Crinecerfont

An Investigational Treatment for Classic Congenital Adrenal Hyperplasia

At Neurocrine Biosciences, we are developing crinecerfont, an investigational, oral, non-steroidal, selective corticotropin-releasing factor type 1 (CRF_1) receptor antagonist for the treatment of classic congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21-OHD).

Overview

Crinecerfont

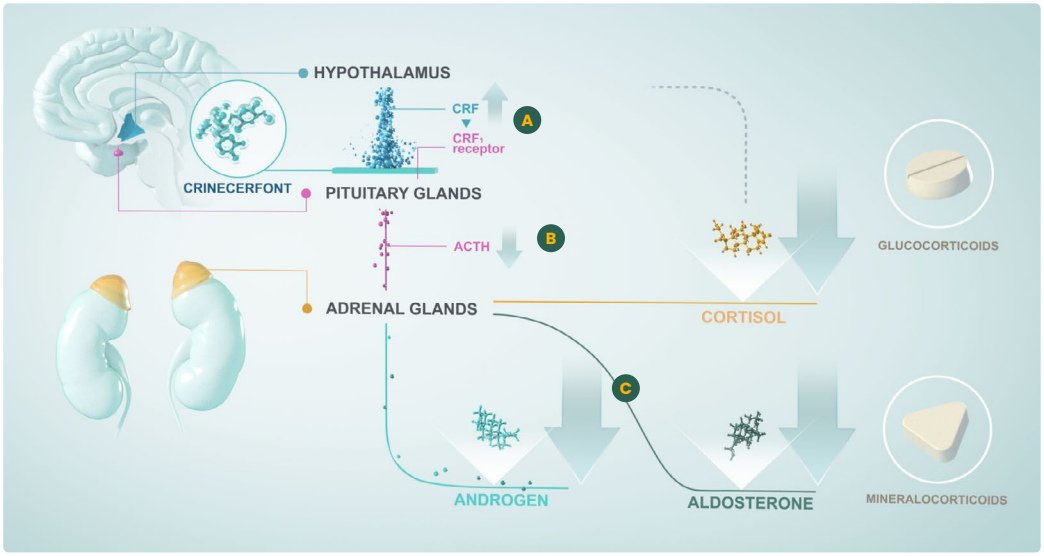
Crinecerfont is an investigational compound in Phase 3 clinical studies for the treatment of classic CAH due to 21-OHD. It has the potential to reduce excessive androgen production, thereby enabling glucocorticoid treatment at more physiologic doses to treat cortisol deficiency that occurs in CAH.

Crinecerfont

Status: Two ongoing Phase 3 studies in adults and children

Crinecerfont is an investigational, oral, non-steroidal, selective CRF_1 receptor antagonist that is being developed for the treatment of classic CAH due to 21-OHD deficiency. It is thought to:

- **A.** Bind to CRF_1 receptors in the pituitary gland, changing their conformation (allosteric binding) to prevent CRF from binding to them.
- **B.** By doing so, crinecerfont is believed to put a brake on the overactive HPA axis by dialing down high ACTH levels…
- **C.** …and potentially decreasing high androgen levels.



Reducing ACTH and androgen level may enable dosing of glucocorticoids at lower, more physiologic levels.

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Clinical Trials

Phase 2 CAHlibrate Clinical Study

Results of the Phase 2 CAHlibrate clinical study evaluating crinecerfont in adults with inadequately controlled classic CAH, showed meaningful reductions in the levels of ACTH, 17-OHP, and A4. In addition, reductions were seen in the levels of testosterone in female participants and A4/testosterone ratio in male participants. High testosterone in females leads to excessive hair growth, menstrual irregularity, and infertility (see CAH fact sheet). In males, it leads to testicular adrenal rest tumors (TARTs) that can impact fertility.

Treatment with crinecerfont in the CAHilbrate Phase 2 study was well tolerated with no related serious adverse events reported. Adverse events reported in two or more participants included headache, upper respiratory tract infection, fatigue, contusion, insomnia, and nausea.

The clinical safety database for crinecerfont includes more than 800 exposures. Crinecerfont has been well tolerated, with no related serious adverse events reported to date in Phase 1 and 2 studies.

Neurocrine Biosciences received Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for crinecerfont in classic CAH due to 21-OHD.

Read more about these study results here, **https://pubmed.ncbi.nlm.nih.gov/34653252/**

Phase 3 CAHtalyst Clinical Studies

We are currently conducting the CAHtalyst™ clinical trial program, consisting of two Phase 3 global registrational studies of crinecerfont in adults (ages 18 years and older), and children and adolescents (ages 2 to 17 years) with classic CAH. Clinical study sites are located in the U.S., Canada, and Europe. As part of the CAHtalyst clinical trial program, participants who complete these trials will be able to continue to receive crinecerfont as part of an open-label extension.

For more information about the CAHtalyst™ adult Phase 3 study, please visit **CAHtalyst.CAHStudies.com** or **ClinicalTrials.gov**.

For more information about the CAHtalyst™ pediatric Phase 3 study, please visit **CAHtalystPeds.CAHStudies.com** or **ClinicalTrials.gov**.

References

1. National Organization for Rare Disorders. Congenital adrenal hyperplasia. Accessed December 18, 2020. https://rarediseases.org/rare-diseases/congenital-adrenal-hyperplasia/.

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