Neurocrine Biosciences Presented One-Year Data from Phase 3 CAHtalyst™ Studies Showing Improvements in Weight-Related Effects of Glucocorticoid Treatment at the 2025 Endocrine Society's Annual Meeting

July 14, 2025

- Adult and pediatric patients with classic congenital adrenal hyperplasia treated with CRENESSITY® (crinecerfont) achieved clinically meaningful weight reductions
- Substantial improvements in insulin resistance were also observed in both adult and pediatric patients treated with CRENESSITY compared with placebo through one year of treatment

SAN DIEGO, July 14, 2025 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced the presentation of new data from the Phase 3 CAHtalyst™ Adult and Pediatric studies showing favorable trends in improvement of weight-related outcomes in patients with classic congenital adrenal hyperplasia who were treated with CRENESSITY® (crinecerfont) for up to one year. These data were presented at the Endocrine Society's Annual Meeting, ENDO 2025, that is taking place July 12-15 in San Francisco.

"It's well established that use of high-dose glucocorticoids pose short- and long-term health risks for people living with congenital adrenal hyperplasia," said Sanjay Keswani, M.D., Chief Medical Officer, Neurocrine Biosciences. "These data presented at ENDO, which include both pediatric and adult patients, showed that the reduction in steroid doses enabled by CRENESSITY can lead to meaningful improvements in cardiometabolic outcomes. The use of CRENESSITY with glucocorticoid treatment is evolving the standard of care for classic congenital adrenal hyperplasia."

The Phase 3 CAHtalyst program was the largest-ever interventional clinical trial program in classic congenital adrenal hyperplasia (CAH) and included 103 pediatric (four to 17 years of age) patients and 182 adult (18 to 58 years of age) patients. Both the CAHtalyst Pediatric study and the CAHtalyst Adult study consisted of an initial six-month, double-blind, placebo-controlled (DBPC) period (28 weeks for the pediatric study and 24 weeks for the adult study) followed by a 24-week open-label (OL) period, during which all patients received CRENESSITY. During both the DBPC and OL periods, glucocorticoid (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.

Adult and pediatric patients receiving CRENESSITY for up to one year saw improvements in key weight-related outcomes:

- Adults taking CRENESSITY experienced greater reductions in body mass index (BMI) at Week 24 versus placebo, with further reductions from baseline observed through Month 12.
- Pediatric patients taking CRENESSITY saw reductions in BMI standard deviation scores (SDS) at Week 28, while those taking placebo saw an increase. Reductions in the CRENESSITY group were maintained through Week 52.
- Among adult and pediatric patients who were overweight or obese at baseline (~70% and ~60%, respectively):
    - A higher percentage of adults achieved a greater than 5% reduction in weight at Week 24 with CRENESSITY versus placebo.
    - A higher percentage of pediatric patients achieved at least a 0.2 reduction from baseline in BMI SDS at Week 28 with CRENESSITY versus placebo.
    - Importantly, the percentage of adult and pediatric patients achieving these thresholds increased through Week 52 for both patients on continuous CRENESSITY and those who switched to CRENESSITY from placebo.
    - In those with insulin resistance, mean homeostatic model assessment for insulin resistance (HOMA-IR) was elevated at baseline; greater reductions in HOMA-IR were observed with CRENESSITY than placebo in both adult and pediatric patients at the end of the DBPC periods, and substantial reductions from baseline were observed through one year of treatment.

Measure	Baseline	Week 24 (adult)/Week	Month 12 (adult)/Week 52	Month 12 (adult)/Week 52

		28 (pediatric) change from Day 1 baseline	(pediatric) change from Day 1 baseline (continuous CRENESSITY group)	(pediatric) change from Day 1 baseline (placebo to CRENESSITY group)
Adult patients				
Mean BMI	30.1 kg/m^2 CRENESSITY; 29.0 kg/m^2 placebo	-0.5 CRENESSITY; -0.2 placebo	-0.8 kg/m^2	-0.4 kg/m^2
Percentage achieving >5% reduction in weight*	-	18% CRENESSITY; 14% placebo	27 %	39 %
HOMA-IR*†	5.3 CRENESSITY; 5.4 placebo	-1.3 CRENESSITY; -0.5 placebo	-1.2	-1.6
Pediatric patients				
Mean BMI SDS	1.2 CRENESSITY; 1.1 placebo	-0.09 CRENESSITY; +0.04 placebo	-0.09	-0.02
Percentage achieving ≥0.2 reduction in BMI SDS*‡	-	15% CRENESSITY; 5% placebo	27 %	21 %
HOMA-IR*†	4.5 CRENESSITY; 6.5 placebo	-1.3 CRENESSITY; +0.05 placebo	-1.8	-2.5

*Among those who were overweight or obese at baseline (adults: 74.6% [91/122] CRENESSITY, 63.3% [38/60] placebo; pediatrics: 58.0% [40/69] CRENESSITY, 58.8% [20/34] placebo).

†Among those with insulin resistance at baseline.

‡Threshold corresponds to an approximate 5% weight reduction in adults.

SDS: standard deviation score.

LSMD: least-squares mean difference.

CRENESSITY has a demonstrated safety profile. Headache, stomach pain, tiredness, nasal congestion and nosebleeds were the most common side effects in children taking CRENESSITY. Fatigue, headache, dizziness, arthralgia, back pain, decreased appetite and myalgia were the most common side effects in adults taking CRENESSITY. Most side effects were temporary and mild to moderate in severity and generally did not lead to discontinuation of the study drug.

Additional presentations, highlighting both new and encore data, at ENDO 2025 include:

Title	Oral Presentation
[NEW] Crinecerfont Allows for More Physiologic Glucocorticoid Treatment with Reduction of Androstenedione to a Normal Range in Adults with Classic Congenital Adrenal Hyperplasia: Post Hoc Analyses of the CAHtalyst Adult Study	OR07-04
Crinecerfont Maintains Reductions in Serum Androstenedione Levels and Glucocorticoid Doses in Children and Adolescents with Classic Congenital Adrenal Hyperplasia: 1-Year Results from the CAHtalyst Pediatric Study	OR07-05

Title	Poster Presentation
[NEW] Crinecerfont Maintains Serum Androstenedione Levels with Reduced Glucocorticoid Doses in Adults with Classic Congenital Adrenal Hyperplasia: 1-Year Results from the CAHtalyst Adult Study	SUN-415

[NEW] Crinecerfont Maintains Adrenocorticotropic Hormone and 17-Hydroxyprogesterone Levels with Reduced Glucocorticoid Doses in Adults with Classic Congenital Adrenal Hyperplasia: 1-Year Results from the CAHtalyst Adult Study	SUN-417
[NEW] Crinecerfont Improves Clinical Outcomes in Adults with Classic Congenital Adrenal Hyperplasia: 1-Year Results from the CAHtalyst Adult Study	SUN-416
[NEW] Evaluation of Potential Drug-Drug Interactions with Crinecerfont	SUN-440
[NEW] Crinecerfont Enables Reduction of Glucocorticoid Doses While Maintaining or Improving Androstenedione in Adults with Classic Congenital Adrenal Hyperplasia: Subgroup Analyses from the Phase 3 CAHtalyst Adult Study	MON-466
[NEW] Treatment Patterns and Changes in Health States in Patients with Classic Congenital Adrenal Hyperplasia: An Analysis of Data from the CAHtalog Registry	MON-467
Crinecerfont Allows for More Physiologic Glucocorticoid Treatment with Reduction of Androstenedione to a Normal Range in Pediatric Patients with Classic Congenital Adrenal Hyperplasia: Post Hoc Analysis of the CAHtalyst Pediatric Study	SAT-418
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	SAT-442
Crinecerfont Reduces Plasma Adrenocorticotropic Hormone and Serum 17-Hydroxyprogesterone Levels in Children and Adolescents with Classic Congenital Adrenal Hyperplasia: 1-Year Results from the CAHtalyst Pediatric Study	SUN-434
Crinecerfont Shows Favorable Trends in Improving Clinical Outcomes in Children and Adolescents with Classic Congenital Adrenal Hyperplasia: 1-Year Results from the CAHtalyst Pediatric Study	SUN-441
Crinecerfont Improves Reproductive Hormones in Classic Congenital Adrenal Hyperplasia: 1-Year Results from the Phase 3 CAHtalyst Adult Study	SUN-414
Crinecerfont Allows for More Physiologic Glucocorticoid Dosing Regimens in Patients with Classic Congenital Adrenal Hyperplasia: Results from the Phase 3 CAHtalyst Adult and CAHtalyst Pediatric Studies	MON-458

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. 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.

Exogenous glucocorticoids (GCs) are necessary to correct the endogenous cortisol deficiency, but historically, doses higher than those for cortisol replacement (supraphysiologic) have been used 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™ Studies
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 could enable customized glucocorticoid (GC) down-titration while androstenedione levels were maintained or improved.

The CAHtalyst Adult study included 182 adult patients 18 to 58 years of age. Similarly, the first question of the study evaluated whether four weeks of CRENESSITY treatment could improve androgen control, and the second question evaluated whether an additional 20 weeks of CRENESSITY treatment could enable GC reduction to physiologic range 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. 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)*

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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