NEWS RELEASE

CRINETICS PHARMACEUTICALS REPORTS POSITIVE INTERIM RESULTS FOR THE ACROBAT EDGE PHASE 2 TRIAL OF PALTUSOTINE (CRN00808) IN ACROMEGALY PATIENTS AND PROVIDES CORPORATE UPDATE

2020-04-06

Crinetics Pharmaceuticals Reports Positive Interim Results for the ACROBAT Edge Phase 2 Trial of Paltusotine (CRN00808) in Acromegaly Patients and Provides Corporate Update

April 6, 2020

| In **Press Releases**

| By **Joe DeMaegd**

- Data from initial patients who have completed the ongoing open label Edge trial show that IGF-1 levels were maintained after 13 weeks of treatment when patients were switched to once daily oral paltusotine from commercially available depot injections of the peptide somatostatin receptor ligands, octreotide or lanreotide.
- ACROBAT Edge recruitment is complete and topline data from all patients in the trial is expected in the fourth quarter of 2020
- Crinetics plans to advance paltusotine into Phase 3 for patients with acromegaly in the first half of 2021 with to-be-marketed formulation and also into Phase 2 for patients with neuroendocrine tumors who suffer from

carcinoid syndrome

- Management to host webcast/conference call Tuesday, April 7, 2020 at 8 a.m. EDT / 5 a.m. PDT

SAN DIEGO, April 06, 2020 (GLOBE NEWSWIRE) — 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 reported interim results from the ongoing ACROBAT Edge Phase 2 trial. Results as of a February 23, 2020 data cutoff showed that acromegaly patients switching from injectable depot therapy to once daily oral paltusotine (formerly CRN00808) maintained IGF-1 levels previously achieved with commercially available depot injections of somatostatin receptor ligands (SRLs).

Interim results from an exploratory analysis of the first 13 patients who entered the Edge trial on octreotide or lanreotide depot monotherapy (group 1) showed that, as of the cutoff date, switching to once daily oral paltusotine maintained patient IGF-1 levels at those achieved with prior depot therapy [mean change from baseline = -0.015 x ULN (95% CI = -0.123, +0.092)]. Ten of the 11(91%) patients in group 1 who completed paltusotine treatment maintained IGF-1 levels within 15% of their respective baseline levels at week 13. No patient required “rescue therapy” with prior injected peptide acromegaly therapy after switching to paltusotine. Of the 12 patients in whom IGF-1 levels were measured two weeks after paltusotine withdrawal, the mean increase of IGF-1 from baseline was 0.74 x ULN ((95% CI = 0.394, 1.083), p<0.001). Paltusotine washed out in a time frame consistent with the approximately 2-day half-life previously measured in a healthy volunteer study. The rapid mean rise in IGF-1 after washout of paltusotine indicated a lack of suppressive effects by remnants of prior depot injected medication. Additionally, paltusotine was well tolerated and there were no discontinuations due to drug-related adverse events. The most common treatment emergent adverse events among patients in group 1 (>10%) were headache, arthralgia, peripheral swelling, back pain and hyperhidrosis. One serious adverse event (headache) was observed in the overall trial as of the data cutoff and determined to be non-treatment related.

“ACROBAT Edge was designed to evaluate a clinically relevant situation in which there is a switch from commercially available long-acting somatostatin receptor ligand injections to paltusotine, a once daily oral alternative. The interim data from this ongoing trial suggest that IGF-1 control can be maintained by daily oral paltusotine after the IGF-1 suppressive effect of the previous peptide depot has worn off,” said Alan Krasner M.D., Chief Medical Officer of Crinetics. “Patients entering this study are representative of approximately two-thirds of acromegaly patients who are treated with SRL monotherapy. Recruitment for ACROBAT Edge is now complete and topline data is anticipated in the fourth quarter of this year.”

“The currently available intramuscular or deep-subcutaneous depot drugs can be painful, and leave many of us with a return of acromegaly symptoms at the end of each monthly injection cycle,” said Jill Sisco, President of the Acromegaly Community, the largest global advocacy and support organization for acromegaly patients. “Travel to physician’s offices or hospitals for these injections can disrupt our daily lives. The potential opportunity to switch to

a once daily oral therapy that could work as well as the currently available injections to lower our IGF-1 levels is very exciting."

"These exciting interim results from Edge show that our oral nonpeptide drug candidate suppressed IGF-1 levels in these acromegaly patients to the same level as commercially available peptide SRL depots and further bolster our confidence in both paltusotine and Crinetics' highly productive drug discovery organization that created it and all our pipeline programs," said Scott Struthers, Ph.D., Founder and Chief Executive Officer of Crinetics. "With these data we are proceeding with plans to begin the Phase 3 stage of our development program for acromegaly in the first half of 2021 when full results from the Phase 2 trials are expected to be available. These results also give us confidence to expand the clinical program for paltusotine to include patients with neuroendocrine tumors (NETs) and we are evaluating how to best integrate this indication into our overall development plans."

The company also provided additional updates on its development programs as follows:

- New enrollment in the ACROBAT Evolve study has been discontinued. The 12 patients already enrolled will continue in the study. The company believes that this interim data from Edge alone is supportive of moving forward into Phase 3. Rather than waiting for Evolve to complete enrollment in the current environment, stopping enrollment now enables data from those patients already enrolled in the study to be available for end of Phase 2 regulatory interactions on the same timeline as data from Edge.
- Phase 1 data for CRN01941 in healthy volunteers showed that the compound did not represent an improvement over paltusotine. Therefore, the company has discontinued its development in order to focus resources on development of paltusotine for both acromegaly and NETs. We believe that the acceleration and increased efficiency offered by focusing on paltusotine offers the best path forward for our sst2 franchise.
- First-in-human enabling activities are ongoing for both the oral nonpeptide ACTH antagonist for the treatment of Cushing's disease and congenital adrenal hyperplasia, and the oral nonpeptide sst5 agonist for the treatment of hyperinsulinism. The start of Phase 1 clinical trials is planned for late 2020 or early 2021 and if successful, the company anticipates PK/PD data from these human proof-of-concept studies in the first half of 2021.
- Management has updated its cash runway guidance to extend into 2022 based on these development program updates.

Conference Call and Webcast

Crinetics' management will host a webcast and conference call Tuesday, April 7, 2020 at 8 a.m. EDT / 5 a.m. PDT to discuss the interim results for the EDGE clinical trial and provide a corporate update. The live call may be accessed by dialing (877) 860-8623 for domestic callers and (720) 405-3401 for international callers and entering the conference code: 6048597. A live webcast of the call will be available from the Investor Calendar section of the company's IR website at **https://ir.crinetics.com/events-and-presentations/events**.

Trial Design for ACROBAT Edge

ACROBAT Edge (NCT03789656) is an ongoing open label, single-arm exploratory study designed to evaluate the safety and efficacy of paltusotine in patients with acromegaly who have not achieved normal IGF-1 levels despite stable therapy with a SRL (group 1) or with a SRL in combination with a dopamine agonist (group 2). Additional exploratory subgroups are also eligible for enrollment in this trial, all of whom have normal IGF-1 at baseline: patients treated with a SRL in combination with a dopamine agonist (group 3), pasireotide LAR monotherapy (group 4), or a SRL in combination with pegvisomant (group 5). Eligible patients receive their last injection of their previous SRL 4 weeks prior to switching to once daily oral paltusotine monotherapy for a 13-week dose titration period, followed by a 4-week drug washout period. The primary endpoint is change in IGF-1 from baseline to the completion of the 13-week dose titration period in a target sample size of 30 patients in groups 1 and 2.

About Paltusotine

Paltusotine (formerly CRN00808) is an orally available nonpeptide biased agonist that is designed to be highly selective for the somatostatin sst2 receptor. It was designed by the Crinetics discovery team to provide a once daily option for patients with acromegaly and neuroendocrine tumors that are currently treated by injected therapies that sell approximately $3.1 billion annually. Non-clinical chronic toxicology studies are complete and no dose limiting toxicity was identified at the maximum feasible doses in rats and dogs. Crinetics previously completed a Phase 1 trial that showed potent suppression of the GH axis in healthy volunteers, which provided clinical proof-of-concept. In addition, the molecule's observed plasma half-life of ~2 days suggested the potential for paltusotine for once daily oral administration. A subsequent Phase 1 trial showed that paltusotine was 70% orally bioavailable.

About Acromegaly

Acromegaly is a serious disease generally caused by a benign growth hormone (GH) secreting tumor in the pituitary. Excess GH secretion causes excess secretion of insulin-like growth factor-1 (IGF-1) from the liver, which causes bone and cartilage overgrowth, organ enlargement, and changes in glucose and lipid metabolism. The symptoms of acromegaly include abnormal growth of hands and feet and changes in shape of the bone and cartilage that result in alteration of facial features. Overgrowth of bone and cartilage and thickening of tissue leads to arthritis, carpal tunnel syndrome, joint aches, enlarged lips, nose and tongue, deepening of voice due to enlarged vocal cords, sleep apnea due to obstruction of airways, and enlargement of heart, liver, and other organs.

Surgical removal of pituitary adenomas, if possible, is the preferred initial treatment for most acromegaly patients. Pharmacological treatments are used for patients that are not candidates for surgery, or when surgery is unsuccessful in achieving treatment goals. Approximately 50% of patients with acromegaly prove to be candidates for pharmacological treatment. Long-acting somatostatin receptor ligands (SRL) are usually the initial pharmacologic treatment, however these drugs require monthly injections and are commonly associated with pain, injection site reactions, and increased burden in the lives of patients. Although over 90% of patients have

demonstrable responses to SRLs (Annals of Internal Medicine. 1992; 117:711-718) only 20-40% of patients achieve normalization of IGF-1 (J Clin Endocrinol Metab 99: 791–799, 2014). Additional pharmacological treatment options include dopamine agonists or GH receptor antagonists which may be used in combination with SRLs.

About Neuroendocrine Tumors

NETs arise from cells of the enteroendocrine system. Tumors in gastroenteropancreatic tissues account for approximately 60% of cases, but in approximately 25% of cases, NETs can also arise from neuroendocrine cells in the lung. In approximately 20% of cases, these tumors are associated with excess secretion of serotonin and other hormones resulting in carcinoid syndrome, which is typically characterized by severe diarrhea and flushing. Patients with grade 1 and 2 NETs and distant metastases have a five-year survival probability of ranging from 30-70% depending on the primary site. NETs are the second most prevalent GI tumor after colon cancer with prevalence estimated to be over 171,000 in the United States.

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 oral selective nonpeptide somatostatin receptor type 2 biased agonist undergoing two Phase 2 clinical trials 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 trial in acromegaly and a Phase 2 trial for the treatment of carcinoid syndrome associated with NETs in 2021. The company is also developing an oral nonpeptide somatostatin sst5 agonist for hyperinsulinism, as well as an oral nonpeptide ACTH antagonist for the treatment of Cushing's disease, congenital adrenal hyperplasia and other diseases of excess ACTH excess. 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 for interim data results to be consistent with final results, once available; the potential for any of our ongoing clinical trials to show safety or efficacy; the potential benefits of paltusotine for acromegaly patients; the potential to initiate a pivotal Phase 3 trial of paltusotine in acromegaly based on interim results obtained to date and the timing thereof; the planned expansion of the paltusotine development program to include the treatment of carcinoid syndrome in patients with NETs and the expected timing thereof, including initiation of a Phase 2 trial in these patients; the anticipated timing of topline data for EDGE and PK/PD data for its other development programs and initiation of

trials thereafter; and the company's anticipated cash runway. 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 risk that interim results of a clinical trial do not necessarily predict final results and that one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data, and as more patient data become available; potential delays in the commencement, enrollment and completion of clinical trials and the reporting of data therefrom; advancement of paltusotine into a Phase 3 trial 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 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.

Contacts:
Marc Wilson
Chief Financial Officer
IR@crinetics.com
(858) 450-6464

Robert H. Uhl
Westwicke ICR
robert.uhl@westwicke.com
(858) 356-5932