About the Balance-CAH Study

(CRN04894-13)

Study Purpose

The Balance-CAH Study (CRN04894-13) is a Phase 2/3 study, with an open-label extension, evaluating the safety, efficacy, and pharmacokinetics of an investigational drug, atumelnant, in patients between 1 and less than 18 years of age living with congenital adrenal hyperplasia (CAH).

This study has 3 parts. Part A (Phase 2) will evaluate the safety and tolerability of atumelnant in pediatric patients living with CAH. Part B (Phase 3) will evaluate the efficacy of atumelnant in reducing the daily supraphysiological glucocorticoid (GC) dose while maintaining adrenal androgen normalization. Part C (OLE) will evaluate the long-term safety and efficacy of atumelnant in pediatric patients that completed participation in either Part A or Part B of this study. Participants will have the opportunity to enter directly into this OLE period, where they will receive atumelnant for up to 5 years. This global study is sponsored by Crinetics Pharmaceuticals, Inc.

About CAH

CAH is a set of autosomal recessive diseases of the adrenal glands due to genetic mutations leading to 21-hydroxylase deficiency (21-OHD). This can result in a lack of cortisol and aldosterone production, leading to lifelong adrenal insufficiency. Cortisol absence can elevate adrenocorticotropic hormone (ACTH) levels and drive excess adrenal androgen production. Prolonged exposure to elevated ACTH can cause adrenal hyperplasia and eventually hyperandrogenism, leading to premature puberty in childhood and infertility in adulthood, among other conditions.

About Atumelnant

Atumelnant is a once-daily melanocortin-2 receptor (MC2R) antagonist. Atumelnant may offer a different mechanism and site (adrenal gland) of action that may allow for rapid and sustained normalization of adrenal androgens and clinically meaningful glucocorticoid reductions to physiologic levels for individuals living with CAH.

In January 2025, Crinetics announced positive results from the TouCAHn Phase 2 sequential dose cohort study in adult individuals living with CAH. The study data showed a rapid, substantial, and sustained significant reduction in serum androstenedione (A4) levels, as well as a significant positive impact on CAH signs and symptoms. No participants in TouCAHn required dose reduction or discontinued from the study.[1]

Atumelnant is an investigational drug, and its safety and effectiveness have not been approved by any regulatory authority.

Crinetics Pharmaceuticals

Balance-CAH

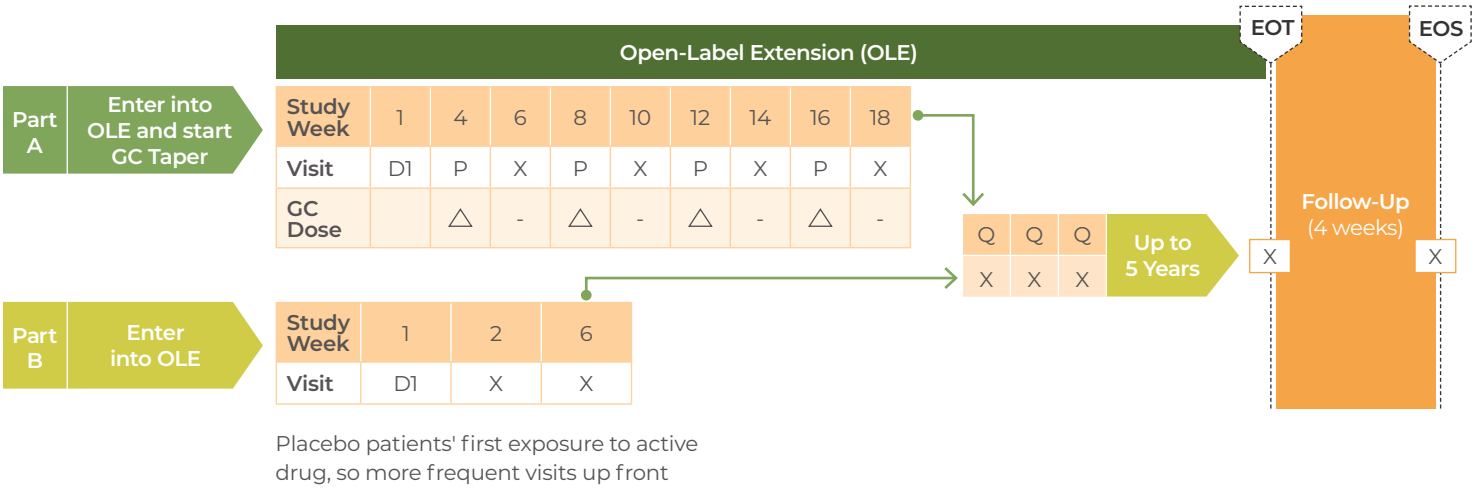
Part A Study Schema

	Screening (6 weeks)	Treatment (8 weeks)								Follow-Up (4 weeks) or OLE			
		GC stable											
Study Week	-6 to -1	1	2	3	4	5	6	7	8	9	10	11	12
Visit	X	D1	X		X		P		X		X		P

Part B Study Schema

	Screening (6 weeks)	Treatment (28 weeks) Randomized, Double-Blind, Placebo-Controlled													Follow-Up (4 weeks) or OLE
		Atumelnant													Participants will either end treatment and complete the follow-up period **OR** Enter an OLE period
		Placebo													
Study Week	-6 to -1	1	4	6	8	10	12	14	16	18	20	24	28	30	32
Visit	X	D1	X	P	X	P	X	P	X	P	X	X	X	X	P

Part C Study Schema



Placebo patients' first exposure to active drug, so more frequent visits up front

△ = indicated time points when GCs may be adjusted; D1 = Day 1; GC = glucocorticoid, OLE = open-label extension; P = phone visit, can be converted to on-site as required; Q = quarterly; X = site visit or Home Health if allowed and available in country

Study Design

The length of study participation will depend on whether an individual is enrolled in Part A or Part B.

- **Part A (Phase 2)** will last up to 18 weeks and will enroll a maximum of 48 participants. Part A includes up to 9 visits that will be conducted at the study site, at home if allowed and available, or over the phone. Participants will be placed into 1 of 4 cohorts based on their age and weight and will receive a dosage of atumelnant between 6 mg to 80 mg, which will be taken orally once daily in the morning. **All participants will remain on their pre-study GC therapies.**
- **Part B (Phase 3)** will last up to 38 weeks and will enroll approximately 105 new participants. Part B includes up to 16 visits that will be conducted at the study site, at home if allowed and available, or over the phone. Participants will be randomized 2:1 to receive either atumelnant or placebo, which will be taken orally once daily in the morning. The dose level of atumelnant will be based on the results of Part A. **All participants will remain on their pre-study GC therapies. However, the dose level of these GC therapies will be adjusted during specific time points in the study based on biomarkers and clinical presentation of the participants.**
- **Part C (OLE)** will last up to 5 years and will enroll up to 153 participants who completed either Part A or Part B. Part C includes up to 30 visits. The exact number of visits will depend on if participants were enrolled in Part A or Part B previously, and will be conducted at the study site, at home if allowed and available, or over the phone. All participants will receive atumelnant, which will be taken orally once daily in the morning. **All participants will remain on their GC therapies. However, the dose level of these GC therapies may be adjusted based on biomarkers and clinical presentation of the participants.**

The investigational drug, study lab tests, imaging, study procedures, and safety assessments are provided at no cost to participants. Additionally, costs for travel may be reimbursed.

Key Eligibility Criteria

- Be between 1 and < 18 years of age
- Have classic CAH due to 21-OHD
- Have elevated morning serum A4 level > upper limit of normal (ULN) during screening obtained prior to GC administration
- Be on stable supraphysiologic GC replacement therapy (e.g., modified-release hydrocortisone, cortisone acetate, prednisolone, prednisone, methylprednisolone, dexamethasone)
- Have a body weight of at least 10 kg
- Other eligibility criteria will apply

1. crinetics.com/crinetics-announces-positive-topline-results-from-phase-2-trial-of-atumelnant-in-congenital-adrenal-hyperplasia-cah

Endpoints

	Part A:	Part B:	Part C:
Primary Objective	To evaluate efficacy of atumelnant, measured by change from baseline in serum A4	To evaluate efficacy of atumelnant in reducing daily GC dose while maintaining adrenal androgen normalization	To evaluate efficacy of atumelnant, measured by change from baseline in A4
Secondary Objectives	• To evaluate efficacy of atumelnant, measured by change from baseline in serum 17-OHP • To measure the pharmacokinetic profile of atumelnant	• To evaluate efficacy of atumelnant to reduce A4 levels, change in 17-OHP, and reduce GC dosing	• To evaluate efficacy of atumelnant, measured by change from baseline in serum 17-OHP • To evaluate efficacy of atumelnant, as assessed by GC need

Learn More

To learn more or to refer a patient for the Balance-CAH Study, scan the QR code or visit **CrineticsCAH.com**. For questions on the mechanism of action or other studies within Crinetics' pipeline, please contact **ClinicalTrials@Crinetics.com**.

Thank you for your interest in the Balance-CAH Study (CRN04894-13).

Notes

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