NEWS RELEASE

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

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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 ≤ 1.0x ULN 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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