Neurocrine Biosciences to Present New Data Analyses for Crinecerfont in Adults with Classic Congenital Adrenal Hyperplasia at ENDO 2021

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- Additional Positive Data from Phase II CAHlibrate Study
- Real-World Data Highlight Impact of CAH in Adult and Pediatric Patients

SAN DIEGO, March 20, 2021 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced that it will present additional positive data from its Phase II CAHlibrate study of crinecerfont, an investigational, oral, non-steroidal corticotropin-releasing factor type 1 (CRF1) receptor antagonist for the potential treatment of classic congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21-OHD), at ENDO 2021, the Endocrine Society's annual meeting, on March 20–23, 2021. These new analyses, based on data from seven male subjects with classic CAH receiving crinecerfont, demonstrate dose-dependent decreases in androstenedione (A4), a key marker of CAH control and precursor to testosterone, with similar dose-dependent decreases in the A4 to testosterone ratio. Testosterone levels were preserved despite the marked reductions in A4, suggesting a positive effect on reproductive hormones and providing early indications of improved testicular function. During the ENDO 2021 Virtual Poster Hall, Neurocrine Biosciences will present the Phase II CAHlibrate data, along with two additional abstracts that highlight real-world data evaluating the impact of CAH in adult and pediatric patients.

"As we continue to evaluate crinecerfont, we find the additional Phase II analyses that we are presenting at ENDO 2021 very encouraging," 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. "These data are consistent with preserved and possibly even improved testicular function in men with classic CAH during 14 days of crinecerfont treatment. These results are an important addition to growing clinical evidence that demonstrates the potential benefit of this investigational compound."

Of the two additional abstracts, one presents analyses from the International CAH (I-CAH) Registry, a research database that includes patients from 29 countries with longitudinal data dating back to 1989, evaluating the impact of CAH on bone age advancement and growth patterns in pediatric patients. In the other abstract, the company will present analyses from a real-world evidence repository of medical and prescription claims and electronic health records demonstrating the impact of possible glucocorticoid-related and disease-related co-morbidities in over 1,100 adult and pediatric patients with assumed classic CAH.

"These real-world data demonstrate the significant clinical impact that both CAH and its long-term treatment with high doses of glucocorticoids have on patients," said Eiry W. Roberts, M.D., Chief Medical Officer at Neurocrine Biosciences. "Through the Phase III CAHtalyst studies in adults and pediatric patients with classic CAH, we hope to demonstrate the potential value of crinecerfont in controlling disease-related symptoms while also creating the opportunity for a reduction in the adverse effects created by current outdated treatment options."

Presentations at ENDO 2021 include:

- Changes in Adrenal and Gonadal Androgens After 14-Day Treatment with CRF1 Receptor Antagonist, Crinecerfont (NBI-74788), in Men with Classic 21-Hydroxylase Deficiency (Poster #8486)
- Growth-Related Characteristics of Patients <18 Years of Age with Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency (21-OHD): Real-World Evidence from the I-CAH Registry (Poster #6719)
- Real-World Evidence of Clinical Outcomes in Patients with Assumed Classic Congenital Adrenal Hyperplasia in the United States (Poster #6968)

All posters will be on display in the virtual poster hall throughout ENDO 2021 starting at 11:00 a.m. ET on March 20, 2021. ENDO 2021 abstracts will also be included in a supplemental issue of the *Journal of the Endocrine Society* following the meeting.

Neurocrine Biosciences is developing crinecerfont, an investigational, oral, non-steroidal corticotropin-releasing factor type 1 (CRF1) receptor antagonist as a novel therapy for the treatment of classic CAH. Crinecerfont is currently being evaluated in global registrational Phase III studies in adults (CAHtalyst Study, clinicaltrials.gov) and pediatric patients (CAHtalyst Pediatric Study, clinicaltrials.gov) with classic CAH.

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 congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21-OHD). 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, androstenedione (A4) and testosterone, 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 hormones. Because of this deficiency, the adrenal glands fail to produce enough cortisol and, in approximately 75% of cases, aldosterone, resulting in a potentially life-threatening condition. The lack of cortisol stimulates the release of high levels of adrenocorticotropic hormone (ACTH) from the pituitary gland, leading to excessive production of adrenal androgens. Elevated androgens can lead to virilization, menstrual irregularities, hirsutism and 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 for more than 60 years, are prescribed to treat cortisol deficiency and reduce the high ACTH levels in order to attempt to control androgen excess. However, the dose and duration of glucocorticoids required to suppress ACTH and control androgen levels are often well above what is needed for replacement dosing to treat cortisol deficiency. Long-term, chronic exposure to greater than physiologic dosing of glucocorticoids can cause metabolic issues, bone loss, growth impairment and infection risk typical of iatrogenic Cushing's syndrome. Classic CAH is a disease that affects approximately 30,000 people in the U.S. and roughly 50,000 people in Europe.

To learn more about CAH, click here.

About Crinecerfont
Crinecerfont is an investigational, oral, non-steroidal corticotropin-releasing factor type 1 (CRF1) receptor antagonist under evaluation for the treatment of classic congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21-OHD). The blockade of CRF receptors in the pituitary has been shown to decrease the release of adrenocorticotropic hormone (ACTH), which in turn decreases the production of adrenal androgens, and potentially the symptoms associated with classic CAH. Adding crinecerfont treatment to glucocorticoid therapy has the potential to reduce the adverse consequences of androgen excess and of long-term exposure to greater than replacement doses of glucocorticoids, enabling patients to better manage the symptoms of classic CAH.

To learn more about crinecerfont, click here.

About Neurocrine Biosciences
Neurocrine Biosciences is a neuroscience-focused, biopharmaceutical company dedicated to discovering, developing and delivering 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*, uterine fibroids* and clinical programs in multiple therapeutic areas. For nearly three decades, Neurocrine Biosciences has specialized in targeting and interrupting disease-causing mechanisms involving the interconnected pathways of the nervous and endocrine systems. For more information, visit neurocrine.com, and follow the company on LinkedIn. (*in collaboration with AbbVie)

Neurocrine Biosciences 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 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: our future financial and operating performance; the impact of the COVID-19 pandemic and efforts to mitigate its spread on our business; risks and uncertainties associated with the scale and duration of the COVID-19 pandemic and resulting global, national, and local disruptions, 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-K for the year ended December 31, 2020. Neurocrine Biosciences disclaims any obligation to update the statements contained in this press release after the date hereof.

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