NEWS RELEASE

CRN04777 (CONGENITAL HYPERINSULINISM) ADVANCES TO PHASE 1 STUDY

2021-02-03

Phase 1 study is designed to provide clinical proof-of-concept by taking advantage of established methods in endocrinology

SAN DIEGO – February 3, 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 the initiation of a Phase 1 study of **CRN04777, an oral, nonpeptide somatostatin receptor type 5 (SST5) agonist** being developed as a treatment for **congenital hyperinsulinism (congenital HI)**. Congenital HI is a rare genetic disease associated with dysregulated insulin production in which excess insulin produces life-threatening hypoglycemia (low blood glucose) beginning at birth. The purpose of this study is to evaluate the safety and tolerability of CRN04777 in healthy adult volunteers. In addition, the study is designed to test the mechanism of action of CRN04777 by measuring its ability to suppress insulin secretion in healthy volunteers following stimulation with either glucose or a sulfonylurea, an agent that increases the secretion of insulin.

“Congenital HI is a truly devastating disease. Early recognition, diagnosis and treatment is imperative to prevent life-threatening hypoglycemia, severe neurological sequelae and developmental delay,” said Sr. Medical Director Chris Ferrara-Cook, M.D., Ph.D., a pediatric endocrinologist who has specialized in the treatment of children with congenital HI throughout her medical career and who is leading this clinical program at Crinetics. “Families with a child diagnosed with congenital HI are burdened with years of constant glucose monitoring and maintenance in an attempt to minimize the degree and frequency of hypoglycemic events. Treatment options are limited, and we believe the current standard of care is inadequate. CRN04777 is a novel therapy under development that focuses

on reducing insulin secretion, with a mechanism of action that we believe could treat all genetic forms of congenital HI. Oral administration has a significant advantage for treating the infants and young children who have the greatest need for novel therapies."

"CRN04777 is another nonpeptide, small molecule drug candidate for a rare, endocrine disease that has emerged from our internal discovery efforts. Like our other clinical programs, including that for paltusotine which has recently completed Phase 2 in acromegaly, this Phase 1 study with CRN04777 is designed to provide important safety and tolerability information as well as evidence of clinical proof-of-concept using established methods in endocrinology," said **Scott Struthers, Ph.D., founder and CEO of Crinetics**. "Through patient advocacy groups like **Congenital Hyperinsulinism International**, we have come to learn the devastating toll this disease has on children with congenital HI and their families. We are ecstatic to bring this drug candidate to the clinic with the hope that it will provide an important new oral therapeutic tool to help these families and their treating physicians."

About the CRN04777-01 Phase 1 Study

Crinetics anticipates enrolling up to 117 healthy volunteers, who will be randomized into cohorts to receive single-ascending doses (SAD) or multiple-ascending doses (MAD) of CRN04777. In the first part of the SAD phase, participants will receive IV glucose to stimulate insulin production and baseline plasma biomarker levels will be recorded. The following day, participants will receive CRN04777 or placebo followed by the IV glucose challenge, and a comparison will be made of plasma biomarker levels to baseline. In the second part of the SAD phase, participants will receive a sulfonylurea to stimulate insulin secretion in the setting of a euglycemic clamp, in which blood glucose levels are maintained ("clamped") via glucose infusion. Baseline plasma biomarker levels as well as the amount of IV glucose required to maintain euglycemia will be recorded. On the next day, participants will be administered CRN04777 or placebo, after which they will receive the sulfonylurea challenge, and a comparison will be made of plasma biomarker levels and IV glucose support to baseline levels. In the MAD phase, volunteers will undergo the sulfonylurea challenge in the setting of a euglycemic clamp at baseline after which they will be administered placebo or ascending doses of study drug daily for 10 days. Levels of IV glucose support, glucose, insulin and C-peptide will be measured after CRN04777 administration and compared to baselines to determine the degree to which CRN04777 can reduce insulin levels. Food effect, safety and tolerability will also be assessed.

In September 2020, it was announced that the **U.S. Food and Drug Administration granted rare pediatric disease designation for CRN04777**. 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 increased insulin secretion from pancreatic β-cells. Congenital HI is a severe form of hyperinsulinism driven by one of more than ten known genetic 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 2,000 and 4,000 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. Early diagnosis is vital to prevent neurological complications due to recurrent low blood sugar, which can result in apnea, seizures, developmental delays, learning disabilities and even death.

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 CRN04777 and the expected timing thereof; the potential to generate data regarding the safety, tolerability, food effects and mechanism of action of CRN04777 from such Phase 1 study in healthy volunteers and the expected timing thereof; the potential that such data will provide

evidence of clinical proof-of-concept of CRN04777; and the potential of CRN04777 to treat all genetic forms of congenital HI. 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, 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.

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.