Neurocrine Biosciences Presents CAHtalyst™ Adult Study Baseline Characteristics and Data on Impact of Supraphysiologic Glucocorticoid Therapy at AACE 2024

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- CAHtalyst™ Study Baseline Characteristics Highlight the Need for New Treatment Options to Reduce Adrenal Androgens and Supraphysiologic Glucocorticoid Dosing in CAH Adult Patients
- Comprehensive Literature Review Identified Potential Psychological and Cognitive Impact of High Glucocorticoid Doses in CAH Patients

SAN DIEGO, May 9, 2024 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced that it will present CAHtalyst™ Adult Phase 3 clinical study baseline characteristics for adults with congenital adrenal hyperplasia (CAH) enrolled in the study, as well as data from a comprehensive literature review assessing the impact of supraphysiologic glucocorticoid (GC) doses on psychiatric disorders and cognition in patients with CAH.

The CAHtalyst Adult study baseline data demonstrate the potential long-term consequences of current CAH treatments, with many patients in young adulthood experiencing disorders found more commonly in people decades older, including osteopenia, hypertension and hyperlipidemia. In addition, the results of a comprehensive literature review showed that many CAH patients receiving supraphysiologic GC doses had an increased risk of psychiatric and cognitive symptoms. These new data were presented at oral presentations and poster sessions at the American Association of Clinical Endocrinology 2024 Annual Meeting in New Orleans.

CAHtalyst Phase 3 Adult Study Baseline Characteristics

Baseline characteristics of 182 adults with CAH enrolled in the CAHtalyst Adult Phase 3 study were summarized in an oral presentation at the conference by Oksana Hamidi, M.D., Associate Professor in the Division of Endocrinology and Metabolism at UT Southwestern Medical Center.

Despite supraphysiologic GC dosing, levels of adrenocorticotropic hormone, 17-hydroxyprogesterone and androstenedione (A4) were elevated at baseline, with levels of testosterone (females) and A4/testosterone (males) also elevated. Common comorbidities included anxiety, osteopenia, depression, hypertension and hyperlipidemia. Overall, close to half of participants were overweight. Forty-seven percent of females reported a history of hirsutism (excessive hair growth) and acne (23%), and testicular adrenal rest tumors were identified in 66% of male participants.

"In the CAHtalyst Phase 3 study in adults, we're seeing the consequence of decades of living with CAH and the clinical consequences of the current treatment paradigm in the baseline characteristics," said Eiry W. Roberts, M.D., Chief Medical Officer at Neurocrine Biosciences. "Despite being in their 30s, many of the CAHtalyst Adult study participants have been diagnosed with disorders that are more common in people twice their age, including osteopenia, hypertension and hyperlipidemia. As we saw in the CAHtalyst Pediatric study baseline data presented at PES2024, adrenal androgen and other steroid markers were also elevated despite supraphysiologic doses of glucocorticoids, demonstrating the need for novel glucocorticoid-independent approaches to reducing adrenal androgens and supraphysiologic glucocorticoid dosing in CAH patients at all ages."

In 2023, Neurocrine Biosciences announced top-line data from the CAHtalyst Pediatric and CAHtalyst Adult Phase 3 clinical studies evaluating the efficacy, safety, and tolerability of crinecerfont in children, adolescents, and adults with CAH due to 21-hydroxylase deficiency. The data from both studies supported two New Drug Applications submitted to the U.S. Food and Drug Administration in April 2024.

Literature Review: Psychological and Cognitive Impact of Supraphysiologic Glucocorticoids

Neurocrine Biosciences also presented the results of a comprehensive review of available literature between 1996–2023 focusing on the use of supraphysiologic doses of hydrocortisone and their effect on psychiatric disorders and cognition in patients with CAH (Poster# 05). The review identified mood and psychotic disorders as the most consistent psychiatric disorders seen. Brain morphology in patients with CAH was altered (white matter microstructure abnormalities), suggesting an increased risk of cognitive impairment with use of supraphysiologic doses of GCs in these patients.

"Glucocorticoids administered at supraphysiologic doses can lead to a spectrum of psychiatric and cognitive symptoms, with the severity correlating with the glucocorticoid dosage given," said Amy Wisniewski, M.D., Research Professor, Psychology at Oklahoma State University. "As a result, increased awareness among healthcare providers is necessary to monitor CAH patients receiving supraphysiologic doses of glucocorticoids for signs of psychiatric and cognitive symptoms. More research is needed to identify the multiple factors, including prolonged exposure to adrenal androgen excess and glucocorticoid-induced deterioration of brain regions, that may determine the cognitive impairment of patients with CAH."

Neurocrine Biosciences abstracts to be presented at the meeting include:

- Baseline Characteristics of Adults with Classic Congenital Adrenal Hyperplasia Enrolled in CAHtalyst, a Phase 3 Study of

Crinecerfont, a Corticotropin-Releasing Factor Type 1 Receptor Antagonist, **Oral Presentation—Dr. Oksana Hamidi, May 10; 11:00-11:15 a.m.**

- The Psychological and Cognitive Impact of Supraphysiological Glucocorticoids in Patients with Congenital Adrenal Hyperplasia: A Comprehensive Review, May 11; 7:30–7:45 a.m. (Poster #05)
- Glucocorticoid Treatment Patterns in Pediatric and Adult Patients with Classic Congenital Adrenal Hyperplasia: Results from the CAHtalog™ Registry, May 10; 10:10–10:25 a.m. (Poster #14)

About Congenital Adrenal Hyperplasia
Congenital adrenal hyperplasia (CAH) is a rare genetic condition that results in an enzyme deficiency that alters the production of adrenal hormones which are essential for life. Approximately 95% of CAH cases are caused by a mutation that leads to deficiency of the enzyme 21-hydroxylase. Severe deficiency of this enzyme leads to an inability of the adrenal glands to produce cortisol and, in approximately 75% of cases, aldosterone. If left untreated, CAH can result in salt wasting, dehydration, and even death.

Glucocorticoids (GCs) are currently used not only to correct the endogenous cortisol deficiency, but doses used are higher than cortisol replacement needed (supraphysiologic) to lower the levels of adrenocorticotropic hormone (ACTH) and adrenal androgens. However, glucocorticoid treatment at supraphysiologic doses has been associated with serious and significant complications of steroid excess, including metabolic issues such as weight gain and diabetes, cardiovascular disease, and osteoporosis. Additionally, long-term treatment with supraphysiologic GC doses may have psychological and cognitive impact, such as changes in mood and memory. Adrenal androgen excess has been associated with abnormal bone growth and development in pediatric patients, female health problems such as acne, excess hair growth and menstrual irregularities, testicular rest tumors in males, and fertility issues in both sexes. To learn more about CAH, click here.

About Crinecerfont
Crinecerfont is an investigational, oral, selective corticotropin-releasing factor type 1 receptor (CRF_1) antagonist being developed to reduce and control excess adrenal androgens through a glucocorticoid-independent mechanism for the treatment of congenital adrenal hyperplasia due to 21-hydroxylase deficiency. Antagonism of CRF_1 receptors in the pituitary has been shown to decrease adrenocorticotropic hormone levels, which in turn decreases the production of adrenal androgens and potentially the symptoms associated with CAH. Our data demonstrate that lowering adrenal androgen levels enables lower, more physiologic dosing of glucocorticoids and thus could potentially reduce the complications associated with exposure to greater than normal glucocorticoid doses in patients with CAH.

To learn more about crinecerfont, click here.

About the CAHtalyst ™ Phase 3 Studies
The CAHtalyst™ Pediatric and Adult Phase 3 global studies are the largest registrational studies conducted to date to evaluate the safety, efficacy, and tolerability of crinecerfont in children and adolescents, and adults respectively, with congenital adrenal hyperplasia due to 21-hydroxylase deficiency. The primary portions of the CAHtalyst Phase 3 studies have completed and enrollment is closed, while the open-label treatment portions of both studies are ongoing.

For more information about the CAHtalyst Pediatric Phase 3 study, please visit ClinicalTrialsPediatric.gov.

For more information about the CAHtalyst Phase 3 study in adults (ages 18 years of age and older), please visit ClinicalTrialsAdult.gov.

About Neurocrine Biosciences, Inc.
Neurocrine Biosciences is a leading neuroscience-focused, biopharmaceutical company with a simple purpose: to relieve suffering for people with great needs, but few options. We are dedicated to discovering and developing life-changing treatments for patients with under-addressed neurological, neuroendocrine and neuropsychiatric disorders. The company's diverse portfolio includes FDA-approved treatments for tardive dyskinesia, chorea associated with Huntington's disease, endometriosis* and uterine fibroids*, as well as a robust pipeline including multiple compounds in mid- to late-phase clinical development across our core therapeutic areas. For three decades, we have applied our unique insight into neuroscience and the interconnections between brain and body systems to treat complex conditions. We relentlessly pursue medicines to ease the burden of debilitating diseases and disorders, because you deserve brave science. For more information, visit neurocrine.com, and follow the company on LinkedIn, X (formerly Twitter), and Facebook.
(**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, but are not limited to, statements regarding the potential benefits to be derived from crinecerfont. Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements include: the crinecerfont NDAs may not be accepted for filing by the FDA or may not obtain regulatory approval or such approval may be delayed; additional regulatory submissions may not occur or be submitted in a timely manner; the FDA may make adverse decisions regarding crinecerfont; crinecerfont may not be found to be safe and/or effective or may not prove to be beneficial to patients; development activities for crinecerfont may not be completed on time or at all; 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; competitive products and technological changes that may limit demand for our products; uncertainties relating to patent protection and intellectual property rights of third parties; our dependence on third parties for development and manufacturing activities related to crinecerfont, and our ability to manage these third parties; our future financial and operating performance; risks and uncertainties associated with the commercialization of our products; 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, 2024. Neurocrine Biosciences disclaims any obligation to update the statements contained in this press release after the date hereof.

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