Neurocrine Biosciences Presents New Two-Year CRENESSITY® (crinecerfont) Data Demonstrating Improvements in Cardiometabolic Outcomes in Adults with Classic Congenital Adrenal Hyperplasia at ENDO 2026

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- Two-year CRENESSITY data in adults showed improvements in cardiometabolic outcomes of insulin resistance, body composition and body weight alongside sustained reductions in glucocorticoid dose
- Among participants who were overweight or obese at baseline, 37% achieved >5% reduction in body weight at 2 years, and 43% of those with insulin resistance at baseline were no longer insulin resistant at 2 years
- Favorable trends in bone health outcomes were observed with CRENESSITY treatment, including improvements in bone mineral density with up to 2 years of treatment
- Patient-reported survey data from adults in the open-label extension suggested improvements in quality of life outcomes and treatment satisfaction, including emotional well-being, energy levels and confidence in managing their classic congenital adrenal hyperplasia with CRENESSITY

SAN DIEGO, June 15, 2026 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced new Phase 3 CAHtalyst® Adult study data demonstrating improved cardiometabolic outcomes alongside sustained glucocorticoid dose reduction through up to two years of treatment with CRENESSITY® (crinecerfont) for classic congenital adrenal hyperplasia. These results, together with additional presentations highlighting improvement in bone outcomes and patient-reported quality of life survey outcomes, were presented at the Endocrine Society's annual meeting, ENDO 2026, in Chicago.

Long-term supraphysiologic glucocorticoid (GC) treatment in adults with classic congenital adrenal hyperplasia (CAH) is associated with obesity, insulin resistance, increased cardiometabolic risk and adverse effects on bone health. In these analyses, adults with classic CAH taking CRENESSITY for up to two years experienced improvements in weight, body composition and insulin resistance, key markers of long-term health, with sustained GC dose reductions and maintenance of baseline androgen control.

"These two-year results provide important evidence on the long-term impact of CRENESSITY for adults living with classic congenital adrenal hyperplasia," said Sanjay Keswani, M.D., Chief Medical Officer, Neurocrine Biosciences. "Sustained improvements across key clinical outcomes, including both cardiometabolic and bone outcomes, underscore the potential of CRENESSITY to meaningfully redefine lifelong disease management and improve health. We are excited to share these new data with the scientific community as we continue to deepen our understanding of the long-term impact of CRENESSITY on patient outcomes and quality of life."

CAHtalyst adult participants (N=182) who completed the 24-week, double-blind, placebo-controlled period and the subsequent six-month, open-label period of the study continued treatment with CRENESSITY in an ongoing open-label extension.

Sustained Improvements in Weight-related and Metabolic Outcomes over Two Years

Cardiometabolic clinical outcomes were evaluated through up to two years of CRENESSITY treatment, including changes in body weight, body mass index (BMI), body composition and insulin resistance, as assessed by the homeostatic model assessment for insulin resistance (HOMA-IR) at Months 12 and 24. To avoid potential confounding from glucagon-like peptide-1 (GLP-1) receptor agonists and/or glucose-dependent insulinotropic polypeptide (GIP) use, data from participants taking these medications (n=9) were excluded from the time the medication was started.

Sustained improvements were observed, with mean reductions from baseline in body weight, BMI and insulin resistance.

- Among participants who were overweight or obese at baseline, more than one-third achieved clinically meaningful weight loss (>5%) at two years, with reductions in fat mass exceeding changes in lean mass.
- Improvements in insulin resistance were also sustained through two years, including among participants with insulin resistance at baseline, 43% of whom were no longer insulin resistant at two years.

Measure	Baseline	Change from Baseline at Month 12	Change from Baseline at Month 24
Mean daily GC dose (mg/m²/day HCe*)	17.6	-6.8 (-37%)	-7.0 (-38%)
Mean BMI (kg/m^2)†‡	32.5	-0.9	-0.9
Percentage of overweight/obese participants who achieved >5% reduction in weight†‡	—	31% (35/114)	37% (35/95)
Change in percent fat mass versus percent lean mass†‡	—	-0.9% versus +0.7%	-0.9% versus +0.8%
Mean HOMA-IR‡§	5.3	-1.5	-1.7
Percentage of participants who achieved HOMA-IR ≤2.5‡§	—	40% (26/65)	43% (24/56)

*HCe denotes hydrocortisone equivalents.
†Among participants who were overweight or obese (BMI ≥25 kg/m^2) at baseline. Clinically meaningful weight loss is defined as >5% reduction in body weight.
‡Data from participants who were taking a GIP/GLP-1 receptor agonist were excluded from the time the medication was started.
§Among participants with insulin resistance (HOMA-IR >2.5) at baseline.

"For many adults with classic congenital adrenal hyperplasia, long-term supraphysiologic glucocorticoid exposure can contribute to weight gain and insulin resistance, adding to cumulative cardiometabolic burden over time," said Oksana Hamidi, D.O., M.S.C.S., Associate Professor of Internal Medicine, Division of Endocrinology, UT Southwestern Medical Center. "What makes these two-year data particularly meaningful is that they demonstrate sustained glucocorticoid reductions alongside improvements in insulin resistance and body composition, outcomes that are closely tied to future cardiometabolic risk and long-term health."

Favorable Trends Observed Across Bone-related Outcomes

Bone-related outcomes were also assessed over two years of CRENESSITY treatment, including bone mineral density (BMD) *z* scores at Months 12, 18 and 24, and mean changes from baseline in bone turnover markers at Months 12 and 18.

Favorable trends were observed in mineral density measurements (lumbar spine and total hip) and bone turnover (formation/resorption).

- BMD *z* scores trended toward incremental improvement over time, with the greatest improvement in the lumbar spine where there is the largest proportion of GC-sensitive bone.
- All bone turnover markers increased from baseline to Month 12, potentially reflecting recovery from suppression caused by supraphysiologic GC doses.
- From Month 12 to Month 18, markers of bone formation remained at similar levels, while markers of bone resorption showed a decreasing trend.

Patient-reported Survey Data Reflect Meaningful Changes in Lived Experience

To understand patient perspectives following long-term CRENESSITY treatment, a cross-sectional survey was conducted among adult U.S. participants (n=48) at their final open-label extension visit.

In the survey, 96% of respondents indicated they were moderately or very satisfied with their experience with CRENESSITY treatment, and a majority of participants reported:

- Having more hope for their future living with classic CAH (98%).
- Feeling more in control of their classic CAH (94%).
- Being more optimistic about reducing the long-term impacts of high-dose GCs (96%) and elevated adrenocorticotropic hormone or androgens (92%).

Large majorities of participants who experienced improvements also reported those changes as meaningful, including less side effects associated with high-dose steroids (93%) and less worry about weight gain associated with high-dose steroids (81%), as well as high levels of treatment satisfaction, with 98% reporting they would recommend CRENESSITY and 96% reporting they preferred treatment with CRENESSITY over treatment without CRENESSITY.

Across analyses, CRENESSITY was generally well tolerated through up to two years of treatment, with no new safety signals observed during long-term follow-up.

These findings build on two-year data presented earlier this year at the American Association of Clinical Endocrinology 2026 Annual Meeting and the Pediatric Endocrine Society 2026 Annual Meeting in adults and pediatrics, respectively.

Presentations at the ENDO 2026 annual meeting included:

CAHtalyst Adult Study Two-Year Results

Title: Weight-Related Outcomes and Insulin Resistance in Adults with Classic Congenital Adrenal Hyperplasia: 2-Year Results from the CAHtalyst Adult Study **(Oral Presentation #ORF32-07)**
Authors: Oksana Hamidi, D.O., et al

Title: Adults with Classic Congenital Adrenal Hyperplasia Taking Crinecerfont Demonstrated Sustained Decreases in Glucocorticoid Doses: 2-Year Results from the CAHtalyst Adult Study **(Poster Presentation #SUN-458)**
Authors: Irina Bancos, M.D., et al

Title: A Cross-sectional Survey on Quality of Life of Adults with Classic Congenital Adrenal Hyperplasia in the United States Participating in CAHtalyst Adult Open-Label Extension Study **(Poster Presentation #SUN-467)**
Authors: Sonal Vaid, M.D., et al

Title: Bone Outcomes in Adults with Classic Congenital Adrenal Hyperplasia Treated with Crinecerfont for Up to 2 Years in CAHtalyst Adult Study **(Poster Presentation #SUN-468)**
Authors: Maria Vogiatzi, M.D., et al

CAHtalyst Pediatric Study Two-Year Results

Title: Characterization of Children and Adolescents with Classic Congenital Adrenal Hyperplasia Who Had Slowed Bone Age Progression and Improved Height Prediction with Crinecerfont **(Oral Presentation #ORF32-05)**
Authors: Maria Vogiatzi, M.D., et al

Title: Long-term Crinecerfont Treatment Reduced ACTH and 17-Hydroxyprogesterone — Clinical Outcomes in Children and Adolescents with Classic Congenital Adrenal Hyperplasia: 2-Year Results from CAHtalyst Pediatric **(Poster Presentation #SAT-465)**
Authors: Natalie Nokoff, M.D., et al

Title: Long-term Crinecerfont Enables Sustained Decreases in Glucocorticoid Doses — Clinical Outcomes in Children and Adolescents with Classic Congenital Adrenal Hyperplasia: 2-Year Results from CAHtalyst Pediatric **(Poster Presentation #SUN-465)**
Authors: Kyriakie Sarafoglou, M.D., et al

Additional Presentations

Title: Long-term Risk of Cardiometabolic Comorbidities Associated with Glucocorticoid Exposure and Androgen Control in Classic Congenital Adrenal Hyperplasia: A Cox Proportional Hazards Analysis from the CAHtalog Registry **("New Therapies and Perspectives for Congenital Adrenal Hyperplasia and Adrenal Insufficiency" Rapid Fire Presentation #ORF32-02 and Poster Presentation #MON-495)**
Authors: Oksana Lekarev, D.O., et al

Title: Crinecerfont Treatment of Classic Congenital Adrenal Hyperplasia Due to 11β-Hydroxylase Deficiency: A Case Series **(Poster Presentation #SAT-466)**
Authors: Kyriakie Sarafoglou, M.D., et al

Title: A Modified Delphi Panel of U.S. Endocrinologists to Align on Minimum Clinically Important Difference in Glucocorticoid Dose and Other Key Considerations in Classic Congenital Adrenal Hyperplasia **(Poster Presentation #SAT-459)**
Authors: Ahmed Khattab, M.D., et al

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. Severe enzyme deficiency leads to an inability of the adrenal glands to produce enough cortisol and, in approximately 75% of cases, aldosterone. Because individuals with CAH are typically 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 adrenal crisis and even death.

Exogenous glucocorticoids (GCs) are necessary to correct the endogenous cortisol deficiency, but historically, doses higher than those needed for cortisol replacement (supraphysiologic) have been used to lower the elevated levels of adrenocorticotropic hormone (ACTH) and adrenal androgens. However, GC 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 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 cardiometabolic and fertility issues in both sexes. The symptoms of high ACTH may include testicular adrenal rest tumors (TARTs).

About CRENESSITY® (crinecerfont)
CRENESSITY is a potent and selective oral corticotropin-releasing factor type 1 receptor (CRF1) antagonist that reduces and controls excess adrenocorticotropic hormone (ACTH) and adrenal androgens through a non-glucocorticoid (GC) mechanism for the treatment of classic congenital adrenal hyperplasia (CAH). Antagonism of CRF1 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.

About the CAHtalyst® Studies
The Phase 3 CAHtalyst global registrational studies were designed to evaluate the safety, efficacy and tolerability of CRENESSITY® (crinecerfont) in children and adults with classic congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency. The CAHtalyst studies were the largest-ever 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.

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 enabled 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.

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 biopharmaceutical company with a simple purpose: to relieve suffering for people with great needs. We are dedicated to discovering, developing and commercializing life-changing treatments for patients with under-addressed neurological, psychiatric, endocrine and immunological disorders. The company's diverse portfolio includes FDA-approved treatments for tardive dyskinesia, chorea associated with Huntington's disease, classic congenital adrenal hyperplasia, hyperphagia in patients with Prader-Willi syndrome, 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 more than 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, Facebook and YouTube. *(*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, including its potential support sustained glucocorticoid dose reductions and contribute to improvements in certain cardiometabolic, bone health and patient-reported outcomes; 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 as to whether the data described in this press release will be replicated in additional studies or will be predictive of efficacy or other clinical outcomes in subsequent clinical studies or real-world use of CRENESSITY; 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, 2026. 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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