NEWS RELEASE

LEAD ACTH ANTAGONIST CRN04894 (CUSHING'S, CAH) ENTERS PHASE 1 STUDY

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SAN DIEGO, February 4, 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 announced that CRN04894, the company's lead **adrenocorticotropic hormone (ACTH) antagonist** for the treatment of diseases associated with excess ACTH such as Cushing's disease and congenital adrenal hyperplasia (CAH), has advanced into the clinic. Based on encouraging preclinical results, Crinetics has initiated a double-blind, randomized, placebo-controlled Phase 1 study of this orally administered, nonpeptide small molecule drug candidate in healthy volunteers. This study will assess the safety and tolerability of single and multiple doses of CRN04894 and will measure the effect of CRN04894 on suppression of cortisol, cortisol precursors, and adrenal androgens following exogenous ACTH stimulation.

Scott Struthers, Ph.D., Founder and Chief Executive Officer of Crinetics, stated "ACTH is the central hormone mediating the endocrine stress response in humans. While disease due to ACTH excess was first described more than a century ago, until now no agents that can block the action of ACTH have been developed and made available for human clinical studies. This is a major step forward towards a new class of therapeutic for patients suffering from devastating diseases of the stress endocrine axis, such as Cushing's disease or congenital adrenal hyperplasia. I am extremely proud of our discovery scientists for crafting a molecule that has the potential to solve this long-standing problem in endocrinology."

"CRN04894 is a nonpeptide, small molecule that is designed to be taken orally to block the interaction of ACTH with its target receptor. It has the potential to offer a life-saving treatment option to patients with Cushing's disease, CAH and related diseases" said **Alan Krasner, M.D. Chief Medical Officer of Crinetics**. "Like the first-in-human study for

our lead endocrine drug candidate, paltusotine, this first-in-human study for CRN04894 is designed to evaluate not just safety and pharmacokinetic data, but also to assess the pharmacologic activity to lower cortisol levels. Serum cortisol is the biomarker used to evaluate treatments of Cushing's disease. It has served as the basis for FDA approval of recent therapies and is a meaningful pharmacodynamic readout to assess the ability of CRN04894 to block ACTH signaling in other conditions of ACTH excess, such as CAH. Like our other programs, we believe that if successful, this healthy volunteer study can provide important clinical proof-of-concept data for the program."

About the CRN04894-01 Phase 1 Study

Crinetics anticipates enrolling approximately 100 healthy volunteers divided into multiple cohorts in the single ascending dose (SAD) and multiple ascending dose (MAD) phases of the study. In the SAD phase, study participants will receive synthetic ACTH during the study to replicate conditions of excess ACTH and create a baseline of elevated serum cortisol. On day 1, volunteers will undergo ACTH stimulation after which they will be administered placebo or ascending doses of study drug. In the MAD phase, participants will undergo ACTH stimulation test at baseline after which they will be administered placebo or ascending doses of study drug daily for 10 days and an ACTH stimulation test will be performed after repeat dosing.

The primary objective is to evaluate the percentage of subjects with treatment-emergent adverse events. In addition to safety, a key endpoint is inhibition of ACTH stimulated serum cortisol levels compared to baseline before treatment with CRN04894. A reduction in serum cortisol could indicate successful blockade of MCR2, the receptor target of ACTH. Pharmacokinetics of CRN04894 will also be assessed.

About CRN04894

Adrenocorticotropic hormone (ACTH) is synthesized and secreted by the pituitary gland and binds to melanocortin type 2 receptor (MC2R), which is selectively expressed in the adrenal gland. This interaction of ACTH with MCR2 stimulates the adrenal production of cortisol, a stress hormone that is involved in the regulation of many systems. Cortisol is involved for example, 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, has exhibited strong binding affinity for MC2R in preclinical models and demonstrated suppression of adrenally derived glucocorticoids and androgens that are under the control of ACTH, while maintaining mineralocorticoid production.

About Cushing's Disease and Congenital Adrenal Hyperplasia

Cushing's disease is a rare disease with a prevalence of approximately 10,000 patients in the United States. It is more common in women, between 30 and 50 years of age. Cushing's disease often takes many years to diagnose and may well be under-diagnosed in the general population as many of its symptoms such as lethargy, depression, obesity, hypertension, hirsutism, and menstrual irregularity can be incorrectly attributed to other more common disorders.

Congenital adrenal hyperplasia (CAH) encompasses a set of disorders that are caused by genetic mutations that result in impaired cortisol synthesis with a prevalence of approximately 27,000 patients in the United States. This lack of cortisol leads to a loss of feedback mechanisms and results in persistently high levels of ACTH, which in turn causes overstimulation of the adrenal cortex. The resulting adrenal hyperplasia and over-secretion of other steroids (particularly androgens) and steroid precursors can lead to a variety of effects from improper gonadal development to life-threatening dysregulation of mineralocorticoids.

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 biased agonist for the treatment of acromegaly, an orphan disease affecting more than 25,000 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 NETs in 2021. 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 the expected timing thereof; the potential to initiate a Phase 2 program of paltusotine in patients with carcinoid syndrome due to NETs and the expected timing thereof; the

initiation and enrollment of a Phase 1 clinical study in CRN04894 and the expected timing thereof; the potential that CRN04894 could represent a new class of therapeutic for patients suffering from devastating diseases; the potential to generate safety, pharmacodynamic, pharmacokinetic and pharmacologic activity data from such Phase 1 study in healthy volunteers with CRN04894 and the expected timing thereof; and the potential that such data will provide important clinical proof-of-concept for Crinetics' CRN04894 program. 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 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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