NEWS RELEASE

Crinetics to Present New Long-Term Data Demonstrating Durable Control of Once-Daily, Oral PALSONIFY™ (Paltusotine) in Acromegaly at ENDO 2025

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Data show that PALSONIFY was well tolerated and IGF-1 levels remained stably controlled during long-term open label extensions of PATHFNDR-1 and PATHFNDR-2 studies

Additional PALSONIFY presentations demonstrate reductions in patient-reported symptom burden, including both symptom severity and rates of symptom flares

SAN DIEGO, July 13, 2025 (GLOBE NEWSWIRE) -- **Crinetics Pharmaceuticals, Inc.** (Nasdaq: CRNX) today announced new data from its clinical development program evaluating once-daily, oral investigational PALSONIFY™ (paltusotine) in acromegaly will be presented in several oral and poster presentations at the Endocrine Society's Annual Meeting, ENDO 2025. Notably, open-label extension (OLE) data from both the pivotal PATHFNDR-1 and PATHFNDR-2 trials will be featured in two presentations, showing the long-term clinical profile of PALSONIFY in people with acromegaly.

"With once-daily, oral PALSONIFY's PDUFA date quickly approaching, we're excited to see a growing body of data that continues to underscore its potential as the next generation of care for people living with acromegaly," said Scott Struthers, Ph.D., Founder and Chief Executive Officer of Crinetics. "Building on the remarkable Phase 3 trial results from the PATHFNDR studies that we've presented at ENDO previously, the new long-term data we're showcasing this year provide further evidence of PALSONIFY's ability to deliver durable IGF-1 control, sustained

improvements in patient symptom burden, and a consistent safety profile."

PATHFNDR-1 Open-Label Extension (OLE) Study

The PATHFNDR-1 Phase 3 trial enrolled adults with acromegaly who were biochemically controlled on monthly injectable somatostatin receptor ligands (SRLs). Following a 36-week randomized, placebo-controlled period, 53 of 58 participants (91%) entered the ongoing single-arm open-label extension. An interim analysis includes data through Week 96 of total study participation (60 weeks in the OLE).

- In patients who transitioned from injected SRLs to once-daily oral PALSONIFY, mean insulin-like growth factor 1 (IGF-1) levels remained stable with IGF-1 (mean ± SE) of 0.93 ± 0.22 at OLE baseline and 0.81 ± 0.21 times the upper limit of normal (ULN) at Week 96, demonstrating durable biochemical control over this time span.
- Growth hormone (GH) levels were also stable, with mean values of 1.0 ± 1.0 ng/mL at baseline and 1.1 ± 1.2 ng/mL at Week 96.
- Symptom control, as measured by the Acromegaly Symptom Diary (ASD)—a seven-item daily patient-reported outcome assessing core acromegaly symptoms such as headache, joint pain, sweating, fatigue, and soft tissue swelling—also remained stable at Week 96.
- PALSONIFY was generally well tolerated.

These results will be included in an oral presentation titled "Disease Control in Patients With Acromegaly Switching From Injected Somatostatin Receptor Ligands to Once-Daily Oral Paltusotine: Interim Results of the PATHFNDR-1 Open-Label Extension," taking place July 13 from 2:45-3:00 PM PT.

PATHFNDR-2 OLE Study

The PATHFNDR-2 trial is a randomized, double-blind, placebo-controlled Phase 3 study evaluating once-daily oral PALSONIFY in adults with biochemically uncontrolled acromegaly (baseline IGF-1 > 1.3 × ULN). After a 24-week RC period, 103 of 106 completers (97.2%) entered the ongoing OLE, along with 11 additional patients who were eligible for the RC phase but enrolled directly into the OLE after the completion of RC phase enrollment. This interim analysis includes efficacy data from 88 patients through Week 84 (corresponding to 60 weeks in the OLE), with safety data reported for all 114 enrolled.

- Patients who had received placebo during the RC phase experienced sustained reductions in IGF-1, with a mean change from baseline of –0.81 × ULN at Week 84 (n=39). Direct-to-OLE participants (n=9) showed similar reductions (–0.75 × ULN), while those who had been treated with PALSONIFY during the RC phase (n=40) maintained control (mean change –0.01 × ULN).
- GH, ASD symptom scores and pituitary tumor size were durably controlled over the study period.
- PALSONIFY was generally well tolerated.

These results will be included in a poster presentation titled “Once-Daily Oral Paltusotine in the Treatment of Patients with Biochemically Uncontrolled Acromegaly: Interim Results of the PATHFNDR-2 Open-Label Extension,” taking place July 14, from 12:00 PM – 1:30 PM PT.

Additional data presented at ENDO 2025 highlighted the impact of PALSONIFY on symptom burden in acromegaly. A pooled analysis of ASD scores from PATHFNDR-1 and PATHFNDR-2 showed that greater proportions of patients treated with PALSONIFY experienced less acromegaly symptom burden compared to placebo, regardless of the magnitude of the symptom effect, treatment history, or state of biochemical disease control. In an analysis of PATHFNDR-1 data, biochemically controlled patients switching from injected SRLs to PALSONIFY saw a significant drop in day to day symptom exacerbations – from over 30% of days on SRLs to just 6.2% during stable PALSONIFY dosing ($p < 0.0001$). All presentations will be posted on **Crinetics.com** at the time of the presentation.

About PALSONIFY™ (Paltusotine)
Crinetics’ lead development candidate, PALSONIFY, is the first investigational once-daily, oral, selectively-targeted somatostatin receptor type 2 (SST2) nonpeptide agonist that has completed Phase 3 clinical development for acromegaly and is in Phase 3 clinical development for carcinoid syndrome associated with neuroendocrine tumors. It was designed to be a once-daily oral option for the control of acromegaly and carcinoid syndrome. In Phase 3 studies, once-daily, oral PALSONIFY maintained IGF-1 levels and symptom control in patients with acromegaly who were switched from monthly injectable medications (PATHFNDR-1) and rapidly decreased IGF-1 levels and symptom burden in medically untreated acromegaly patients (PATHFNDR-2). IGF-1 is the primary biomarker endocrinologists use to manage acromegaly patients. Results from a Phase 2 study in carcinoid syndrome demonstrated rapid and sustained reductions in flushing episodes and bowel movement frequency, which are the most common symptoms of carcinoid syndrome, leading to the initiation of a Phase 3 trial for control of carcinoid syndrome in patients with neuroendocrine tumors.

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. Crinetics’ lead development candidate, PALSONIFY (paltusotine), is the first investigational once-daily, oral, selective somatostatin receptor type 2 (SST2) nonpeptide agonist that is in clinical development for acromegaly and carcinoid syndrome associated with neuroendocrine tumors. Atumelnant is currently in development for congenital adrenal hyperplasia and ACTH-dependent Cushing’s syndrome. 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 (including thyroid eye disease), diabetes, obesity and GPCR-targeted oncology indications.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical facts contained in this press release are forward-looking statements, including statements regarding the plans and timelines for the clinical development of atumelnant and PALSONIFY, including the therapeutic potential and clinical benefits or safety profile thereof; the expected timing of the PDUFA target action date for our NDA submission to the FDA and of a potential EMA decision for our MAA for PALSONIFY for the treatment or maintenance of treatment of acromegaly in the United States and other applicable jurisdictions, and the plans and timelines for the commercial launch PALSONIFY if approved; and the therapeutic potential for our development candidates. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplates,” “believes,” “estimates,” “predicts,” “potential,” “upcoming” or “continue” or the negative of these terms or other similar expressions. These forward-looking statements speak only as of the date of this press release and are subject to a number of risks, uncertainties and assumptions, including, without limitation, initial or topline data that we report may change following completion or a more comprehensive review of the data related to the clinical studies and such data may not accurately reflect the complete results of a clinical study, and the FDA and other regulatory authorities may not agree with our interpretation of such results; geopolitical events may disrupt Crinetics’ business and that of the third parties on which it depends, including delaying or otherwise disrupting its clinical studies and preclinical studies, manufacturing and supply chain, or impairing employee productivity; the success of Crinetics’ clinical studies and nonclinical studies; regulatory developments in the United States and foreign countries; clinical studies and preclinical studies may not proceed at the time or in the manner expected, or at all; the timing and outcome of research, development and regulatory review is uncertain, and Crinetics’ drug candidates may not advance in development or be approved for marketing; and the other risks and uncertainties described in the Company’s periodic filings with the Securities and Exchange Commission (SEC). The events and circumstances reflected in the company’s forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Additional information on risks facing Crinetics can be found under the heading “Risk Factors” in Crinetics’ periodic filings with the SEC, including its annual report on Form 10-K for the year ended December 31, 2024 and quarterly report on Form 10-Q for the quarter ended March 31, 2025. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by applicable law, Crinetics does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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