Neurocrine Biosciences to Present Wide-Ranging One-Year Data from Phase 3 CAHtalyst™ Pediatric Study at Pediatric Endocrine Society 2025 Annual Meeting

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One-Year Data Show Lasting Reductions in Glucocorticoid Doses and Improvements in Clinical Outcomes with CRENESSITY™ (crinecerfont) in Pediatric Patients with Classic Congenital Adrenal Hyperplasia

SAN DIEGO, May 16, 2025 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced it will present new data from the Phase 3 CAHtalyst™ Pediatric study showing lasting reductions in glucocorticoid doses in pediatric patients with classic congenital adrenal hyperplasia who received CRENESSITY™ (crinecerfont) for up to one year. In addition, the study showed that for patients on CRENESSITY, adrenocorticotropic hormone, 17-hydroxyprogesterone and androstenedione remained below baseline levels, despite substantially decreased glucocorticoid doses. Results also showed improvements in clinical outcomes, including body mass index and insulin resistance. These data will be presented at the Pediatric Endocrine Society (PES) 2025 Annual Meeting taking place from May 15-18, 2025, in National Harbor, MD.

"These results demonstrate that CRENESSITY has the potential to transform the treatment landscape for children and adolescents living with classic congenital adrenal hyperplasia," said Eiry W. Roberts, M.D., Chief Medical Officer, Neurocrine Biosciences. "By simultaneously addressing the underlying hormonal imbalances and allowing for a reduction in glucocorticoid doses, we're seeing improvements in clinical outcomes, including reductions in body mass index and insulin resistance."

The Phase 3 CAHtalyst Pediatric study was part of the largest-ever interventional clinical trial program in classic congenital adrenal hyperplasia (CAH) including 103 pediatric patients, four to 17 years of age. The trial consisted of a 28-week, double-blind, placebo-controlled (DBPC) period, during which patients with classic CAH on supraphysiologic glucocorticoid (GC) doses were randomized 2:1 to receive CRENESSITY or placebo, and a 24-week, open-label (OL) period, during which all patients received CRENESSITY. During both the DBPC and OL periods, GC doses were kept stable for the first four weeks and then decreased as tolerated toward more physiologic levels while maintaining or improving androstenedione (A4) relative to Day 1 baseline. Three separate analyses examined the effect of CRENESSITY on:

- Changes in serum A4 levels and GC doses.
- Changes in adrenocorticotropic hormone (ACTH) and 17-hydroxyprogesterone (17-OHP) levels.
- Clinical outcomes.

Long-term, sustained reductions in high GC doses, in addition to improvements in key clinical outcomes, were observed in pediatric patients with up to one year of treatment with CRENESSITY:

- Reductions in supraphysiologic GC doses observed with 28 weeks of treatment with CRENESSITY were maintained during long-term treatment of up to one year.
    - Importantly, for patients who were randomized to CRENESSITY during the DBPC period, the proportion who achieved a GC dose within the physiologic range (i.e., ≤11 mg/m^2/d hydrocortisone equivalents) was stable from Week 28 (30%) to Week 52 (32%).
- Pre-glucocorticoid ACTH, 17-OHP and A4 levels were reduced to below Day 1 baseline levels in children and adolescents with classic CAH taking CRENESSITY for up to one year, even after significant reductions in GC dose.
- Improvements were observed in body mass index (BMI) and insulin resistance in children and adolescents with classic CAH taking CRENESSITY for up to one year. In addition, hirsutism in female participants did not worsen, despite significant reductions in GC dose.

Measure	**Baseline**	**Week 52 change from baseline (continuous**	**Week 52 change from baseline (placebo to**

		CRENESSITY group)	CRENESSITY group)
Mean GC dose	16.4 mg/m^2/d	-2.9 mg/m^2/d	-1.1 mg/m^2/d
Mean BMI SD scores	1.2 CRENESSITY; 1.1 placebo	-0.09	-0.02
Average homeostatic model assessment of insulin resistance	2.8 CRENESSITY; 3.3 placebo	-0.72	-1.3
Mean hirsutism VAS scores (out of 100) in female participants	13.7 CRENESSITY; 21.6 placebo	-3.2	+1.9

BMI: body mass index; SD: standard deviation; VAS: visual analog scale.

CRENESSITY was generally well tolerated, with no adrenal crises reported in the DBPC period. The most common adverse reactions with CRENESSITY were headache (25% versus 6% for placebo), abdominal pain (13% versus 0%), fatigue (7% versus 0%), nasal congestion (7% versus 3%) and epistaxis (4% versus 0%).

GC Dosing Regimens in the Phase 3 CAHtalyst™ Adult and CAHtalyst Pediatric Studies

Additional data will be presented regarding changes in GC regimens in both adult and pediatric patients with classic CAH. Hydrocortisone dosing frequency was more likely to decrease with CRENESSITY, as was switching to dexamethasone- and prednisolone-free regimens. These changes may reduce both the CAH treatment burden and the risk of adverse effects of chronic treatment with high-dose GCs.

Additional poster presentations at the PES 2025 Annual Meeting include:

- Treatment Patterns and Changes in Health States in Pediatric Patients with Classic Congenital Adrenal Hyperplasia: An Analysis of Data from the CAHtalog™ Registry
- Crinecerfont Enables Reduction of Glucocorticoid Doses While Maintaining or Improving Androstenedione in Pediatric Patients with Classic Congenital Adrenal Hyperplasia: Subgroup Analyses from the CAHtalyst™ Pediatric Phase 3 Study
- Crinecerfont Allows for More Physiologic Glucocorticoid Treatment with Greater Reductions of Androstenedione in Pediatric Patients with Classic Congenital Adrenal Hyperplasia: Analyses of Individual Patient Data from the CAHtalyst™ Pediatric Study

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 steroid hormones, such as cortisol, aldosterone and adrenal androgens, which are essential for life. Approximately 95% of CAH cases are caused by variants of the *CYP21A2* gene that leads to deficiency of the enzyme 21-hydroxylase. Severe deficiency of this enzyme leads to an inability of the adrenal glands to produce enough cortisol and, in approximately 75% of cases, aldosterone. Because individuals with CAH are still able to produce androgens, the unused precursors that would normally be used to make cortisol instead result in the production of excess amounts of androgens. If left untreated, CAH can result in salt wasting, dehydration and even death.

Historically, exogenous glucocorticoids (GCs) have been used to correct the endogenous cortisol deficiency, but doses higher than those for cortisol replacement (supraphysiologic) are needed to lower the elevated levels of adrenocorticotropic hormone (ACTH) and adrenal androgens. However, GC treatment at high 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 high-dose GCs may have psychological and cognitive impacts, 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 excess facial hair growth and menstrual irregularities, in addition to fertility issues in both sexes. The symptoms of high ACTH may include testicular adrenal rest tumors (TARTs) or ovarian adrenal rest tumors (OARTs).

About The CAHtalyst™ Pediatric Study
The Phase 3 CAHtalyst global registrational studies were designed to evaluate the safety, efficacy and tolerability of CRENESSITY in children and adults with classic congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency. The CAHtalyst studies were the largest-ever interventional clinical trial program in classic CAH, including 285 pediatric and adult patients.

The CAHtalyst Pediatric study included 103 pediatric patients four to 17 years of age. The study tested two questions. The first question evaluated whether four weeks of CRENESSITY treatment could improve androgen control. The second question evaluated whether an additional 24 weeks of CRENESSITY treatment enabled customized glucocorticoid (GC) down-titration while androstenedione levels were maintained or improved.

Data from the CAHtalyst Phase 3 studies supported approval of CRENESSITY by the U.S. Food and Drug Administration in December 2024. The open-label extension treatment portions of both studies are ongoing.

About CRENESSITY™ (crinecerfont)
CRENESSITY is a potent and selective, oral corticotropin-releasing factor type 1 receptor (CRF_1) antagonist developed to reduce

and control excess adrenocorticotropic hormone (ACTH) and adrenal androgens through a non-glucocorticoid (GC) mechanism for the treatment of classic congenital adrenal hyperplasia (CAH). Antagonism of CRF_1 receptors in the pituitary has been shown to decrease ACTH levels, which in turn decreases the production of adrenal androgens and potentially the symptoms associated with CAH. The robust clinical study data demonstrate that lowering adrenal androgen levels with CRENESSITY enables lower, more physiologic dosing of GCs to replace missing cortisol.

CRENESSITY comes in capsules and an oral solution. The capsule formulation is available in 50 mg and 100 mg doses. The oral solution is available as a 50 mg/mL strength formulation. For adults 18 years of age and older, the recommended dosage is 100 mg twice daily taken orally with a meal. For pediatric patients four to 17 years of age weighing less than 55 kg (121 lbs), the recommended dosage is based on body weight and is administered twice daily, taken orally with a meal. For pediatric patients weighing more than 55 kg (121 lbs), the recommended dosage is 100 mg twice daily taken orally with a meal. Healthcare providers can work with patients to determine the appropriate formulation for use depending on patient needs. Patients receiving CRENESSITY should continue GC therapy for cortisol replacement.

Important Information

Approved Uses
CRENESSITY (crinecerfont) is a prescription medicine used together with glucocorticoids (steroids) to control androgen (testosterone-like hormone) levels in adults and children 4 years of age and older with classic congenital adrenal hyperplasia (CAH).

IMPORTANT SAFETY INFORMATION

Do not take CRENESSITY if you:

Are allergic to crinecerfont, or any of the ingredients in CRENESSITY.

CRENESSITY may cause serious side effects, including:

Allergic Reactions. Symptoms of an allergic reaction include tightness of the throat, trouble breathing or swallowing, swelling of the lips, tongue, or face, and rash. If you have an allergic reaction to CRENESSITY, get emergency medical help right away and stop taking CRENESSITY.

Risk of Sudden Adrenal Insufficiency or Adrenal Crisis With Too Little Glucocorticoid (Steroid) Medicine. Sudden adrenal insufficiency or adrenal crisis can happen in people with congenital adrenal hyperplasia who are not taking enough glucocorticoid (steroid) medicine. You should continue taking your glucocorticoid (steroid) medicine during treatment with CRENESSITY. Certain conditions such as infection, severe injury, or shock may increase your risk for sudden adrenal insufficiency or adrenal crisis. Tell your healthcare provider if you get a severe injury, infection, illness, or have planned surgery during treatment. Your healthcare provider may need to change your dose of glucocorticoid (steroid) medicine.

Before taking CRENESSITY, tell your healthcare provider about all of your medical conditions, including if you are pregnant or plan to become pregnant, or are breastfeeding or plan to breastfeed.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

The most common side effects of CRENESSITY in adults include tiredness, headache, dizziness, joint pain, back pain, decreased appetite, and muscle pain.

The most common side effects of CRENESSITY in children include headache, stomach pain, tiredness, nasal congestion, and nosebleeds.

These are not all the possible side effects of CRENESSITY. Call your healthcare provider for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit MedWatch at www.fda.gov/medwatch or call 1-800-FDA-1088.

Dosage Forms and Strengths: CRENESSITY is available in 50 mg and 100 mg capsules, and as an oral solution of 50 mg/mL.

Please see full **Prescribing Information**.

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. 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, classic congenital adrenal hyperplasia, 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 and Facebook. *(*in collaboration with AbbVie)*

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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 CRENESSITY for the treatment of classic congenital adrenal hyperplasia (CAH); the value and benefits CRENESSITY brings to patients with CAH; the ability of Neurocrine Biosciences to ensure patients have access to CRENESSITY; and whether the results from our clinical trials of CRENESSITY are indicative of real-world results. Factors that could cause actual results to differ materially from those stated or implied in the forward-looking statements include, but are not limited to, the following: risks and uncertainties associated with Neurocrine Biosciences' business and finances in general, as well as risks and uncertainties associated with the commercialization of CRENESSITY, including the extent to which patients and physicians accept and adopt CRENESSITY; whether CRENESSITY receives adequate reimbursement from third-party payors; risks and uncertainties relating to competitive products and technological changes that may limit demand for CRENESSITY; risks associated with the Company's dependence on third parties for development and manufacturing activities related to CRENESSITY, and the ability of the Company to manage these third parties; risks that additional regulatory submissions for CRENESSITY may not occur or be submitted in a timely manner; risks that the FDA or other regulatory authorities may make adverse decisions regarding CRENESSITY; risks that post-approval CRENESSITY commitments or requirements may be delayed; risks that CRENESSITY may be precluded from commercialization by the proprietary or regulatory rights of third parties, or have unintended side effects, adverse reactions or incidents of misuse; risks and uncertainties relating to competitive products and technological changes that may limit demand for CRENESSITY; 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, 2025. Neurocrine Biosciences disclaims any obligation to update the statements contained in this press release after the date hereof other than required by law.

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SOURCE Neurocrine Biosciences, Inc.

Neurocrine Biosciences, Inc., Media: Aimee White, 1-858-354-7865, media@neurocrine.com; Investors: Todd Tushla, 1-858-617-7143, ir@neurocrine.com