NEWS RELEASE

CRINETICS ANNOUNCES POSITIVE INITIAL FINDINGS FROM ONGOING OPEN-LABEL PHASE 2 STUDY OF PALTUSOTINE FOR THE TREATMENT OF CARCINOID SYNDROME

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- Significant Reductions in Frequency and Intensity of Both Bowel Movements and Flushing Episodes Were Observed
- Paltusotine was Well-Tolerated with an Overall Pharmacokinetic Profile that was Consistent with Prior Studies
- Phase 2 Study Enrollment is Complete (N=36), and Topline Results Expected in 1H 2024
- Management to Host a Conference Call Today at 5:00 p.m. Eastern Time

SAN DIEGO – December 18, 2023 – 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 initial findings from its ongoing open-label Phase 2 carcinoid syndrome (CS) study of paltusotine, an oral, once-daily investigational compound being developed for the treatment of acromegaly and CS.

“We are very encouraged by these strong initial findings in our Phase 2 study of paltusotine in people with carcinoid syndrome,” said Scott Struthers, Ph.D., founder and chief executive officer of Crinetics. “These initial results show the potential of paltusotine to significantly reduce both frequency and intensity of bowel movements and flushing, the key carcinoid syndrome symptoms. Further, paltusotine was well-tolerated and the overall pharmacokinetic profile was consistent with prior studies. After completing this Phase 2 study next quarter, we anticipate sharing the results with the FDA to align on the design of a Phase 3 program.”

Key Highlights from Ongoing Open-label Phase 2 Study of Paltusotine in Carcinoid Syndrome:

The Phase 2 study is a randomized, open-label, parallel group, multi-center study evaluating the safety, tolerability, pharmacokinetics, and efficacy of paltusotine in people living with carcinoid syndrome. Participants were randomized to receive either 40 mg or 80 mg of paltusotine, with the ability to dose titrate based on tolerability or inadequate control of symptoms during the first four weeks of treatment. At the time of this initial data snapshot, safety data were available for 27 participants, 23 of whom had completed at least two weeks of the randomized treatment period and 15 of whom had completed the full 8-week randomized treatment period. Thirteen of the 15 participants (87%) who completed the randomized treatment phase enrolled in the long-term extension phase of the study.

The initial findings indicate that:

- Administration of paltusotine resulted in rapid and sustained reductions in bowel movement (BM) frequency and flushing episodes:
    - 65% reduction of excess bowel movements (defined as daily bowel movements above the upper limit of normal, 3/day) for patients with >3/day at baseline
    - 65% reduction of flushing frequency for patients with >1/day at baseline
- Exposure of paltusotine in people with carcinoid syndrome was consistent with prior clinical studies
- Paltusotine was generally well-tolerated with a safety profile consistent with prior clinical studies
    - There were no treatment-related severe or serious adverse events (AEs), with the majority of treatment-related AEs being mild-to-moderate.
    - The most frequently reported AEs included diarrhea, headache, and abdominal pain.
- Enrollment in the study is complete, with a total of 36 participants enrolled. Topline data from the complete study is expected in the first half of 2024.

Data Review Conference Call

Crinetics will hold a conference call and live webcast on Monday, December 18 at 5:00 p.m. Eastern Time to discuss the initial findings from the Phase 2 study. To participate, please dial 1-877-451-6152 (domestic), 1-201-389-0879 (international), or request a callback **here** and refer to conference ID 13742964. To access the webcast, click **here**. Following the live event, a replay will be available on the Investors section of the Company's website.

About the Phase 2 Study

The Phase 2 study is a randomized, open-label, parallel group, multi-center study evaluating the safety, tolerability, pharmacokinetics and efficacy of paltusotine in people living with carcinoid syndrome. This study consists of a

randomized treatment phase followed by a long-term extension phase. Enrollment in the study is complete, and a total of 36 patients with documented carcinoid syndrome requiring medical therapy were randomized to receive either 40 mg or 80 mg of daily oral paltusotine. The treatment phase of the study is expected to be completed in the first quarter of 2024. For additional information, please visit clinicaltrials.gov (**NCT05361668**).

About Carcinoid Syndrome

Carcinoid syndrome is found in approximately 20% of patients with neuroendocrine tumors (NETs). NETs are a rare, slow-growing type of cancer that arise most often in the digestive tract. When these tumors metastasize to the liver, carcinoid syndrome can occur and is most commonly characterized by diarrhea and flushing. While injectable depot somatostatin receptor ligand (SRL) therapies are mainstay treatments for carcinoid syndrome, these injections are associated with considerable treatment burden and offer inadequate relief of carcinoid syndrome symptoms for many patients.

About Paltusotine

Paltusotine is the first oral, once-daily selectively-targeted somatostatin receptor type 2 (SST2) agonist and is currently in investigational Phase 3 studies for acromegaly and a Phase 2 study for carcinoid syndrome. It was designed by the Crinetics discovery team to provide an efficacious and convenient once-daily option for people living with acromegaly and neuroendocrine tumors. In Phase 2 studies and the recently completed PATHFNDR-1 Phase 3 study, paltusotine maintained IGF-1 levels in acromegaly patients who switched from monthly injectable medications to paltusotine. IGF-1 is the primary biomarker endocrinologists use to manage acromegaly patients. Initial findings from an ongoing Phase 2 study in carcinoid syndrome further support paltusotine's potential beyond acromegaly.

About Crinetics Pharmaceuticals

Crinetics Pharmaceuticals is a clinical stage pharmaceutical company focused on the discovery, development, and commercialization of novel therapeutics for endocrine diseases and endocrine-related tumors. **Paltusotine**, an investigational, first-in-class, oral somatostatin receptor type 2 (SST2) agonist, is in Phase 3 clinical development for acromegaly and Phase 2 clinical development for carcinoid syndrome associated with neuroendocrine tumors. Crinetics has demonstrated pharmacologic proof-of-concept in a Phase 1 clinical study for **CRN04894** a first-in-class, investigational, oral ACTH antagonist, that is currently in Phase 2 clinical studies for the treatment of Cushing's disease and congenital adrenal hyperplasia. All of the Company's **drug candidates** are orally delivered, small molecule new chemical entities resulting from in-house drug discovery efforts, including additional discovery programs addressing a variety of endocrine conditions such as hyperparathyroidism, polycystic kidney disease, Graves' disease, thyroid eye disease, hyperinsulinism, diabetes and obesity.

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