# Neurocrine Biosciences Presents Data on Treatment of Patients with Congenital Adrenal Hyperplasia at ECE 2023

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- **Post Hoc Analyses of Phase 2 Study of Crinecerfont in Adults with CAH Demonstrate Androgen Reduction Across a Broad Range of Glucocorticoid Doses**
- **Post Hoc Analyses of Phase 3 Study Demonstrate EFMODY® (hydrocortisone modified-release hard capsules) Reduced Androgen Levels Compared to Immediate-Release Hydrocortisone in Patients with CAH**

SAN DIEGO, May 12, 2023 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX), a leading neuroscience-focused biopharmaceutical company, today announced that it will present new analyses of Phase 2 data of the investigational drug crinecerfont in adults with classic congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21-OHD) and post hoc analyses of Phase 3 data for EFMODY® (hydrocortisone modified-release hard capsules). EFMODY is approved by the European Commission for the European Economic Area (including Northern Ireland) (EEA) and by the UK Medicines and Healthcare Products Regulatory Agency (MHRA) for the treatment of adults and adolescents (12 years and older) with CAH. These new data and an additional poster showing Phase 2 data of crinecerfont in adolescents with classic CAH will be presented at ECE 2023, the 25th European Congress of Endocrinology in Istanbul, Turkey from May 13–16.

In previously reported Phase 2 study data, crinecerfont treatment for 14 days led to clinically meaningful reductions of 17–hydroxyprogesterone (17OHP), adrenocorticotropic hormone (ACTH), and androstenedione in adults with classic CAH due to 21-OHD. Post hoc analyses of these data released today assessed whether baseline hormone levels and glucocorticoid (GC) doses correlated with treatment response. A strong correlation was found between baseline level and change from baseline to Day 14 for 17OHP, ACTH, and androstenedione, with the greatest reductions from baseline observed in subjects with the highest baseline hormone level. These results indicate that adults with classic CAH who have more elevated baseline hormone levels have the potential for a greater response to treatment with crinecerfont. However, reductions in androgen levels were seen in patients regardless of their GC dose at baseline. See the abstract (Poster #274; Response to Crinecerfont Treatment in Adults with Classic Congenital Adrenal Hyperplasia is Correlated with Elevated Baseline Hormone Levels, but Not Glucocorticoid Dose) for more information here.

"Androgen excess is a hallmark feature of classic congenital adrenal hyperplasia. These analyses demonstrate that the effectiveness of crinecerfont in reducing androgen levels in this study correlated with baseline hormone level, irrespective of GC dose. Patients with higher baseline androgens experienced greater reductions following treatment with crinecerfont, which supports the potential of crinecerfont in providing improved androgen control across a broad range of CAH patients," said Eiry W. Roberts, M.D., Chief Medical Officer at Neurocrine Biosciences. "We plan to announce top-line data from our Phase 3 CAHtalyst clinical studies of crinecerfont in children, adolescents, and adults in the fourth quarter of 2023."

Treatment of adults with crinecerfont was generally well tolerated with no related serious adverse events reported. Adverse events reported in two or more participants included headache, upper respiratory tract infection, fatigue, contusion (bruising), insomnia, nasopharyngitis, pyrexia, and nausea.

EFMODY has been shown to replicate the natural circadian rhythm of cortisol and reduce androgen levels in CAH patients. In a Phase 3 study, adults with classic CAH were randomized to continue standard therapy with immediate-release hydrocortisone or receive EFMODY modified-release hydrocortisone capsules (MRHC) at the same hydrocortisone dose equivalent. In the MRHC group, it was found that MRHC (which demonstrated similar bioavailability to immediate-release hydrocortisone) provided a greater reduction in 17-OHP standard deviation score 24-hour profile than was seen in the standard therapy group. The more physiological exposure pattern provided by MRHC means that patients previously on other GC therapy, experienced greater reduction in androgen levels at an equivalent dose of MRHC. These data will be part of an oral presentation (Oral Presentation, May 15, 2:20–2:30pm: Switching Patients with Congenital Adrenal Hyperplasia to Modified-Release Hydrocortisone Capsules: Relative Bioavailability and Disease Control). See more information here.

"Findings of these new analyses of the EFMODY study provide prescribing physicians with dosing guidance for this alternative to immediate-release hydrocortisone, which reduces androgen levels at similar dose levels, while replicating cortisol diurnal rhythm in patients with CAH," Dr. Roberts added.

In the entire EFMODY development clinical trial program, the overall most common serious adverse events were acute adrenal insufficiency (4.2 percent of patients treated with EFMODY). Other common reactions in relation to EFMODY were fatigue (11.7 percent of patients), headache (7.5 percent), increased appetite (5.8 percent), dizziness (5.8 percent) and increased weight (5.8 percent).

**Additional Presentation:**

– *Selected as one of the Top 40 Posters at ECE*
(Poster #P1); Crinecerfont (NBI-74788), a Novel $CRF_1$ Receptor Antagonist, Lowers Adrenal Androgens and Precursors in Adolescents with

Classic Congenital Adrenal Hyperplasia

Neurocrine Biosciences is developing crinecerfont, an investigational, oral, steroid-independent, selective corticotropin-releasing factor type 1 receptor ($CRF_1$) antagonist for the treatment of classic CAH due to 21-OHD. Neurocrine has completed enrollment in Phase 3 global registrational studies of crinecerfont in adults (18 years of age and older) and children and adolescents (2 to 17 years of age) with classic CAH, called the CAHtalyst ™ and CAHtalyst ™ Pediatric studies, respectively. As part of the CAHtalyst clinical trial program, participants who complete these trials will be able to continue to receive crinecerfont as part of an open-label extension.

Classic CAH is a rare autosomal disease caused by a genetic defect in one of the enzymes (21-OHD) involved in the production of adrenal hormones. The disorder is characterized by cortisol deficiency and often also aldosterone deficiency, elevated adrenocorticotropic (ACTH) levels, and excess production of adrenal androgens (including androstenedione). Cortisol deficiency can lead to adrenal crises, while androgen excess can lead to virilization in females, abnormalities in growth leading to short stature, early puberty, and infertility.

EFMODY was developed by Diurnal Ltd. and is a preparation of hydrocortisone that has been specifically designed to replicate the natural circadian rhythm of cortisol, when given in a twice-a-day "toothbrush" regimen, (administered last thing at night before sleep and first thing in the morning on waking), to improve androgen control and chronic fatigue in patients with cortisol deficiency. It is a multi-particulate formulation presented as a capsule and is available in doses of 5 mg and 10 mg. Neurocrine Biosciences acquired Diurnal Group plc. in November 2022.

**About Classic Congenital Adrenal Hyperplasia (CAH)**
Congenital adrenal hyperplasia (CAH) refers to a group of genetic conditions that result in an enzyme deficiency that alters the production of adrenal hormones. Approximately 95 percent 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 percent of cases, aldosterone. If left untreated, classic CAH can result in salt wasting, dehydration, and even death.

There are currently no steroid-independent treatments approved by the U.S. Food and Drug Administration (FDA) for classic CAH. Glucocorticoids, the current standard of care, are used to correct the endogenous cortisol deficiency and to try to reduce the high adrenocorticotropic hormone (ACTH) levels resulting in androgen excess. However, standard glucocorticoid treatment at dosing well above the normal physiological level for androgen control has been associated with serious and significant complications of steroid excess, including metabolic abnormalities, increased cardiovascular risk, bone loss, fractures, growth impairment, muscle weakness, and increased infection risk. Androgen excess has been associated with virilization in females, abnormalities in growth leading to short stature, early puberty, and infertility.

To learn more about CAH, click here.

**About Crinecerfont**
Crinecerfont is an investigational, oral, steroid-independent, selective corticotropin-releasing factor type 1 receptor ($CRF_1$) antagonist under evaluation for the treatment of classic 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 could decrease the production of adrenal androgens and potentially the symptoms associated with classic CAH. Research also suggests that lowering androgen levels may enable lower, more physiologic dosing of glucocorticoids and thus 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 CAHtalyst ™ Studies**
Neurocrine Biosciences has completed enrollment in Phase 3 global registrational studies of crinecerfont in adults (18 years of age and older) and children and adolescents (ages 2 to 17 years of age) with classic CAH. As part of the CAHtalyst ™ clinical trial program, participants who completed these trials will be able to continue to receive crinecerfont as part of an open-label extension. We plan to announce top-line data from our Phase 3 CAHtalyst clinical studies in the fourth quarter of 2023.

Treatment with crinecerfont was generally well tolerated in adolescent and adult participants with no related serious adverse events or discontinuations due to adverse events. Treatment-emergent adverse events reported in two or more participants included headache, dizziness, upper respiratory tract infection, fatigue, contusion (bruising), insomnia, nasopharyngitis, pyrexia, and nausea.

For more information about the adult CAHtalyst ™ Phase 3 study, please visit cahtalyst.cahstudies.com and ClinicalTrials.gov.

For more information about the pediatric CAHtalyst ™ Phase 3 study, please visit cahtalystpeds.cahstudies.com and ClinicalTrials.gov.

**About EFMODY®**
EFMODY is a modified-release preparation of hydrocortisone that has been specifically designed to replicate the natural circadian rhythm of cortisol when given in a twice-a-day "toothbrush" regimen (last thing at night before sleep and first thing in the morning on waking) to reduce excess androgens and chronic fatigue in patients with diseases of cortisol deficiency. In 2021, EFMODY received marketing authorization from the Medicines and Healthcare products Regulatory Agency (MHRA) in Great Britain (England, Wales, and Scotland) and from the European Commission in the European Economic Area (including Northern Ireland).

**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, 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_)

Neurocrine and the Neurocrine logo are registered trademarks and CAHtalyst is a trademark of Neurocrine Biosciences, Inc. EFMODY is a registered

trademark of Diurnal Ltd.

**Neurocrine Biosciences 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 potential benefits of crinecerfont to patients and future clinical development plans as well as statements regarding the potential benefits to be derived from certain of our products. 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; risks and uncertainties associated with the commercialization of our products; the risk that 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; 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 our products and/or product candidates may not occur or be submitted in a timely manner; risks that 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; risks and uncertainties relating to competitive products and technological changes that may limit demand for our products; risks associated with 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; 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, 2023. Neurocrine Biosciences disclaims any obligation to update the statements contained in this press release after the date hereof.

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Linda Seaton, 1-858-617-7292, media@neurocrine.com, Investors, Todd Tushla, 1-858-617-7143, ir@neurocrine.com