NEWS RELEASE

CRINETICS ANNOUNCES POSITIVE INITIAL FINDINGS AT ENDO 2024 FOR ATUMELNANT IN TWO ONGOING, OPEN-LABEL STUDIES FOR THE TREATMENT OF CONGENITAL ADRENAL HYPERPLASIA (CAH) AND ACTH-DEPENDENT CUSHING'S SYNDROME (ADCS)

2024-06-03

SAN DIEGO – June 3, 2024 – **Crinetics Pharmaceuticals, Inc.** (Nasdaq: CRNX) today announced initial findings from the development program of its second clinical product candidate, atumelnant* (CRN04894), a novel, once-daily oral adrenocorticotropic hormone (ACTH) receptor antagonist. The results, presented at the Endocrine Society's annual meeting (ENDO2024), include initial data from the Phase 1b/2a, open-label study in participants with ACTH-dependent Cushing's syndrome (ADCS) conducted in collaboration with the National Institutes of Health, and the Phase 2 open-label TouCAHn study in participants with congenital adrenal hyperplasia (CAH).

"Despite knowing about ACTH's pivotal role in the endocrine stress response for nearly a century, no other ACTH antagonist drug candidates have been developed and studied in humans. Achieving physiologically normal hormone levels is critical for people living with CAH and ADCS, and today's data show an impressive ability of atumelnant to reduce key disease drivers like A4 or cortisol to healthy levels," said Scott Struthers, Ph.D., founder and chief executive officer of Crinetics. "These data also reinforce the strength of our in-house discovery engine and our ability to purposefully design medicines with groundbreaking mechanisms of action like atumelnant, the second novel drug candidate in our pipeline to have demonstrated remarkable results in clinical studies."

Once Daily Oral Atumelnant (CRN04894) Induces Rapid and Profound Reductions of Androstenedione and 17-hydroxyprogesterone in Participants with Classical Congenital Adrenal Hyperplasia: Initial Results from A 12-week,

Phase 2, Open-label Study (Abstract #**MON-677**):
In this initial analysis of this Phase 2 trial (TouCAHn), people with classic CAH were treated with once-daily, oral atumelnant and assessed for safety and efficacy. The trial continues to enroll three treatment cohorts: 80 mg once daily (n=9), 40 mg once daily (n=9) and 120 mg once daily (n=6).

Data presented at ENDO (n=10) reflect a cutoff date of May 21, 2024. Available data for 80 mg includes: n=4 at 12 weeks of treatment, with two additional participant's data up to six weeks of treatment. For 40 mg, available data was with n=4 for two weeks of treatment. The TouCAHn study is ongoing, with topline results from the complete study expected in the second half of 2024.

Baseline biomarker levels for subjects in Cohort 1 were:

- Androstenedione (A4) mean: 838 ng/dL
- 17-hydroxyprogesterone (17-OHP) mean: 9,880 ng/dL

Initial results from Cohort 1:

- Atumelnant resulted in profound, rapid and sustained reductions in key adrenal steroids that are hallmarks of CAH.
- 100% of participants had A4 levels below the upper limit of normal (ULN) at two weeks with atumelnant, which was sustained through 12 weeks.
- A4 reductions, a potential endpoint in registrational trials, from the baseline mean were:
    - 91% at two weeks (n=6)
    - 93% at six weeks (n=6)
    - 96% at 12 weeks (n=4)
- 17-OHP changes in serum levels from the baseline mean were:
    - 97% at two weeks (n=6)
    - 95% at six weeks (n=6)
    - 94% at 12 weeks (n=4)

Two-week data from the first four patients in Cohort 2 (40 mg atumelnant once daily) are also presented at ENDO2024.

No severe or serious treatment emergent adverse events have been observed to date, and no participants have discontinued from the trial. All AEs to-date have been mild to moderate and transient. There were no significant changes in safety labs or electrocardiograms. The most common treatment-emergent adverse events included: fatigue (3), headache (2) and upper respiratory tract infection (2).

“In CAH, androgen production can go into overdrive and have a profound effect on people living with this difficult-to-manage disease,” said Dr. Umasuthan Srirangalingam, consultant physician in endocrinology and diabetes at University College London Hospitals NHS Foundation Trust and TouCAHn investigator. “Atumelnant’s unique ability to inhibit ACTH directly at its receptor sets it apart from how we’ve historically pursued controlling androgen production through supra-physiological doses of glucocorticoids. It’s compelling to see initial Phase 2 results showing atumelnant dramatically reduced A4 and 17-OHP.”

Atumelnant (CRN04894) Induces Rapid and Sustained Reductions in Serum and Urine Cortisol in Patients with ACTH-dependent Cushing Syndrome During a Phase 1b/2a, Single Center, 10-day, Inpatient, Open-label Study (Abstract #**MON-680**):
Initial data from five ACTH-dependent Cushing’s syndrome trial participants who completed 10 days of once- daily oral atumelnant treatment (80 mg) in this dose-finding study shows rapid and profound impact on cortisol:

- In all participants, 24h urine free cortisol was below the upper limit of normal during the treatment period even while receiving oral hydrocortisone replacement. UFC normalization has been recommended by the U.S. Food and Drug Administration as a primary endpoint for drugs that decrease cortisol levels in Cushing’s syndrome.
- All five participants (100%) experienced serum cortisol <5 mcg/dL within 10 days of administration.
- Two or more clinical symptoms improved in all patients.

“This initial data showed atumelnant’s ability to rapidly reduce — and normalize — cortisol levels in people with ADCS,” said Dr. Lynnette Nieman, senior investigator, National Institutes of Health, and principal investigator of the Phase 1b/2a atumelnant trial. “As a clinician and investigator, I’ve witnessed the unmet needs in this patient population for 40 years. I am hopeful for further promising results as we continue our research on this drug candidate”

Atumelnant was generally well tolerated. Adverse events were mild to moderate, with the most frequently reported being headache, nausea and decreased appetite, consistent with symptoms of adrenal insufficiency. Predefined biochemical adrenal insufficiency (morning serum cortisol <5 mcg/dL) was observed in all participants treated to date. This effect was anticipated based on the known pharmacology of atumelnant, and related symptoms reversed with oral hydrocortisone replacement treatment. Two participants with pre-existing steatosis had small increases in ALT (<1.5x ULN). There have been no early discontinuations from the study to date.

Conference Call and Webcast
Crinetics will host an investor conference call on June 3, 2024, at 4:30 pm Eastern Time to discuss the initial findings from these two studies.
Dial-in Details:

Domestic: 1-800-717-1738
International: 1-646-307-1865
Conference ID: 81415

Participants can use Guest dial-in #s above and be answered by an operator OR click the Call me™ link for instant telephone access to the event.

Call me™: **https://emportal.ink/3K5zWA3**
Webcast: **https://viavid.webcasts.com/starthere.jsp?ei=1673017&tp_key=a62184f9a6**

ABOUT ATUMELNANT (CRN04894)
Atumelnant, our second investigational compound, is the first once-daily, oral adrenocorticotropic hormone (ACTH) receptor antagonist that acts selectively at the melanocortin type 2 receptor (MC2R) on the adrenal glands. Diseases associated with excess ACTH can have significant impact on physical and mental health. Atumelnant has exhibited strong binding affinity for MC2R in preclinical models and has demonstrated suppression of adrenally derived glucocorticoids and androgens that are under the control of ACTH. Data in a Phase 1 healthy volunteer study demonstrated pharmacologic proof-of-concept for atumelnant, with reductions in both serum cortisol levels and 24-hour urine free cortisol excretion in the presence of sustained, disease-like ACTH concentrations. Atumelnant is currently in Phase 2 studies for Congenital Adrenal Hyperplasia and ACTH-dependent Cushing's syndrome.

ABOUT THE TouCAHn STUDY
TouCAHn is an open-label, global, Phase 2 study designed to evaluate the efficacy, safety, and pharmacokinetics of atumelnant when administered up to 12 weeks in participants with CAH caused by 21-hydroxylase deficiency. The study is ongoing and aims to enroll up to 30 patients, aged 18-75, with classic CAH and on a stable dose of glucocorticoid replacement for at least 6 months. Key endpoints include early morning androstenedione (A4), 17-hydroxyprogesterone (17-OHP) levels and safety.

For more information about the study, please visit clinicaltrials.gov (**NCT05907291**).

ABOUT THE PHASE 1B/2A STUDY IN ACTH-DEPENDENT CUSHING'S SYNDROME
The Phase 1b/2a, is the first-in-disease, open-label, multiple-ascending dose exploratory study to evaluate safety, tolerability, pharmacokinetics, and pharmacodynamic biomarker responses associated with atumelnant over a 10-day treatment period in participants with ACTH-dependent Cushing's syndrome. The study is being conducted in collaboration with the National Institutes of Health and led by Dr. Lynnette Nieman. Participants will receive oral atumelnant once daily for 10 days, followed by monitoring during four wash-out days. The study is ongoing and aims to enroll 18 people.

The content in this release is the sole responsibility of Crinetics Pharmaceuticals, Inc. and does not necessarily represent the official views or imply endorsement of the National Institutes of Health. For more information about the study, please visit clinicaltrials.gov (**NCT05804669**).

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 in Phase 2 clinical development for carcinoid syndrome associated with neuroendocrine tumors. Crinetics is also developing atumelnant (CRN04894), an investigational, first-in-class, oral ACTH antagonist, that is currently completing Phase 2 clinical studies for the treatment of congenital adrenal hyperplasia and Cushing's disease. 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, diabetes and obesity.

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, including the therapeutic potential and clinical benefits or safety profile thereof; the expected timing of additional data and topline results from studies of atumelnant in CAH and ADCS; the target enrollment in studies of atumelnant; and the potential outcomes of the Phase 2 participants with CAH and the Phase 1b/2a trial for participants with ADCS. 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; unexpected adverse side effects or inadequate efficacy of the Company's product candidates that may limit their development, regulatory approval and/or commercialization; 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, 2023 and its Quarterly report on Form 10-Q for the quarter ended March 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.

Contact:
Corey Davis
LifeSci Advisors
cdavis@lifesciadvisors.com
(212) 915-2577

Media:
Natalie Badillo
Head of Corporate Communications
nbadillo@crinetics.com
(858) 345-6075

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