



NEWS RELEASE

# CRINETICS PHARMACEUTICALS UNVEILS PARATHYROID HORMONE RECEPTOR ANTAGONIST PROGRAM AT ASBMR

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SAN DIEGO, September 27, 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 its intent to develop a nonpeptide oral parathyroid hormone (PTH) receptor antagonist for the treatment of hypercalcemia associated with primary hyperparathyroidism (HPT) and other diseases of PTH receptor type 1 (PTHr1) over-activation. Details of the preclinical efforts supporting this newly disclosed program will be presented in a late-breaking poster at the upcoming annual meeting of the American Society for Bone and Mineral Research (ASBMR), which is being held October 1-4, 2021.

“Like all our product candidates, our family of novel PTHr1 antagonists are small molecules generated through our in-house discovery efforts. They are designed to specifically block PTHr1, which positions them to potentially address all conditions of excess PTH, whether it’s primary hyperparathyroidism due to parathyroid tumors or hyperplasia; secondary hyperparathyroidism due to chronic kidney disease (CKD); or malignancy-associated hypercalcemia,” stated **R. Scott Struthers, Ph.D., founder and chief executive officer** at Crinetics. “This is our first presentation at ASBMR, and I am eager to discuss our new program with this scientific community. It represents an important expansion of our pipeline and an opportunity to broaden the reach of our drug development efforts to multiple large patient populations with high unmet need.”

PTH regulates calcium and phosphate homeostasis in bone and kidney through activation of its receptor, PTHr1. Increased activation of PTHr1, either via PTH or PTH-related peptide (PTHrP) can lead to skeletal, renal,

gastrointestinal, and neurological problems.

“While PTHR1 is crucial for regulation of calcium homeostasis and metabolic bone health, to our knowledge there are no medications available or in development targeting this receptor for the treatment of PTH or PTHrP-driven diseases,” added **Alan Krasner, M.D., Crinetics’ chief medical officer**. “Our PTHR1 antagonists have the potential to improve the outcomes and experience of patients with parathyroid disease; CKD, or cancer. We look forward to the continued advancement of this preclinical program into IND-enabling studies and then into a healthy volunteer, pharmacologic proof-of-concept phase 1 study. In this way, we expect to leverage utilization of endocrine biomarkers very early in drug development, a paradigm that has now been validated with three internally discovered new chemical entities in our clinical pipeline.”

The Crinetics poster, titled, “Discovery of Potent and Orally Bioavailable Nonpeptide Parathyroid Hormone Receptor Type-1 (PTHr1) Antagonists for the Treatment of Primary Hyperparathyroidism (PHPT),” will be presented by Elizabeth Rico-Bautista, Ph.D., principal scientist at Crinetics. It will be presented during the Late-Breaking Poster Session II at the ASBMR annual meeting on October 3, 2021, from 1:00 – 03:00 p.m. Pacific Time and may be accessed in the virtual conference environment for 30 days following the conclusion of the meeting. In addition, it will be available on the Crinetics website in accordance with the society’s embargo policy.

#### About PTH Receptor Antagonists

Crinetics’ PTH receptor type-1 antagonists have been designed and optimized by the Crinetics discovery team with the goal of providing a once-daily oral option for patients with primary hyperparathyroidism, humoral hypercalcemia of malignancy (HHM), and other diseases of excess PTH receptor activation. We are in the late stages of selecting a lead candidate from this family of compounds, which we anticipate will enable us to initiate IND-enabling studies in 2022.

#### About Hyperparathyroidism and HHM

The two most common causes of hypercalcemia are hyperparathyroidism and malignancy. Hyperparathyroidism may be classified as primary (PHPT), in which a benign tumor or hyperplasia involving one or more of the four parathyroid glands causes overproduction of parathyroid hormone (PTH). Primary HPT affects approximately 100,000 new patients per year in the U.S. and, while it can often be cured surgically, there are an estimated 480,000 nonsurgically treated patients in the US. Advanced solid tumors or multiple myeloma also produce PTH-related peptide (PTHrP), a protein of similar structure to PTH that acts on the same receptor, PTHR1. Increased production of PTH (or PTHrP) triggers the release of calcium from bones, causing hypercalcemia. Hypercalcemia can cause loss

of appetite, nausea, vomiting, dehydration, constipation, memory loss, confusion, bone loss, kidney stones, and pancreatitis. HHM impacts an estimated 50,000 to 200,000 patients annually in the US . The metabolic abnormalities seen in chronic kidney disease can lead to a state of sustained secondary hyperparathyroidism and the formation of hyperplastic parathyroid glands. In these patients, chronic excess PTH stimulation of bone forming osteoblast cells can lead to high turnover bone disease and worsening metabolic abnormalities. More than 13M patients in the US have chronic kidney disease, many of whom suffer from persistent secondary hyperparathyroidism.

#### 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 and syndromic 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 PTH receptor antagonists for patients with primary hyperparathyroidism, HHM, secondary hyperparathyroidism due to chronic kidney disease and other diseases of excess PTH receptor activation; the potential of Crinetics' PTH receptor antagonist program to improve the outcomes and experience of patients with parathyroid disease, CKD, or cancer; plans to identify and advance a lead candidate for development, including potential IND-enabling studies in 2022 and a healthy volunteer, pharmacologic proof-of-concept phase 1 study; 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: the results of preclinical studies and early clinical trials are not necessarily predictive of future results; 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, nonclinical studies and preclinical studies for paltusotine, CRN04894, CRN04777, its PTH receptor antagonist program 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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