

Neurocrine Biosciences Reports Positive Phase II Data for Crinecerfont in Adults with Congenital Adrenal Hyperplasia at ENDO Online 2020

June 8, 2020

Neurocrine Biosciences Reports Positive Phase II Data for Crinecerfont in Adults with Congenital Adrenal Hyperplasia at ENDO Online 2020

- Crinecerfont Demonstrates Meaningful Reductions in Key Disease Biomarkers After 14 Days of Treatment
- Initiation of Global Registrational Study of Crinecerfont in Adults Planned for Second Half 2020

SAN DIEGO, June 8, 2020 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced positive data from its completed open-label, multiple-dose, dose-finding, Phase II clinical study of crinecerfont (NBI-74788), demonstrating meaningful reductions in all three key disease hormone markers in adult patients with classic congenital adrenal hyperplasia (CAH), a genetic disorder affecting the adrenal glands. Crinecerfont treatment produced meaningful reductions in elevated adrenocorticotropic hormone (ACTH) and 17-hydroxyprogesterone (17-OHP) levels (by 54% to 75%) at all doses studied, together with a dose-related decrease in androstenedione (A4) levels, ranging from 21% to 64% (Figure 1). At the highest dose of crinecerfont (100 mg twice daily), 75% of patients showed a response of at least 50% reduction from baseline for each of the three hormone markers at day 14 (Table 1). Treatment with crinecerfont was well tolerated with a favorable safety profile 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 full data set from the Phase II study assessing the safety, tolerability, pharmacokinetics and pharmacodynamics of crinecerfont, an investigational, oral, non-steroidal corticotropin-releasing factor type 1 (CRF1) receptor antagonist, is available as part of a recorded presentation at the [Endocrine Society's ENDO Online 2020 meeting](#), can be accessed at this [link](#), and on Neurocrine Biosciences' corporate website under Investors at www.neurocrine.com.

Figure 1: Crinecerfont Treatment Led to Meaningful Reductions in ACTH, 17-OHP and A4

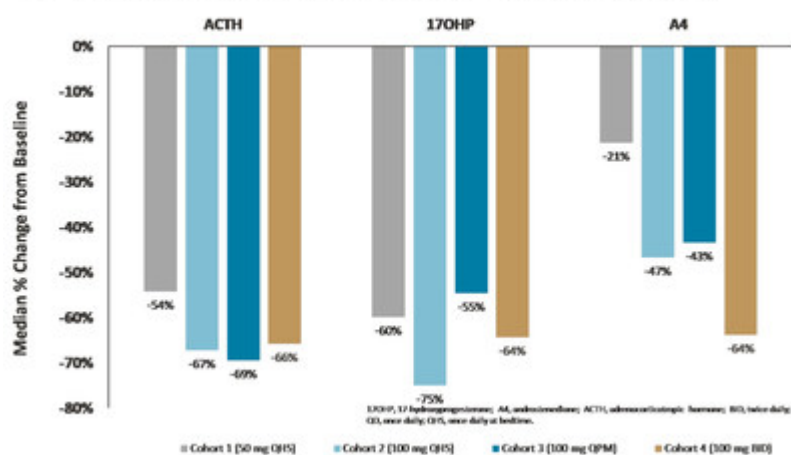


Table 1: Number and Percentage of Participants in Each Cohort Demonstrating a $\geq 50\%$ Reduction from Baseline in ACTH, 17-OHP and Androstenedione (A4)

$\geq 50\%$ reduction from baseline, n/N (%)	Cohort 1: 50 mg QHS	Cohort 2: 100 mg QHS	Cohort 3: 100 mg QPM	Cohort 4: 100 mg BID
ACTH	4/8 (50.0)	5/6 (83.3)	5/7 (71.4)	6/8 (75.0)
17-OHP	4/8 (50.0)	4/6 (66.7)	4/7 (57.1)	6/8 (75.0)
Androstenedione (A4)	2/8 (25.0)	3/6 (50.0)	3/7 (42.9)	6/8 (75.0)

"There continues to be a need for effective treatment options that are well tolerated in patients with classic CAH. Patients with this genetic disorder require glucocorticoid replacement therapy, but often at high doses to manage their excessive adrenal androgen production. At the same time, side effects from chronic treatment with supraphysiologic amounts of glucocorticoids can cause serious long-term health consequences including bone loss and metabolic dysfunction," said Richard Auchus, M.D., Ph.D., the study's lead investigator and Professor of Internal Medicine, Division of Metabolism, Endocrinology & Diabetes at Michigan Medicine. "It is encouraging to see that crinecerfont, a non-steroidal therapy, provided meaningful reductions in three key disease biomarkers in patients with classic CAH. These data suggest that crinecerfont has the potential to improve CAH symptoms and to reduce the burden of daily glucocorticoid exposure for these patients. Hopefully, this approach might provide a new treatment option to better manage the androgen excess of classic CAH while mitigating the adverse consequences of current treatment schemes."

Neurocrine Biosciences plans to initiate a single, global registrational study of crinecerfont in adult patients with classic CAH in the second half of 2020. Classic CAH is a genetic disorder, in which an enzyme deficiency alters the production of adrenal steroids. Because of this deficiency, the adrenal glands fail to produce enough cortisol and, sometimes, aldosterone, resulting in a potentially life-threatening condition.

"We are pleased that crinecerfont was effective in producing a meaningful, dose-related reduction of adrenal androgens and other key biomarkers of disease in patients with classic CAH and was well tolerated in this study," said Eiry W. Roberts, M.D., Chief Medical Officer at Neurocrine Biosciences. "In addition, data from the study was successful in identifying an effective dosing regimen for further evaluation in a single, global registration study in adults with classic CAH. We hope to demonstrate that crinecerfont is a valuable, non-steroidal, treatment option for patients to manage the burdensome symptoms of classic CAH, while also reducing the need for chronic supraphysiologic dosing with glucocorticoids."

Crinecerfont Phase II Study Design

The Phase II open-label, multiple-dose, dose-finding study assessed the safety, tolerability, pharmacokinetics and pharmacodynamics of crinecerfont in 18 adults with classic 21-hydroxylase deficiency CAH. The study's sequential-cohort design evaluated four crinecerfont oral dosing regimens: 50 mg at bedtime (Cohort 1; n=8); 100 mg at bedtime (Cohort 2; n=7); 100 mg once-daily with an evening meal (Cohort 3; n=8); and 100 mg twice-daily with meals (Cohort 4; n=8). Participants in Cohorts 1 and 2 could enroll in Cohorts 3 and/or 4. Each regimen was administered for 14 consecutive days. ACTH, 17-OHP and A4, key disease hormone markers in CAH patients, were measured over a 24-hour period at baseline and after 14 consecutive days of dosing.

About Classic Congenital Adrenal Hyperplasia (CAH)

Classic CAH is a genetic disorder, in which an enzyme deficiency alters the production of adrenal steroids. Because of this deficiency, the adrenal glands fail to produce enough cortisol and, sometimes, aldosterone, resulting in a potentially life-threatening condition. The lack of cortisol stimulates the release of high levels of adrenocorticotrophic hormone (ACTH) from the pituitary gland, leading to excessive adrenal androgen levels. These levels can lead to virilization, menstrual irregularities, hirsutism, acne in females and accelerated growth and precocious puberty in childhood (resulting in short stature and fertility problems in both males and females).

Corticosteroids, the current standard of care, are used both to correct the endogenous cortisol deficiency and to reduce the high ACTH levels and androgen excess. However, the dose and duration of glucocorticoids required to suppress ACTH are often well above the normal physiological level of cortisol, which can result in serious complications typical of iatrogenic Cushing's syndrome, including metabolic issues, bone loss, growth impairment, and infection risk. Classic CAH is a disease that affects approximately 20,000 to 30,000 people in the United States and approximately 50,000 people in Europe.

About Crinecerfont

Crinecerfont is a novel, potent, selective, oral, non-steroidal corticotropin-releasing factor type 1 (CRF1) receptor antagonist under evaluation for the treatment of classic CAH. The blockade of CRF receptors in the pituitary has been shown to decrease the release of adrenocorticotrophic hormone (ACTH), which in turn decreases the production of adrenal androgens, and potentially the symptoms associated with CAH. Lowering ACTH and adrenal androgen levels could reduce the amount of glucocorticoid treatment necessary for disease control and thus could avoid the complications associated with long-term supraphysiologic glucocorticoid therapy.

Neurocrine Biosciences plans to initiate a single, global registrational study of crinecerfont in adult patients with classic CAH in the second half of 2020 and recently restarted enrollment for the Phase IIa pediatric study in adolescents with classic CAH.

About Neurocrine Biosciences

Neurocrine Biosciences is a neuroscience-focused, biopharmaceutical company with 28 years of experience discovering and developing life-changing treatments for people with serious, challenging and under-addressed neurological, endocrine and psychiatric disorders. The company's diverse portfolio includes FDA-approved treatments for tardive dyskinesia, Parkinson's disease, endometriosis* and uterine fibroids*, and clinical development programs in multiple therapeutic areas including a gene therapy for Parkinson's disease, chorea in Huntington disease, congenital adrenal hyperplasia, epilepsy, and polycystic ovary syndrome*. Headquartered in San Diego, Neurocrine Biosciences specializes in targeting and interrupting disease-causing mechanisms involving the interconnected pathways of the nervous and endocrine systems. For more information, visit [neurocrine.com](https://www.neurocrine.com), and follow the company on [LinkedIn](#). (*in collaboration with AbbVie)

Forward-Looking Statements

In addition to historical facts, this press release contains forward-looking statements that involve a number of risks and uncertainties. These statements include statements regarding the potential benefits of crinecerfont to patients and future clinical development plans. Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements include the risk that crinecerfont will not be found to be safe and/or effective or may not prove to be beneficial to patients; that development activities for crinecerfont may not be completed on time or at all; risks that clinical development activities may be delayed for regulatory or other reasons, may not be successful or replicate previous and/or interim clinical trial results, or may not be predictive of real-world results or of results in subsequent clinical trials; risks that regulatory submissions for crinecerfont may not occur or be submitted in a timely manner; risks that crinecerfont may not obtain regulatory approvals; or that the U.S. Food and Drug Administration or regulatory authorities outside the U.S. may make adverse decisions regarding crinecerfont; and other risks described in the Company's periodic reports filed with the Securities and Exchange Commission, including without limitation the Company's quarterly report on Form 10-Q for the quarter ended March 31, 2020. Neurocrine disclaims any obligation to update the statements contained in this press release after the date hereof.



View original content to download multimedia: <http://www.prnewswire.com/news-releases/neurocrine-biosciences-reports-positive-phase-ii-data-for-crinecerfont-in-adults-with-congenital-adrenal-hyperplasia-at-endo-online-2020-301072072.html>

SOURCE Neurocrine Biosciences, Inc.

Navjot Rai (Media), 858-617-7623, media@neurocrine.com; Todd Tushla (Investors), 858-617-7143, ir@neurocrine.com