NEWS RELEASE

CRINETICS REPORTS POSITIVE TOP-LINE RESULTS FROM CRN04777 PHASE 1 MAD COHORTS

2022-03-30

SAN DIEGO – March 30, 2022 – **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 positive top-line results from the multiple-ascending dose (MAD) cohorts of healthy volunteers in a first-in-human Phase 1 clinical study of CRN04777. These results showed a rapid and sustained reduction of insulin secretion, including in a pharmacologic model of congenital hyperinsulinism (HI). CRN04777 is the company's investigational nonpeptide somatostatin receptor type 5 (SST5) agonist in development as an oral treatment for **congenital monogenic and syndromic hyperinsulinism**.

"We are very excited to see the strong pharmacologic proof-of-concept data from the MAD cohorts that build upon the trial's single-ascending dose (SAD) cohorts that were presented at the Congenital HI International Virtual Research Conference in 2021," explained **Scott Struthers, Ph.D., founder and chief executive officer** of Crinetics. "Consistent with the SAD findings, data from the MAD cohorts showed that CRN04777 inhibited insulin secretion when administered orally once daily over the course of 10 days and eliminated the need for glucose support in a model of hyperinsulinism. We plan to meet with global regulators to discuss the results from our Phase 1 study and plans for advancing the clinical program in HI patients."

These newly announced data are from 27 healthy volunteers who received once daily oral doses of CRN04777 (30 mg, 60 mg, or 120 mg) or placebo for 10 days with daily sampling to measure levels of fasting plasma glucose and insulin. Results showed CRN04777 treatment led to rapid, sustained and dose-dependent decreases in fasting insulin, which in-turn led to dose-dependent increases in fasting plasma glucose. Pharmacokinetic and exposure profiles were consistent with expectations from the SAD cohorts, with CRN04777 being orally bioavailable with a

half-life of approximately 40 hours. Increasing CRN04777 exposures were observed with increasing doses and the study drug was well-tolerated. No serious adverse events (SAEs) were reported and no discontinuations due to adverse events occurred. All adverse events were considered to be mild-to-moderate.

On Day -2 (prior to CRN04777 dosing) and on Day 10 of CRN04777 dosing in each of the MAD cohorts, participants underwent a challenge with a sulfonylurea, which induces excess insulin secretion and pharmacologically mimics the effects of the most common genetic mutations in congenital HI. To avoid the occurrence of hypoglycemia as a result of increased insulin secretion, subjects undergoing the sulfonylurea challenge were evaluated using the euglycemic clamp procedure, meaning they received intravenous (IV) glucose support, with the glucose infusion rate increasing in automated fashion to maintain safe glucose levels. One hour after the sulfonylurea challenge on Day 10, the dose of CRN04777 was administered resulting in a dose-proportional and rapid reduction of insulin secretion and glucose infusion rate requirement compared to baseline. In participants receiving 120 mg of CRN04777, the need for IV glucose support was eliminated for most subjects.

Alan Krasner, M.D., chief medical officer at Crinetics, added, "CRN04777 is the only oral product candidate in clinical development we are aware of that is designed to treat all hyperinsulinism patients, regardless of their underlying genetic mutation. With these latest findings, we have added confidence in CRN04777's potential to prevent hypoglycemia and to help alleviate the enormous treatment burden for children with this disease. We believe these results strongly support clinical studies evaluating CRN04777 in children suffering from hyperinsulinism."

Data Review Conference Call

Crinetics will hold a conference call and live audio webcast today, March 30, 2022, at 4:30 p.m. Eastern Time to discuss results from MAD cohorts of the Phase 1 trial of CRN04777. To participate, please dial 1-877-407-0789 (domestic) or 1-201-689-8562 (international) and refer to conference ID 13727857. To access the webcast, click **here**. Following the live event, a replay will be available on the **Events** page of the Company's website.

About the Phase 1 CRN04777 study

The primary purpose of the Phase 1 study was to assess safety and tolerability following single and multiple doses of CRN04777 administered to healthy volunteers. In addition, pharmacologic proof of concept was sought through two distinct methods of stimulating insulin secretion to mimic hyperinsulinism. During the first part of the SAD phase, healthy adult volunteers received IV glucose to stimulate insulin production and baseline plasma biomarker responses were recorded. The following day, participants received CRN04777 or placebo followed by the IV glucose

challenge, and a comparison was made of plasma biomarker levels to baseline. In the second part of the SAD phase, participants received a sulfonylurea to stimulate insulin secretion in the setting of a euglycemic clamp, and baseline plasma biomarker levels as well as the amount of IV glucose required to maintain euglycemia were recorded. On the next day, participants received the sulfonylurea prior to receiving CRN04777 or placebo and a comparison was made of plasma biomarker levels and IV glucose support to baseline levels. As previously reported, oral administration of CRN04777 showed rapid dose-dependent suppression of insulin secretion in healthy adults who were administered single-ascending doses of CRN04777.

In the MAD phase, volunteers underwent the sulfonylurea challenge in the setting of a euglycemic clamp at baseline, after which they were administered placebo or ascending doses of study drug daily for 10 days. Levels of IV glucose support, glucose and insulin were measured after CRN04777 administration and compared to baseline levels to determine the degree to which CRN04777 could reduce insulin levels.

About CRN04777

CRN04777 is a highly optimized, orally available, nonpeptide SST5-selective agonist that is designed to reduce the excess secretion of insulin in patients with congenital monogenic and syndromic HI, and other diseases of insulin excess. Oral administration of CRN04777 has been shown to potently inhibit insulin secretion and normalize glucose levels in preclinical models of hyperinsulinism. In 2021, Crinetics initiated a Phase 1 clinical study in healthy volunteers to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of CRN04777. Results from the Phase 1 study demonstrated pharmacologic proof-of-concept for CRN04777, with strong dose-dependent suppression of insulin secretion in healthy volunteers.

The U.S. Food and Drug Administration granted rare pediatric disease designation for CRN04777 for the treatment of congenital hyperinsulinism. A rare pediatric disease is defined as a serious or life-threatening disease, which primarily affects individuals aged from birth to 18 years and affects fewer than 200,000 people in the United States.

About Congenital Hyperinsulinism

Hyperinsulinism (HI) is a heterogeneous condition in which dangerously low blood sugar levels are caused by inappropriate insulin secretion from pancreatic β-cells. Congenital HI is a severe form of hyperinsulinism driven by one of more than ten known mutations in certain genes involved in regulating insulin secretion. The incidence of congenital HI is approximately 1 in 30,000 to 50,000 new births in the United States, and it is estimated that there are between 1,500 and 2,000 congenital HI patients in the U.S. While this is a rare disease, congenital HI is a leading cause of persistent hypoglycemia in infants and children. Hyperinsulinism can also be one of a complex of findings

associated with Beckwith-Wiedemann syndrome, Sotos syndrome, Kabuki syndrome, and Turner syndrome. The estimated prevalence of these syndromic forms of HI is approximately 2,000 patients in the U.S. For all forms of HI, early diagnosis is vital to prevent acute life-threatening complications of hypoglycemia including apnea, seizures, and coma as well as brain damage and developmental delays that can occur from recurrent hypoglycemia.

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 26,000 people in the United States. A Phase 3 clinical program in acromegaly with paltusotine is underway. Crinetics also plans to advance paltusotine into 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.

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 benefits of CRN04777 for patients with congenital and other forms of hyperinsulinism; plans to meet with regulators and to advance CRN04777 into a clinical program in patients for the treatment of hyperinsulinism; plans to advance paltusotine into a Phase 2 trial for the treatment of carcinoid syndrome associated with neuroendocrine tumors and plans to advance other pipeline product candidates. 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" 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 risks and uncertainties inherent in Crinetics' business, including, without limitation: preliminary data that we report may change following a more comprehensive review of the data related to the clinical trials and such data may not accurately reflect the

complete results of a clinical trial, and the FDA and other regulatory authorities may not agree with our interpretation of such results; advancement of CRN04777 into later stage trials is dependent on and subject to the receipt of further feedback from the FDA; 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 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; 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 trials and nonclinical studies; regulatory developments in the United States and foreign countries; Crinetics may use its capital resources sooner than it expects; 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 documents the company files from time to time with the SEC. 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:
Marc Wilson
Chief Financial Officer
IR@crinetics.com
(858) 450-6464

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

Aline Sherwood
Scienta Communications
asherwood@scientapr.com
(312) 238-8957

Source: Crinetics Pharmaceuticals, Inc.