NEWS RELEASE

CRN04777 DEMONSTRATES PHARMACOLOGIC PROOF-OF-CONCEPT WITH STRONG DOSE-DEPENDENT SUPPRESSION OF INSULIN SECRETION IN PHASE 1 SINGLE ASCENDING DOSE STUDY

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– CRN04777 Phase 1 Program Progressing to Multiple Ascending Dose Cohorts to Advance Development as a Treatment for Congenital Hyperinsulinisms –

– Demonstrated Dose-dependent Reductions in Glucose-stimulated and Sulfonylurea-induced Insulin Secretion –

– Management Hosting Webcast to Discuss Findings Today at 4:30 p.m. Eastern Time –

SAN DIEGO, September 15, 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 positive preliminary findings from the single ascending dose (SAD) cohorts of a first-in-human Phase 1 clinical study with **CRN04777** demonstrating pharmacologic proof-of-concept for this investigational oral, nonpeptide somatostatin receptor type 5 (SST5) agonist being developed as a treatment for congenital hyperinsulinism (HI).

“Congenital HI patients and their families live in constant fear of hypoglycemia. It is an ever-present danger that significantly impacts all aspects of daily life for these vulnerable patients and their families. Current treatment options are very limited and not universally effective, resulting in a high burden of care,” explained **Chris Ferrara-**

Cook M.D, Ph.D., a pediatric endocrinologist and senior medical director at Crinetics who has specialized in the treatment of children with hyperinsulinism throughout her medical career.

Alan Krasner, M.D., chief medical officer at Crinetics, added, "We are very encouraged by these single ascending dose data that clearly demonstrate proof-of-SST5 agonism and resultant inhibition of insulin secretion with CRN04777 exposure in healthy volunteers. We are excited by the possibility that CRN04777 may serve as an oral treatment to normalize glucose levels in any child born with congenital HI regardless of their specific genetic mutation and eagerly look forward to better understanding its full potential with additional clinical studies."

The 80 healthy volunteers who enrolled in the SAD cohorts were administered oral doses of CRN04777 (0.5 mg to 120 mg) or placebo. The pharmacologic effects of CRN04777 were evaluated using two distinct methods. First, oral administration of CRN04777 showed rapid dose-dependent suppression of insulin secretion in response to an intravenous bolus of glucose in an Intravenous Glucose Tolerance Test, or IVGTT. In a second method, oral administration of CRN04777 rapidly eliminated the need for IV glucose support in individuals who were administered a sulfonylurea, a class of drugs that induces insulin secretion analogous to the most common genetic defect in congenital HI patients. The reductions in insulin secretion and resulting changes in plasma glucose in these pharmacologic evaluations suggest that CRN04777 binds and activates pancreatic β-cell SST5 to inhibit insulin secretion, as designed. CRN04777 was well tolerated in the healthy volunteers who enrolled in these SAD cohorts and all adverse events were considered mild or moderate.

These newly announced findings will be presented during the 2021 Congenital Hyperinsulinism International Virtual Research Conference. The presentation, titled: "Single Dose Results from a Phase 1 Clinical Trial of CRN04777, an Orally Bioavailable SST5-Selective, Nonpeptide Somatostatin Agonist for the Treatment of Congenital Hyperinsulinism: Pharmacokinetics and Pharmacodynamics in Healthy Volunteers," will be made available to conference attendees in the Clinical Trials and Industry Engagement track from 1:00 PM – 2:05 PM Eastern Time on September 18th. **Congenital Hyperinsulinism International** is a nonprofit organization dedicated to providing information, resources and support to the global congenital HI community.

Julie Raskin, executive director of Congenital Hyperinsulinism International (CHI), added, "For many congenital HI families, life revolves around trying to maintain normal blood sugar levels in a loved one to avoid brain damage. New treatments are necessary so children and adults with congenital HI can lead a normal life. We applaud the work being done at Crinetics to address this rare disease and are looking forward to the discussion of this compelling Phase 1 data with the broader congenital HI community at our upcoming conference."

"Congenital HI patients and their families are a source of inspiration for our company and it is tremendously rewarding to see that we may be able to bring our drug discovery and development talents to their aid," said **Scott Struthers, Ph.D.**, founder and chief executive officer of Crinetics. "The pharmacologic proof-of-concept data

presented today represent yet another major step forward for Crinetics and are a testament to the abilities and hard work of all our staff and collaborators. Taking a broader view, these data have allowed us to achieve the important goal of expanding our clinical pipeline to three new chemical entities: **paltusotine**, **CRN04894** and CRN04777, each with clinically demonstrated pharmacologic proof-of-concept. We look forward to continuing to advance these compounds and others in our growing pipeline."

In addition to the ongoing Phase 1 trial of CRN04777, Crinetics also continues to advance its Phase 3 PATHFNDR program evaluating paltusotine in acromegaly and the multiple ascending dose (MAD) portion of its Phase 1 trial evaluating CRN04894, an investigational, oral, nonpeptide adrenocorticotropic hormone (ACTH) antagonist. Data from the MAD portions of the Phase 1 CRN04777 and CRN04894 trials are now expected in Q1 2022.

Data Review Conference Call

Crinetics will hold a conference call and live audio webcast today, September 15, 2021, at 4:30 p.m. Eastern Time to discuss the results of the CRN04777 SAD cohorts. To participate, please dial 877-407-0789 (domestic) or 201-689-8562 (international) and refer to conference ID 13723002. Visit **the event page** to access the webcast. The archived webcast will be available for 90 days.

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 HI, 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, we initiated a Phase 1 clinical study in healthy volunteers to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of CRN04777. Currently, subjects are being enrolled in this Phase 1 study and will be randomized into cohorts to receive multiple ascending doses of CRN04777. Levels of IV glucose support, glucose, and insulin will be measured after CRN04777 administration and compared to baselines to determine the degree to which CRN04777 can reduce insulin levels. 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 for congenital hyperinsulinism**. A rare pediatric disease is defined to include 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 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 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 symptoms associated with other genetic diseases such as 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 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 26,000 people in the United States. A Phase 3 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 hyperinsulinism; the design and timing of data from the MAD portion of the

Phase 1 clinical trial of CRN04777; 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. 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: 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; 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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