NEWS RELEASE

Crinetics Announces FDA Approval of PALSONIFY™ (paltusotine) for the Treatment of Adults with Acromegaly

2025-09-25

Novel nonpeptide SST2 agonist PALSONIFY advances the treatment paradigm as the first once-daily, oral therapy approved by the FDA to treat acromegaly

Approval based on data from two pivotal Phase 3 trials where PALSONIFY was well tolerated and resulted in rapid, durable, and consistent biochemical control and reduced symptom burden

Launch of lead product PALSONIFY marks a pivotal milestone for Crinetics as the premier endocrine-focused global pharmaceutical company

Investor call to be held today at 6:00 pm ET

SAN DIEGO, Sept. 25, 2025 (GLOBE NEWSWIRE) -- **Crinetics Pharmaceuticals, Inc.** (Nasdaq: CRNX) today announced that the U.S. Food and Drug Administration (FDA) approved PALSONIFY™ (paltusotine) for the first-line treatment of adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option. PALSONIFY, a selectively-targeted somatostatin receptor type 2 nonpeptide (SST2) agonist, is now the first once-daily, oral treatment approved for adults with acromegaly.

"With the FDA approval of our lead therapy Palsonify, today marks a new era for those living with acromegaly and also for Crinetics as a company," said Scott Struthers, Ph.D., Founder and Chief Executive Officer of Crinetics. "We are very pleased to be fulfilling our commitment to transforming patient lives. This approval is the first to come

from our deep pipeline of first-in-class, small molecule drugs. This would not be possible without the help and partnership of people living with acromegaly, their caretakers, our employees, and the clinical researchers and health care professionals who contributed to Palsonify's successful development program. Thank you to all involved."

The approval is based on data from the **PATHFNDR-1** and **PATHFNDR-2** Phase 3 pivotal trials, which evaluated PALSONIFY's safety and efficacy in previously treated and medically untreated adults with acromegaly. Across both trials, PALSONIFY consistently demonstrated rapid onset, reliable biochemical control, and sustained efficacy.

Participants also reported significant reductions in signs and symptoms associated with acromegaly as measured by the Acromegaly Symptom Diary (ASD) — an FDA-aligned patient-reported outcome tool developed to capture the symptoms that matter to people living with acromegaly. Symptoms include headaches, joint pain, sweating, fatigue, weakness, swelling, and/or numbness/tingling. PALSONIFY was generally well-tolerated, with no serious adverse events reported in the randomized controlled portion of the trials.

Long-term results from the open-label extension (OLE) phases of both trials were presented at this year's Endocrine Society's annual meeting, ENDO 2025, providing further evidence of PALSONIFY's ability to deliver durable IGF-1 control, sustained improvements in patient symptom burden, and a consistent safety profile. Ninety-one percent of patients from PATHFNDR-1 and 97 percent of completers from PATHFNDR-2 enrolled in the OLE.

"The PATHFNDR clinical development program set a new standard for acromegaly treatment by demonstrating the ability of Palsonify to drive both biochemical and symptom control, regardless of the degree of underlying disease severity," said Dr. Shlomo Melmed, Executive Vice President of Medicine and Health Sciences and Dean of the Medical Faculty at Cedars-Sinai. "The approval of Palsonify is a significant advancement for our patients, as there is an unmet need for an easy-to-administer and safe therapeutic option with a rapid action and durable response that can consistently manage acromegaly."

"For people living with acromegaly, treatment once meant burdensome injections, breakthrough symptoms, and lifestyle sacrifices just to stay on track," said Jill Sisco, President of Acromegaly Community. "What matters most to our community – maintaining consistent control so the disease doesn't control us – led us to partner with the FDA on Externally Led Patient-Focused Drug Development meetings. This new treatment reflects that our voices have been heard in shaping the next generation of acromegaly care."

PALSONIFY is expected to be available in the U.S. in early October. Crinetics is ensuring broad access to PALSONIFY by working closely with payers, healthcare providers, and patient advocacy organizations to support those who may benefit from this treatment.

As part of this commitment, Crinetics has launched CrinetiCARE®, a comprehensive support program designed to assist people living with acromegaly throughout their treatment journey. CrinetiCARE provides disease and product education, benefit verification, financial assistance resources, and access to dedicated nurse educators who can offer support with treatment onboarding and ongoing adherence. For more information, visit **www.CrinetiCARE.com** or the PALSONIFY product website **Palsonify.com**.

A Marketing Authorization Application (MAA) for paltusotine in acromegaly is currently under review for use in the European Union, and the current timeline for the Committee for Medicinal Products and Human Use (CHMP) opinion is the first half of 2026. Crinetics is in partnership with Sanwa Kagaku Kenkyuso (SKK) to develop and commercialize paltusotine for acromegaly in Japan.

Paltusotine is also being evaluated for the treatment of carcinoid syndrome in the pivotal Phase 3 CAREFNDR trial.

Conference Call and Webcast
Crinetics will host an investor conference call at 6:00 p.m. Eastern Time to discuss the FDA approval of PALSONIFY. Following the live event, a replay will be available on the Investors section of the Company's website.

Dial-in Details:
Domestic: 1-833-470-1428
International: 1-646-844-6383
Conference ID: 120796
Webcast: **https://events.q4inc.com/attendee/443074040**

PALSONIFY™ (paltusotine) INDICATION:
PALSONIFY is a somatostatin receptor agonist indicated for the treatment of adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS:

- Cholelithiasis and Its Complications: Cholelithiasis, including related complications such as acute cholecystitis and pancreatitis, have been reported. Monitor patients periodically. Discontinue PALSONIFY if complications of cholelithiasis occur and treat appropriately.
- Hyperglycemia and Hypoglycemia: Hyperglycemia, diabetes mellitus, or hypoglycemia, may occur. Monitor blood glucose levels when PALSONIFY treatment is initiated or when dosage is altered. Adjust antidiabetic treatment accordingly.

- Cardiovascular Abnormalities: Cardiac conduction abnormalities and other ECG changes such as PR interval prolongation, bradycardia, sinus arrest, and atrioventricular block may occur in patients with acromegaly and were reported in PALSONIFY clinical trials. Dosage adjustments of concomitant drugs that have bradycardic effects may be necessary.
- Thyroid Function Abnormalities: Somatostatin analogs may suppress the secretion of thyroid-stimulating hormone, which may result in hypothyroidism. Periodic assessment of thyroid function is recommended.
- Steatorrhea and Malabsorption of Dietary Fats: Somatostatin analog treatment may result in malabsorption of dietary fats and subsequent symptoms of steatorrhea, loose stools, abdominal bloating, and weight loss. If new or worsening symptoms are reported with PALSONIFY, evaluate patients for potential pancreatic exocrine insufficiency and manage accordingly.
- Vitamin B_{12} Deficiency: Vitamin B_{12} deficiency may occur. Monitor vitamin B_{12} levels, if clinically indicated.

ADVERSE REACTIONS:
Most common adverse reactions (>5%) are diarrhea, abdominal pain, nausea, decreased appetite, sinus bradycardia, hyperglycemia, palpitations, and gastroenteritis.

DRUG INTERACTIONS:

- Strong or Moderate CYP3A4 Inducers: may decrease PALSONIFY exposure. May require an increased dosage of PALSONIFY.
- Proton Pump Inhibitors: may decrease PALSONIFY exposure. May require an increased dosage of PALSONIFY. Avoid concomitant use of proton pump inhibitors in patients who are already on PALSONIFY 60 mg.
- Cyclosporine: may decrease cyclosporine exposure. May require cyclosporine dosage adjustment when used with PALSONIFY; follow therapeutic monitoring recommendations.

Please report adverse events to Crinetics Pharmaceuticals at 1-833-CRN-INFO (1-833-276-4636) or FDA at 1-800-FDA-1088 or **www.fda.gov/medwatch**.

Please see **Full Prescribing Information** including **Patient Information.**

About PALSONIFY™ (Paltusotine)
PALSONIFY, a selectively-targeted somatostatin receptor type 2 (SST2) nonpeptide agonist is the first and only once-daily, oral therapy approved for the treatment of adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option. 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. Paltusotine is also in Phase 3 clinical development for carcinoid syndrome associated with neuroendocrine tumors (CAREFNDR). 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.

About Crinetics Pharmaceuticals

Crinetics Pharmaceuticals is a global pharmaceutical company committed to transforming the treatment of endocrine diseases and endocrine-related tumors through science rooted in patient needs. Crinetics is focused on discovering, developing, and commercializing novel therapies, with a core expertise in targeting G-protein coupled receptors (GPCRs) with small molecules that have specifically tailored pharmacology and properties.

Crinetics' lead product, PALSONIFY™ (paltusotine), is the first once-daily, oral treatment approved by the U.S. FDA for the treatment of adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option. Paltusotine is also in clinical development for carcinoid syndrome associated with neuroendocrine tumors. Crinetics' deep pipeline of 10+ disclosed programs includes late-stage investigational candidate atumelnant, which is currently in late-stage development for congenital adrenal hyperplasia and ACTH-dependent Cushing's syndrome. Additional discovery programs address a variety of endocrine conditions such as neuroendocrine tumors, Graves' disease (including Graves' hyperthyroidism and Graves' orbitopathy, or thyroid eye disease), polycystic kidney disease, hyperparathyroidism, 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 approval of additional product candidates in our pipeline; the timeline of availability of PALSONIFY in the U.S.; the timeline of the Committee for Medicinal Products and Human Use (CHMP)'s opinion regarding PALSONIFY; the plan to develop and commercialize paltusotine for acromegaly in Japan; the plans and timelines for the clinical development of atumelnant and paltusotine for the treatment of carcinoid syndrome, including the therapeutic potential and clinical benefits or safety profiles thereof and the timeline for global enrollment for CAREFNDR; or the therapeutic potential for our development candidates to transition to clinical development. 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, data that we report may change following completion or a more

comprehensive review of the data related to the clinical studies, and the FDA and other regulatory authorities may not agree with our interpretation of such 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; 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; unexpected adverse side effects, complications and/or drug interactions or inadequate efficacy of the Company's product candidates that may limit their development, regulatory approval and/or commercialization; the Company's dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the success of Crinetics' clinical studies and nonclinical studies; regulatory developments or political changes, including policies related to pricing and pharmaceutical drug reimbursement, 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; Crinetics may use its capital resources sooner than expected or our cash burn rate may accelerate; any future impacts to our business resulting from geopolitical developments outside our control; 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. 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.

Photos accompanying this announcement are available at:

https://www.globenewswire.com/NewsRoom/AttachmentNg/c29d44d5-f6d5-43e3-b4b1-47972cb05d71

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Source: Crinetics Pharmaceuticals, Inc.

Palsonify Pills

Palsonify pills

Palsonify Logo

Palsonify tablets

Crinetics Exterior

Crinetics headquarters in San Diego, CA