Neurocrine Biosciences Reports Positive Interim Results from Phase II Study of NBI-74788 in Adults with Classic Congenital Adrenal Hyperplasia

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- NBI-74788 Achieved Study Goals and Demonstrated Reductions in Key Disease Biomarkers Exceeding Predetermined Threshold for Proof-of-Concept

- Based on Interim Results, Company Plans to Meet with FDA to Discuss the Registration Program in Adult and Pediatric Patients with Congenital Adrenal Hyperplasia

SAN DIEGO, March 12, 2019 /PRNewswire/ -- Neurocrine Biosciences, Inc. (NASDAQ: NBIX) today announced positive interim results from a Phase II proof-of-concept study evaluating the safety, tolerability, pharmacokinetics and pharmacodynamics of NBI-74788, a proprietary corticotropin-releasing factor type 1 (CRF1) receptor antagonist, in adult patients with classic congenital adrenal hyperplasia (CAH). The results from this ongoing Phase II open-label study demonstrated a reduction of at least 50 percent from baseline in 17-hydroxyprogesterone (17-OHP) and adrenocorticotropic hormone (ACTH) levels in more than 50 percent of CAH patients treated with NBI-74788 for 14 days. Meaningful reductions were also observed in other biomarkers, including androstenedione. NBI-74788 was shown to be well tolerated with no serious adverse events reported to date. The Company plans to meet with the FDA to discuss the registration program for NBI-74788 in adult and pediatric patients with CAH, a genetic disorder affecting the adrenal glands.

"Patients with classic CAH currently have limited treatment options besides more and more glucocorticoids. The management of their genetic disorder is complex due to the highly variable clinical features and response to therapy, which also changes over time. Most patients receive supraphysiologic doses of glucocorticoids chronically to manage their disease, which frequently leads to serious long-term health consequences," said Richard Auchus, M.D., Ph.D., the study's lead investigator and Professor of Internal Medicine, Division of Metabolism, Endocrinology & Diabetes at University of Michigan Health System. "The interim results from this Phase II study of NBI-74788 are encouraging, as they indicate a clinically meaningful reduction in key biomarkers. These data provide encouragement that NBI-74788 has potential as a new treatment option to help patients avoid the complications associated with current therapeutic options for classic CAH."

Classic CAH is a rare genetic disorder caused by a deficiency of the 21-hydroxylase enzyme, which alters the production of cortisol and other adrenal steroids, leading to adrenal insufficiency, overgrowth of the adrenal glands, and excess androgen levels. Classic CAH can lead to adrenal crisis, virilization, hirsutism, precocious puberty, fertility problems and abnormal growth. The standard of care for classic CAH requires a lifelong regimen with high-dose corticosteroids, which cause additional serious long-term clinical problems, including bone loss, Cushing's syndrome and metabolic issues.

"We are very encouraged by the positive interim results of NBI-74788 in this Phase II proof-of-concept study demonstrating the pharmacological effects of CRF1 antagonism on key biomarkers in patients with CAH," said Eiry W. Roberts, M.D., Chief Medical Officer at Neurocrine Biosciences. "We look forward to meeting with the FDA to discuss the registration program to bring this potential new treatment option to patients with classic CAH."

NBI-74788 Phase II Study Design

The NBI-74788 Phase II clinical study is an open-label, multiple-dose, dose-escalation study to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of NBI-74788 in approximately 30 adults with a documented medical diagnosis of classic 21-hydroxylase deficiency CAH. The study includes a sequential-cohort design with three NBI-74788 dose cohorts, with each dose administered for 14 consecutive days.

About NBI-74788

NBI-74788 is a proprietary, potent, selective, orally-active, non-peptide corticotropin-releasing factor type 1 (CRF1) receptor antagonist under evaluation for the treatment of classic CAH. Blockade of CRF receptors in the pituitary has been shown to decrease the release of adrenocorticotropic hormone (ACTH), which in turn decreases the production of adrenal steroids, including androgens, and potentially the symptoms associated with CAH. Research suggests that lowering ACTH levels could reduce the amount of corticosteroid treatment necessary for CAH patients to thrive and avoid the effects associated with long-term steroid therapy.

About Classic Congenital Adrenal Hyperplasia (CAH)

Classic CAH is a genetic disorder that results in an enzyme deficiency that alters the production of adrenal steroids. Because of this deficiency, the adrenal glands have little to no cortisol biosynthesis resulting in a potentially life-threatening condition. If left untreated, classic CAH can result in salt wasting, dehydration and eventually death. Even with cortisol replacement, persistent elevation of adrenocorticotropic hormone (ACTH) from the pituitary gland results in excessive androgen levels leading to virilization and menstrual irregularities in females; both males and females may also experience precocious puberty, short stature, hirsutism, acne and fertility problems. Classic CAH is a disease that affects approximately 20,000 to 30,000 people in the United States.

There are currently no non-steroidal FDA-approved treatments for classic CAH. Corticosteroids, the current standard of care, are used to both correct the endogenous cortisol deficiency and reduce the excessive ACTH levels and androgen excess. However, the dose and duration of steroid use required to suppress ACTH is well above the normal physiological level of cortisol, which can result in serious and common complications, including metabolic issues, bone loss, growth impairment, and iatrogenic Cushing's syndrome.

About Neurocrine Biosciences

Neurocrine Biosciences, a San Diego based biopharmaceutical company, is focused on developing treatments for neurological and endocrine related disorders. The company discovered, developed and markets INGREZZA® (valbenazine) capsules, the first FDA-approved product indicated for the treatment of adults with tardive dyskinesia, an involuntary movement disorder. Discovered and developed through Phase II clinical trials by Neurocrine, ORILISSA® (elagolix), the first FDA-approved oral medication for the management of endometriosis with associated moderate to severe pain in over a decade, is marketed by AbbVie as part of a collaboration to develop and commercialize elagolix for women's health. Neurocrine's clinical development programs include opicapone as an adjunctive therapy to levodopa/DOPA decarboxylase inhibitors in Parkinson's disease patients, elagolix for uterine fibroids with AbbVie, valbenazine for the treatment of Tourette syndrome, and NBI-74788 for the treatment of congenital adrenal hyperplasia (CAH). For more information and the latest updates from Neurocrine Biosciences, please visit **www.neurocrine.com**.

Forward-Looking Statements

In addition to historical facts, this press release may contain forward-looking statements that involve a number of risks and uncertainties. Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are risks and uncertainties associated with Neurocrine's product candidate NBI-74788 and the Phase II study in general, including the risk that NBI-74788 will not be found to be safe and/or effective, or that final results of the study will replicate the interim results. Specifically, the risks and uncertainties the Company faces for NBI-74788 include risks that development activities may not be completed on time or at all; risks that clinical development activities may be delayed for regulatory or other reasons, may not be successful or replicate previous and/or interim clinical trial results, or may not be predictive of real-world results or of results in subsequent clinical trials; risks that regulatory submissions may not occur or be submitted in a timely manner; risks that NBI-74788 may not obtain regulatory approvals; or that the U.S. Food and Drug Administration or regulatory authorities outside the U.S. may make adverse decisions regarding the Company's product candidates; 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-K for the year ended December 31, 2018. Neurocrine disclaims any obligation to update the statements contained in this press release after the date hereof.

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