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CAHtalyst™ Pediatric Study: Global Safety and Efficacy Study of Crinecerfont for the Treatment of Classic Congenital Adrenal Hyperplasia (CAH) due to 21-Hydroxylase Deficiency (21-OHD) in Pediatric Participants

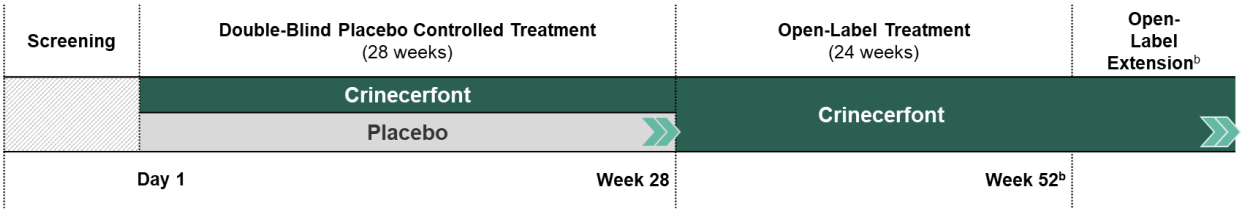
Thank you for contacting Neurocrine Biosciences with your unsolicited Medical Information request regarding the CAHtalyst Pediatric (NCT04806451) study, investigating the use of crinecerfont for the treatment of classic CAH due to 21-OHD in pediatric participants.

Crinecerfont is an investigational, oral, selective corticotropin-releasing factor type 1 receptor (CRF_1) antagonist being developed to help reduce and control excess adrenal androgens through a steroid-independent mechanism for the treatment of CAH. Crinecerfont is currently not approved by the US Food and Drug Administration (FDA) or another regulatory body for the treatment of any indication.[1-4]

CAH2006 (CAHtalyst™ Pediatric Study): Phase 3 Study in Pediatric Participants (eligible ages: 2-17 years) with Classic CAH

The crinecerfont Phase 3 CAHtalyst Pediatric study (NCT04806451) was designed to evaluate the efficacy, safety, and tolerability of crinecerfont vs. placebo in 103 pediatric male and female participants (eligible ages: 2-17 years of age) with classic CAH due 21-OHD. There was a 28-week randomized, double blind, placebo-controlled period, followed by 24 weeks of open-label treatment with crinecerfont capsules, administered orally, twice daily (**Figure 1**). The primary outcome measure was the change from baseline in serum androstenedione (A4) at Week 4, with secondary outcome measures including, but not limited to, change from baseline in serum 17-hydroxyprogesterone (17-OHP) at Week 4, percent change from baseline in glucocorticoid (GC) daily dose (in hydrocortisone dose equivalents adjusted for body surface area) while maintaining androgen control at Week 28, change from baseline in body mass index, bone age advancement, and salivary 17-OHP at Week 28, and change from baseline in predicted adult height at Week 52. Key inclusion criteria included a medically confirmed diagnosis of classic CAH due to 21-OHD and stable GC doses prior to study start. Key exclusion criteria included a known or suspected diagnosis of any of the other known forms of classic CAH or a history of bilateral adrenalectomy, hypopituitarism, or other condition requiring chronic GC therapy. At the end of the study, participants have the opportunity to continue to receive crinecerfont as part of an open-label extension.[5]

Figure 1. CAH2006: Study Design[5a]:



[a]Enrollment completed; [b]Duration of participation in the study is ~14 months for the core study and will be a variable amount of time per participant for the open-label extension.

The Phase 3 CAHtalyst Pediatric study met its primary endpoint, demonstrating that treatment with crinecerfont resulted in a statistically significant decrease from baseline in serum A4 at Week 4 vs. placebo, following a GC stable period (p=0.0002). The study also met key secondary endpoints, with a statistically significant percent reduction from baseline in GC daily dose vs. placebo while maintaining androgen control at Week 28 (p<0.0001), and a statistically significant decrease from baseline in serum 17-OHP at Week 4 vs. placebo (p< 0.0001). Approximately 30% of participants receiving crinecerfont achieved a reduction to a physiological GC daily dose while maintaining androgen control compared to 0% of participants receiving placebo at Week 28 (p=0.0009, p-value not adjusted for multiplicity).[4]

During the phase 3 double-blind, placebo-controlled period of the CAHtalyst Pediatric study, crinecerfont was generally well tolerated. The most common adverse events were headache, fever, vomiting, upper respiratory tract infection, and nasopharyngitis. There were few serious adverse events, with none assessed as related to crinecerfont.[4]

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For more information about the CAHtalyst Pediatric study, please visit ClinicalTrials.gov.

This letter is provided in response to your unsolicited medical information inquiry. Please feel free to contact Neurocrine Medical Information at (877) 641-3461 or medinfo@neurocrine.com if you would like to request additional information.

References:

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2. Newfield RS, Sarafoglou K, Fechner PY, et al. Crinecerfont, a CRF1 Receptor Antagonist, Lowers Adrenal Androgens in Adolescents with Congenital Adrenal Hyperplasia [published online ahead of print, 2023 May 22]. *J Clin Endocrinol Metab*. 2023; dgad270. doi:10.1210/clinem/dgad270.
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4. Neurocrine.com. (2023). Neurocrine Biosciences Announces Phase 3 Pediatric Study Results of Crinecerfont in Children and Adolescents for the Treatment of Congenital Adrenal Hyperplasia Met Primary and Key Secondary Endpoints [Press release]. Retrieved from: https://neurocrine.gcs-web.com/news-releases/news-release-details/neurocrine-biosciences-announces-phase-3-pediatric-study-results. Accessed October 5, 2023.
5. Global safety and efficacy registration study of crinecerfont in pediatric patients with classic congenital adrenal hyperplasia (CAHtalyst Pediatric Study). ClinicalTrials.gov identifier: NCT04806451. Updated April 13, 2023. Accessed October 5, 2023. https://clinicaltrials.gov/ct2/show/NCT04806451.