NEWS RELEASE

CRINETICS' ONCE-DAILY ORAL PALTUSOTINE ACHIEVED THE PRIMARY AND ALL SECONDARY ENDPOINTS IN THE PHASE 3 PATHFNDR-2 STUDY IN ACROMEGALY PATIENTS

2024-03-19

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. 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 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.

Contact:
Corey Davis
LifeSci Advisors
cdavis@lifesciadvisors.com
(212) 915-2577

Media:
Natalie Badillo
Head of Corporate Communications
nbadillo@crinetics.com
(858) 345-6075

Source: Crinetics Pharmaceuticals, Inc.