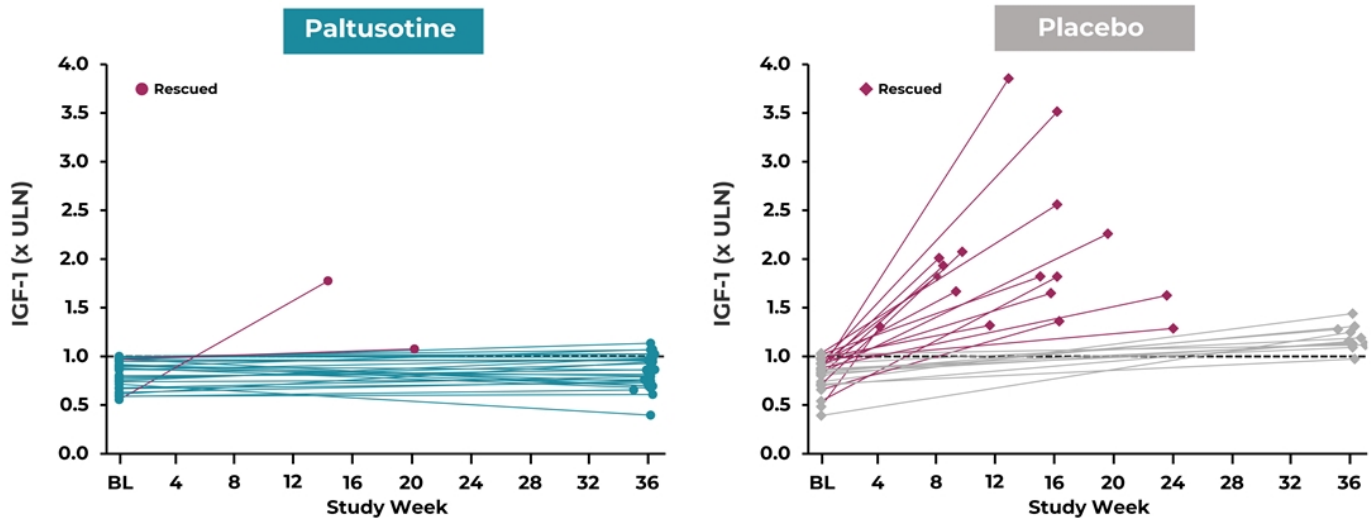
Secondary Endpoint #1 Achieved: Paltusotine Treatment Maintained Control of IGF-1



Least Squares (LS) Mean (± SE) is shown and estimated based on an analysis of covariance.
If participant was rescued, IGF-1 values measured just prior to rescue are used.

Participants on Paltusotine Maintained IGF-1 Levels

IGF-1 xULN at Baseline and End of Randomized Controlled Phase (EOR) for Each Participant



EOR: End of Randomized Controlled Phase. If participant was rescued, IGF-1 values measured prior to rescue are used.
Rescue: If there were two consecutive IGF-1 ≥ 1.3 xULN on 60 mg AND exacerbation of acromegaly clinical signs/symptoms as determined by the investigator.

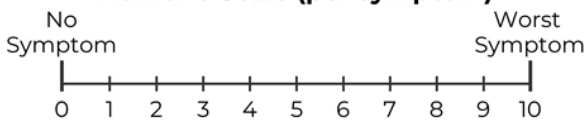
Patients Reported Symptom Severity Using the Acromegaly Symptoms Diary (ASD)

- ASD was developed in accordance with FDA guidance to evaluate symptoms of acromegaly in clinical studies*
- Seven symptoms were rated from 0 (no symptom) to 10 (worst symptom); total ASD score 0 to 70
- A daily checklist for symptoms was collected prior to and during study treatment

Symptoms Evaluated in the ASD

Headache pain
Joint pain
Sweating
Fatigue
Leg weakness
Swelling
Numbness/tingling
Total Score (0-70)

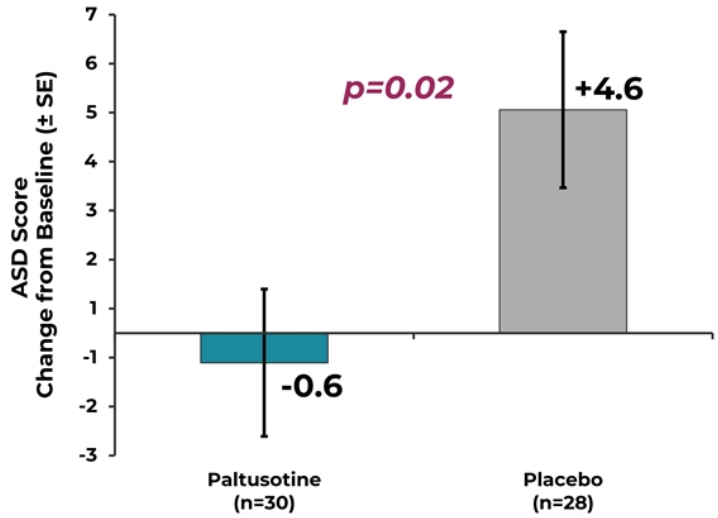
Numeric Scale (per symptom)



*Martin et al. Journal of Patient-Reported Outcomes (2023) 7:15; https://doi.org/10.1186/s41687-023-00541-7

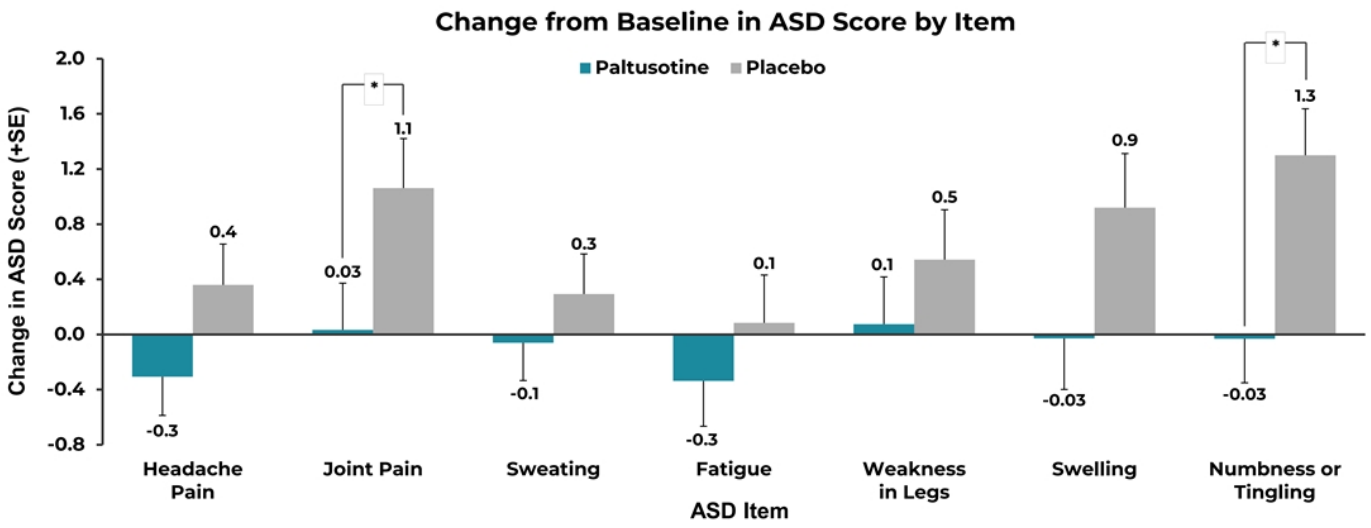
Secondary Endpoint #2 Achieved: Paltusotine Treatment Maintained Control of Acromegaly Symptoms

Change from Baseline to EOR in Total ASD Score



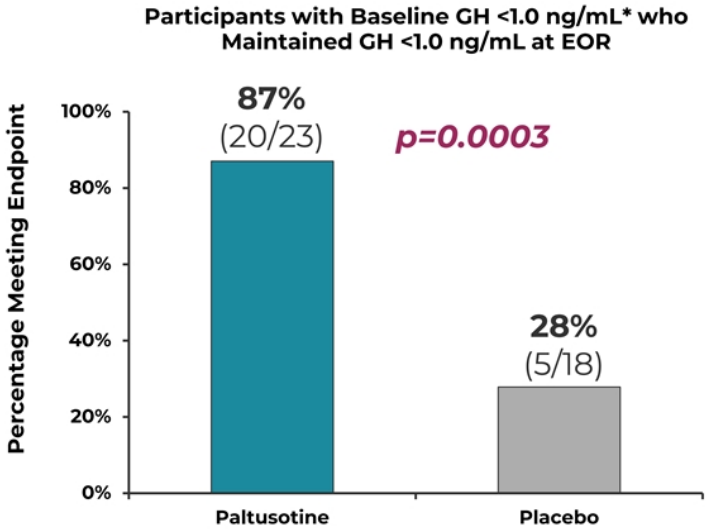
EOR: End of Randomized Controlled Phase. ASD scores measured prior to rescue or discontinuation are used.
Baseline ASD scores were 13.2 for paltusotine and 10.9 for placebo.

Paltusotine Treatment Maintained Control Across All Individual Symptom Components of ASD



*p<0.05.
EOR: End of Randomized Controlled Phase, ASD scores measured prior to rescue or discontinuation are used. Each symptom is on a 0 (no symptom) to 10 (worst symptom) scale.

Secondary Endpoint #3 Achieved: Paltusotine Treatment Maintained Growth Hormone Control



*Endocrine Society Clinical Practice guidelines recommend target GH levels < 1.0 ng/mL; Katznelson et al. J Clin Endocrinol Metab 99: 3933–3951, 2014
Participants who were rescued or stopped the assigned treatment before week 34 did not meet the protocol-defined endpoint.
EOR: End of Randomized Controlled Phase
n: 23 out 30 paltusotine participants and 18 out of 28 placebo participants entered the study with a baseline GH <1.0 ng/mL

Paltusotine was Well-Tolerated with No Severe or Serious Adverse Events

Treatment-Emergent Adverse Events	Paltusotine N=30 n (%)	Placebo N=28 n (%)
Any	**24 (80%)**	**28 (100%)**
Mild	14 (47%)	10 (36%)
Moderate	10 (33%)	15 (54%)
Severe	0	3 (11%)
Treatment-related	**11 (37%)**	**4 (14%)**
Serious		
Not treatment-related	0	1 (4%)
Treatment-related	0	0
Leading to dose reduction	**1 (3%)**	**0**
Leading to rescue	**2 (7%)**	**17 (61%)**
Leading to death	**0**	**0**

Severe TEAEs in placebo were arthralgia in 1 participant, peripheral swelling/fatigue/pain in extremity in 1 participant, and leukopenia in 1 participant.
Serious TEAE in placebo was acute cholecystitis.

PATHFNDR-1 Adverse Events Summary

Treatment Emergent Adverse Events ≥5%	Paltusotine N=30 n (%)	Placebo N=28 n (%)
Common Acromegaly Symptoms		
Arthralgia	8 (27%)	16 (57%)
Headache	6 (20%)	10 (36%)
Peripheral swelling	2 (7%)	10 (36%)
Fatigue	2 (7%)	5 (18%)
Muscular weakness	1 (3%)	3 (11%)
Paraesthesia	0	7 (25%)
Hyperhidrosis	0	4 (14%)
Common SRL Side Effects		
Diarrhoea	7 (23%)	4 (14%)
Abdominal pain	5 (17%)	3 (11%)
Nausea	3 (10%)	2 (7%)
Abdominal distension	2 (7%)	1 (4%)
Flatulence	2 (7%)	1 (4%)
Other		
Constipation	2 (7%)	4 (14%)
Urinary tract infection	2 (7%)	2 (7%)
Nasopharyngitis	2 (7%)	1 (4%)
Dyspnoea	1 (3%)	2 (7%)
Hyperglycaemia	1 (3%)	2 (7%)
Dizziness	1 (3%)	2 (7%)
Back pain	1 (3%)	2 (7%)
COVID-19	0	6 (21%)
Asthenia	0	4 (14%)
Pain in extremity	0	3 (11%)

Includes AEs occurring during rescue period. Rates were similar when rescue period is excluded.

The frequency of adverse events considered related to acromegaly was notably lower in participants treated with paltusotine compared to placebo (30% vs. 86% respectively).

PATHFNDR-1 Safety Summary

- Paltusotine was well-tolerated with no severe or serious adverse events reported in the active arm
- The most frequently (>10%) reported adverse events included arthralgia, diarrhea, headache, abdominal pain and nausea
- No safety signals were observed in vital signs, ECGs, or laboratory values during treatment with paltusotine
- No clinically significant changes were observed in pituitary tumor size as measured by MRI
- Safety results in PATHFNDR-1 comparable to that observed in entire clinical program to date

Crinetics' Approach to Address Unmet Needs of People with Acromegaly, Prescribers, and Healthcare Systems

As a trusted member of the global endocrine community, Crinetics aspires to bring the first once daily, oral selectively targeted SST2 agonist* to patients

For Patients

- Once daily oral
- Consistent symptom control
- Room temperature storage
- Home delivery
- Patient support services

For Physicians

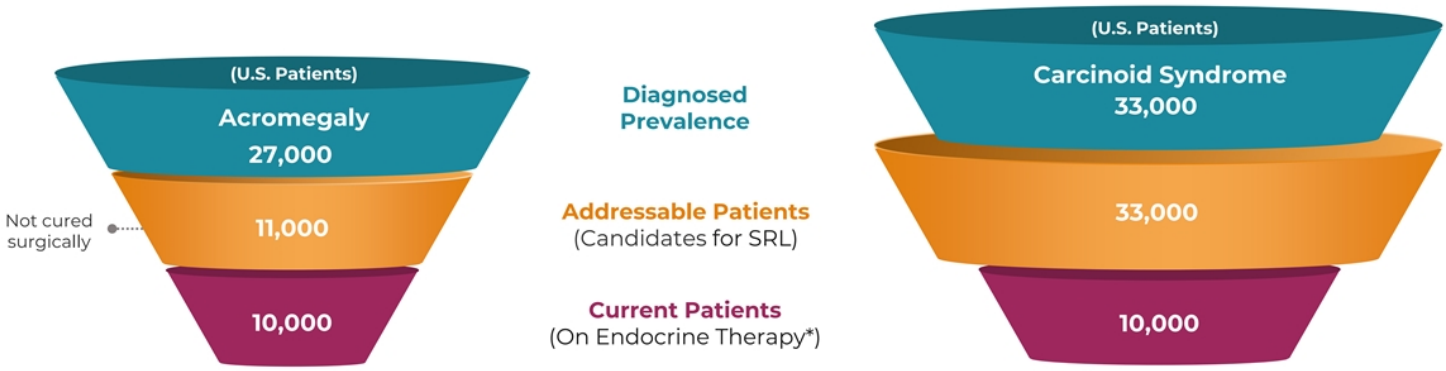
- Reliable, consistent, and durable IGF-1 control
- Simple dose selection
- Low drug interaction risk
- HCP support services

For the Healthcare System

- Potential reduced patient out-of-pocket costs
- At-home option reduces costs compared to in-office administration
- At-home option saves HCP resources

* If paltusotine receives regulatory approval. Clinical studies to support applications for regulatory approval are ongoing; HCP: Healthcare Provider.

Paltusotine: Initial Multi-Billion Dollar U.S. Market Opportunity in Acromegaly and Carcinoid Syndrome



$70K	Average Annual WAC for Injectables	$100K
$700M	Current Market for Endocrine Therapy (U.S.)	$1,000M
$800M	Total Addressable Market for Endocrine Therapy (U.S.)	$3,300M

*Endocrine therapy includes SRLs, dopamine agonists, and growth hormone antagonists
WAC: Wholesale acquisition cost; Sources: Company data on file

Anticipated Paltusotine Milestones

- **4Q23** Preliminary results from carcinoid syndrome Phase 2 study
- **1Q24** Results from PATHFNDR-2 Phase 3 study in untreated acromegaly patients
- **2024** Acromegaly NDA submission
- **2024** Anticipated carcinoid syndrome Phase 3 start
- **Ongoing:** Acromegaly open label extension studies
  - N > 120 and increasing
  - Some Phase 2 patients have been treated with paltusotine for up to 3 years

Q&A

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Chief Medical Officer