Neurocrine Biosciences Presents Findings Contributing to the Growing Body of Evidence on the Impact of High-Dose Glucocorticoids on Clinical Outcomes in Congenital Adrenal Hyperplasia

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- Most Studies Meeting the Literature Review Criteria Found That a Higher Glucocorticoid Dose was Statistically Significantly Associated with Adverse Clinical Outcomes
- Findings Presented at the 2025 International Society for Pharmacoeconomics and Outcomes Research Annual Meeting

SAN DIEGO, May 14, 2025 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) presented today a systematic literature review illustrating the relationship between higher glucocorticoid dose and adverse clinical outcomes, including decreased bone mineral density, increased insulin resistance and higher body mass index, in patients with congenital adrenal hyperplasia. This study was presented at the 2025 International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Annual Meeting in Montreal, Canada.

Congenital adrenal hyperplasia (CAH) is a rare, lifelong genetic condition linked to overproduction of adrenal androgens and cortisol deficiency. CAH is traditionally treated with lifelong high-dose glucocorticoids (GCs), which increase the risk of complications across multiple aspects of health. However, the relationship between GC dose and adverse clinical outcomes in CAH has not been fully explored. This systematic literature review was conducted to analyze the relationship between GC dose and clinical outcomes, and is the first to capture the impact of higher GC dose on the incidence and severity of all relevant adverse clinical outcomes in patients with CAH.

"CAH requires lifelong glucocorticoid therapy to manage adrenal androgen excess and cortisol deficiency, but high doses often lead to significant complications, including cardiometabolic, bone and growth issues," said Eiry W. Roberts, M.D., Chief Medical Officer, Neurocrine Biosciences. "This review highlights the significant clinical burden of long-term, high-dose glucocorticoid use in CAH patients and the challenges clinicians face in optimizing treatment. The emergence of new therapeutic options offers hope for potentially reducing reliance on high-dose glucocorticoids, representing an important advancement in the management of CAH."

The systematic literature review, conducted using PubMed and Embase, identified 105 publications, of which 65% (n=68) included patients with CAH; 55% (n=58) were adults. The most commonly reported outcomes were bone health (43%; n=45), cardiometabolic (41%; n=43) and height and growth (24%; n=25).

More than half (62%, n=65/105) of the publications found statistically significant associations between GC dose and clinical outcomes.

- Of these, 98% (n=64/65) concluded that higher GC doses were significantly linked to adverse clinical outcomes, including decreased bone mineral density, increased insulin resistance and higher body mass index.
- The remaining 38% (n=40/105) of the publications did not reach statistically significant relationships between GC dose and clinical outcomes: nine (9%) reported trends in adverse clinical outcomes, 29 (28%) reported no trend and two (2%) reported trends in improved clinical outcomes.

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 (21-OH). 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 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 new therapeutic options which may reduce reliance on high-dose glucocorticoids for people affected by CAH, and the benefit that such treatments may bring to these individuals. 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: data that we report may change following a more comprehensive review of the data related to the study; risks and uncertainties associated with Neurocrine Biosciences' business and finances in general, as well as risks and uncertainties associated with the commercialization of the Company's products; risks that the Company's products may be precluded from development by the proprietary rights of third parties, or have unintended side effects or adverse reactions; risks and uncertainties relating to competitive products and technological changes that may limit demand for the Company's products; risks associated with our dependence on third parties for development and manufacturing activities related to the Company's products, and our ability to manage these third parties; risks that the FDA or other regulatory authorities may make adverse decisions regarding our products; risks associated with potential generic entrants for our products; 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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