NEWS RELEASE

CRINETICS PRESENTS NEW DATA AT ENDO 2024 THAT INCREASES THAT INCREASES BODY OF EVIDENCE POSITIONING ONCE-DAILY, ORAL PALTUSOTINE AS POTENTIAL FIRST-CHOICE TREATMENT OPTION FOR ACROMEGALY

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SAN DIEGO – June 3, 2024 – **Crinetics Pharmaceuticals, Inc.** (Nasdaq: CRNX) today presented findings from its clinical development program evaluating oral, once-daily investigational paltusotine in acromegaly. Data presented included results of the Phase 3 PATHFNDR-2 trial, a new analysis of patient reported outcome (PRO) data from the Phase 3 PATHFNDR-1 trial, and interim long-term efficacy and safety results at 42 months from the open-label ACROBAT Advance extension study. The data were presented today at the Endocrine Society's Annual Meeting (ENDO2024), with findings from PATHFNDR-1 accepted for publication as a manuscript in The Journal of Clinical Endocrinology & Metabolism.

"The depth and breadth of our clinical development program for once-daily, oral paltusotine under investigation for the treatment of acromegaly is on display at ENDO 2024, demonstrating its rapid, durable effect on both biochemical and symptom control in these studies," said Scott Struthers, Ph.D., founder and chief executive officer of Crinetics. "Notably, based on patient reported outcome data captured daily by the Acromegaly Symptom Diary, a new analysis from the PATHFNDR-1 trial showed that paltusotine was able to drive significant and important differences in the frequency of acromegaly breakthrough symptom exacerbations compared to prior treatment with standard of care medications. We look forward to submitting a New Drug Application in the second half of this year and potentially changing the acromegaly treatment paradigm."

Efficacy and Safety of Once-daily Oral Paltusotine in Medically Untreated Patients with Acromegaly: Results from the Phase 3, Randomized, Placebo-controlled PATHFNDR-2 Study (Abstract #**MON-694**):
PATHFNDR-2 was a randomized, double-blind, placebo-controlled trial with a 24-week treatment period, followed by an optional open-label extension study evaluating paltusotine in 111 participants with active acromegaly (IGF-1 > 1.1 ULN) who were not pharmacologically treated. Results demonstrated:

- 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%).
- This represents the second Phase 3 trial showing a significant difference in symptoms favoring paltusotine.
- Response to paltusotine was rapid, with the majority of the effect in IGF-1 reductions observed between weeks two and four, and sustained throughout treatment.
- Among those treated with paltusotine, a reduction in IGF-1 levels occurred in 92.6% of patients (n=50/54) by the end of treatment.
- 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.

Use of the Acromegaly Symptom Diary (ASD) in a Phase 3, Placebo-Controlled Study of Once-Daily, Oral Paltusotine in Patients with Acromegaly Switched from Injected Octreotide or Lanreotide (Abstract #**MON-156**):
PATHFNDR-1 was a randomized, double-blind, placebo-controlled trial with a 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 receptor ligands (SRL). The study enrolled participants with acromegaly who were biochemically controlled on octreotide or lanreotide depot monotherapy.

The study met the primary endpoint and all three secondary endpoints, as previously announced. Findings clearly demonstrated that once-daily, oral paltusotine maintained biochemical and symptom control in patients with acromegaly switched from SRL. Paltusotine was well tolerated with no severe or serious TEAEs.

In a new analysis of PATHFNDR-1 data presented at ENDO2024, Acromegaly Symptom Diary (ASD) scores for patients at screening (and on injected SRL, the current standard of care) were compared to scores while on paltusotine (n=25). The ASD is a novel PRO tool developed in accordance with U.S. Food and Drug Administration (FDA) guidance to assess disease-related symptom burden. Paltusotine was associated with statistically significant reductions in the frequency of breakthrough acromegaly symptom exacerbations for total ASD scores, most

bothersome symptom, headache, joint pain, sweating, fatigue, numbness/tingling, sleep difficulty and memory difficulty. Numerical differences favoring paltusotine were seen for the remaining symptoms of leg weakness and swelling.

“Patients with acromegaly often suffer from unpredictable breakthrough symptoms, despite receiving regular painful depot injections of the available first line medical treatments,” said Alan Krasner, M.D., chief endocrinologist at Crinetics. “The data from PATHFNDR-1 suggest that once daily oral paltusotine may be associated with less day-to-day symptom variability compared to the injections. Reducing the burden of the disease, as well as the burden of its treatment, are key goals of the paltusotine development program.”

Long-Term Safety and Efficacy of Once-Daily Oral Paltusotine in the Treatment of Patients with Acromegaly: Update from ACROBAT Study (Abstract #**MON-695**):
ACROBAT Advance is an ongoing, six-year, single-arm, open-label extension study of paltusotine in the treatment of patients with acromegaly. This analysis includes interim results as the first enrolled patients approach four years of treatment. Enrolled patients had completed either the ACROBAT Edge or Evolve Phase 2 parent studies.

Results demonstrated:

- Once-daily oral paltusotine treatment was well-tolerated, with stable biochemical and symptom control, comparable to that observed with prior injected SRLs.
- Parent study baseline median IGF-I levels were 1.15× ULN (0.84, 1.46; n=43). In ACROBAT Advance, median IGF-1 levels were 1.14× ULN (0.89, 1.29; n=40), 1.06× ULN (0.87, 1.24; n=35), and 1.08× ULN (0.87, 1.57; n=10) at months 12, 24, and 42, respectively.
- Important clinical outcomes including acromegaly symptoms, blood pressure, HbA1c, and residual pituitary tumor size were stable over the period of observation.
- Paltusotine continues to be well- tolerated. The most common adverse events (AEs) (reported at least during the study) were arthralgia (37.2%), headache (30.2%), and fatigue (23.3%). One serious drug-related AE (cholelithiasis) was reported. Of the eight patients who discontinued the study, two were due to AEs (mild or moderate).

Preparation of regulatory filings for paltusotine based on PATHFNDR-1 and PATHFNDR-2 data are currently underway, with a New Drug Application submission to the FDA planned in the second half of 2024.

About Paltusotine
Paltusotine is the first oral, once-daily selectively-targeted somatostatin receptor type 2 (SST2) agonist, and has completed its randomized, controlled 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** and **PATHFNDR-2** Phase 3 studies, paltusotine maintained IGF-1 levels in patients with acromegaly who were switched from monthly injectable medications to paltusotine (PATHFNDR-1) and decreased IGF-1 levels in medically untreated patients (PATHFNDR-2). 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 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 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 is also developing atumelnant (CRN04894), an investigational, first-in-class, oral ACTH antagonist, that is currently completing 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 and commercialization of paltusotine, including the therapeutic potential and clinical benefits or safety profile thereof; the expected publication of findings from PATHFNDR-1; and the expected timing of an NDA submission for paltusotine for the treatment or maintenance of treatment of acromegaly in the United States. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplates,” “believes,” “estimates,” “predicts,” “potential,” “upcoming” or “continue” or the negative of these terms or other similar expressions. 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, initial or topline data that we report may change following completion or 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; unexpected adverse side effects or inadequate efficacy of the Company’s product candidates that may limit their development, regulatory approval and/or commercialization; 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; 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, and its Quarterly report on Form 10-Q for the quarter ended March 31, 2024. 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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