Neurocrine Biosciences Announces Classic Congenital Adrenal Hyperplasia Supplement Published Today in The Journal of Clinical Endocrinology & Metabolism

January 21, 2025

SAN DIEGO, Jan. 21, 2025 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced publication of a classic congenital adrenal hyperplasia (CAH)-focused supplement in *The Journal of Clinical Endocrinology & Metabolism (JCEM)*, sponsored by the company. The supplement, titled "Challenges and Opportunities in the Management of Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency Throughout the Lifetime," contains eight review articles that provide a comprehensive look at the clinical, psychosocial, treatment-related and day-to-day challenges faced by individuals with classic CAH. *JCEM* is a leader in disseminating research that supports healthcare providers, patients and caregivers in advancing the understanding and management of various endocrinology conditions, such as CAH.

"Our understanding of the genetics, pathophysiology, and complications of CAH has exploded over the last 20 years," said Dr. Richard Auchus, M.D., Ph.D., Principal Investigator, Professor of Pharmacology and Internal Medicine, Division of Metabolism, Endocrinology, and Diabetes at the University of Michigan. "These reviews capture the many dimensions of this complex condition and its management. The limitations of traditional glucocorticoid treatment, particularly in under-resourced areas, create a large disease burden, multiple co-morbidities, and poor outcomes for many patients. The authors are optimistic that this evolving knowledge and emerging treatments, such as corticotropin-releasing factor type 1 receptor antagonists, hold great promise for more personalized care, with improved androgen control and less glucocorticoid-related health consequences in patients."

The *JCEM* supplement is a collection of reviews authored by leading endocrinologists and researchers and sponsored by Neurocrine Biosciences. It explores various aspects of classic CAH management, including pathophysiology, clinical manifestations, treatment challenges, barriers to care, psychosocial impact and advances in treatment, including CRENESSITY™ (crinecerfont), a potent and selective oral corticotropin-releasing factor type 1 receptor (CRF_1) antagonist. CRENESSITY is the first and only classic CAH treatment that directly reduces excess adrenocorticotropic hormone and downstream adrenal androgen production, allowing for glucocorticoid dose reduction. The articles aim to provide healthcare professionals with up-to-date insights and evidence-based approaches that can enhance clinical practice and patient care.

"We are honored to support this important educational content in collaboration with *The Journal of Clinical Endocrinology & Metabolism*," said Eiry W. Roberts, M.D., Chief Medical Officer, Neurocrine Biosciences. "Neurocrine is committed to empowering patients, caregivers and healthcare providers with the knowledge and support to navigate the life-long challenges of treating and living with CAH."

The eight reviews include:

- Genetics and Pathophysiology of Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency (Yang M and White PC)
- Clinical Manifestations and Treatment Challenges in Infants and Children with Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency (Nokoff NJ, Buchanan C and Barker JM)
- Challenges in Adolescent and Adult Males with Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency (Claahsen-van der Grinten HL, Adriaansen BPH and Falhammar H)
- Clinical Manifestations and Challenges in Adolescent and Adult Females with Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency (Engberg H, Nordenström A and Hirschberg AL)
- Mental Health Issues Associated with Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency, (Sandberg DE, Gardner M and Lapham ZK)
- Life With Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency: Challenges and Burdens (Witchel SF, Miller T, McCann E and Gupta A)
- Barriers to the Management of Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency (Eitel KB and Fechner PY)

- Future Directions in the Management of Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency (Sarafoglou K and Auchus RJ)

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 not only to correct the endogenous cortisol deficiency, but doses used are higher than cortisol replacement needed (supraphysiologic) to lower the 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 impact, 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, testicular rest tumors in males and fertility issues in both sexes.

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 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 nose bleeds.

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 (formerly Twitter) 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. 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 September 30, 2024. 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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