Neurocrine Biosciences Announces Positive Top-Line Data from Phase 3 Study of Crinecerfont in Adults for the Treatment of Congenital Adrenal Hyperplasia (CAH)

September 12, 2023

CAHtalyst ™Met Primary Endpoint Demonstrating a Statistically Significant Decrease from Baseline Daily Glucocorticoid Dose with Androgen Control

Key Secondary Endpoint Achieved Statistically Significant Decrease in Androstenedione at Week 4 versus Placebo

Key Secondary Endpoint Demonstrated a Statistically Significant Number of Patients on Crinecerfont Achieved a Reduction to a Physiologic Glucocorticoid Dose versus Placebo

Crinecerfont Was Generally Well-Tolerated

SAN DIEGO, Sept. 12, 2023 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced positive top-line data from the Phase 3 CAHtalyst™ Adult Study evaluating the efficacy, safety, and tolerability of crinecerfont in adults with classic congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21-OHD).

The Phase 3 study met its primary endpoint at Week 24, demonstrating that treatment with crinecerfont resulted in a statistically significant percent reduction in daily glucocorticoid (GC) dose versus placebo while maintaining androgen control (p-value <0.0001).

The study also met important key secondary endpoints, with a statistically significant decrease in androstenedione at Week 4 versus placebo (p-value <0.0001). At Week 24, approximately 63% of patients on crinecerfont achieved a reduction to a physiologic GC dose versus approximately 18% on placebo (p-value <0.0001).

Crinecerfont was generally well tolerated. The most common adverse events during the double-blind, placebo-controlled period of the trial were fatigue, headache, and coronavirus infection. There were few serious adverse events, with none assessed as related to crinecerfont.

"I am gratified to see the extremely positive and clinically meaningful results from this study, the largest ever interventional trial conducted in this rare disease. It required a global effort, and the top-line results confirm our confidence in crinecerfont as a potential first-in-class medication and first-ever non-glucocorticoid treatment option for patients living with CAH," said Richard Auchus, M.D., Ph.D., Principal Investigator, Professor of Pharmacology and Internal Medicine, Division of Metabolism, Endocrinology, and Diabetes at the University of Michigan. "It has been 60 years since we've seen a significant treatment advance for patients with CAH, and the data from this study suggest that crinecerfont might improve their outcomes and quality of life."

"CAH patients suffer from a number of debilitating symptoms and have had suboptimal treatment options with existing standard of care for their whole lives. These data, along with data from the open label treatment period, will allow us to proceed with our regulatory submissions to the FDA in 2024 and European Medicines Agency afterwards," said Kevin Gorman, Ph.D., Chief Executive Officer, Neurocrine Biosciences.

"CAH is a difficult disorder to live with for patients and their caregivers, taking a huge toll physically and mentally," said Eiry Roberts, M.D., Chief Medical Officer at Neurocrine Biosciences. "For physicians, the current treatment paradigm is problematic, relying on glucocorticoids for a dual purpose: not only to address the underlying cortisol deficiency but typically at supraphysiologic doses to treat androgen excess resulting in well-known complications over the long-term. The CAHtalyst Phase 3 Adult data bring us one step closer to a new approach to treating CAH with a therapy that has demonstrated the ability to substantially reduce glucocorticoid doses while maintaining or improving androgen control."

Additional information regarding the results from the Phase 3 CAHtalyst study will be discussed at the Morgan Stanley 21st Annual Global Healthcare Conference at 10:50 a.m. Eastern Time on September 12 in New York. The live presentation will be webcast and may be accessed on the Company's website under Investors at www.neurocrine.com. A replay of the presentation will be available on the website approximately one hour after the conclusion of the event and will be archived for approximately one month. Additional data from the Phase 3 CAHtalyst study will be provided in a peer-reviewed medical journal or at a medical conference at a future date.

Data from the Phase 3 CAHtalyst Pediatric Study will be available, as planned, in early Q4 2023.

About Classic Congenital Adrenal Hyperplasia
Congenital adrenal hyperplasia (CAH) refers to a group of genetic conditions that result 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 (21-OHD). In classic CAH, 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, classic CAH can result in salt wasting, dehydration, and even death.

There are currently no non-glucocorticoid treatments approved by the U.S. Food and Drug Administration (FDA) for classic CAH. Glucocorticoids (GCs), the current standard of care, are used not only to correct the endogenous cortisol deficiency but typically used at greater than physiologic (supraphysiologic) doses to try to suppress the high levels of corticotropin-releasing factor (CRF) and adrenocorticotropic hormone (ACTH) that result in androgen excess. 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. 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 steroid-independent mechanism for the treatment of congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21-OHD). Antagonism of CRF type 1 receptors in the pituitary has been shown to decrease adrenocorticotropic hormone (ACTH) levels, which in turn decreases the production of adrenal androgens and potentially the symptoms associated with classic CAH. Our data demonstrates that lowering 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 classic CAH.

To learn more about crinecerfont, click here.

About the CAHtalyst ™ Phase 3 Study in Adults
The CAHtalyst™ Phase 3 global registrational study was designed to evaluate the safety, efficacy, and tolerability of crinecerfont in adults (18 years of age and older) with classic congenital adrenal hyperplasia (CAH) due to 21-OHD. The study enrolled 182 female and male patients with CAH and consisted of a 24-week randomized, double-blind, placebo-controlled period followed by one-year of open-label crinecerfont treatment and optional open-label extension. The study started in December 2020, and the open-label treatment portion is still ongoing.

For more information about the CAHtalyst Phase 3 study in adults, please visit Clinical TrialsAdult.gov.

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

About Neurocrine Biosciences
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, Parkinson'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, Twitter, and Facebook.
(**in collaboration with AbbVie)*

Forward-Looking Statement
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 clinical results from, and our future development plans with respect to, crinecerfont, as well as the therapeutic potential and clinical benefits or safety profile of crinecerfont. Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements include: top-line data that we report may change following a more comprehensive review of the data related to the clinical studies and such data may not accurately reflect the complete results of the clinical study; risks that regulatory submissions for our products and/or product candidates may not occur or be submitted in a timely manner; our products and/or product candidates 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 our products and/or product candidates; our products and/or product candidates will not be found to be safe and/or effective or may not prove to be beneficial to patients; that development activities for our products and/or product candidates may not be completed on time or at all; 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; 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 our products and our product candidates, 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 June 30, 2023. Neurocrine Biosciences disclaims any obligation to update the statements contained in this press release after the date hereof.

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