UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 3, 2024

Crinetics Pharmaceuticals, Inc.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-38583**	**26-3744114**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

6055 Lusk Boulevard **San Diego, California**	**92121**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (858) 450-6464

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	CRNX	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On June 3, 2024, Crinetics Pharmaceuticals, Inc. (the "Company," "Crinetics," "we," "us," or "our") issued a press release and made available a corporate presentation announcing positive 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 ("ENDO 2024"), include initial data from the Phase 1b/2a, open-label study in ACTH-dependent Cushing's syndrome conducted in collaboration with the National Institutes of Health, and the Phase 2 open-label TouCAHn study in congenital adrenal hyperplasia. Copies of the press release and corporate presentation are attached as Exhibits 99.1 and 99.3, respectively, to this Current Report on Form 8-K and are incorporated herein by reference. The press release and corporate presentation will also be available under the "Investors" section of the Company's website. The Company intends to deliver the corporate presentation during a conference call and live webcast with the investment community on June 3, 2024, at 4:30 p.m. Eastern Time.

Also on June 3, 2024, the Company issued a press release announcing findings from its clinical development program evaluating oral, once-daily investigational paltusotine in acromegaly. The data was presented at ENDO 2024 and included results of the Phase 3 PATHFNDR-2 trial, a new analysis of patient reported outcome data from the Phase 3 PATHFNDR-1 trial, and interim long-term efficacy and safety results at 42 months from the open-label ACROBAT Advance extension study. A copy of the press release is attached as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference. The press release will also be available under the "Investors" section of the Company's website.

The information that is solely contained in this Item 7.01 of this Current Report on Form 8-K, including in Exhibit 99.3 hereto, is being "furnished" and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended, is not subject to the liabilities of that section and is not deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except as shall be expressly set forth by specific reference in such a filing.

* Proposed international non-proprietary name under review.

Item 8.01 Other Events.

The information regarding the press releases referred to in Item 7.01 of this Current Report on Form 8-K is incorporated herein by reference. Copies of the press releases are attached as Exhibits 99.1 and 99.2 to this Current Report on Form 8-K and are incorporated herein by reference.

Forward-Looking Statements

This report 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 report are forward-looking statements. These forward-looking statements speak only as of the date of this report and are subject to a number of known and unknown risks, uncertainties and assumptions, including, without limitation, the 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 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.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release dated June 3, 2024.
99.2	Press Release dated June 3, 2024.
99.3	Corporate Presentation.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Crinetics Pharmaceuticals, Inc.

Date: June 3, 2024

By: /s/ R. Scott Struthers, Ph.D.
R. Scott Struthers, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 99.1

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)

100% of Participants (n=6) With CAH Maintained Androstenedione (A4) Below the Upper Limit of Normal at all Time Points on Atumelnant (80 mg)

CAH Participants Achieved More Than a 90% Reduction of A4 and 97% Reduction of 17-OHP on Atumelnant (80 mg), Beginning at Two Weeks and Sustained Through 12 Weeks

In the ADCS Trial, Atumelnant (80 mg) Normalized 24-hr Urinary Free Cortisol Levels for 100% of Participants (n=5) During Treatment

Management to Host Investor Conference Call Today at 4:30 PM ET and Onsite KOL Event at ENDO for Investors and Analysts at 6:00 PM ET

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

* Proposed international nonproprietary name under review

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

Following the live event, a replay will be available on the Investors section of the Company's website.

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 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, 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

Exhibit 99.2

Crinetics Presents New Data at ENDO 2024 that Increases Body of Evidence Positioning Once-Daily, Oral Paltusotine as Potential First-Choice Treatment Option for Acromegaly

First Scientific Presentation of PATHFNDR-2 Acromegaly Safety and Efficacy Data Following Positive Topline Announcement, Showing Rapid and Sustained IGF-1 Responses in People Treated with Paltusotine

New PATHFNDR-1 Patient-Reported Outcomes Analysis Showed Paltusotine Lessened Day-to-Day Breakthrough Symptom Exacerbations versus Prior Treatment with Standard of Care Injections, as Assessed by Acromegaly Symptom Diary

Long-Term Data from Open-Label ACROBAT Advance Extension Study Demonstrated Durable Safety, IGF-1, and Symptom Control at Up to 42-Months of Paltusotine Treatment

Crinetics Expects to Complete NDA Submission for Paltusotine in 2H 2024

SAN DIEGO – June 3, 2024 – Crinetics Pharmaceuticals, Inc. (Nasdaq: CRNX) today presented findings from its clinical development program evaluating oral, once-daily investigational paltusotine in acromegaly. Data presented included results of the Phase 3 PATHFNDR-2 trial, a new analysis of patient reported outcome (PRO) data from the Phase 3 PATHFNDR-1 trial, and interim long-term efficacy and safety results at 42 months from the open-label ACROBAT Advance extension study. The data were presented today at the Endocrine Society's Annual Meeting (ENDO2024), with findings from PATHFNDR-1 published as a manuscript in *The Journal of Clinical Endocrinology & Metabolism.*

"The depth and breadth of our clinical development program for once-daily, oral paltusotine under investigation for the treatment of acromegaly is on display at ENDO 2024, demonstrating its rapid, durable effect on both biochemical and symptom control in these studies," said Scott Struthers, Ph.D., founder and chief executive officer of Crinetics. "Notably, based on patient reported outcome data captured daily by the Acromegaly Symptom Diary, a new analysis from the PATHFNDR-1 trial showed that paltusotine was able to drive significant and important differences in the frequency of acromegaly breakthrough symptom exacerbations compared to prior treatment with standard of care medications. We look forward to submitting a New Drug Application in the second half of this year and potentially changing the acromegaly treatment paradigm."

Efficacy and Safety of Once-daily Oral Paltusotine in Medically Untreated Patients with Acromegaly: Results from the Phase 3, Randomized, Placebo-controlled PATHFNDR-2 Study (Abstract #MON-694):

PATHFNDR-2 was a randomized, double-blind, placebo-controlled trial with a 24-week treatment period, followed by an optional open-label extension study evaluating paltusotine in 111 participants with active acromegaly (IGF-1 > 1.1 ULN) who were not pharmacologically treated. Results demonstrated:

- The study met statistical significance ($p<0.0001$) on the primary endpoint, based on the proportion of participants taking paltusotine (56%) who achieved an insulin-like growth factor 1 (IGF-1) level ≤ 1.0 times the upper limit of normal (xULN) compared to those taking placebo (5%).
- This represents the second Phase 3 trial showing a significant difference in symptoms favoring paltusotine.
- Response to paltusotine was rapid, with the majority of the effect in IGF-1 reductions observed between weeks two and four, and sustained throughout treatment.
- Among those treated with paltusotine, a reduction in IGF-1 levels occurred in 92.6% of patients (n=50/54) by the end of treatment.
- Paltusotine was generally well-tolerated and no serious adverse events were reported in participants treated with paltusotine. The frequency of participants with at least one treatment emergent adverse event (TEAE) was comparable in the paltusotine treatment arm and placebo arm.

- The most commonly reported TEAEs in paltusotine-treated participants included: diarrhea, headache, arthralgia and abdominal pain. The frequency of adverse events considered related to acromegaly was notably lower in paltusotine treated participants compared to placebo treated participants.

Use of the Acromegaly Symptom Diary (ASD) in a Phase 3, Placebo-Controlled Study of Once-Daily, Oral Paltusotine in Patients with Acromegaly Switched from Injected Octreotide or Lanreotide (Abstract #MON-156):

PATHFNDR-1 was a randomized, double-blind, placebo-controlled trial with a 36-week treatment period, followed by an optional open-label extension study evaluating paltusotine in participants with acromegaly switching from standard-of-care injected depot somatostatin receptor ligands (SRL). The study enrolled participants with acromegaly who were biochemically controlled on octreotide or lanreotide depot monotherapy.

The study met the primary endpoint and all three secondary endpoints, as previously announced. Findings clearly demonstrated that once-daily, oral paltusotine maintained biochemical and symptom control in patients with acromegaly switched from SRL. Paltusotine was well tolerated with no severe or serious TEAEs.

In a new analysis of PATHFNDR-1 data presented at ENDO2024, Acromegaly Symptom Diary (ASD) scores for patients at screening (and on injected SRL, the current standard of care) were compared to scores while on paltusotine (n=25). The ASD is a novel PRO tool developed in accordance with U.S. Food and Drug Administration (FDA) guidance to assess disease-related symptom burden. Paltusotine was associated with statistically significant reductions in the frequency of breakthrough acromegaly symptom exacerbations for total ASD scores, most bothersome symptom, headache, joint pain, sweating, fatigue, numbness/tingling, sleep difficulty and memory difficulty. Numerical differences favoring paltusotine were seen for the remaining symptoms of leg weakness and swelling.

“Patients with acromegaly often suffer from unpredictable breakthrough symptoms, despite receiving regular painful depot injections of the available first line medical treatments,” said Alan Krasner, M.D., chief endocrinologist at Crinetics. “The data from PATHFNDR-1 suggest that once daily oral paltusotine may be associated with less day-to-day symptom variability compared to the injections. Reducing the burden of the disease, as well as the burden of its treatment, are key goals of the paltusotine development program.”

Long-Term Safety and Efficacy of Once-Daily Oral Paltusotine in the Treatment of Patients with Acromegaly: Update from ACROBAT Study (Abstract #MON-695):

ACROBAT Advance is an ongoing, six-year, single-arm, open-label extension study of paltusotine in the treatment of patients with acromegaly. This analysis includes interim results as the first enrolled patients approach four years of treatment. Enrolled patients had completed either the ACROBAT Edge or Evolve Phase 2 parent studies.

Results demonstrated:

- Once-daily oral paltusotine treatment was well-tolerated, with stable biochemical and symptom control, comparable to that observed with prior injected SRLs.
- Parent study baseline median IGF-I levels were 1.15× ULN (0.84, 1.46; n=43). In ACROBAT Advance, median IGF-1 levels were 1.14× ULN (0.89, 1.29; n=40), 1.06× ULN (0.87, 1.24; n=35), and 1.08× ULN (0.87, 1.57; n=10) at months 12, 24, and 42, respectively.
- Important clinical outcomes including acromegaly symptoms, blood pressure, HbA1c, and residual pituitary tumor size were stable over the period of observation.
- Paltusotine continues to be well-tolerated. The most common adverse events (AEs) (reported at least during the study) were arthralgia (37.2%), headache (30.2%), and fatigue (23.3%). One serious drug-related AE (cholelithiasis) was reported. Of the eight patients who discontinued the study, two were due to AEs (mild or moderate).

Preparation of regulatory filings for paltusotine based on PATHFNDR-1 and PATHFNDR-2 data are currently underway, with a New Drug Application submission to the FDA planned in the second half of 2024.

ABOUT PALTUSOTINE

Paltusotine is the first once-daily, oral selectively-targeted somatostatin receptor type 2 (SST2) agonist, and has completed its randomized, controlled 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 carcinoid syndrome. In Phase 2 studies and the recently completed PATHFNDR-1 and PATHFNDR-2 Phase 3 studies, paltusotine maintained IGF-1 levels in patients with acromegaly who were switched from monthly injectable medications to paltusotine (PATHFNDR-1) and decreased IGF-1 levels in medically untreated patients (PATHFNDR-2). IGF-1 is the primary biomarker endocrinologists use to manage acromegaly patients. Results from the Phase 2 study in carcinoid syndrome further support paltusotine's potential use beyond acromegaly.

ABOUT ACROMEGALY

Acromegaly is a serious rare disease generally caused by a pituitary adenoma, a benign tumor in the pituitary that secretes growth hormone (GH). Excess GH secretion causes excess secretion of IGF-1 from the liver. Prolonged exposure to increased levels of IGF-1 and GH leads to progressive and serious systemic complications, often resulting in bone, joint, cardiovascular, metabolic, cerebrovascular, or respiratory disease. Acromegaly symptoms include headache, joint aches, fatigue, sleep apnea, severe sweating, hyperhidrosis/oily skin, bone and cartilage overgrowth, abnormal growth of hands and feet, enlargement of heart, liver, and other organs and alteration of facial features. Uncontrolled acromegaly results in increased mortality and has a debilitating impact on daily functioning and quality of life.

Surgical removal of pituitary adenomas, if possible, is the preferred initial treatment for most acromegaly patients. Pharmacotherapy is used for patients who 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 pharmacotherapy. Injectable depot somatostatin analogues are the most common initial pharmacologic treatment; however, these drugs require monthly depot injections with large gauge needles that are commonly associated with pain, injection site reactions, and an increased burden on the lives of patients.

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 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, 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 and commercialization of paltusotine, including the therapeutic potential and clinical benefits or safety profile thereof; the expected publication of findings from PATHFNDR-1; and the expected timing of an NDA submission for paltusotine for the treatment or maintenance of treatment of acromegaly in the United States. 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

Exhibit 99.3

Crinetics Pharmaceuticals

Initial Phase 2 Results From Atumelnant* (CRN04894) in Congenital Adrenal Hyperplasia (CAH) and ACTH-dependent Cushing's Syndrome (ADCS)

June 3rd, 2024

* Proposed international nonproprietary name under review

Safe Harbor Statement

This presentation contains forward-looking statements. Crinetics Pharmaceuticals, Inc. ("Crinetics," the "company," "we," "us," or "our") cautions you that statements contained in this presentation 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 benefits of atumelnant (CRN04894) in patients with Congenital Adrenal Hyperplasia ("CAH") or ACTH-Dependent Cushing's syndrome ("ADCS"); the potential benefits of paltusotine for acromegaly patients and patients with carcinoid syndrome; the potential for the PATHFNDR program to support registration of paltusotine for all acromegaly patients who require pharmacotherapy; the expected plans and timing for data and data readouts from ongoing clinical studies; plans and timing for sharing the full results of the Phase 2 study of atumelnant with the FDA to align on one or more Phase 3 programs; the plans and timelines for the clinical development of atumelnant and paltusotine, including the therapeutic potential and clinical benefits or safety profile thereof as well as atumelnant's ability to revolutionize the treatment for CAH and ADCS or our ability to commercialize atumelnant globally; the expected timing of the submission of a new drug application for paltusotine for the treatment of acromegaly or for carcinoid syndrome and the plans and timelines for the commercial launch paltusotine if approved; the expected timing of initiation of a Phase 3 program in patients with carcinoid syndrome; our plans to identify and create new drug candidates for additional diseases or the potential for any such new drug candidates to show safety or efficacy and the expected plans and timing for candidate selection and clinical development of such candidates; our plans to identify and create new drug candidates for additional diseases; the direction or trajectory of the Company's potential future growth, the receipt of any revenues from product sales and the ability of such revenues to support continued growth, and our expected plans and timing for commercialization of paltusotine, altumenant and other product candidates pending regulatory approval. In some cases, you can identify forward-looking statements by terms such as "may," "believe," "anticipate," "could," "should," "estimate," "expect," "intend," "plan," "project," "will," "contemplate," "predict," "continue," "forecast," "aspire," "lead to," "designed to," "goal," "potential," "target," "our vision," "our mission" or the negative of or other similar terms.

These statements speak only as of the date of this presentation, involve known and unknown risks, uncertainties, assumptions, and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, without limitation: topline and initial data that we report may change following 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; the risk that preliminary results of preclinical studies or clinical studies 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, the possibility of unfavorable new clinical data and further analyses of existing clinical data; potential delays in the commencement, enrollment and completion of clinical studies and the reporting of data therefrom; the FDA or other regulatory agencies may require additional clinical studies or changes to our planned clinical studies of paltusotine prior to and in support of the approval of a New Drug Application or applicable foreign regulatory approval; international conflicts may disrupt our business and that of the third parties on which we depend, including delaying or otherwise disrupting our clinical studies and preclinical studies, manufacturing and supply chain, or impairing employee productivity; our dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the success of our clinical studies, nonclinical studies and preclinical studies; regulatory developments or price restrictions in the United States and foreign countries; unexpected adverse side effects or inadequate efficacy of our product candidates that may limit their development, regulatory approval and/or commercialization; our ability to obtain and maintain intellectual property protection for our product candidates; we may use our capital resources sooner than we expect; and other risks described under the heading "Risk Factors" in documents we file from time to time with the Securities and Exchange Commission ("SEC"). Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. 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 and, except as required by applicable law, we do 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. This presentation also contains estimates relating to addressable patients, addressable market or the potential market opportunity for our product. Projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Crinetics' Vision for Atumelnant*

A single pill, taken once a day, that reliably enables people struggling with either CAH or ADCS to achieve **normal, healthy hormone levels** that will improve their daily lives.

OUR MISSION

To revolutionize the treatment paradigm for CAH and ADCS with an unprecedented, transformative therapy and bring this medicine to all people around the world.

*Atumelnant is a clinical stage investigational compound that has not yet been approved by any regulatory authority.

CAH: Congenital adrenal hyperplasia. ADCS: ACTH-dependent Cushing's syndrome.

Profound, Rapid and Sustained Reductions of A4 and 17-OHP in Congenital Adrenal Hyperplasia with Atumelnant

EFFICACY

- ☑ **100%** (n=6/6) of participants maintained androstenedione (A4) <ULN at all time points on atumelnant (80 mg)
  - *A4 and related androgens are key drivers of disease pathophysiology*
  - *A4 is a potential endpoint in registrational trials*
- ☑ **>90% reduction of A4** and **97% reduction of 17-OHP** on atumelnant (80 mg) beginning at 2 weeks and sustained through 12 weeks
- ☑ **Two female participants resumed regular menstrual cycles** on atumelnant (80 mg) who had not menstruated in > 2 years previously

SAFETY

- ☑ Atumelnant has been well-tolerated with no treatment-related severe or serious adverse events

More data from additional patients and dose levels expected in 2H 2024

ULN: Upper limit of normal. 17-OHP: 17-Hydroxyprogesterone. A4: Androstenedione.
Data presented represents data cut off date of May 21st, 2024. Available data: 80 mg: n=4 at 12 weeks; n=2 at 6 weeks; 40 mg: n=4 for 2 weeks.

Crinetics Pharmaceuticals

Profound, Rapid and Sustained Reduction of Excess Cortisol in ACTH-dependent Cushing's Syndrome with Atumelnant

EFFICACY

- ☑ **100%** (n=5/5) of participants achieved normal 24h Urinary Free Cortisol (UFC) on atumelnant (80 mg)
  - *UFC normalization has been recommended by FDA as a primary endpoint*
- ☑ **ALL** patients experienced improvements in 2 or more clinical symptoms

SAFETY

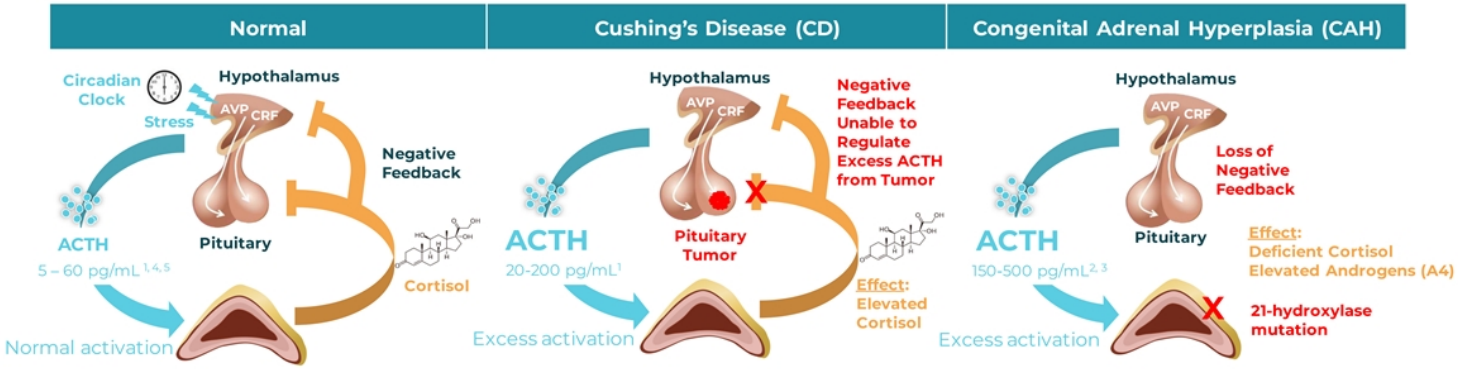
- ☑ Atumelnant was generally well-tolerated

More data from additional patients and dose levels expected in 2H 2024

5 ULN: Upper limit of normal. UFC: Urine free cortisol.

Crinetics Pharmaceuticals

Disruptions in the HPA Axis Lead to Diseases of Excess ACTH and Excess Adrenal Activation



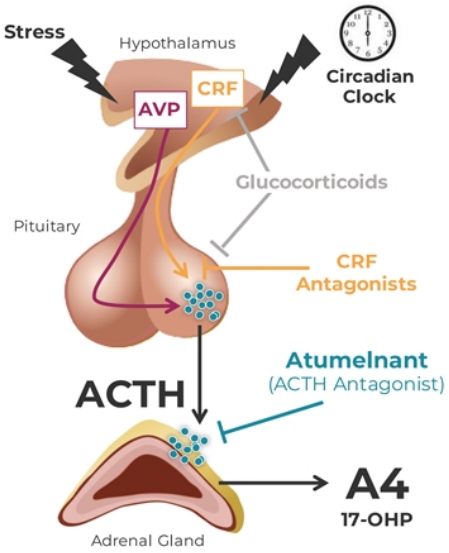
Cause	ACTH-secreting tumor	Inability to produce cortisol leads to loss of negative feedback & excess ACTH
U.S. Prevalence	11,200	27,000
Symptoms	Central obesity and round face; Dorsal and supraclavicular fat pads; Hypertension; Stretch marks; Bone loss; Hyperglycemia; Psychiatric disturbances	Adrenal insufficiency; Infertility; Hirsutism; Short stature; Precocious puberty; ambiguous genitalia at birth, Adrenal rest tumors

Raff et al. *Compr Physiol* 2015, Petersen *Acta Pediatr Scand* 1981, NBIX ENDO Online 2020 presentation, Oster et al., *Endocrine Reviews* 2017.
HPA: Hypothalamic-pituitary-adrenal. A4: Androstenedione; 17-OHP: 17-hydroxyprogesterone, ACTH: Adrenocorticotropic hormone.

Crinetics Pharmaceuticals

CONGENITAL ADRENAL HYPERPLASIA

Atumelnant: Second Clinical Asset in Late-Stage Development Skillfully Crafted to Help Subjects Reach Their Treatment Goals



Lead Indication: Congenital Adrenal Hyperplasia (CAH)

Estimated ~27,000 people in the US based on genetic prevalence

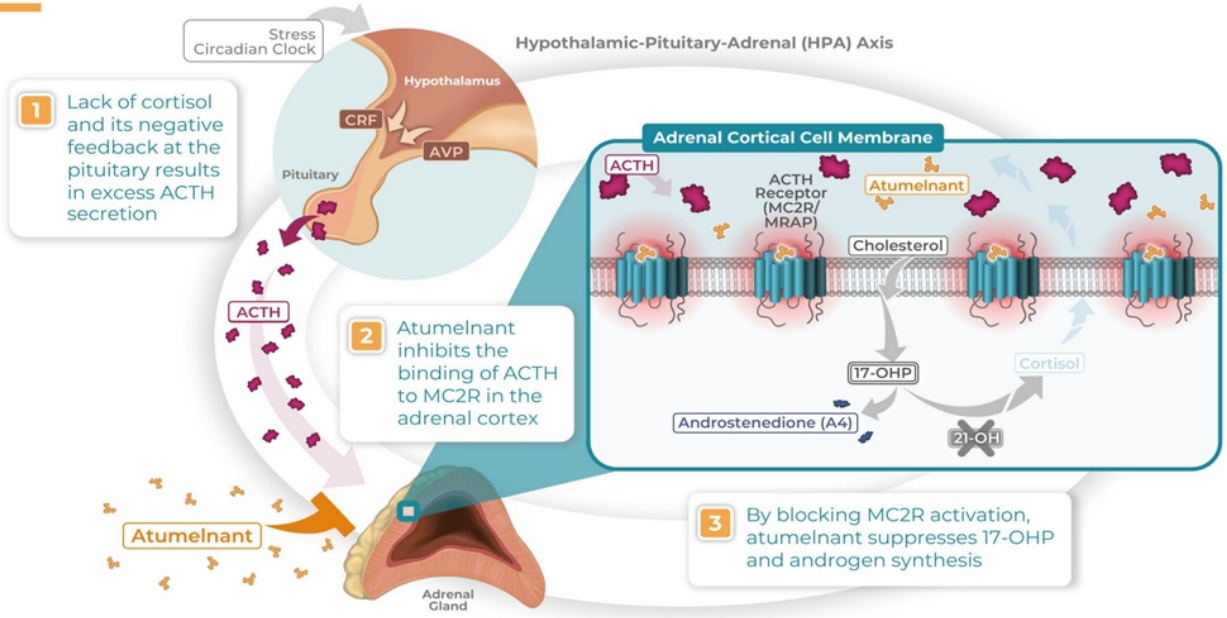
Treatment Goals

- Normalize/eliminate adrenal androgen production
- Restore normal menstrual cycles and fertility in women
- Shrink testicular adrenal rest tumors, alleviate pain, restore fertility in men
- Avoid complications of glucocorticoid excess (e.g weight gain, hypertension, bone disease) and enable physiologic replacement levels

AVP: arginine vasopressin, CRF: corticotropin releasing factor; A4: Androstenedione; 17-OHP: 17-hydroxyprogesterone, ACTH: Adrenocorticotropic hormone.

Crinetics Pharmaceuticals

Atumelnant: The First Oral, Selective ACTH Antagonist



Atumelnant is an investigational drug being evaluated in clinical studies for CAH. Atumelnant has not yet been approved by any regulatory authority.
A4: Androstenedione; 17-OHP: 17-hydroxyprogesterone, ACTH: Adrenocorticotropic hormone. MC2R: Melanocortin receptor 2.

Crinetics Pharmaceuticals

Updated Design and Status: Phase 2 Atumelnant in Congenital Adrenal Hyperplasia (CAH) (TouCAHn)

TOUCAHN

Key Eligibility Criteria

N=24

- Male or female participants ≥18 to 75 years. Age: ≥16 years (US)
- Classic 21-hydroxylase deficiency
- On ≥15mg Hydrocortisone equivalent daily dose
- A4 >1.5xULN

Treatment Arms:

- 3 cohorts, each 12 weeks (N=6-12)

80 mg Once Daily (n=9)

40 mg Once Daily (n=9)

120 mg Once Daily (n=6)

Pre-trial glucocorticoid therapy (dose and regimen) maintained throughout the trial

Objectives: Evaluate the Safety, Efficacy, and Pharmacokinetics of atumelnant

Primary Endpoint: Change from baseline in morning serum A4 at week 12
Secondary Endpoint: Change from baseline in morning serum 17-OHP at week 12
Primary Safety Assessment: Incidence of TEAEs throughout the study

A4: Androstenedione; ULN: Upper limit of normal; 17-OHP: 17 hydroxyprogesterone; TEAE: Treatment emergent adverse event.
Baseline is defined as the last morning window value (i.e. the average of any early morning samples on or after 06:00 but prior to 11:00) prior to the first dose of atumelnant.

Crinetics Pharmaceuticals

Demographics and Baseline Characteristics

	40 mg N=4	80 mg N=6	All Participants N=10
Age (yrs), mean (range)	24.3 (22-27)	35.2 (25-42)	30.8 (22-42)
Female, n (%)	0	5 (83%)	5 (50%)
BMI (kg/m²)*, mean (range)	26.5 (21.7-30.2)	30.9 (22.3-35.8)	29.0 (21.7-35.8)
Baseline Biomarker levels			
A4 (ng/dL), mean (range)	1,680 (1,180-2,465)	838** (116-2,755)	1,175 (116-2,755)
17-OHP (ng/dL), mean (range)	15,600 (12,150-22,800)	9,880 (4,740-24,300)	12,168 (4,740-24,300)
ACTH (pg/mL), mean (range)	658 (115-1,082)	554 (155-1,009)	596 (115-1,082)
Glucocorticoid dose* (mg/day), mean (range)**	28 (20-40)	35 (25-40)	32 (20-40)

Upper limit of normal (ULN):
- A4 (ng/dL) – Male: 150, Female: 200
- 17-OHP (ng/dL) – Male: 220, Female (luteal): 285
- ACTH (pg/mL): 63

* One participant in 80mg had no height assessment at baseline and was excluded in the summary. ** Central laboratory data reported. 2 participants entered the study based on elevated A4 levels measured locally that were >1.5 ULN. *** In hydrocortisone equivalents. Available data: 80 mg: n=4 for 12 weeks; n=6 for 6 weeks; 40 mg: n=4 for 2 weeks.

Crinetics Pharmaceuticals

No Significant Safety Signals Reported

Summary of TEAEs by Preferred Term
(Reported by ≥2 of Total Participants)

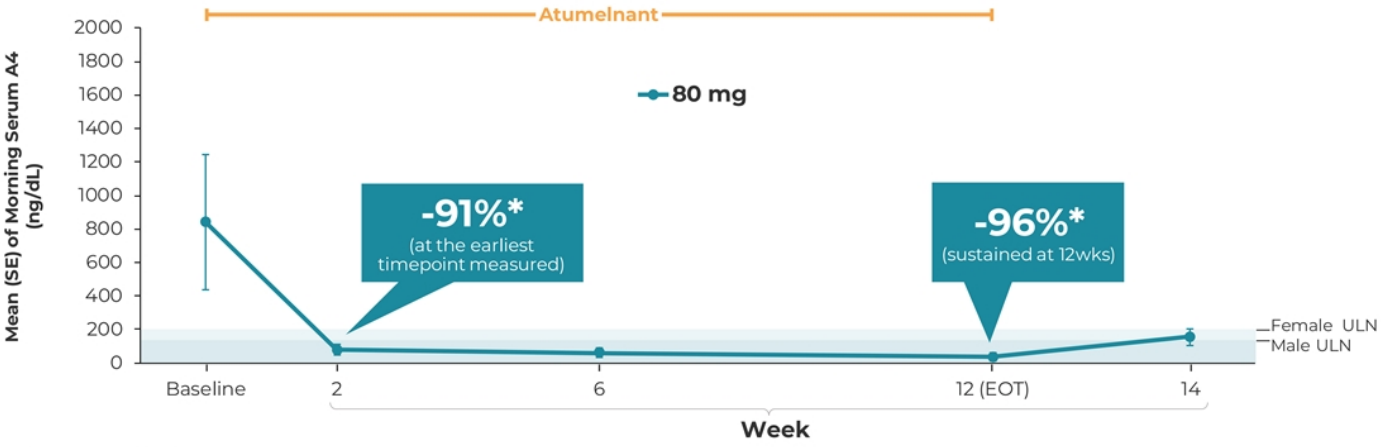
Preferred Term	40 mg N=4 n (%)	80 mg N=6 n (%)	All N=10 n (%)
Participants with at least 1 TEAE	3 (75%)	4 (67%)	7 (70%)
Fatigue	2 (50%)	1 (17%)	3 (30%)
Headache	2 (50%)	0	2 (20%)
Upper respiratory tract infection	0	2 (33%)	2 (20%)

- No severe or serious adverse events and no discontinuations
- Both atumelnant 80 mg and 40 mg have been generally well tolerated
- All adverse events have been either mild or moderate and transient
- No significant changes in safety labs or electrocardiograms

Data presented represents data cut off date of May 21st, 2024. Available data: 80 mg: n=4 for 12 weeks; n=6 for 6 weeks; 40 mg: n=4 for 2 weeks.
TEAE = treatment emergent adverse event.

Crinetics Pharmaceuticals

Atumelnant (80 mg) Profoundly and Rapidly Reduced Mean A4, Sustained at 12 Weeks



Number of Participants:

80 mg	6	6	6	4	4

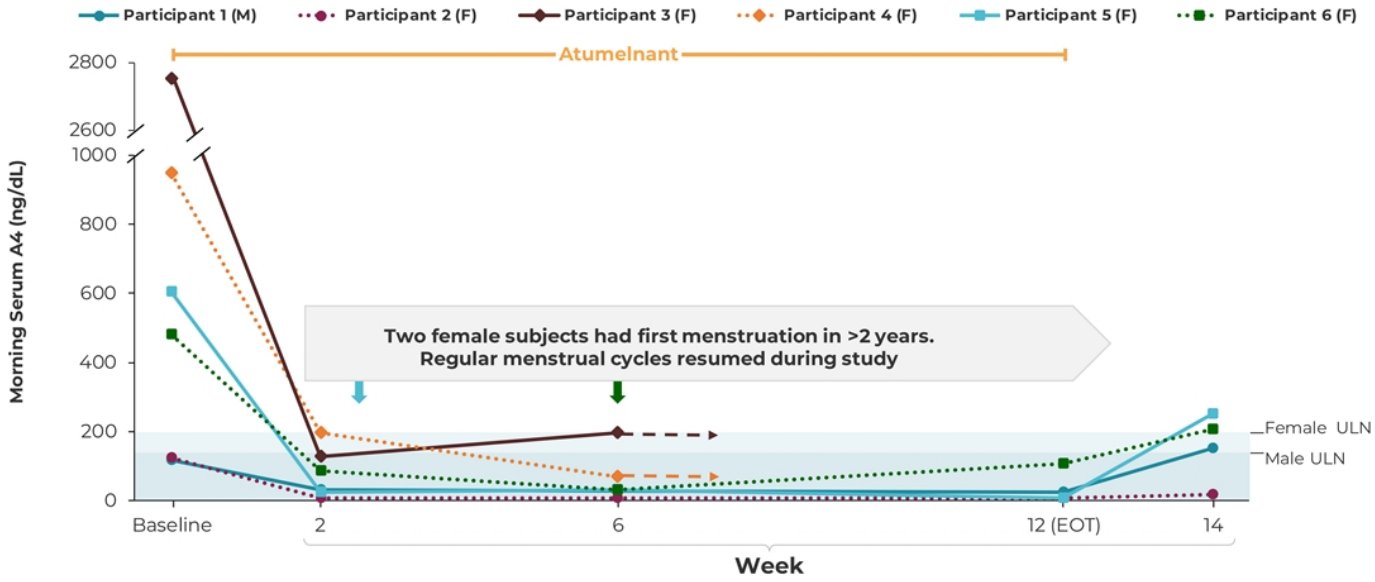
* Percent change between mean baseline and mean post-baseline value.

13 ULN: Upper limit of normal. EOT: End of Treatment

Available data: 80 mg: n=4 for 12 weeks; n=6 for 6 weeks.

Crinetics Pharmaceuticals

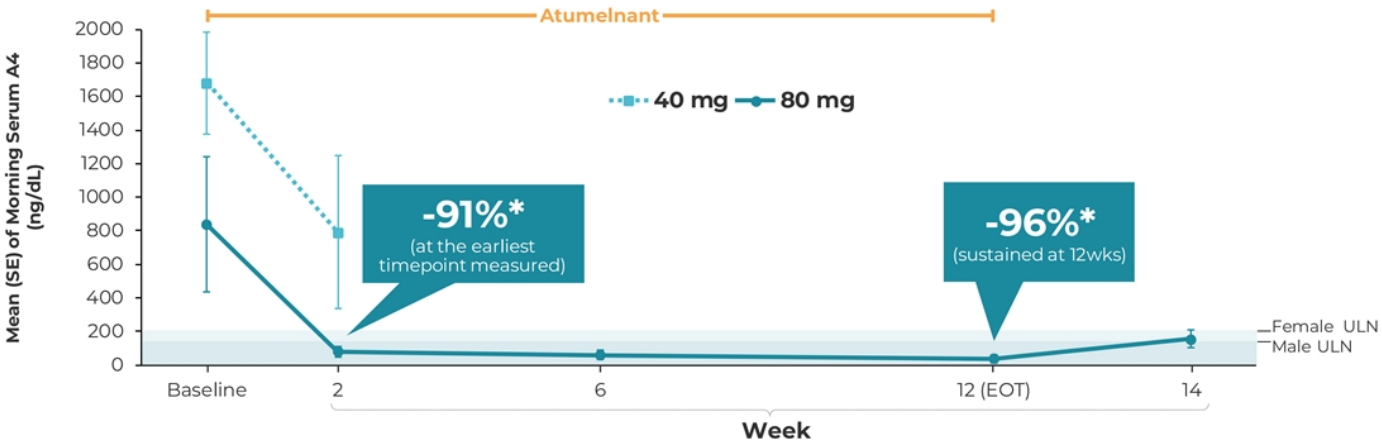
Atumelnant (80 mg) Induced Rapid, Profound and Sustained Reduction of A4 in all Participants



M: Male; F: Female, EOT: End of Treatment. Participant 5 reported resumed menses on day 18, Participant 6 reported resumed menses on day 42. Captured as part of a menstrual cycle diary in the study. Available data: 80 mg: n=4 for 12 weeks; n=6 for 6 weeks.

Crinetics Pharmaceuticals

Atumelnant (40 mg) Also Lowered A4 Levels



Number of Participants:

40 mg	4	4	0	0	0
80 mg	6	6	6	4	4

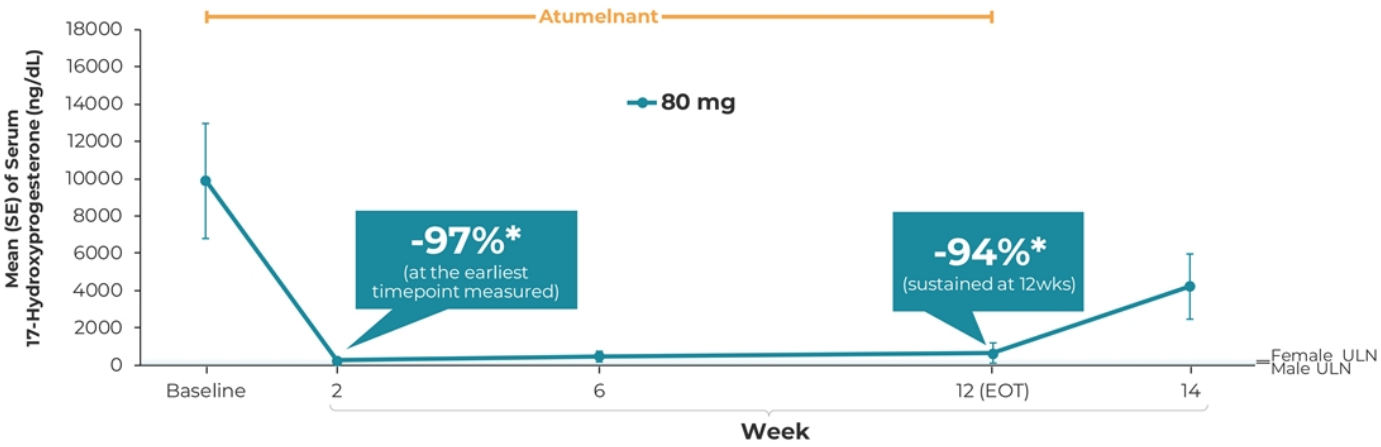
* Percent change between mean baseline and mean post-baseline value.

15 ULN: Upper limit of normal, EOT: End of Treatment.

Available data: 80 mg: n=4 for 12 weeks; n=6 for 6 weeks; 40 mg: n=4 for 2 weeks.

Crinetics Pharmaceuticals

Atumelnant (80 mg) Profoundly and Rapidly Reduced Mean 17-OHP, Sustained at 12 Weeks



Number of Participants:

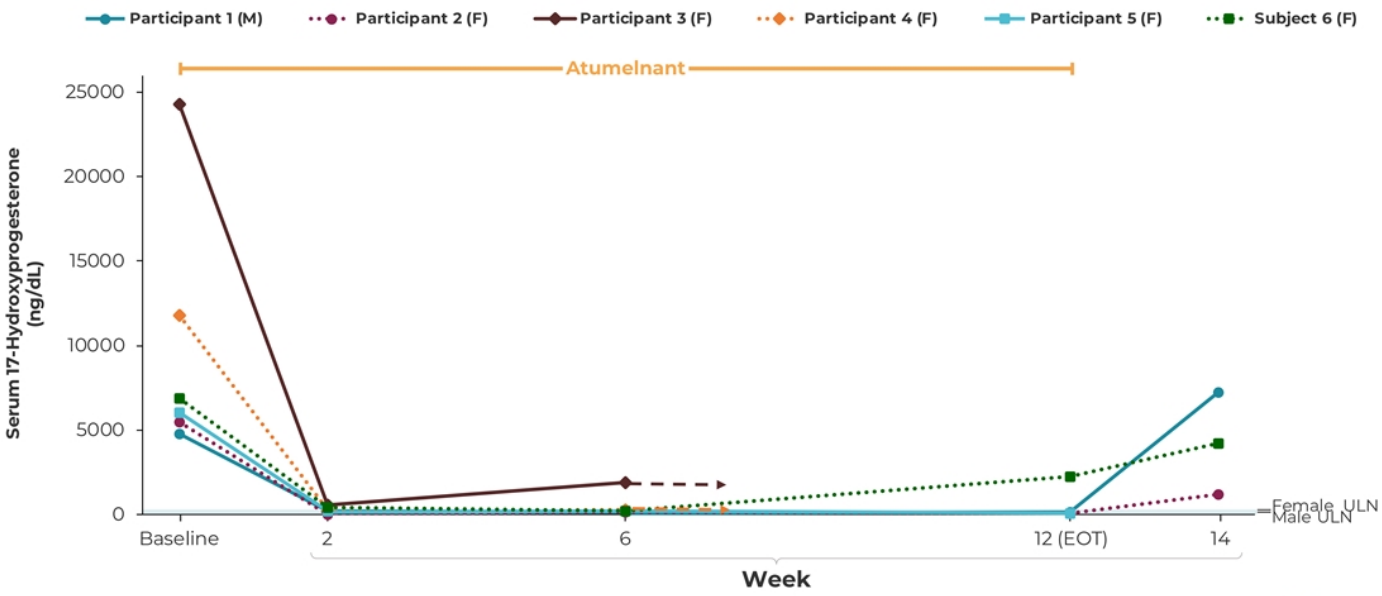
80 mg	6	6	6	4	3

* Percent change between mean baseline and mean post-baseline value.

16 ULN: Upper limit of normal, EOT: End of Treatment.

Available data: 80 mg: n=4 for 12 weeks; n=6 for 6 weeks.

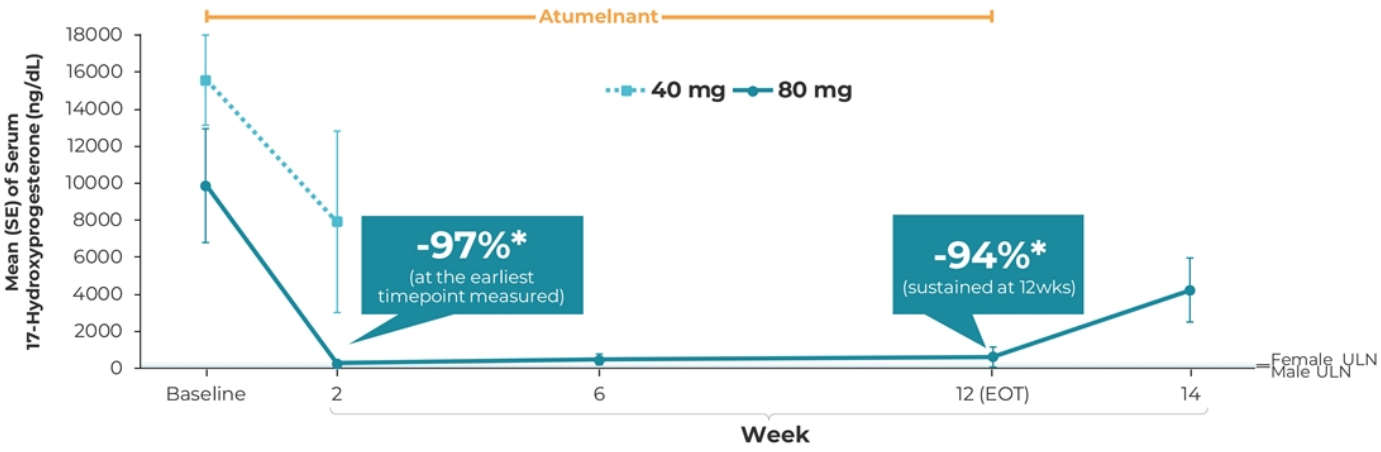
Atumelnant (80 mg) Induced Rapid, Profound and Sustained Reduction of 17-OHP in all Participants



17 EOT: End of Treatment.
Available data: 80 mg: n=4 for 12 weeks; n=6 for 6 weeks.

Crinetics Pharmaceuticals

Atumelnant (40 mg) Also Lowered 17-OHP Levels



Number of Participants:

40 mg	**4**	**4**	**0**	**0**	**0**
80 mg	**6**	**6**	**6**	**4**	**3**

* Percent change between mean baseline and mean post-baseline value.

18 ULN: Upper limit of normal, EOT: End of Treatment.

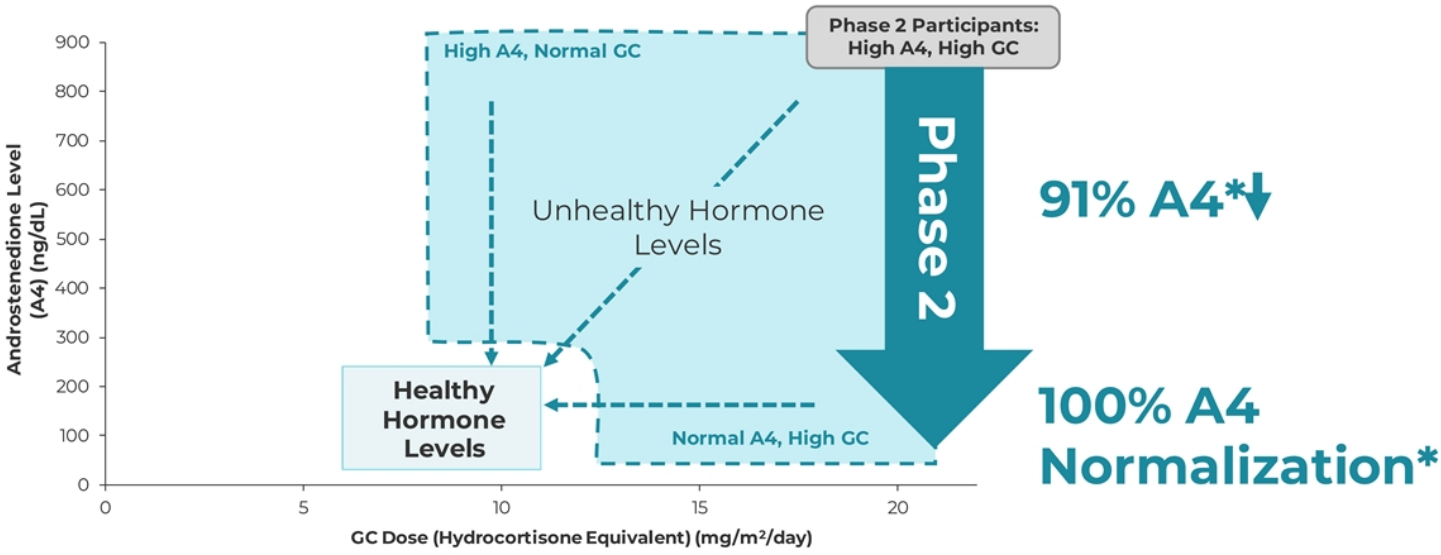
Available data: 80 mg: n=4 for 12 weeks; n=6 for 6 weeks; 40 mg: n=4 for 2 weeks.

Crinetics Pharmaceuticals

Goal: Achieving Healthy Hormone Levels with Atumelnant

Normalize A4 at Physiologic Glucocorticoid Replacement

Phase 3 study to be designed to benefit all patients with unhealthy hormone levels (A4 or GC)

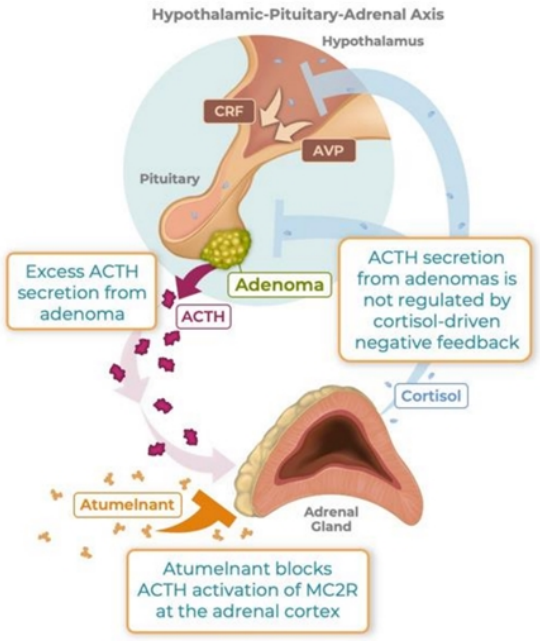


GC: glucocorticoid; A4: androstenedione. *Phase 2 results with 80 mg atumelnant at 2 weeks..

Crinetics Pharmaceuticals

ACTH DEPENDENT CUSHING'S SYNDROME

Atumelnant in ACTH-dependent Cushing's Syndrome



ACTH-dependent Cushing's Syndrome (ADCS)

Treatment Goals

- Control cortisol levels and reduce associated complications (e.g., cardiovascular disease, infections, thromboembolism, diabetes, fractures)
- Correct ADCS symptoms and patient reported outcomes (weight gain, fatigue etc.)
- Lower systolic blood pressure and lower doses of BP meds
- Reduce androgens, restore menstruation, reduce hirsutism (women) and acne
- Improvement in glucose control

Kim SH, Han S, Zhao J, et al. Discovery of CRN04894: A novel potent selective MC2R antagonist. *ACS Med Chem Lett*. 2024;15(4):478-485.
ACTH: adrenocorticotrophic hormone; AVP: arginine vasopressin; CRF: corticotropin-releasing factor.

Crinetics Pharmaceuticals

Despite Recent Medical Advances, Optimal ADCS Medical Treatment Remains Elusive

Unpredictable outcomes with existing therapies

~50-80% efficacy but with unpredictable effects and lack of response in many patients

Therapies given multiple times daily

Unacceptable delay to cortisol normalization

Laborious Titration schedules (every 2+ weeks or longer)

"Change in treatment should be considered if cortisol levels are persistently elevated after 2–3 months on max tolerated doses" [1]

Multiple Limiting Adverse events

- Hepatotoxicity
- Hypokalemia
- Hypertension
- Hyperandrogenism
- Hypogonadism
- QT prolongation

1. Fleseriu, Maria, et al. "Consensus on diagnosis and management of Cushing's disease: a guideline update." *The Lancet Diabetes & Endocrinology* 9:847-875, 2021.
ADCS: ACTH-dependent Cushing's syndrome.

Open-Label Trial of Atumelnant in ACTH-dependent Cushing's Syndrome (ADCS)

Sequential Multiple Ascending Dose Cohorts

Key Eligibility Criteria

N=18

- Male or female, aged 18-75 years
- ADCS or Ectopic ACTH syndrome

Treatment Arms:

- 3 cohorts, 10 days treatment

80 mg Once Daily (n=6)

120 mg Once Daily (n=6)

TBD (n=6)

Objectives: Evaluate the Safety and PK of Atumelnant for the Treatment of Cushing's Syndrome

Primary Endpoints: Safety, tolerability and pharmacokinetics assessments

Secondary Endpoints:

- Change from baseline in early morning serum cortisol at Day 11

Exploratory Endpoints:

- To demonstrate the lowering of 24-hour urinary free cortisol
- Proportion of participants who normalize UFC at Day 10

Dose in third cohort of study will be determined after review of results from first two cohorts at 80 mg and 120 mg

Crinetics Pharmaceuticals

Demographics and Baseline Characteristics

	80 mg N=5
Age (yrs), median (range)	47 (34-55)
Male, n (%)	4 (80%)
BMI (kg/m²), median, (range)	36 (24-43)
24h mUFC (ug/24h), median (range)	252 (99-293)
ACTH (pg/mL), median (range)	49 (26-1,504)

Reference range (RR): <45 ug/24h for mUFC and 5-46 pg/mL for ACTH.
BMI: Body mass index. UFC: Urine free cortisol. ACTH: Adrenocorticotropic hormone.

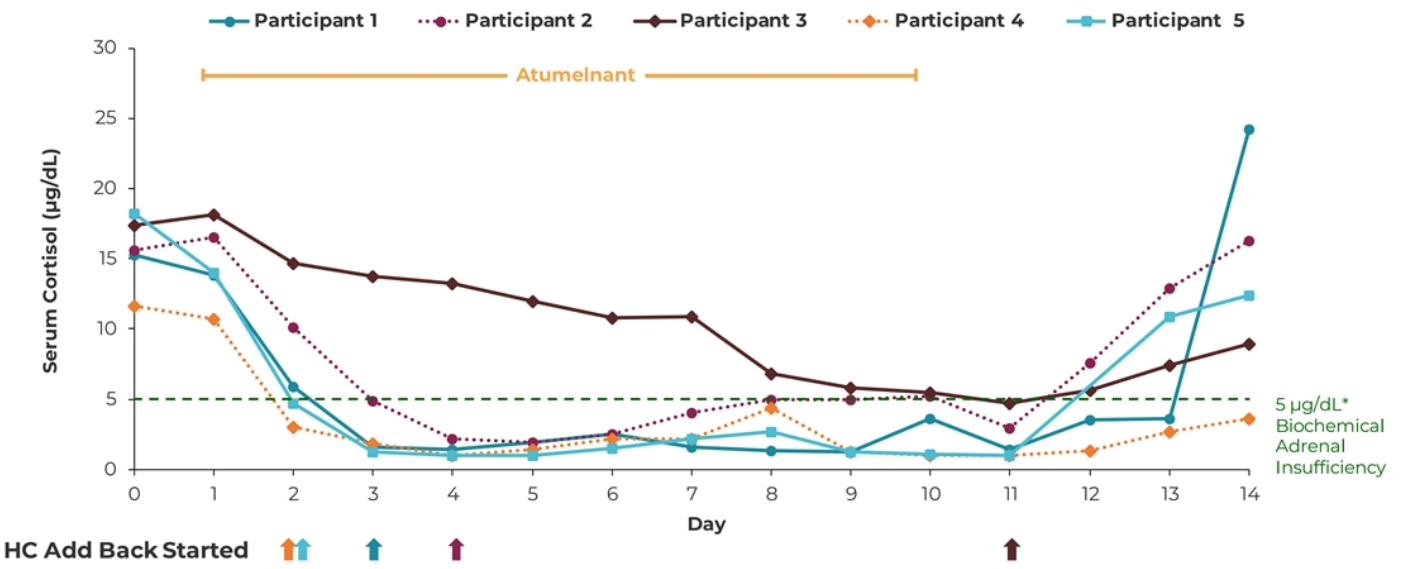
Crinetics Pharmaceuticals

Safety and Tolerability

- Atumelnant 80 mg was generally well tolerated in this study
- Predefined biochemical adrenal insufficiency (serum cortisol <5 µg/dL) observed in all patients treated to date. Consistent with the known mechanism and pharmacology
- Two participants with pre-existing steatosis had small increases in ALT (<1.5x ULN)
  - No changes in bilirubin or AST
- Other AEs reported were mild to moderate:
  - Headache (4/5) and anorexia/nausea (4/5) coincided with AM cortisol <5 mcg/dL; most symptoms improved with HC add-back
  - Fatigue, malaise, itching, edema, sinus congestion each once

ALT: Alanine Transaminase. ULN: Upper limit of normal. AST: Aspartate Aminotransferase. AE: Adverse event.

Morning Serum Cortisol: All Participants Rapidly Achieved Serum Cortisol Levels <5 µg/dL

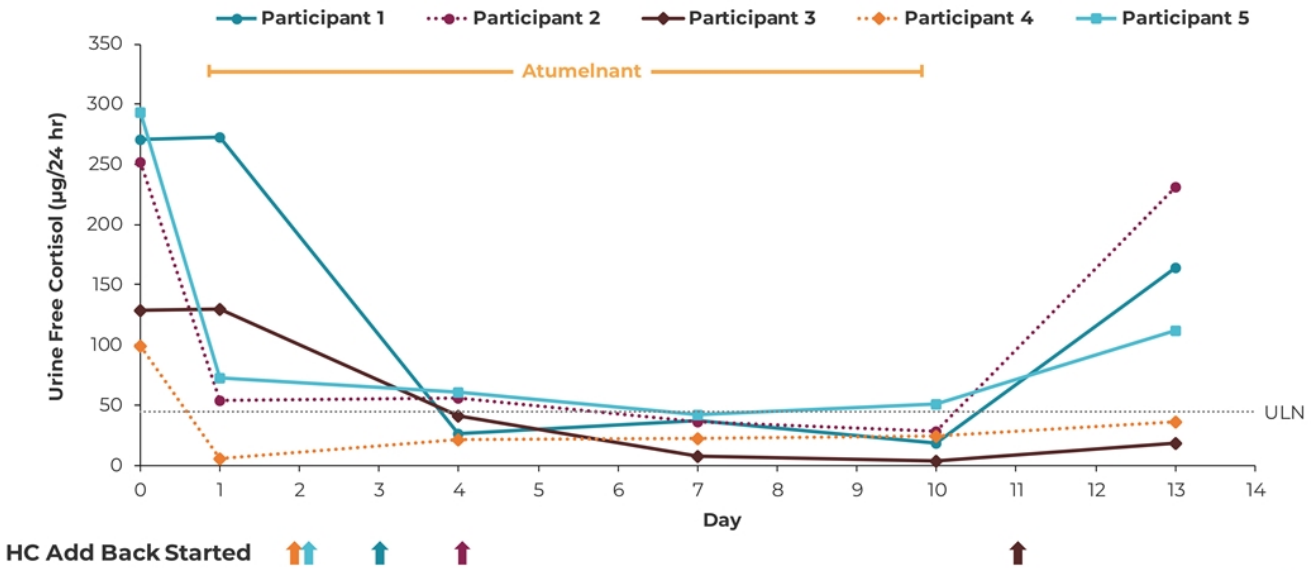


HC Add Back Started

26 HC: Hydrocortisone.

Crinetics Pharmaceuticals

24h Urine Free Cortisol: Sustained at or Below the ULN and Maintained Control with Hydrocortisone (HC) Add Back



HC Add Back Started

27 ULN: Upper limit of normal.

Crinetics Pharmaceuticals

Every Participant Experienced Improvement in Multiple Clinical and/or Cushing's Lab Features

		Participant					
		1	2	3	4	5	Total
Clinical Features	Insomnia	●	●	-	●	●	4/4
	Irritability	-	●	-	●	●	3/3
	Malaise	-	-	-	-	●	1/1
	Poor concentration	●	●	●	●	●	4/5
	Anxiety/depression	-	●	●	●	●	3/4
	Fatigue	●	-	-	●	●	2/3
	Low Libido	●	●	-	-	●	2/3
	Brain Fog	●	●	●	●	●	3/5
	Hypertension	●	●	●	●	●	3/5
	Swelling/bloating	●	-	●	●	●	2/4
Laboratory Features of ADCS	Normalization of neutrophilia	●	-	●	●	-	3/3
	Normalization of leukocytosis	-	-	●	●	-	2/2
	Normalization of low testosterone	●	●	●	●	-	3/4

● Reported and improved ● Reported but not improved - Not reported as bothersome or abnormal at entry

ADCS: ACTH-dependent Cushing's syndrome.

Atumelnant Program: Summary of Results and Next Steps

Summary: Phase 2 Data Exceeded Expectations with Unprecedented Effects

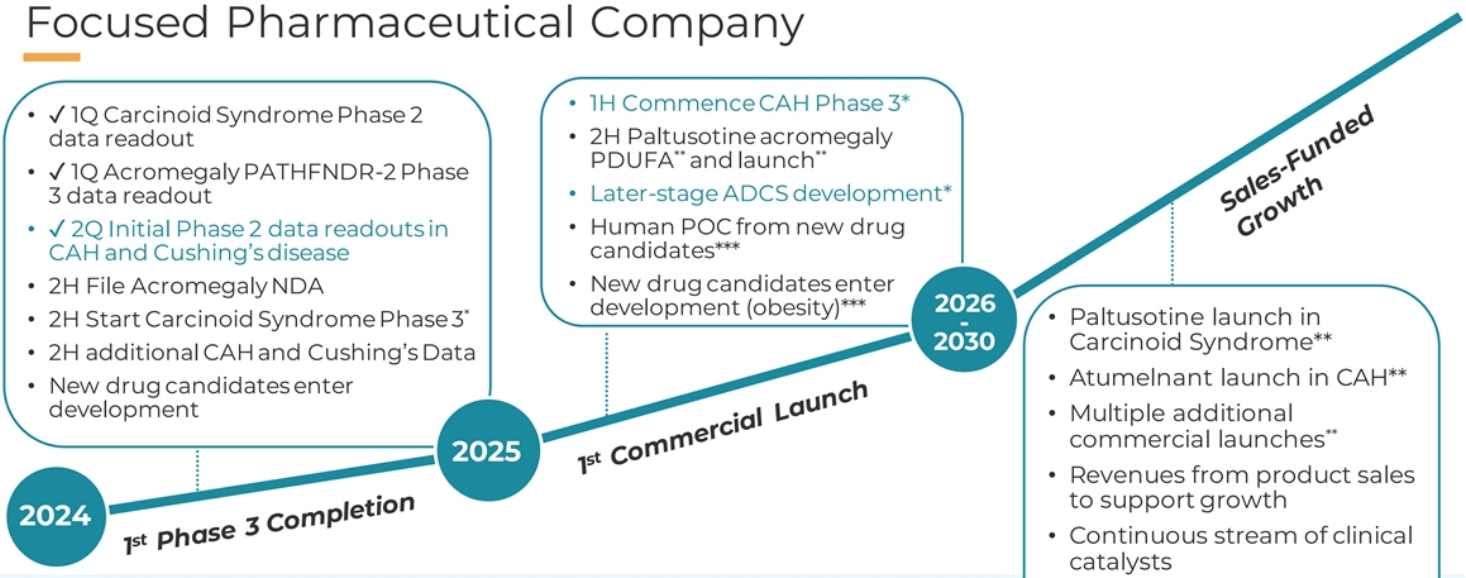
- Profound, rapid and sustained biomarker reduction in *both* CAH and ADCS
- Generally safe and well-tolerated
- Early signs of clinical symptom improvement in both CAH and ADCS
- Initial data support advancing towards Phase 3 in CAH
- Initial data support advancing towards later stage development in ADCS

Immediate Next Steps

- Complete the Phase 2 study in CAH (TouCAHn) and report top-line data in 2H 2024
- Complete the Phase 1b/2a study in ADCS and report additional data 2H 2024
- Design Phase 3 trial for CAH and align with regulators
- Design ADCS later stage development plan and align with regulators

 CAH: Congenital adrenal hyperplasia. ADCS: ACTH-dependent Cushing's syndrome.

Crinetics is Building the Premier Fully Integrated Endocrine-Focused Pharmaceutical Company



Strategic Approach to **Growing Long-term Value**

*Pending alignment with FDA **Pending NDA submission, acceptance and regulatory approval
***Pending clinical development of new drug candidates for additional diseases

NDA: New drug application. CAH: Congenital adrenal hyperplasia; PDUFA: Prescription Drug User Fee Act. ADCS: ACTH-dependent Cushing's syndrome. POC: Proof of concept.

Crinetics Pharmaceuticals

Q&A

Scott Struthers, Ph.D.
Founder and Chief Executive Officer

Dana Pizzuti, M.D.
Chief Medical & Development Officer

Alan Krasner, M.D.
Chief Endocrinologist

Jim Hassard
Chief Commercial Officer

Crinetics Pharmaceuticals