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

October 5, 2023

- ***CAHtalyst ™Pediatric Study Met Primary Endpoint Demonstrating a Statistically Significant Decrease from Baseline in Serum Androstenedione in Children and Adolescents with Congenital Adrenal Hyperplasia***
- ***Key Secondary Endpoint Demonstrated a Statistically Significant Decrease from Baseline in Daily Glucocorticoid Dose while Maintaining Androgen Control***
- ***Crinecerfont Was Generally Well-Tolerated***
- ***Company to Host Conference Call and Webcast Today at 8:00 a.m. ET with Management and Dr. Richard Auchus, Professor of Pharmacology and Internal Medicine, Division of Metabolism, Endocrinology, and Diabetes at the University of Michigan***

SAN DIEGO, Oct. 5, 2023 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced positive top-line data from the Phase 3 CAHtalyst™ Pediatric Study evaluating the efficacy, safety, and tolerability of crinecerfont in children and adolescents with classic congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency. Crinecerfont is an oral, selective corticotropin-releasing factor type 1 receptor antagonist being investigated to help reduce and control excess adrenal androgens through a steroid-independent mechanism.

"The outstanding safety and efficacy results reported today for the CAHtalyst Pediatric study and last month for the CAHtalyst Adult study demonstrate the potential benefit of crinecerfont across all groups studied, including children, adolescents and adults," said Kevin Gorman, Ph.D., Chief Executive Officer, Neurocrine Biosciences, Inc.

"As a pediatric endocrinologist, I'm highly encouraged by the results from the CAHtalyst Pediatric study and the potential of crinecerfont to shift the treatment paradigm for a disorder that has seen little innovation in many decades," said Kyriakie Sarafoglou, M.D., Professor, Department of Pediatrics and Department of Experimental and Clinical Pharmacology, Divisions of Endocrinology and Genetics & Metabolism, University of Minnesota. "The data suggest that crinecerfont might enable us to smooth out the numerous adjustments we have to make in glucocorticoid doses to manage high androgen levels as children grow, potentially improving clinical outcomes related to androgen excess as well as chronic supraphysiologic glucocorticoid dosing."

The Phase 3 Pediatric study met its primary endpoint, demonstrating that treatment with crinecerfont resulted in a statistically significant decrease in serum androstenedione from baseline at Week 4 versus placebo following a glucocorticoid (GC) stable period ($p = 0.0002$).

Importantly and consistent with the results from the Phase 3 CAHtalyst Adult study, crinecerfont treatment led to a statistically significant percent reduction from baseline in daily GC dose while maintaining androgen control at Week 28 versus placebo ($p < 0.0001$). Approximately 30% of participants receiving crinecerfont achieved a reduction to a physiologic GC dose while maintaining androgen control compared to 0% of participants receiving placebo. The study also met the other key secondary endpoint demonstrating a statistically significant decrease in serum 17-hydroxyprogesterone from baseline at Week 4 versus placebo ($p < 0.0001$).

	P-value	
Common Endpoints in CAHtalyst ™Phase 3 Studies	**Adult n = 182**	**Pediatric n = 103**
Serum Androstenedione – Change from baseline at Week 4	<0.0001	0.0002
GC Total Daily Dose – Percent change from baseline at Week 24 (Adult) / Week 28 (Pediatric), while maintaining androgen control	<0.0001	<0.0001
Achieving Reduction to Physiologic GC Dose – At Week 24 (Adult) / Week 28 (Pediatric), while maintaining androgen control	<0.0001	0.0009*
*p-value not adjusted for multiplicity		

Crinecerfont was generally well tolerated. During the double-blind, placebo-controlled period of the trial, 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.

There was a high rate of completion (>95%) in the 28-week double-blind, placebo-controlled treatment period of the trial, similar to the >95% completion rate observed in the double-blind, placebo-controlled portion of the CAHtalyst Adult study.

"The CAHtalyst studies represent the largest interventional clinical trial program conducted in both pediatric and adult CAH patients to date and enrolled a patient population that reflects the unmet need in this condition, with both adult and pediatric patients having inadequate androgen control at baseline despite supraphysiologic glucocorticoid dosing," said Eiry W. Roberts, M.D., Chief Medical Officer at Neurocrine Biosciences, Inc. "The results from these studies suggest that crinecerfont could represent a new standard of care for CAH patients with the ability to reduce androgen levels through a non-glucocorticoid mechanism. I am particularly excited about our positive results in the pediatric patient population and what improved androgen control in the setting of reduced glucocorticoid doses could mean for important outcomes related to growth and development."

The data from the CAHtalyst Pediatric and Adult studies, including data from the open-label treatment periods, will support regulatory submissions to the FDA in 2024 and later to the European Medicines Agency. Additional information regarding the results from both Phase 3 CAHtalyst studies will be provided at the Company's December 2023 Analyst Day and in a peer-reviewed medical journal.

Conference Call and Webcast Today at 8:00 a.m. Eastern Time
The Company will discuss the results, baseline characteristics and additional data from the Phase 3 CAHtalyst Pediatric and CAHtalyst Adult studies on a Conference Call at 8:00 a.m. ET today. Management will be joined by Richard Auchus, M.D., Ph.D., Principal Investigator in the CAHtalyst Adult study and Professor of Pharmacology and Internal Medicine, Division of Metabolism, Endocrinology, and Diabetes at the University of Michigan. Participants can access the live conference call by dialing 800-895-3361 (U.S.) or 785-424-1062 (International) using the conference ID: NBIX. The webcast and supplementary materials for the call can also be accessed on the Company's website under Investors at www.neurocrine.com. A replay of the webcast will be available on the website approximately one hour after the conclusion of the event and will be archived for approximately one month.

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_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 ™ Pediatric Phase 3 Study
The CAHtalyst™ Phase 3 global registrational study was designed to evaluate the safety, efficacy, and tolerability of crinecerfont in children and adolescents (2–17 years of age) with classic congenital adrenal hyperplasia (CAH) due to 21-OHD. The study enrolled 103 female and male patients with CAH and consisted of a 28-week randomized, double-blind, placebo-controlled period followed by 24 weeks of open-label crinecerfont treatment and optional open-label extension. The study started in July 2021, and the open-label treatment portion is still 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, 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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