NEWS RELEASE

CRINETICS PHARMACEUTICALS PIPELINE PROGRESS ON DISPLAY AT ENDO 2021

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SAN DIEGO, March 22, 2021 — **Crinetics Pharmaceuticals, Inc**. (Nasdaq: CRNX), a clinical stage pharmaceutical company focused on the discovery, development, and commercialization of novel therapeutics for rare endocrine diseases and endocrine-related tumors, today provided details of four presentations that were made at the Endocrine Society's annual ENDO 2021 congress on the company's **product pipeline**. A late-breaking e-poster and oral presentation provided details of the preclinical findings supporting the company's development of CRN04894 and CRN04777. In addition, a summary of the previously announced ACROBAT Edge Phase 2 results as well as details of an improved tablet formulation of paltusotine were presented:

- Selective Somatostatin 5 (SST5) and Somatostatin 2 (SST2) Nonpeptide Agonists Potently Suppress Glucose- and Tolbutamide-Stimulated Dynamic Insulin Secretion from Isolated Human Islets
- Effects of CRN04894, a Nonpeptide Orally Bioavailable ACTH Antagonist, on Corticosterone in Rodent Models of ACTH Excess
- Pharmacokinetics and Safety of an Improved Oral Formulation of Paltusotine, a Selective, Nonpeptide Somatostatin Receptor 2 (SST2) Agonist for the Treatment of Acromegaly
- Safety and Efficacy of Switching Injected Peptide Long-Acting Somatostatin Receptor Ligands to Once Daily Oral Paltusotine: ACROBAT Edge Phase 2 Study

"I have never been more excited to share our data with the audience at ENDO. We believe CRN04894, which is now in Phase 1 development, represents an important advancement in the field of the endocrine stress axis. We also presented encouraging findings from our SST5 agonist program, from which we developed CRN04777. I am especially excited about this candidate, which I believe , if successfully developed and approved, has the potential

to offer real benefit to kids with congenital HI and their families," stated Scott Struthers, Ph.D., president and CEO of Crinetics. "In addition to our early-stage pipeline programs, we presented information from the Phase 2 ACROBAT Edge study and the new formulation of paltusotine to be used in our Phase 3 acromegaly program."

Crinetics presented a late-breaking e-poster describing the potential of SST5 receptor agonists to regulate glucose-stimulated insulin secretion from human islet cells. One of somatostatin's roles in maintaining blood glucose concentrations is to regulate insulin secretion, yet the lack of highly selective agonists has previously hampered efforts to identify the role of the individual somatostatin receptor subtypes in this process. In its preclinical efforts, Crinetics observed that SST5 receptor agonists were potent inhibitors of insulin secretion in the healthy pancreas and under conditions that stimulate excess insulin secretion. Based on these results, the company believes that a selective SST5 agonist may have therapeutic value in the treatment of congenital HI, which is a condition associated with dysregulated insulin secretion. Based on these preclinical findings, Crinetics advanced **CRN04777, an experimental oral nonpeptide SST5 agonist**, into a clinical program for congenital HI. CRN04777 is currently being evaluated in a Phase 1 trial designed to evaluate safety, pharmacokinetics, and clinical proof-of-concept by employing well-established methods for evaluating insulin secretion.

Crinetics also discussed preclinical results related to **CRN04894, an oral nonpeptide ACTH antagonist**, during a live oral presentation at ENDO 2021. CRN04894 recently advanced into a Phase 1 clinical program in healthy volunteers that is designed to evaluate safety, pharmacokinetics, and clinical proof-of-concept by measuring the ability of CRN04894 to suppress cortisol, cortisol precursors and adrenal androgens following exogenous ACTH stimulation. Preclinical data featured in the oral presentation showed that repeat dosing of CRN04894 suppressed plasma corticosterone levels in a robust and dose-dependent manner in animal models of ACTH excess. Results also showed that after seven days, the weight gain and adrenal gland hypertrophy caused by excess ACTH were reduced. This evidence supports the further evaluation of CRN04894 in conditions such as Cushing's disease and congenital adrenal hyperplasia (CAH), which are associated with excessive ACTH.

"ENDO 2021 was our first opportunity to present the entirety of our growing clinical-stage pipeline, including the supportive evidence for our emerging programs in congenital HI and diseases of ACTH excess like Cushing's disease and CAH," added Alan S. Krasner, M.D., Crinetics' chief medical officer. "We are extremely excited to expand our development efforts to three clinical programs with more expected from our experienced in-house discovery team."

In addition to the company's pipeline programs, Crinetics presented two posters on **paltusotine, (formerly CRN00808) for the treatment of acromegaly**, including results from the Phase 2 ACROBAT Edge study. Edge was a single-arm study designed to evaluate the impact of switching patients with acromegaly from monthly injected somatostatin receptor ligands (SRLs) to paltusotine, an experimental oral, once-daily, nonpeptide SST2 receptor

agonist. Edge enrolled individuals who had not achieved normal insulin-like growth factor-1 (IGF-1) levels despite receiving long-acting octreotide or lanreotide. As previously reported, after 13 weeks of treatment 20 of 23 participants who completed the dosing period maintained their IGF-1 to levels within 20% of their baseline or lower. The most common treatment-emergent adverse events (>10%) included: headache, arthralgia, fatigue, peripheral swelling, paresthesia and hyperhidrosis. There were no discontinuations due to adverse events and no treatment-related serious adverse events.

Crinetics plans to advance paltusotine into a Phase 3 clinical program in acromegaly in the first half of 2021 using a new tablet formulation. **Results of a Phase 1 pharmacokinetic study reported at ENDO 2021** demonstrated that this new once-daily tablet formulation of paltusotine had a fasting requirement of only 0.5-1 hour, compared to the 2-hour requirement of the prior capsule formulation. The tablet formulation also showed improved dose-proportional exposure up to 80 mg, which offers the potential for greater dosing flexibility compared to the prior formulation. In addition, the new tablet formulation was observed to be less sensitive to effects of acid lowering drugs, such as proton pump inhibitors (PPIs). In planned Phase 3 studies of paltusotine, the new tablet formulation will be administered with a 1-hour post-dose fast without the exclusion of acid lowering drugs.

All presentations made at the annual ENDO 2021 congress may be accessed in the virtual conference environment through April 30, 2021. In addition, they will be available on the **Crinetics website**.

About Paltusotine

Paltusotine (formerly CRN00808) is an investigational, orally available nonpeptide agonist that is designed to be highly selective for the somatostatin receptor type 2 (SST2). It was designed by the Crinetics discovery team to provide a once-daily option for patients with acromegaly and neuroendocrine tumors, which are currently treated by injected therapies that have approximately $3.2 billion in revenues annually. A previously completed Phase 1 trial of paltusotine showed clinical proof of concept by providing evidence of potent suppression of the growth hormone (GH) axis in healthy volunteers. In Phase 2 trials, paltusotine maintained insulin-like growth factor-1 (IGF-1) levels in acromegaly patients who switched from injectable depot medications to once-daily oral paltusotine. IGF-1 is the primary biomarker endocrinologists use to manage their acromegaly patients. Based on these findings, Crinetics plans to advance paltusotine into a Phase 3 program for acromegaly in the first half of 2021.

About CRN04777

CRN04777 is an investigational, orally available selective nonpeptide somatostatin receptor type 5 (SST5) agonist designed to reduce insulin secretion and is intended to be a universal treatment for patients with congenital

hyperinsulinism (HI). Congenital HI is a severe form of hyperinsulinism that, if not identified and treated early, can lead to life-threatening hypoglycemia, severe neurological sequelae and developmental delay. Congenital HI is driven by mutations in certain genes involved in regulating insulin secretion and occurs in approximately 1 in 30,000 to 50,000 new births in the United States. In 2020, the U.S. Food and Drug Administration granted rare pediatric disease designation for CRN04777 for the treatment of congenital HI. CRN04777 is being evaluated in a Phase 1 study in healthy volunteers to assess safety, tolerability, and clinical proof of concept.

About CRN04894

CRN04894 is an investigational, orally available, nonpeptide adrenocorticotropic hormone (ACTH) antagonist designed to selectively block the interaction of ACTH at the melanocortin type 2 receptor (MC2R), which is predominantly expressed in the adrenal gland. ACTH is synthesized and secreted by the pituitary gland and binds to MC2R to stimulate the production of cortisol, a stress hormone that is involved in the regulation of many systems. Cortisol is involved in the regulation of blood sugar levels, metabolism, inflammation, blood pressure, and memory formulation. Diseases associated with excess of ACTH, therefore, can have significant impact on physical and mental health. Crinetics' ACTH antagonist, CRN04894, exhibited strong binding affinity for MC2R and demonstrated suppression of adrenally derived glucocorticoids that are under the control of ACTH, while maintaining mineralocorticoid production in preclinical models. CRN04894 is being evaluated in a Phase 1 study in healthy volunteers to assess safety, tolerability, and clinical proof of concept.

About Crinetics Pharmaceuticals

Crinetics Pharmaceuticals is a clinical stage pharmaceutical company focused on the discovery, development, and commercialization of novel therapeutics for rare endocrine diseases and endocrine-related tumors. The company's lead product candidate, paltusotine (formerly CRN00808), is an investigational, oral, selective nonpeptide somatostatin receptor type 2 (SST2) agonist for the treatment of acromegaly, an orphan disease affecting more than 26,000 people in the United States. Crinetics plans to advance paltusotine into a Phase 3 program in acromegaly and a Phase 2 trial for the treatment of carcinoid syndrome associated with neuroendocrine tumors. The company is also developing CRN04777, an investigational, oral, nonpeptide somatostatin receptor type 5 (SST5) agonist for congenital hyperinsulinism, as well as CRN04894, an investigational, oral, nonpeptide ACTH antagonist for the treatment of Cushing's disease, congenital adrenal hyperplasia, and other diseases of excess ACTH. All of the company's drug candidates are new chemical entities resulting from in-house drug discovery efforts and are wholly owned by the company. For more information, please visit crinetics.com.

Forward-Looking Statements

Crinetics cautions you that statements contained in this press release 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 to initiate a Phase 3 program of paltusotine in acromegaly and a Phase 2 program for the treatment of carcinoid syndrome associated with neuroendocrine tumors and the expected timing thereof; the enrollment of Phase 1 clinical studies for CRN04894 and CRN0477 and the expected timing of thereof; the potential for the new tablet formulation of paltusotine to offer greater dosing flexibility and less sensitivity to effects of acid lowering drugs compared to the prior formulation; the potential to generate safety, pharmacodynamic, pharmacokinetic and pharmacologic activity data from such Phase 1 studies in healthy volunteers with CRN04894 and CRN04777; the potential that such data will provide important clinical proof-of-concept for Crinetics' CRN04894 and CRNX04777 programs; the ability of Crinetics' in-house discovery team to expand its development efforts into additional clinical programs; and the potential for CRN04777, if successfully developed and approved, to benefit congenital HI patients. The inclusion of forward-looking statements should not be regarded as a representation by Crinetics that any of its plans will be achieved. Actual results may differ from those set forth in this press release due to the risks and uncertainties inherent in Crinetics' business, including, without limitation: advancement of paltusotine into a Phase 3 program for acromegaly or a program for carcinoid syndrome is dependent on and subject to the receipt of further feedback from the FDA; the COVID-19 pandemic may disrupt Crinetics' business and that of the third parties on which it depends, including delaying or otherwise disrupting its clinical trials and preclinical studies, manufacturing and supply chain, or impairing employee productivity; the company's dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the success of Crinetics' clinical trials and nonclinical studies for paltusotine, CRN04894, CRN04777 and its other product candidates; regulatory developments in the United States and foreign countries; unexpected adverse side effects or inadequate efficacy of the company's product candidates that may limit their development, regulatory approval and/or commercialization; Crinetics may use its capital resources sooner than it expects; and other risks described under the heading "Risk Factors" in documents the company files from time to time with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and Crinetics undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. 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.

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