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): March 19, 2024

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.)**

6055 Lusk Boulevard **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 March 19, 2024, Crinetics Pharmaceuticals, Inc. (the "Company," "Crinetics," "we," "us," or "our") issued a press release and made available a corporate presentation announcing positive topline results from PATHFNDR-2 (NCT05192382), the second of two Phase 3 studies evaluating the efficacy and safety of oral, once-daily investigational paltusotine for the treatment of acromegaly. Copies of the press release and corporate presentation are attached as Exhibits 99.1 and 99.2, respectively, to this Current Report on Form 8-K, and are incorporated herein by reference. The press release and 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 March 19, 2024, at 8:30 a.m. Eastern Time.

The information that is solely contained in this Item 7.01 of this Current Report on Form 8-K, including in Exhibit 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.

The information regarding the press release referred to in Item 7.01 of this Current Report on Form 8-K is incorporated herein by reference. A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

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 and CRN04894, including the therapeutic potential and clinical benefits or safety profile thereof; 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 expected plans and timing for commercialization of paltusotine and other product candidates pending regulatory approval; the ability for paltusotine to effectively provide symptom control and biochemical control in acromegaly patients; and the commercialization of paltusotine as the first once-daily, oral SRL for the treatment of acromegaly; the commercial acceptance of paltusotine as a new medical treatment for acromegaly with improvements in treatment experience and access to care for patients and medical providers; the potential for our discovery program for endocrine diseases including hyperparathyroidism, polycystic kidney disease, Graves' disease, thyroid eye disease, diabetes and obesity to progress to drug candidates and 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 report and are subject to a number of known and unknown risks, uncertainties and assumptions, including, without limitation, topline results 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, the possibility of unfavorable new clinical data and further analyses of existing clinical data, and the FDA and other regulatory authorities may not agree with our interpretation of such results; and the other risks and uncertainties described in the company's periodic filings with the Securities and Exchange Commission ("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 filings with the SEC, including its annual report on Form 10-K for the year ended December 31, 2023. 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 March 19, 2024
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: March 19, 2024

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

Exhibit 99.1

Crinetics' Once-Daily Oral Paltusotine Achieved the Primary and All Secondary Endpoints in the Phase 3 PATHFNDR-2 Study in Acromegaly Patients

56% of Participants on Paltusotine Achieved IGF-1 ≤1.0 xULN vs. 5% on Placebo (p<0.0001)

Paltusotine was Generally Well-tolerated with No Serious Adverse Events

Positive Topline Results Support Planned NDA Submission to the FDA in 2H 2024

Management Will Host a Conference Call Today at 8:30 a.m. Eastern Time

SAN DIEGO – March 19, 2024 – Crinetics Pharmaceuticals, Inc. (Nasdaq: CRNX) a clinical stage pharmaceutical company focused on the discovery, development and commercialization of novel therapeutics for endocrine diseases and endocrine-related tumors, today announced positive topline results from PATHFNDR-2, the second of two Phase 3 studies evaluating the efficacy and safety of oral, once-daily investigational paltusotine for the treatment of acromegaly.

PATHFNDR-2 (NCT05192382) was a randomized, double-blind, placebo-controlled 24-week treatment period followed by an optional open-label extension study evaluating paltusotine in 111 participants with acromegaly who were not pharmacologically treated. The study met statistical significance (p<0.0001) on the primary endpoint, based on the proportion of participants taking paltusotine (56%) who achieved an insulin-like growth factor 1 (IGF-1) level ≤ 1.0 times the upper limit of normal (xULN) compared to those taking placebo (5%). All secondary endpoints also met statistical significance:

	Paltusotine (n=54)	Placebo (n=57)	p-value
Primary Endpoint:			
Proportion of participants who achieved an IGF-1 level ≤ 1.0 xULN, % (n)	56% (30/54)	5% (3/57)	<0.0001
Secondary Endpoints:			
Change from baseline in IGF-1 level (xULN)	-0.82	0.09	<0.0001
Proportion of participants who achieved IGF-1 level of <1.3 xULN at EoR*	67%	14%	<0.0001
Change from baseline in Acromegaly Symptoms Diary (ASD) total score	-2.67	2.75	0.004
Proportion of participants who achieved growth hormone (GH) level of <1.0ng/mL at EoR	57%	18%	<0.0001

* EoR: End of Randomized control phase

"These positive topline results of PATHFNDR-2 are incredibly exciting for both patients with acromegaly and the healthcare providers who treat them," 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 demonstrates that paltusotine can provide both symptom control as well as biochemical control in patients who are not currently on pharmacologic treatment. If approved, the prospect that paltusotine can offer an innovative, once-daily oral alternative represents a significant step forward in improving the treatment experience for patients."

In PATHFNDR-2, paltusotine was generally well-tolerated and no serious 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 treatment arm and placebo arm. The most commonly reported TEAEs in paltusotine-treated participants included: diarrhea, headache, arthralgia and abdominal pain. The frequency of adverse events considered related to acromegaly was notably lower in paltusotine treated participants compared to placebo treated participants.

“Paltusotine continues to exceed expectations. Today, PATHFNDR-2 delivered statistically significant topline results across the board,” said Scott Struthers, Ph.D., founder and chief executive officer of Crinetics. “Building upon the success of PATHFNDR-1, the totality of data underscores the potential of paltusotine to provide an important new treatment option for all people living with acromegaly, if approved. We intend to submit a New Drug Application (NDA) to the U.S. Food and Drug Administration in the second half of 2024, and our team is actively preparing for a potential 2025 launch. We are deeply grateful to all the individuals who participated in this study, the skilled clinical staff who provided exceptional care, and the dedicated Crinetics team from around the globe. This collective endeavor has brought an important new potential acromegaly treatment option closer to becoming a reality.”

Data Review Conference Call

Crinetics will hold a conference call and live webcast on Tuesday, March 19 at 8:30 a.m. Eastern Time to discuss topline results from the PATHFNDR-2 Phase 3 study. To participate, please dial 1-888-886-7786 (domestic) or 1-416-764-8658 (international), or request a callback here and refer to conference ID 95442954. To access the webcast, click here. A presentation to accompany the webcast can be found here. Following the live event, a replay will be available on the Investors section 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 ≤ 1.0x ULN on octreotide or lanreotide depot monotherapy. The participants were randomized to receive once-daily, oral paltusotine for 36 weeks or placebo. PATHFNDR-2 (NCT05192382) enrolled 111 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. 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 investigational Phase 3 studies for acromegaly and a Phase 2 study for carcinoid syndrome. It was designed by the Crinetics' discovery team to provide an efficacious and convenient once-daily option for people living with acromegaly and carcinoid syndrome. 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 acromegaly patients. Results from the Phase 2 study in carcinoid syndrome further support paltusotine's potential use beyond acromegaly.

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 in 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, an investigational, first-in-class, oral ACTH antagonist, that is currently in Phase 2 clinical studies for the treatment of congenital adrenal hyperplasia and Cushing's disease. 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, 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 and CRN04894, including the therapeutic potential and clinical benefits or safety profile thereof; 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 expected plans and timing for commercialization of paltusotine and other product candidates pending regulatory approval; the ability for paltusotine to effectively provide symptom control and biochemical control in acromegaly patients; and the commercialization of paltusotine as the first once-daily, oral SRL for the treatment of acromegaly; the commercial acceptance of paltusotine as a new medical treatment for acromegaly with improvements in treatment experience and access to care for patients and medical providers; the potential for our discovery program for endocrine diseases including hyperparathyroidism, polycystic kidney disease, Graves' disease, thyroid eye disease, diabetes and obesity to progress to drug candidates and 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 known and unknown risks, uncertainties and assumptions, including, without limitation, topline results 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, the possibility of unfavorable new clinical data and further analyses of existing clinical data, and the FDA and other regulatory authorities may not agree with our interpretation of such results; and the other risks and uncertainties described in the company's periodic filings with the Securities and Exchange Commission (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 filings with the SEC, including its annual report on Form 10-K for the year ended December 31, 2023. 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

pathfndr2
Paltusotine Acromegaly Therapy Featuring a Non-Invasive Daily Regimen

Crinetics Pharmaceuticals

Topline Results from Paltusotine Phase 3 PATHFNDR-2 Study

A Randomized, Placebo-Controlled, Multicenter Study to Evaluate the Safety And Efficacy of Paltusotine in Subjects with Non-pharmacologically Treated Acromegaly

March 19, 2024

Safe Harbor Statement

This presentation contains forward-looking statements. Crinetics Pharmaceuticals, Inc. ("Crinetics," the "company," "we," "us," or "our") 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 strategic objectives for paltusotine; 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 the submission of a new drug application for paltusotine for the treatment of acromegaly and related open label extension studies; plans and timing for sharing the full results of the Phase 2 study of paltusotine in carcinoid syndrome with the FDA to align on a Phase 3 program and the plans and enrollment in related open label extension studies; the potential benefits of CRN04894 in patients with Congenital Adrenal Hyperplasia or Cushing's Disease and the expected plans and timing for data and topline data readouts from ongoing clinical studies; the potential benefits of PTH receptor antagonists for patients with hyperparathyroidism, the potential benefits of TSH antagonist for Graves' Disease or thyroid eye disease; the potential for any of our ongoing clinical studies to show safety or efficacy; the potential of our ongoing discovery efforts to target future indications for hyperparathyroidism, polycystic kidney disease, Graves diseases, thyroid eye disease, or diabetes/obesity, and the expected plans and timing for candidate selection and clinical development of such candidates; our plans to identify and create new drug candidates for additional diseases or the potential for any such new drug candidates to show safety or efficacy; the direction or trajectory of the Company's potential future growth, the receipt of any revenues from product sales and the ability of such revenues to support continued growth, and our expected plans and timing for commercialization of paltusotine and other product candidates pending regulatory approval; the commercialization of paltusotine as the first once-daily, oral SRL for the treatment of acromegaly; the ability for paltusotine to effectively provide symptom control and biochemical control in acromegaly patients; and the commercial acceptance of paltusotine as a new medical treatment for acromegaly with improvements in treatment experience and access to care for patients and medical providers. In some cases, you can identify forward-looking statements by terms such as "may," "believe," "anticipate," "could," "should," "estimate," "expect," "intend," "plan," "project," "will," "contemplate," "predict," "continue," "forecast," "aspire," "lead to," "designed to," "goal," "potential," "target" or the negative of or other similar terms.

These statements speak only as of the date of this presentation, involve known and unknown risks, uncertainties, assumptions, 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 and initial 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, the possibility of unfavorable new clinical data and further analyses of existing clinical data; 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; international conflicts 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. 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.

Phase 3 Study Met the Primary and All Secondary Endpoints and Paltusotine Was Well-Tolerated

PRIMARY ENDPOINT

- ✅ **56% of participants achieved IGF-1 ≤ 1.0xULN vs 5% on placebo (p<0.0001)**

SECONDARY ENDPOINTS

- ✅ **Change from baseline in IGF-1 (p<0.0001) – Key secondary endpoint**
- ✅ **67% achieved IGF-1 <1.3×ULN (p<0.0001)**
- ✅ **Change from baseline in Total Acromegaly Symptoms Diary (ASD) score (p=0.004)**
- ✅ **Proportion of subjects with GH <1.0 ng/mL at Week 22 (p<0.0001)**

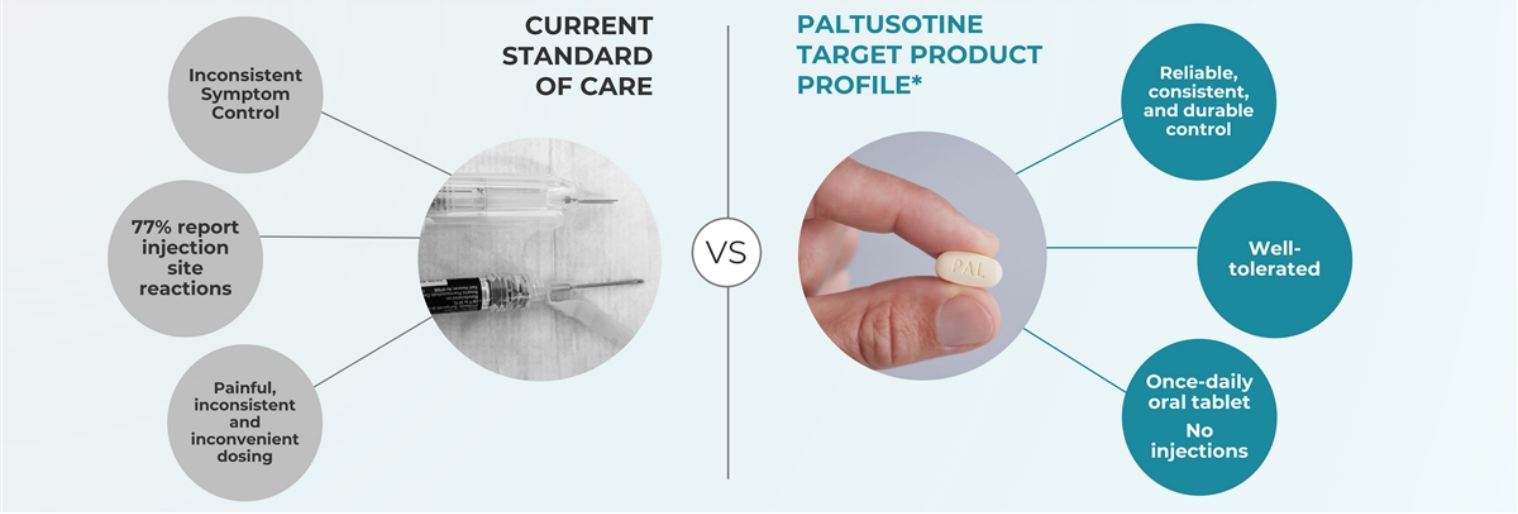
SAFETY

- ✅ **Paltusotine was generally well-tolerated with no serious adverse events**
- ✅ **Paltusotine demonstrated no new safety signals**

The PATHFNDR Program Provides a Uniquely Rich Data Set Assessing BOTH Biochemical AND Symptom Control in Acromegaly

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

Paltusotine: Designed to Allow People with Acromegaly and Carcinoid Syndrome to Focus on Living



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

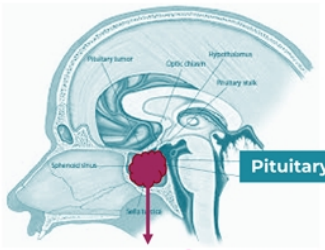
References 1. Geer EB, Sisco J, Adelman DT, et al. Patient reported outcome data from acromegaly patients treated with injectable somatostatin receptor ligands (SRLs) in routine clinical practice. *BMC Endocr Disord.* 2020;20(1):117. doi:10.1186/s12902-020-00595-4; 2. Strasburger CJ, Karavitaki N, Störmann S, et al. Patient-reported outcomes of parenteral somatostatin analogue injections in 195 patients with acromegaly. *Eur J Endocrinol.* 2016;174(3):355-62. doi:10.1530/EJE-15-1042; 3. Fleseriu et al. Frontiers in Endocrinology; March 2021, Vol.12; 4. Boyd et al. Pancreas 2013;42: 878—882.

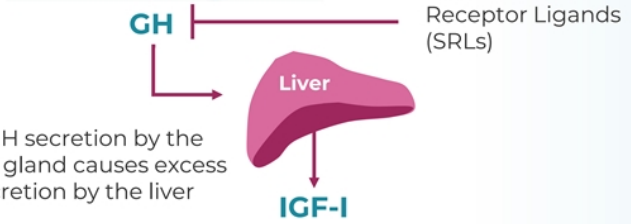
Crinetics Pharmaceuticals

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





Excess GH secretion by the pituitary gland causes excess IGF-1 secretion by the liver

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

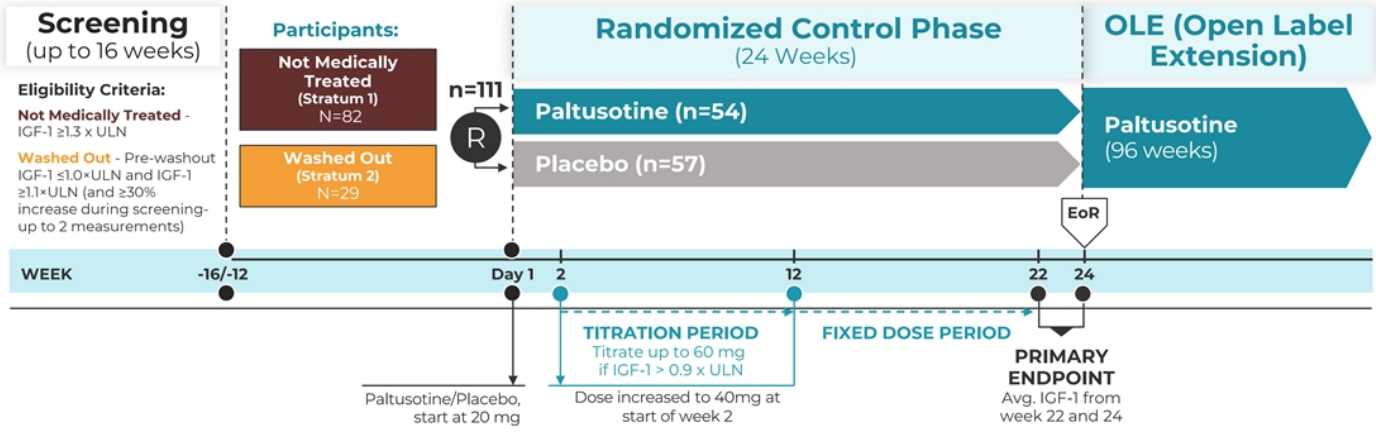
- Hypertension
- Hypopituitarism
- Hepatomegaly
- Impaired Glucose Tolerance
- Thyroid Hypertrophy

- 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.

Crinetics Pharmaceuticals

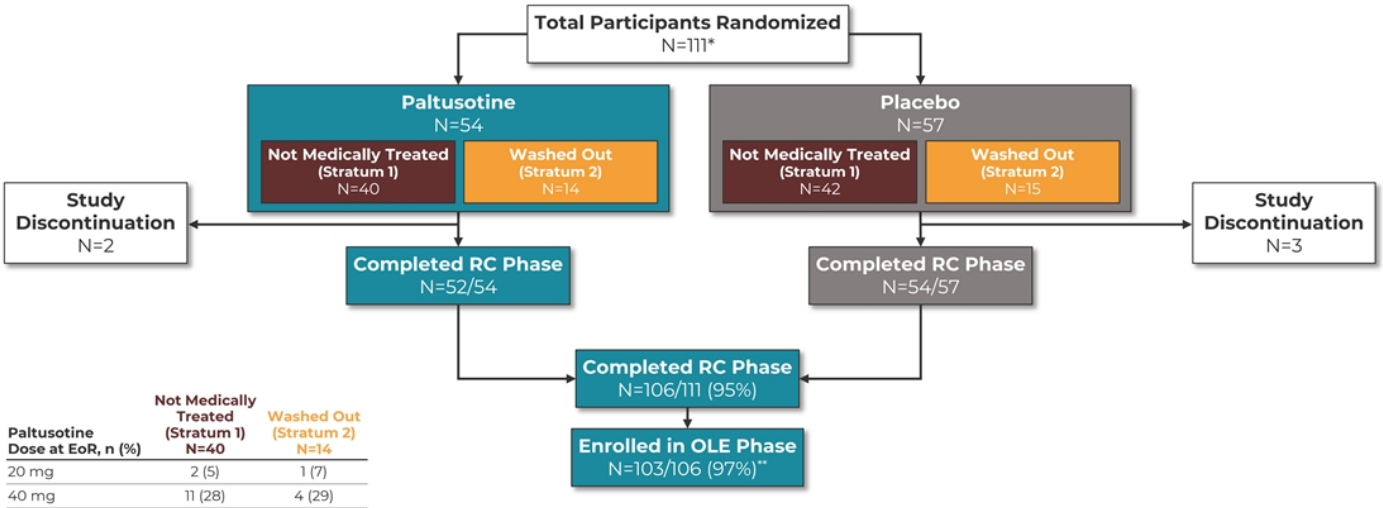
Evaluated Once Daily Oral Paltusotine in Non-pharmacologically Treated Acromegaly



Not Medically Treated (Stratum 1) – Medically Naïve: no prior medical therapy. **Previously Treated**: no medical therapy within 4 months prior to screening.
Washed Out (Stratum 2) – Controlled on octreotide or lanreotide for at least 3 months but agreed to stop injections during the screening period.
IGF-1 Baseline: defined as the average of pre-dose Day 1 IGF-1 and last IGF-1 value measured just prior to Day 1.
EoR: End of Randomized controlled phase. If participant was 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 ≥ 1.5x ULN on 60 mg *AND* exacerbation of acromegaly clinical signs/symptoms as determined by the investigator.

95% of Participants Completed the Randomized Control Phase of PATHFNDR-2 and 97% Enrolled in the Open Label Extension

PATHFNDR-2 Participant Disposition



Paltusotine Dose at EoR, n (%)	Not Medically Treated (Stratum 1) N=40	Washed Out (Stratum 2) N=14
20 mg	2 (5)	1 (7)
40 mg	11 (28)	4 (29)
60 mg	27 (68)	9 (64)

RC = Randomized Control.
* 112 Participants randomized, one subject randomized in error and never dosed.
** An additional 11 participants directly enrolled into the OLE, after confirming eligibility.

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Participant Characteristics

Participant Characteristics	Paltusotine N=54	Placebo N=57	Overall N=111
Female, n (%)	**26 (48%)**	**33 (58%)**	**59 (53%)**
Age at informed consent - Mean (SD), years	**47.5 (13.6)**	**45.9 (12.3)**	**46.7 (12.9)**
Weight - Mean (SD), kg	**86.1 (19.9)**	**82.4 (18.7)**	**84.2 (19.3)**
BMI - Mean (SD), kg/m²	**29.6 (5.4)**	**28.7 (5.2)**	**29.1 (5.3)**
Geographic region, n (%)			
Latin America	19 (35%)	17 (30%)	36 (32%)
Europe and Israel	14 (26%)	18 (32%)	32 (29%)
China	8 (15%)	15 (26%)	23 (21%)
India	7 (13%)	4 (7%)	11 (10%)
United States	6 (11%)	3 (5%)	9 (8%)

BMI=Body Mass Index

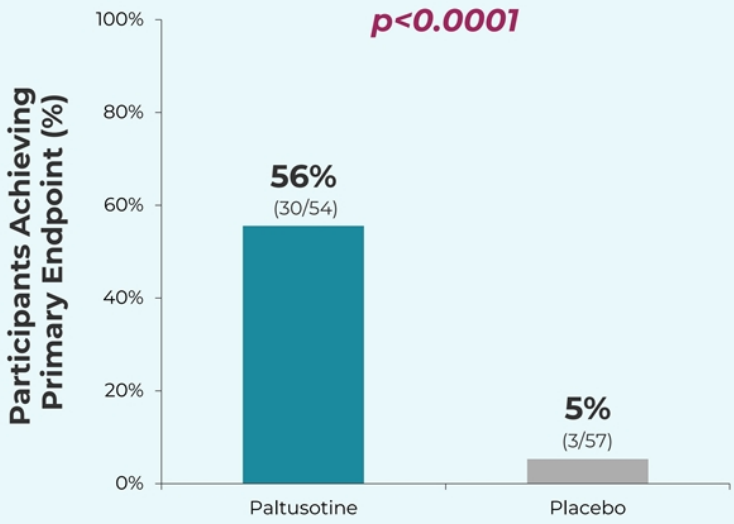
Disease Characteristics and Previous Treatment

Disease Characteristics and Previous Treatment	Paltusotine N=54	Placebo N=57	Overall N=111
Duration since acromegaly diagnosis - Mean (SD), months	**97.9 (95.7)**	**77.1 (69.4)**	**87.2 (83.5)**
Pituitary surgery performed - n (%)	**50 (93%)**	**49 (86%)**	**99 (89%)**
Pituitary Radiation - n (%)*	**2 (4%)**	**3 (5%)**	**5 (5%)**
Baseline IGF-1 x ULN - Mean (SD)	**2.0 (0.81)**	**2.2 (1.10)**	**2.1 (0.97)**
Baseline GH - Mean (SD), Median, ng/mL	**3.0 (2.90), 2.1**	**9.4 (24.15), 2.3**	**6.3 (17.64), 2.3**
Prior SRL at time of screening(Stratum 2)**			
Octreotide, n (%)***	6 (11%)	11 (19%)	17 (15%)
Monthly Dose: 10 mg / 20 mg / ≥30 mg (n)	0 / 3 / 3	1 / 4 / 6	1 / 7 / 9
Lanreotide, n (%)	8 (15%)	3 (5%)	11 (10%)
Monthly Dose: 60 mg / 90 mg / 120 mg (n)	1 / 2 / 5	2 / 0 / 1	3 / 2 / 6

* Pituitary radiation therapy performed >3 years before screening.
** Washed out subjects were controlled on medical therapy for at least 3 months but agreed to washout for 4 months prior to beginning study treatment.
***One subject washed out from oral octreotide taking 60 mg/day is not included.

Crinetics Pharmaceuticals

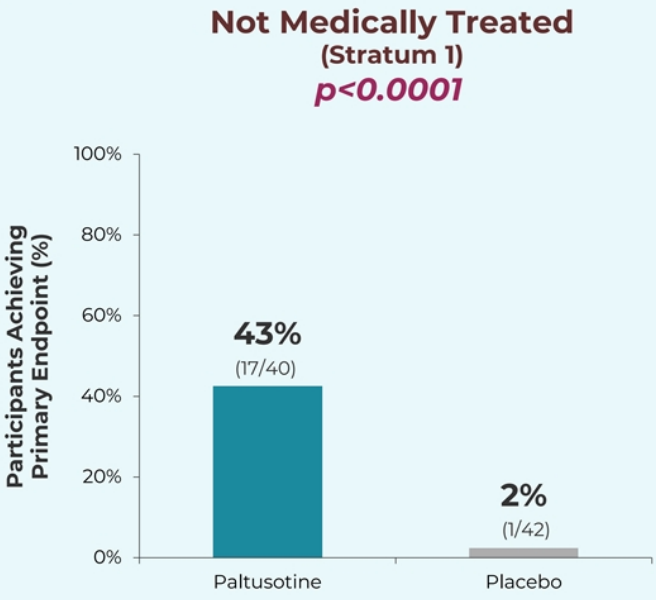
Primary Endpoint Met: 56% of Participants on Paltusotine Achieved IGF-1 ≤1.0xULN

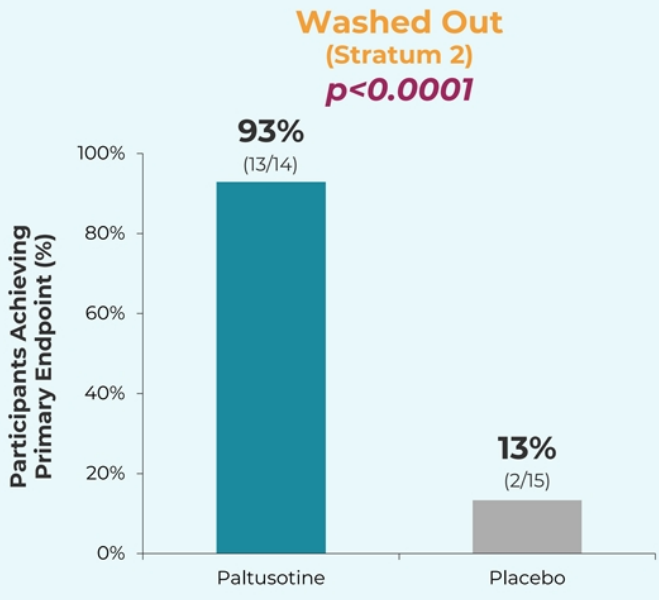


10 Participants who were rescued or stopped the assigned treatment before week 24 were considered not to have met the primary endpoint.

Crinetics Pharmaceuticals

Paltusotine Achieved Statistically Significant Responses (IGF-1 ≤1.0xULN) in Both Patient Populations



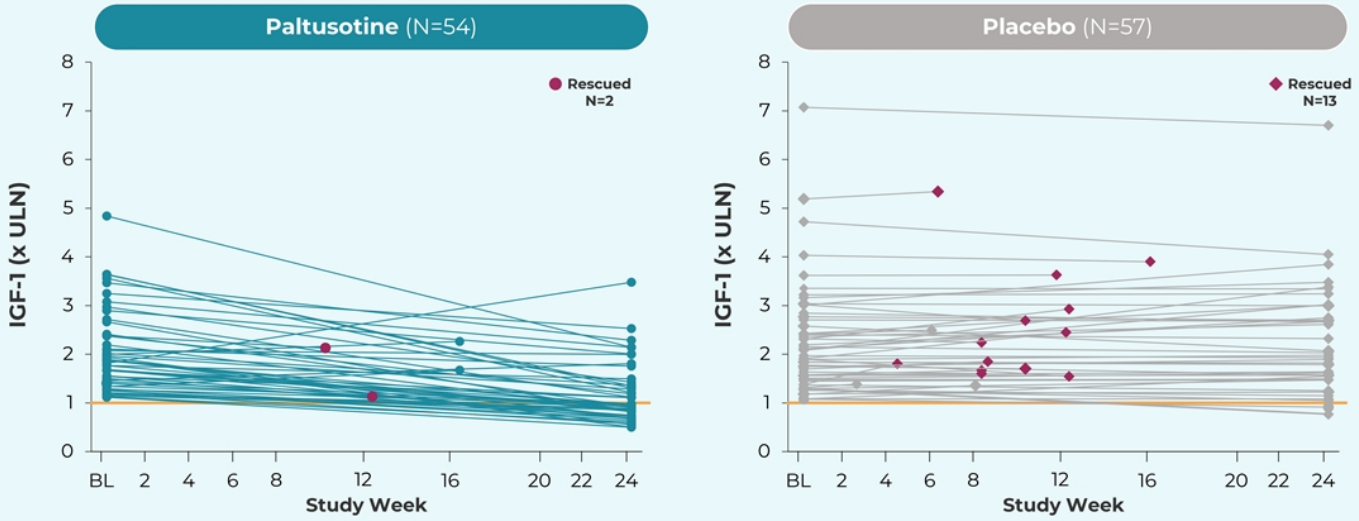


11 Participants who were rescued or stopped the assigned treatment before week 24 were considered not to have met the primary endpoint.

Crinetics Pharmaceuticals

Paltusotine Reduced IGF-1 Levels in 50/54 (93%) of Participants

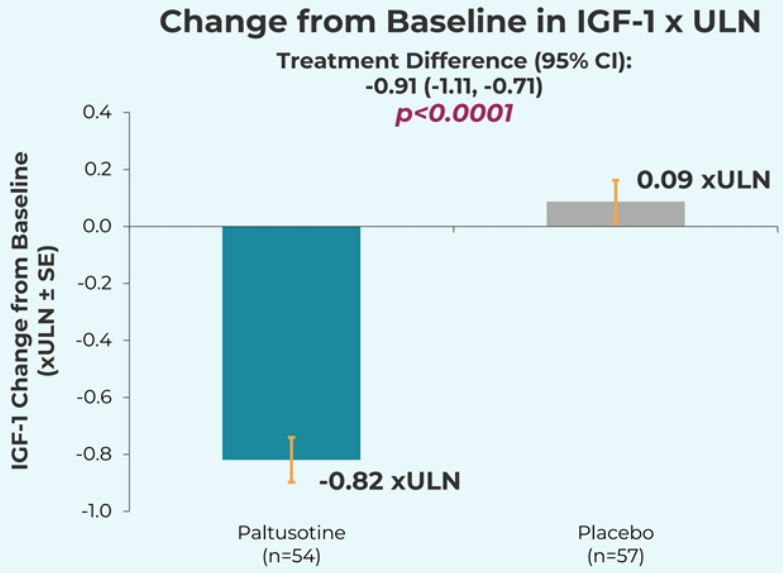
IGF-1 x ULN at Baseline and End of Randomized Control Phase (EoR) for Each Participant



IGF-1 values measured prior to rescue or discontinuation are used.

Crinetics Pharmaceuticals

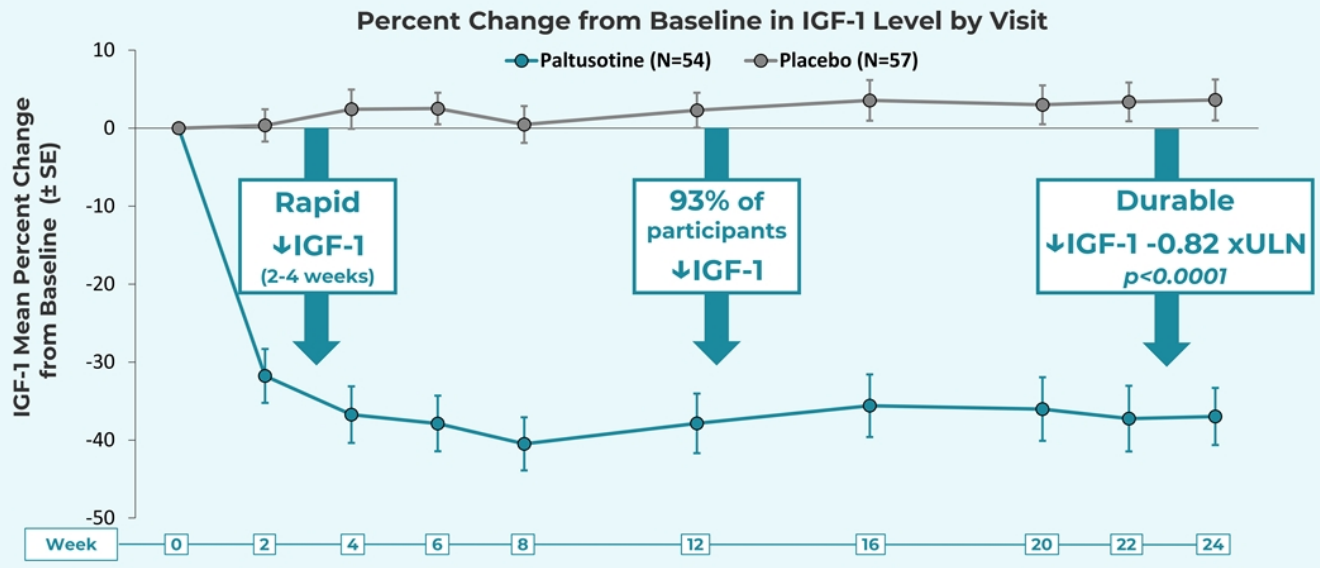
Key Secondary Endpoint Achieved: Paltusotine Treatment Significantly Decreased IGF-1 Levels



Least Squares (LS) Mean (± SE) is shown and estimated based on an analysis of covariance.
IGF-1 values measured prior to rescue or discontinuation are used.

Crinetics Pharmaceuticals

Paltusotine Treatment Rapidly (Within 2-4 Weeks) and Durably Decreased IGF-1 Levels



IGF-1 values measured prior to rescue or discontinuation are carried forward

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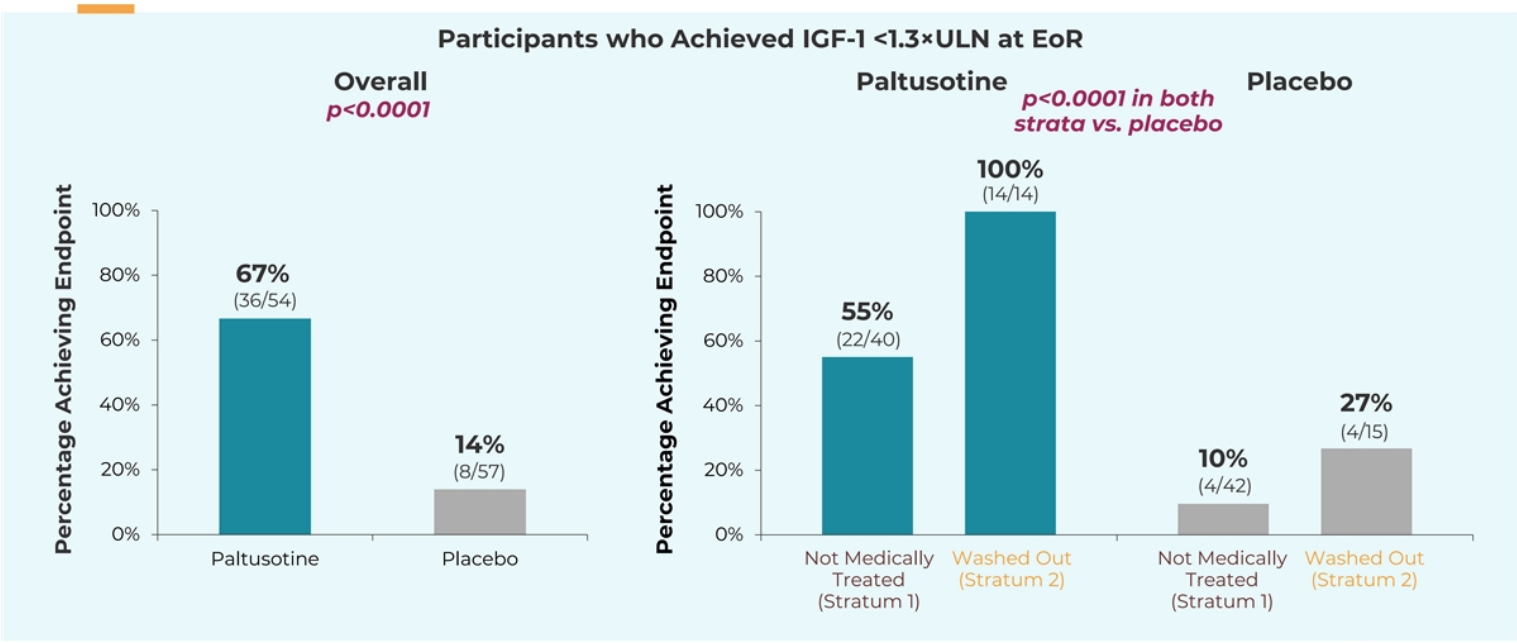
Secondary Endpoint #2 Met: 67% of Participants Achieved IGF-1 <1.3×ULN with Paltusotine



EoR: End of Randomized control phase; Participants who were rescued or stopped the assigned treatment before week 24 were considered not to have met the endpoint.

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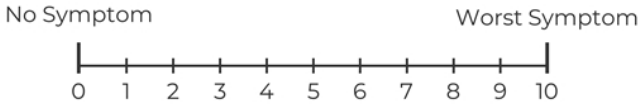
Participants Reported Symptom Severity Using the Acromegaly Symptoms Diary (ASD)

- ASD was developed in accordance with FDA guidance to evaluate symptoms of acromegaly in clinical trials*
- Each symptom was rated from 0 (no symptom) to 10 (worst symptom), Total 0 to 70
- A daily checklist for symptoms was collected for participants 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)

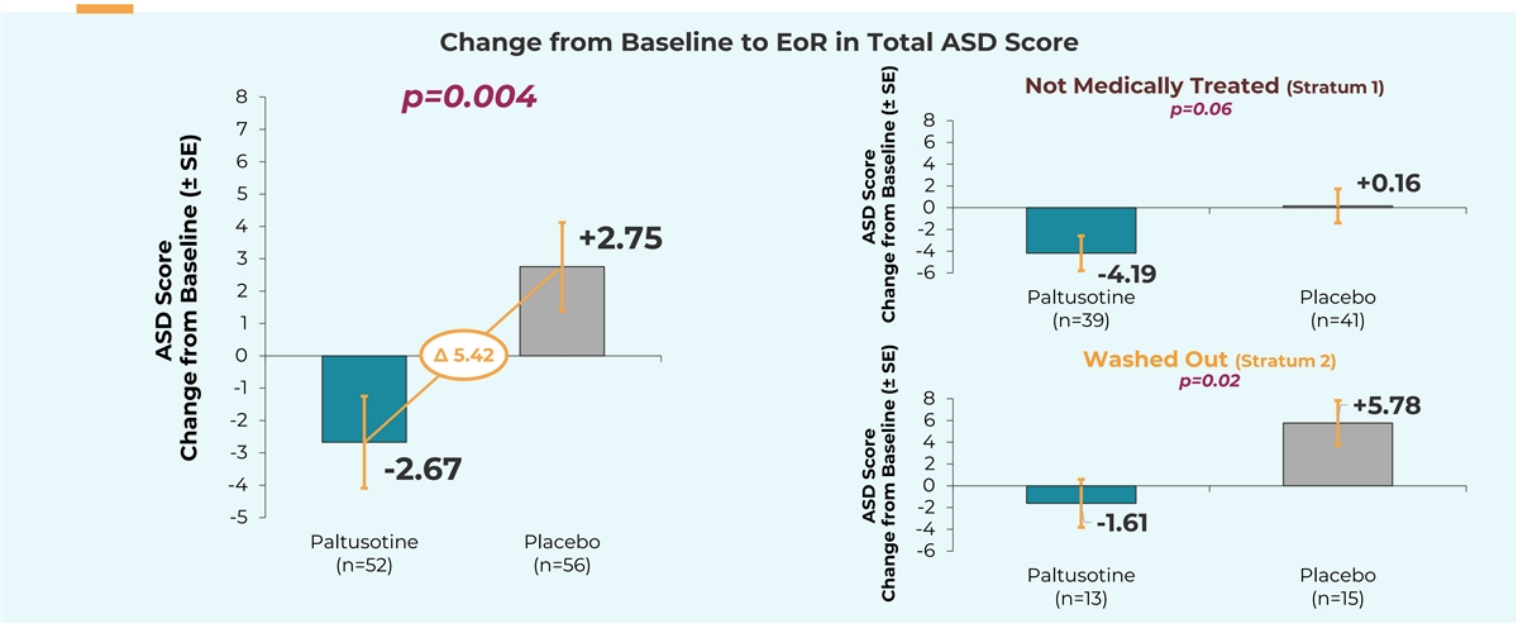
Numeric Scale (per symptom)



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

Crinetics Pharmaceuticals

Secondary Endpoint #3 Achieved: Paltusotine Treatment Improved Acromegaly Symptoms



Least Squares (LS) Mean is estimated based on an analysis of covariance.
EoR: End of Randomized control phase. ASD scores measured prior to rescue or discontinuation are used.

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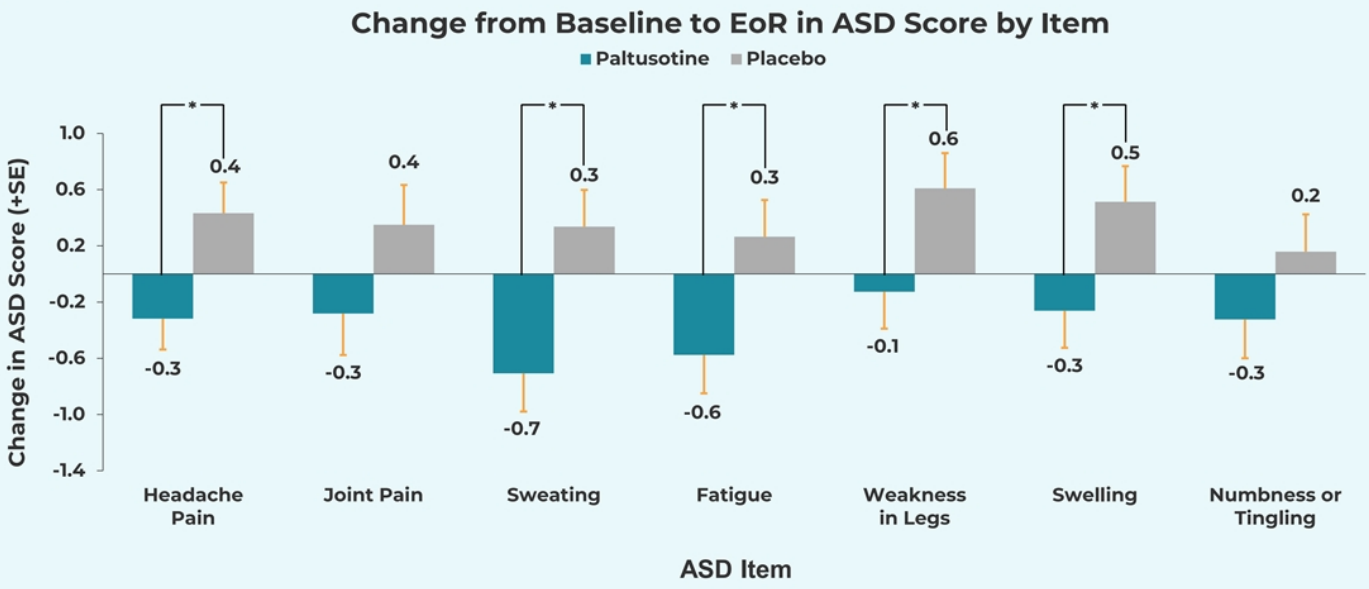
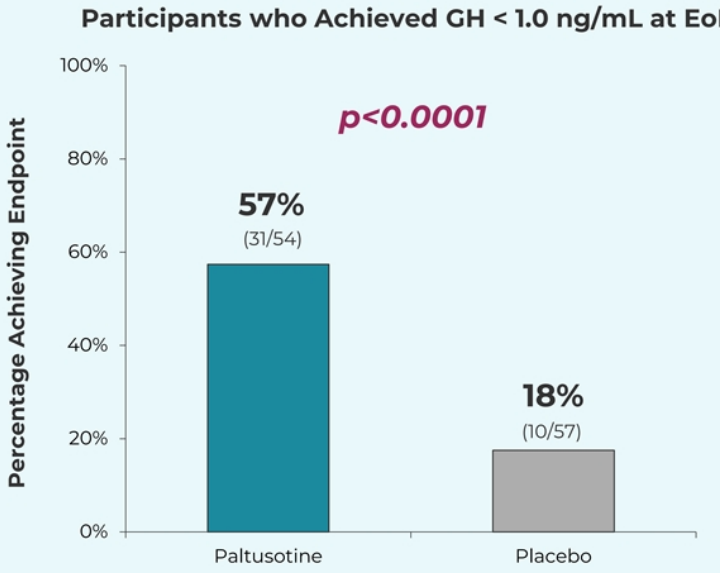
Paltusotine Treatment Improved All Individual Symptom Components of ASD



* p<0.05. P-value is estimated based on an analysis of covariance.
Least Squares (LS) Mean is presented and estimated based on an analysis of covariance.
EoR: End of Randomized Control Phase, ASD scores measured prior to rescue or discontinuation are used.
Each symptom is on a 0 (no symptom) to 10 (worst symptom) scale.

Crinetics Pharmaceuticals

Secondary Endpoint #4 Met: Paltusotine Treatment Achieved Target Growth Hormone Levels in 57% of Subjects



Participants who are rescued or stop the assigned treatment before week 22 did not meet endpoint. GH was measured prior to randomization and at W22, as a mean of 5 separate blood levels measured within a 3 hour period. EoR: End of randomized control phase.

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Paltusotine was Generally Well-Tolerated with No Serious Adverse Events

Treatment-Emergent Adverse Events (TEAEs)	Paltusotine N=54 n (%)	Placebo N=57 n (%)
Any	**49 (91%)**	**49 (86%)**
Mild	47 (87%)	45 (79%)
Moderate	15 (28%)	26 (46%)
Severe	2 (4%)	5 (9%)
Treatment-related	**26 (48%)**	**15 (26%)**
Serious	**0**	**1 (2%)**
Not treatment-related	0	1 (2%)
Treatment-related	0	0
Leading to dose reduction	**3 (6%)**	**1 (2%)**
Leading to rescue	**2 (4%)**	**13 (23%)**
Leading to death	**0**	**0**

Paltusotine Demonstrated No New Safety Signals

TEAEs with an Incidence of ≥5% in Total Participants

TEAE	Paltusotine N=54 n (%)	Placebo N=57 n (%)
Diarrhoea	18 (33%)	10 (18%)
Headache	**11 (20%)**	**19 (33%)**
Arthralgia	**6 (11%)**	**13 (23%)**
Abdominal pain	6 (11%)	2 (4%)
Paresthesia	**5 (9%)**	**3 (5%)**
Nausea	5 (9%)	2 (4%)
Abdominal discomfort	5 (9%)	1 (2%)
Upper respiratory tract infection	4 (7%)	10 (18%)
Fatigue	**3 (6%)**	**8 (14%)**
Dyspepsia	3 (6%)	6 (11%)
Anemia	3 (6%)	5 (9%)
Back pain	3 (6%)	4 (7%)
Urinary tract infection	3 (6%)	4 (7%)
Asthenia	3 (6%)	3 (5%)
Peripheral swelling	**2 (4%)**	**6 (11%)**
Hyperhidrosis	**1 (2%)**	**5 (9%)**

- Safety profile in PATHFNDR-2 comparable to that observed in clinical program to date
- TEAEs (**bold**) are symptoms known to be associated with acromegaly

Includes AEs occurring during rescue period. Rates were similar when rescue period is excluded AE's commonly associated with symptoms of acromegaly are shown in bold.

PATHFNDR-2 Safety Summary

- Paltusotine was generally well-tolerated with no serious adverse events reported
- The most frequently (>10%) reported adverse events included diarrhoea, headache, arthralgia, and abdominal pain
- No new safety signals were observed in adverse events, vital signs, ECGs, or laboratory values during treatment with paltusotine
- Paltusotine treatment was associated with stable or reduced pituitary tumor size, as measured by MRI

Ongoing Open Label Extension Studies:
Currently ~225 participants treated up to 4yrs

PATHFNDR Program Provides a Uniquely Rich Data Set Assessing *BOTH* Biochemical *AND* Symptom Control in Acromegaly

Paltusotine data now support NDA filing for broad use in acromegaly

- Previously, ***PATHFNDR-1*** met all pre-specified endpoints in **maintenance of control when switching from SRLs**
- Today, ***PATHFNDR-2*** met all pre-specified endpoints in **patients not medically treated** who had elevated IGF-1 levels at baseline

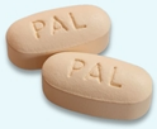
First commercial launch for Crinetics, pending FDA approval of paltusotine for acromegaly

Aspiration: *to launch an important new medical treatment for acromegaly patients and medical providers:*

- ***The first once-daily, oral SRL***
- ***Reducing treatment burden***
- ***Reducing access barriers***
- ***Delivering rapid, durable, and consistent control***

Today → **2H24** → **2025**

Acromegaly NDA submission
Carcinoid syndrome Phase 3 start
pending alignment with FDA



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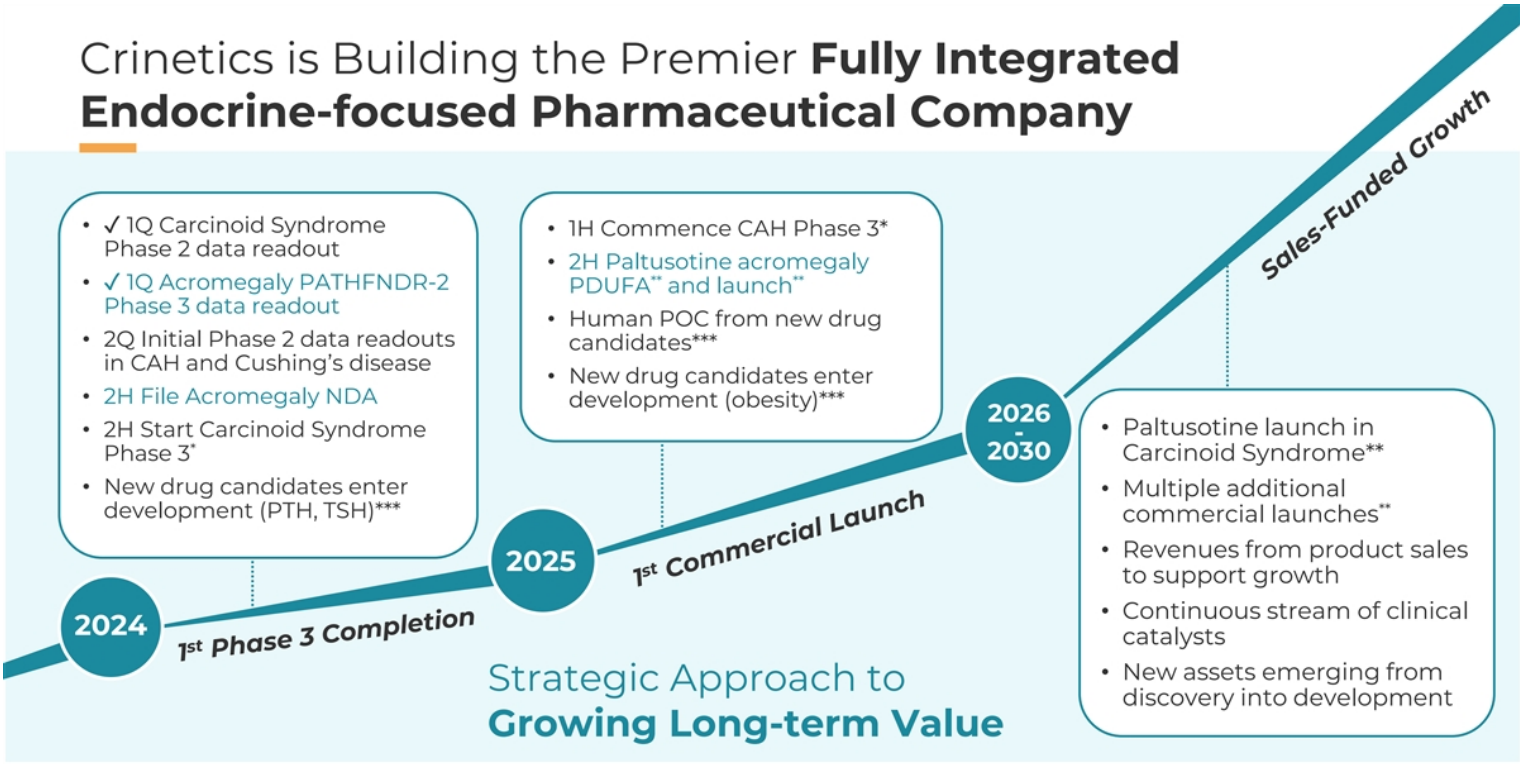
Crinetics is Building the Premier **Fully Integrated Endocrine-focused Pharmaceutical Company**



Strategic Approach to **Growing Long-term Value**

* Pending alignment with FDA. ** Pending NDA submission, acceptance and regulatory approval.
*** Pending identification, creation and clinical development of new drug candidates for additional diseases.
CAH: congenital adrenal hyperplasia; PTH: parathyroid hormone; TSH: thyroid stimulating hormone; POC: proof of concept.

Crinetics Pharmaceuticals

Q&A

Scott Struthers, Ph.D.
Founder and Chief Executive Officer

Dana Pizzuti, M.D.
Chief Medical & Development Officer

Alan Krasner, M.D.
Chief Endocrinologist

Marc Wilson
Chief Financial Officer

Jim Hassard
Chief Commercial Officer

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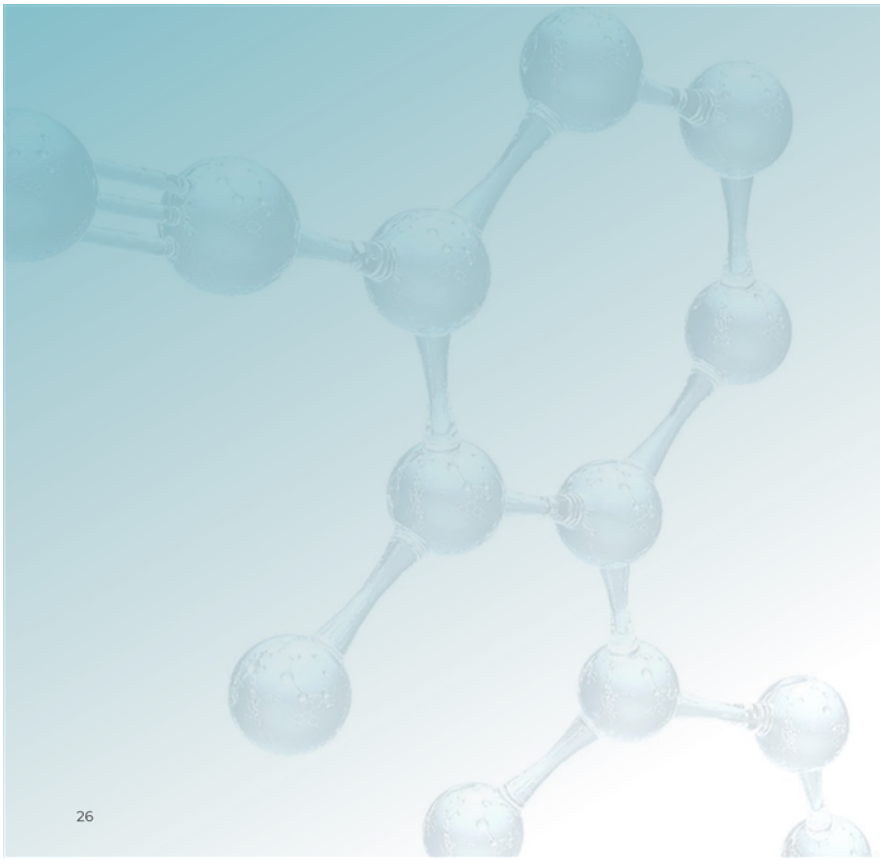

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Thank You