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): January 10, 2025

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 January 10, 2025, Crinetics Pharmaceuticals, Inc. (the "Company," "Crinetics," "we," "us," or "our") issued a press release and made available a corporate presentation announcing positive topline results from its open-label, Phase 2 congenital adrenal hyperplasia ("CAH") study of atumelnant, a novel, once-daily oral adrenocorticotropic hormone ("ACTH") receptor antagonist candidate being developed for the treatment of classic CAH and ACTH-dependent Cushing's syndrome. Copies of the press release and corporate presentation are attached as Exhibits 99.1 and 99.2, 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 January 10, 2025, at 8:30 a.m. Eastern Time.

The information contained in this Item 7.01 of this Current Report on Form 8-K, including in Exhibits 99.1 and 99.2 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 (the "Exchange Act"), 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 (the "Securities Act"), or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

The information regarding the press release referred to in Item 7.01 of this Current Report on Form 8-K is incorporated herein by reference. A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act. All statements other than statements of historical facts contained in this Current Report on Form 8-K are forward-looking statements. These forward-looking statements speak only as of the date of this Current Report on Form 8-K 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 reports on Form 10-Q for the quarters ended March 31, 2024, June 30, 2024, and September 30, 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 January 10, 2025
99.2	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 hereunto duly authorized.

Crinetics Pharmaceuticals, Inc.

Date: January 10, 2025

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 Topline Results From Phase 2 Trial of Atumelnant in Congenital Adrenal Hyperplasia (CAH)

Substantial, Rapid and Sustained Statistically Significant Reductions of Key Biomarkers Achieved Across Doses, Including up to 80% Mean Reduction of Androstenedione

Meaningful Improvements Demonstrated in Multiple Clinical Signs and Symptoms of CAH Affecting Patient Health

Safety and Efficacy Data Support Initiation of Phase 3 Clinical Trial

Management to Host Investor Conference Call Today at 8:30 AM ET

SAN DIEGO – January 10, 2025 – Crinetics Pharmaceuticals, Inc. (Nasdaq: CRNX) today announced positive topline results from an open-label, Phase 2 congenital adrenal hyperplasia (CAH) study of investigational atumelnant, a novel, once-daily oral adrenocorticotropic hormone (ACTH) receptor antagonist candidate being developed for the treatment of classic CAH and ACTH-dependent Cushing's syndrome.

"These exciting results show atumelnant not only lowered key biomarkers, but also had a significant impact on the signs and symptoms of CAH that are important to the overall health of people living with this condition," said Scott Struthers, Ph.D., founder and chief executive officer of Crinetics. "We are eager to move forward with a global Phase 3 pivotal trial for adults in CAH, as we simultaneously prepare to start a Phase 2b/3 trial in pediatric patients this year. Our internally discovered pipeline now has two drug candidates with positive late stage data, and we look forward to submitting INDs for four additional candidates now in first-in-human enabling studies, as we continue our strategy for building the premier global endocrine company."

"There has been a long-standing interest in using a potent, selective antagonist of the ACTH receptor for the treatment of CAH and other diseases of ACTH excess, leading to the design of atumelnant by Crinetics scientists" said Dr. Alan Krasner, M.D., chief endocrinologist of Crinetics. "This Phase 2 study demonstrated that atumelnant was well tolerated and resulted in a reduction of adrenal androgen levels so rapid and robust that it allowed patients to realize meaningful improvements in long-term, pre-existing medical challenges, even within the short 12-week treatment period of this study."

Highlights from the Phase 2 TouCAHn Trial
The TouCAHn trial is an open-label, global, Phase 2 study designed to evaluate the efficacy, safety, and pharmacokinetics of atumelnant when administered for 12 weeks in people with CAH caused by 21-hydroxylase deficiency. The study enrolled 28 patients across 3 dose cohorts with classic CAH on a stable dose of glucocorticoid replacement.

Primary endpoints included change from baseline in morning serum androstenedione (A4) levels and incidence of treatment-emergent adverse events. Change from baseline in morning serum 17-hydroxyprogesterone (17-OHP) was also evaluated as a secondary endpoint.

Results
For all doses, treatment with atumelnant resulted in rapid, substantial and sustained statistically significant reduction in A4 levels, the key biomarker for disease control (results in chart below).

Primary Endpoint

Atumelnant, Dosed Once Daily	Mean A4 Baseline* (ng/dL)	A4 Change from Baseline at Week 12 (ng/dL)**
40 mg (n=11)	1,213	-619 (p=0.0003)
80 mg (n=11)	1,231	-774 (p<0.0001)
120 mg (n=6)	1,064	-954 (p<0.0001)

*Morning serum levels **Least square mean change

Additionally, rapid, substantial and sustained statistically significant reductions in 17-OHP, a confirmatory secondary biomarker of disease control, were achieved across doses. Treatment with atumelnant also had a significant impact on CAH signs and symptoms, including:

- Substantial reduction and normalization of testosterone in the majority of female participants (8/13),[1] with 6 of the 11 impacted participants resuming menses
- Consistent reduction in total adrenal volume observed across dose cohorts
- Resolution of androgen mediated polycythemia in 5 of the 6 impacted participants

Atumelnant has been generally well tolerated with no treatment-related severe or serious adverse events to date, irrespective of disease severity or dose level. No participants required dose reduction or discontinued from the trial. All adverse events to-date have been mild to moderate and generally transient. No consistent clinically important trends were observed across key safety parameters, including clinical safety laboratory values, physical examination, electrocardiogram or vital signs. The most common treatment-emergent adverse events included headache (7/28) and fatigue (5/28).

Conference Call and Webcast
Crinetics will host an investor conference call on January 10, 2025, at 8:30 am Eastern Time to discuss the topline results from this study. Following the live event, a replay will be available on the Investors section of the Company's website.

Dial-in Details:
Domestic: 1-800-445-7795
International: 1-785-424-1699
Conference ID: CRNXQ4

Webcast: https://viavid.webcasts.com/starthere.jsp?ei=1703675&tp_key=d409cb44ff

ABOUT ATUMELNANT
Atumelnant, Crinetics' 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 gland. 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 from a 12-week Phase 2 study demonstrated compelling treatment benefits of atumelnant, evidenced by the rapid, substantial and sustained statistically significant reductions in key CAH disease related biomarkers, including androstenedione and 17-hydroxyprogesterone, in a diverse population. Atumelnant is currently in development for congenital adrenal hyperplasia and ACTH-dependent Cushing's syndrome.

For more information about the Phase 2 TouCAHn study in classic CAH, please visit clinicaltrials.gov (NCT05907291).

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, 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, 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 ACTH-dependent Cushing's syndrome; the expected timing and initiation of Phase 3 studies of atumelnant in CAH; the therapeutic potential and clinical benefits or safety profile of paltusotine; and the future development and focus of Crinetics. 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, June 30, 2024, and September 30, 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.

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[1] Sample size includes female participants not on hormonal contraceptives with intact uterus. Those with restored menses following atumelnant treatment included three previously amenorrheic participants and three with previously irregular menses.

Exhibit 99.2

Crinetics Pharmaceuticals

Topline Phase 2 Results from Atumelnant in Congenital Adrenal Hyperplasia (CAH)

January 10, 2025

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 plans and timelines for the clinical development of atumelnant, including the therapeutic potential and clinical benefits or safety profile in patients with CAH or Cushing's Disease and the expected plans and timing for ongoing clinical studies and related initiatives. 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" 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 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; 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 suggest changes to our planned clinical studies; 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; 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; 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 our drug candidates may not advance in development or be approved for marketing; 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. 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.

Atumelnant Positive Phase 2 Results: Demonstrated Strong Effect on Both Biomarkers and Clinical Outcomes in CAH

EFFICACY

- **Rapid, substantial, sustained statistically significant reduction of A4 in all dose groups:** Up to 80% mean reduction on atumelnant as soon as 2 weeks, sustained at 12 weeks
- **Dose response demonstrated**
- **Substantial reductions in 17-OHP across dose groups:** Up to 67% mean reduction at 12 weeks
- **Broad improvement in signs and symptoms:** Resumption of menses, resolution of androgen-mediated polycythemia and consistent reductions in total adrenal volume seen in many participants

SAFETY

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

Efficacy and safety support progressing to Phase 3

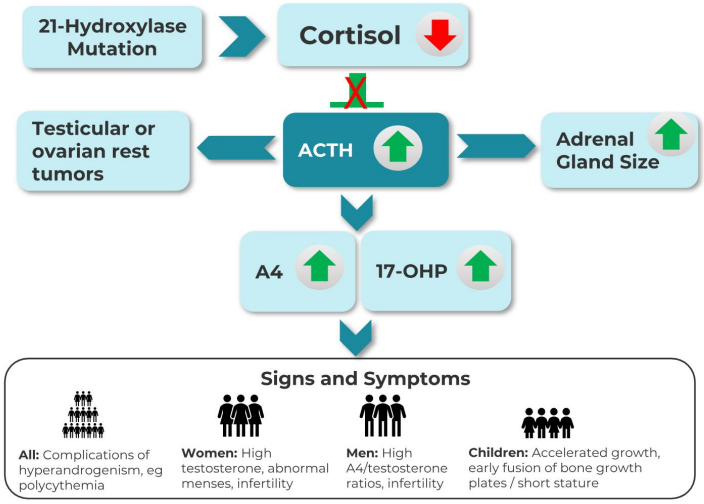
A4: Androstenedione; 17-OHP: 17-hydroxyprogesterone.

Atumelnant is an investigational drug. The safety and efficacy of atumelnant have not been established. In clinical studies, atumelnant was well-tolerated with no severe or serious adverse events.

Crinetics Pharmaceuticals

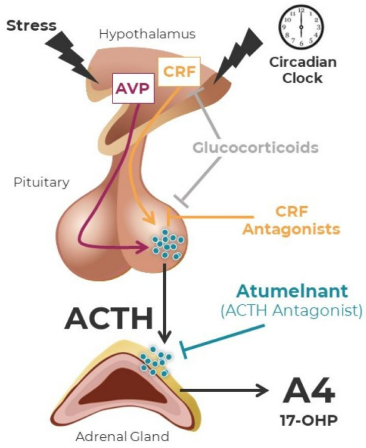
Atumelnant is the First and Only ACTH Antagonist in Clinical Development for Congenital Adrenal Hyperplasia

EXCESS ACTH IS THE FUNDAMENTAL DRIVER OF CAH SIGNS AND SYMPTOMS



ATUMELNANT MECHANISM OF ACTION

Hypothalamic-Pituitary-Adrenal (HPA) Axis in CAH



Reference: 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.

Abbreviations: ACTH, adrenocorticotrophic hormone; AVP, arginine vasopressin; CRF, corticotropin-releasing factor; MC2R, melanocortin type 2 receptor; MRAP, melanocortin 2 receptor accessory protein; 17-OHP, 17-hydroxyprogesterone; 21-OH, 21-hydroxylase;

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CAH Affects ~17,000 Addressable Adult and Pediatric Patients in the US

Treatment Goals in Adults with CAH

- Reduction of A4 and other androgens to address hyperandrogenism, which can manifest as excessive facial hair, acne and polycythemia
- Restore normal menstrual cycles and fertility in women
- Shrink testicular adrenal rest tumors, alleviate pain and restore fertility in men
- Eliminate excessive exposure to glucocorticoids to minimize steroid therapy related adverse effects including weight gain, cardiovascular issues, diabetes, and osteoporosis

Abram
Living with CAH

CAH Has a Range of Clinical Implications

"There's so many different facets of a person's life that it can affect. It can demoralize people. It takes a toll."

– Spouse of a CAH Patient

Crinetics Pharmaceuticals

Phase 2 Open-Label Study of Atumelnant in CAH Designed to Evaluate Safety, Efficacy and Pharmacokinetics

TOUCAHN

Key Eligibility Criteria

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

Treatment Arms:

- Completed cohorts, each 12 weeks (n=28)

40 mg Once Daily (n=11)

80 mg Once Daily (n=11)

120 mg Once Daily (n=6)

Primary Endpoint: Change from baseline in pre-GC morning serum A4 at week 12
Secondary Endpoint: Change from baseline in pre-GC morning serum 17-OHP at week 12
Primary Safety Assessment: Incidence of TEAEs throughout the study
Pre-trial glucocorticoid therapy (dose and regimen) maintained throughout the trial

A4: Androstenedione; ULN: Upper limit of normal; 17-OHP: 17 hydroxyprogesterone; TEAE: Treatment emergent adverse event. PK: pharmacokinetics

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Demographics and Baseline Characteristics

	40 mg N=11	80 mg N=11	120 mg N=6	All Participants N=28
Age (yrs), mean (range)	28.0 (20-45)	33.0 (22-42)	34.0 (22-47)	31.3 (20-47)
Female, n (%)	4 (36.4%)	8 (72.7%)	3 (50.0%)	15 (53.6%)
BMI (kg/m²)*, mean (range)	29.7 (21.7-42.2)	31.7 (22.3-41.4)	25.3 (19.7-27.6)	29.5 (19.7-42.2)
Baseline Biomarker levels				
A4 (ng/dL), mean (range)**	1,213 (409-2,600)	1,231 (116-2,755)	1,064 (383-2,025)	1,188 (116-2,755)
17-OHP (ng/dL), mean (range)	14,371 (2,720-24,250)	16,876 (4,740-44,000)	11,630 (453-30,400)	14,767 (453-44,000)
ACTH (pg/mL), mean (range)	434 (36-1,082)	466 (155-1,009)	1216 (204-5,700)	614 (36-5,700)
Hydrocortisone equivalent (mg/day), mean (range)	28.8 (20-40)	30.8 (20-40)	23.3 (20-30)	28.4 (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.

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12 Weeks of Treatment with Atumelnant Was Well Tolerated

- Once daily dosing of 40, 80 and 120 mg of atumelnant **generally well tolerated**
- **No severe or serious adverse events** observed to date
- TEAEs **mild to moderate in nature**, most were transient and did not require intervention
- No negative clinical trends relative to vital signs, physical examination or electrocardiograms (ECG)
- Clinical safety laboratory parameters did not reveal any consistent negative trends
  - 1 participant at 120 mg experienced AST/ALT increases without increases in bilirubin and with values reverting to baseline off study drug
- All participants completed 12 weeks of dosing and **no TEAEs required dose reduction** / cessation of treatment

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Overview of Treatment-Emergent Adverse Events

	40 mg N=11 n (%)	80 mg N=11 n (%)	120 mg N=6 n (%)	All Participants N=28 n (%)
Any Treatment-Emergent Adverse Events (TEAE)	8 (72.7%)	7 (63.6%)	5 (83.3%)	20 (71.4%)
Mild	5 (45.5%)	4 (36.4%)	4 (66.7%)	13 (46.4%)
Moderate	3 (27.3%)	3 (27.3%)	1 (16.7%)	7 (25.0%)
Severe	0	0	0	0
Any Related TEAE	4 (36.4%)	3 (27.3%)	4 (66.7%)	11 (39.3%)
Any Serious TEAE	0	0	0	0
Any Serious Related TEAE	0	0	0	0
Any TEAE of Special Interest (adrenal insufficiency)	1 (9.1%)	1 (9.1%)	0	2 (7.1%)
Any TEAE Leading to Discontinuation of Study Drug	0	0	0	0
Any TEAE Leading to Discontinuation of Study	0	0	0	0
Any Fatal TEAE	0	0	0	0

No severe or serious TEAEs observed during Phase 2 study

Crinetics Pharmaceuticals

Atumelnant Was Well Tolerated

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

Preferred Term	40 mg N=11 n (%)	80 mg N=11 n (%)	120 mg N=6 n (%)	All Participants N=28 n (%)
Participants with at least 1 TEAE	8 (72.7%)	7 (63.6%)	5 (83.3%)	20 (71.4%)
Headache	2 (18.2%)	3 (27.3%)	2 (33.3%)	7 (25.0%)
Fatigue	3 (27.3%)	1 (9.1%)	1 (16.7%)	5 (17.9%)
Decreased appetite	2 (18.2%)	0	0	2 (7.1%)
Adrenal insufficiency	1 (9.1%)	1 (9.1%)	0	2 (7.1%)
Anxiety	1 (9.1%)	1 (9.1%)	0	2 (7.1%)
Diarrhea	1 (9.1%)	1 (9.1%)	0	2 (7.1%)
Influenza	1 (9.1%)	1 (9.1%)	0	2 (7.1%)
Activated partial thromboplastin time prolonged	1 (9.1%)	0	1 (16.7%)	2 (7.1%)
Nausea	1 (9.1%)	0	1 (16.7%)	2 (7.1%)
Upper respiratory tract infection	0	2 (18.2%)	0	2 (7.1%)
Breast pain	0	1 (9.1%)	1 (16.7%)	2 (7.1%)

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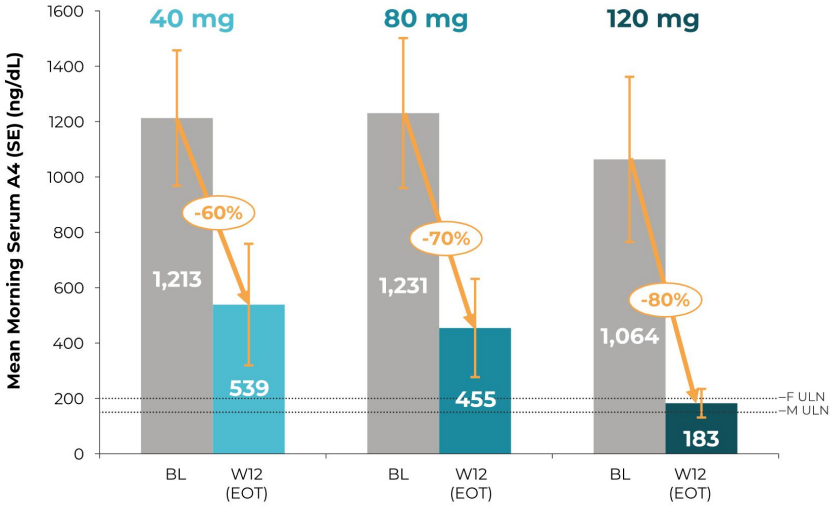
Rapid, Substantial and Sustained A4 Reductions, the Key Biomarker for CAH Disease Control

- Across each cohort, baseline A4 levels were significantly elevated (>1,000 ng/dL)
- All dose cohorts saw substantial decreases vs. baseline, with the magnitude of response increasing with dose
- The 120 mg cohort experienced the largest A4 reduction, with a mean decline of 80% at Week 12

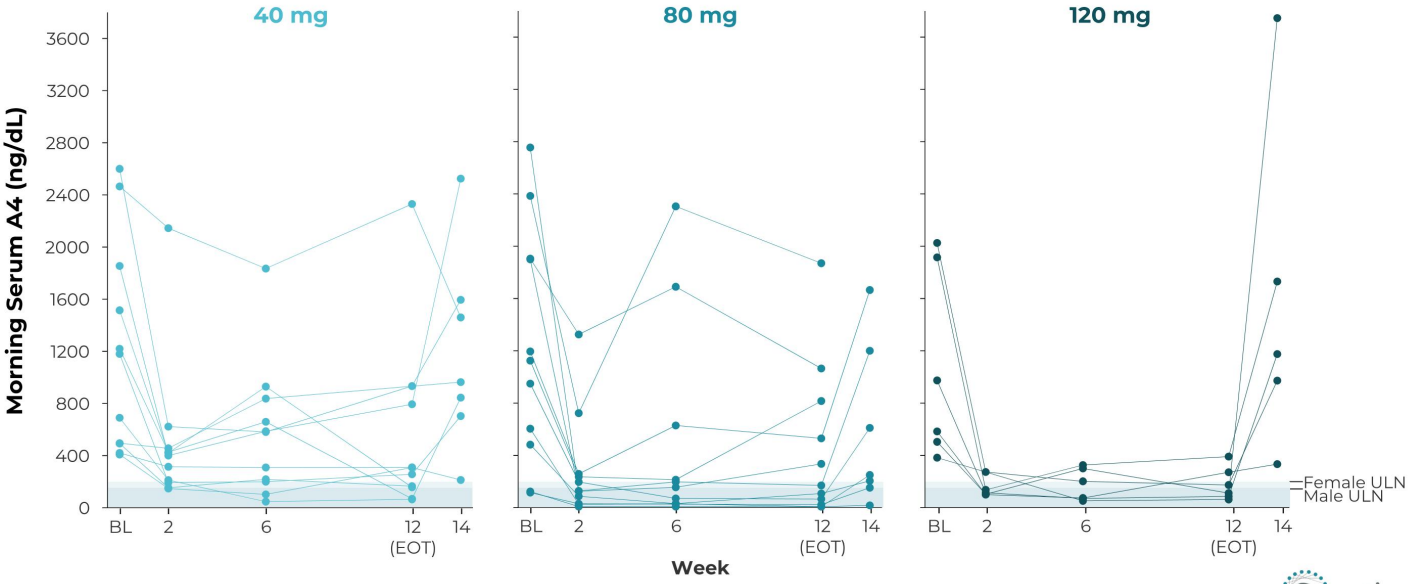


Primary Endpoint: CFB in pre-GC morning serum A4 at week 12			
A4 CFB (ng/dL) at week 12, LSM	-619	-774	-954
p-value	*p=0.0003*	*p<0.0001*	*p<0.0001*

Participants At Baseline: 40 mg N=11; 80 mg N=11; 120 mg N=6.
11 Participants At Week 12: 40 mg N=10; 80 mg N=11; 120 mg N=6.
CFB: change from baseline, LSM: Least-square-mean

Crinetics Pharmaceuticals

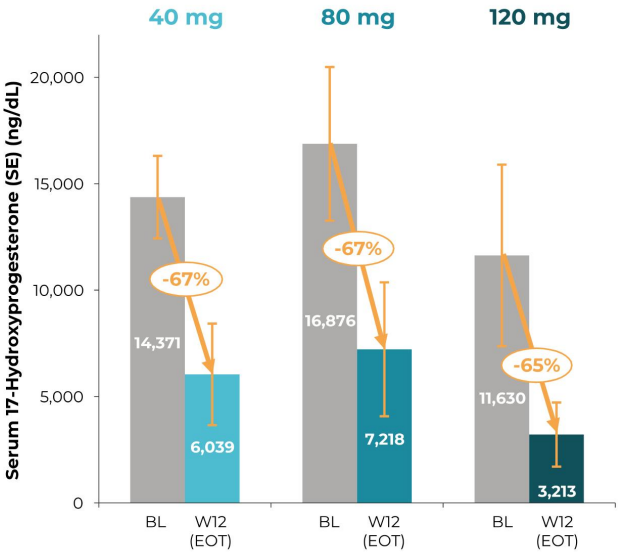
The Majority of Participants at 80mg and 120 mg* Achieved A4<ULN by Week 2



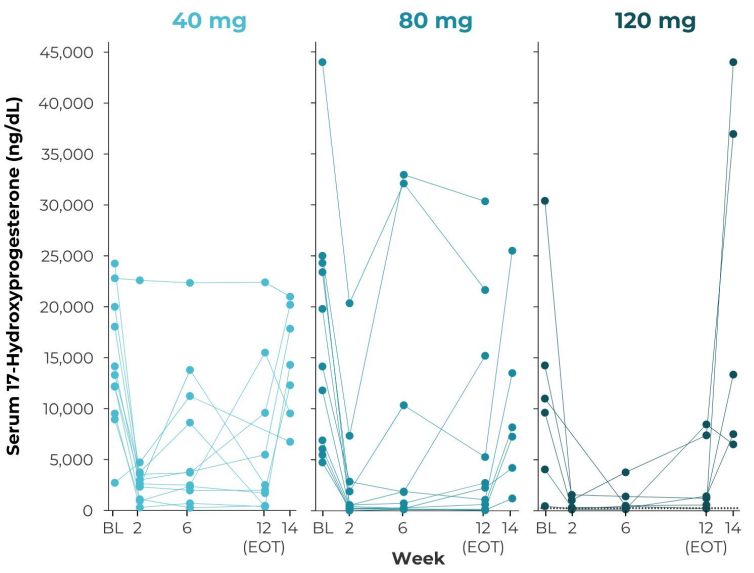
*7/11 participants at 80 mg and 4/6 at 120 mg achieved A4<ULN by week 2

Rapid, Substantial and Sustained Reductions in 17-OHP, a Confirmatory Secondary Biomarker of Disease Control

Mean 17-OHP at Baseline and Week 12



Individual 17-OHP by Study Week



Participants At Baseline: 40 mg N=11; 80 mg N=11; 120 mg N=6.
Participants At Week 12: 40 mg N=10; 80 mg N=11; 120 mg N=6.
CFB: change from baseline, LSM: Least-square-mean

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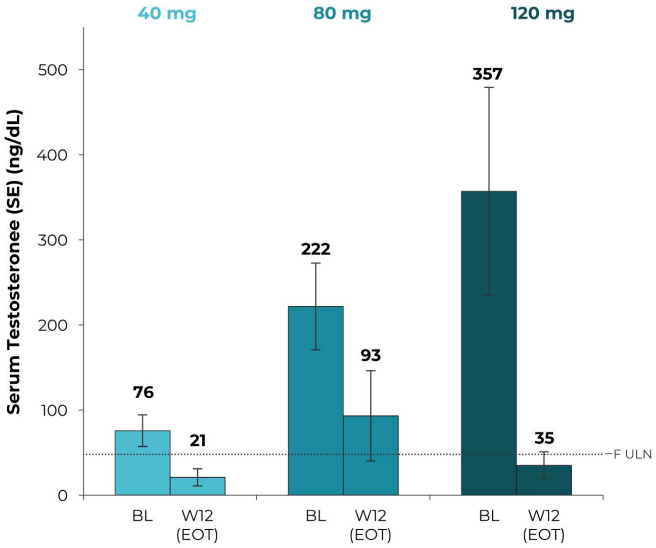
Female Participants Experienced Improvements in Reproductive Health

Many Participants Resumed Menses While Enrolled in the Study

- **6/11** female participants (not on hormonal contraceptives with intact uterus) resumed menses during the study
  - Includes 3 previously amenorrheic female participants, and 3 participants with previous irregular menses
- **8/13** female participants with baseline testosterone >ULN achieved normal testosterone levels at Week 12

Substantial Reduction in Testosterone in All Female Participants (N=14)



14 Number of female participants at each dose level with evaluable testosterone: 40 mg N=3; 80 mg N=8; 120 mg N=3.

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Case Study: Lifelong Adrenal Enlargement Improved on Atumelnant within 12 weeks

Consistent Decrease in Adrenal Volume Across Dose Cohorts

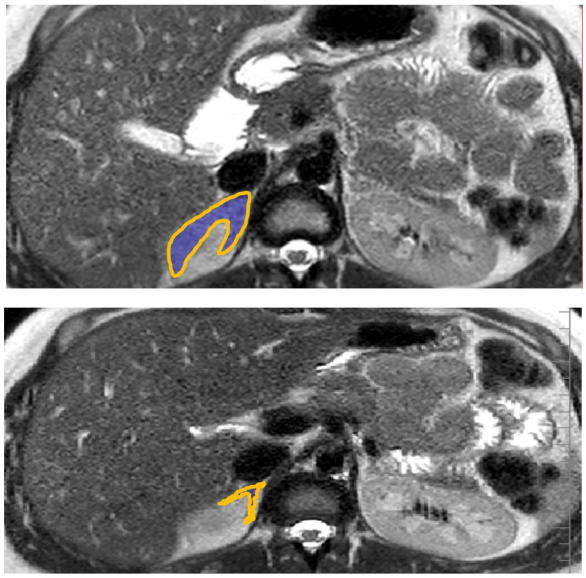
- Normal total adrenal gland volume of 8-10 mL
- Study median baseline total volume of 19.7 mL*
- 1.6-5.2 mL mean reductions in total adrenal volume observed across dose groups

Example 120mg Participant

- Male CAH trial participant taking 30 mg daily hydrocortisone
- Substantial adrenal size reduction** observed in 12 weeks
- Clinically important reductions at 12 weeks relative to baseline in:
  - A4 (**-91%**)
  - 17-OHP (**-91%**)
  - A4/Testosterone ratio (**-89%**)
  - Exploratory marker 21-Deoxycortisol (**-96%**)

-79%
Reduction

Example 120mg Participant



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* In patients with evaluable MRIs at baseline and at 12 Weeks.
**77% reduction observed in the left adrenal (not shown).

Significant Clinical Improvements Achieved with Atumelnant Treatment

CAH Manifestations	Achieved following 12 weeks of treatment with atumelnant
Overproduction of androgens, and androgen precursors	Normalization of A4 in many participants and substantial reduction in 17-OHP levels (across dose groups)
Females: • **Elevated testosterone levels** • **Absent/irregular menses**	Testosterone substantially reduced/normalized in the majority of participants; 6/11 participants resumed menses
Males: Elevated A4/testosterone ratio	Clinically relevant reductions in many participants
Adrenal gland hyperplasia	Consistent reductions in adrenal volume
Androgen mediated polycythemia (linked to increased cardiovascular risks)	Resolution in 5/6 participants with polycythemia
Hirsutism and acne	Improvements reported, longer treatment likely needed for full effects

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Summary of Results and Next Steps

Summary: Successful Phase 2 Results

- Rapid and sustained treatment effect, including in participants with high baseline A4
- Clinical activity observed across all doses (once daily 40, 80 and 120 mg)
  - Dose response demonstrated
  - 80 mg and 120 mg as the likely therapeutic doses of choice
- Evidence of meaningful improvement in multiple clinical signs and symptoms
- No serious adverse events and no severe related adverse events
- All participants completed 12 weeks of treatment

Next Steps

- Initiate Phase 3 pivotal trial in adult CAH population in 1H25
- Start Phase 2/3 pivotal trial in pediatric CAH population

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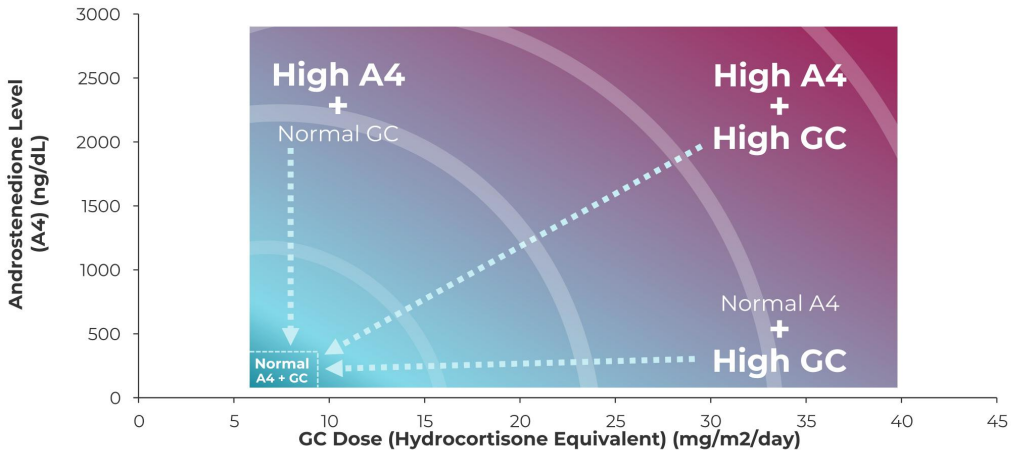
Atumelnant Vision: Healthier Hormone Levels for People Living with CAH



A single pill taken once a day, that eliminates excess ACTH driven adrenal activation *and its clinical sequalae* for people struggling with Congenital Adrenal Hyperplasia

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Q&A

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Abbreviations

17-OHP	17-hydroxyprogesterone
A4	Androstenedione
ACTH	Adrenocorticotrophic hormone
ALT	Alanine Transaminase
AST	Aspartate Transaminase
AVP	Arginine Vasopressin
BL	Baseline
BMI	Body Mass Index
CAH	Congenital adrenal hyperplasia
CRF	Corticotropin releasing factor
EOT	End of treatment
GC	Glucocorticoid
TEAE	Treatment emergent adverse event
TART	Testicular adrenal rests tumors
ULN	Upper limit of normal