Spruce Biosciences Announces Topline Results from CAHmelia-204 in Adult CAH and CAHptain-205 in Adult and Pediatric CAH

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CAHmelia-204 Study of 200mg Once-Daily (QD) Tildacerfont in Adult Congenital Adrenal Hyperplasia (CAH) Did Not Achieve Primary Endpoint of Glucocorticoid (GC) Reduction

Dose-Ranging Data from CAHptain-205 Study of Tildacerfont in Adult and Pediatric CAH Suggests Higher Doses and Twice-Daily (BID) Dosing May Be Necessary for Efficacy in CAH

Evaluation of Strategic Opportunities and Cost-Reduction Activities Underway

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Dec. 10, 2024-- Spruce Biosciences, Inc. (Nasdaq: SPRB), a late-stage biopharmaceutical company focused on developing and commercializing novel therapies for neurological and endocrine disorders with significant unmet medical need, today announced topline results from its CAHmelia-204 study of tildacerfont in adult CAH and its CAHptain-205 study of tildacerfont in adult and pediatric CAH.

“We are very grateful to all the patients, families, investigators, and the entire CAH community who supported the CAHmelia-204 and CAHptain-205 clinical trials. We garnered invaluable safety and exposure response data on tildacerfont from these studies, which suggests that higher doses and more frequent dosing may be necessary for efficacy in CAH,” said Javier Szwarcberg, M.D., M.P.H., Chief Executive Officer of Spruce. “Moving forward, we plan to evaluate a full range of strategic options for Spruce in addressing diseases with serious unmet need for patients. In the interim, the CAHmelia-204 and CAHptain-205 clinical trials will be discontinued, and we will be winding down Spruce’s investment in tildacerfont for the treatment of CAH as we conserve financial resources and look to maximize shareholder value.”

CAHmelia-204 was a Phase 2b, randomized, double-blind, placebo-controlled clinical trial that evaluated the safety and efficacy of tildacerfont in reducing supraphysiologic GC usage in 100 adults with classic CAH on a mean GC dose of 35mg/day of hydrocortisone equivalents (HCe) (19mg/m^2/day) and mean androstenedione (A4) level of 214 ng/dL at baseline.

The clinical trial did not achieve the primary efficacy endpoint of the absolute change in daily GC dose from baseline at week 24. 200mg QD of tildacerfont demonstrated a placebo-adjusted reduction from baseline in daily GC dose of 0.7mg HCe (95% CI: -4.3 to 2.9, p=0.7). Approximately 98% of patients were highly compliant with study drug. Tildacerfont was generally safe and well tolerated with no serious adverse events (SAEs).

“Although the study missed its primary endpoint, the data offers valuable insights that will shape the future of CAH management and research,” said Jung Hee Kim, M.D., M.S., Ph.D., Principal Investigator and Associate Professor of Internal Medicine, Seoul National University Hospital and College of Medicine. “I am grateful to the nearly 400 CAH patients who shared their information with us and look forward to presenting our findings at upcoming conferences in 2025.”

CAHptain-205 was a Phase 2 open-label, 4-week, sequential cohort clinical trial, that evaluated the safety, pharmacodynamics (changes in A4 levels), and pharmacokinetics of QD and BID doses of tildacerfont from 50mg QD to 400mg BID in pediatric and adult patients with CAH. A trend was observed of larger reductions from baseline in A4 levels with higher BID doses of tildacerfont. Tildacerfont was generally safe and well tolerated across all doses with no drug-related SAEs.

“This study was well-run with excellent compliance,” said Paul Thornton, M.B.B.S., Principal Investigator and Medical Director of the Endocrine and Diabetes Program at a CAH Center of Excellence. “The data suggests that a twice-daily dosing may be more effective.”

About CAHmelia-204

CAHmelia-204 was a Phase 2b, randomized, double-blind, placebo-controlled clinical trial that evaluated the safety and efficacy of tildacerfont in reducing supraphysiologic glucocorticoid (GC) usage in 100 adults with classic congenital adrenal hyperplasia (CAH) on supraphysiologic doses of GCs with normal or near normal levels of androstenedione (A4) at baseline. In the first part of the clinical trial, patients were randomized to receive 200mg of tildacerfont once-daily (QD) or placebo for 24 weeks. During the second part of the clinical trial, all patients received 200mg of tildacerfont QD for 52 weeks. Throughout the trial, tapering of GCs was guided according to a pre-specified algorithm based on A4 normalization. The primary endpoint of the clinical trial was the absolute change in daily GC dose in hydrocortisone equivalents (HCe) from baseline through week 24.

About CAHptain-205

CAHptain-205 was a Phase 2 open-label clinical trial, which utilized a sequential nine cohort design, to evaluate the safety, efficacy, and pharmacokinetics of tildacerfont in adults and children between two and 17 years of age with CAH. Cohorts 1-3 evaluated weight-adjusted doses of tildacerfont between 50mg QD and 200mg QD in pediatric CAH patients between two and 17 years of age and assessed changes in androgen levels over 12 weeks of treatment as well as the ability to reduce daily GC dose based on A4 normalization. Cohorts 4-9 evaluated weight-adjusted doses of tildacerfont of 200mg twice-daily (BID) and 400mg BID in adults and children between two and 17 years of age with CAH to assess changes in androgen levels over four weeks of treatment.

About Congenital Adrenal Hyperplasia (CAH)

CAH is an autosomal recessive disease, driven by a mutation in the gene that encodes an enzyme necessary for the synthesis of key adrenal hormones. In CAH patients, the body is not able to produce cortisol, leading to serious health consequences. The absence of cortisol alters the normal

feedback cycle of the hypothalamic-pituitary-adrenal (HPA) axis and leads to excess secretion of adrenocorticotropic hormone (ACTH), hyperplasia of the adrenal gland, and consequently high levels of adrenal androgen production. As a result, CAH patients may suffer from premature puberty, impaired fertility, hirsutism, acne, the development of adrenal rest tumors, and an impaired quality of life, and additionally for females, virilized genitalia and menstrual irregularities. Currently, the only way to downregulate the production of excess androgens in CAH patients is to administer supraphysiologic doses of GCs, which present specific side effects, including increased risks of developing diabetes, cardiovascular disease, stunted growth, osteoporosis, thin skin, gastrointestinal disorders, and decreased lifespan.

About Tildacerfont

Tildacerfont is a potent and highly selective, non-steroidal, once-daily oral antagonist of the CRF_1 receptor, which is the receptor for corticotropin-releasing factor (CRF), a hormone that is secreted by the hypothalamus. The CRF_1 receptor is abundantly expressed in the pituitary gland where it is the primary regulator of the HPA axis. By blocking the CRF_1 receptor, tildacerfont has the potential to address the uncontrolled cortisol feedback regulatory pathway in CAH, and in turn reduce the production of ACTH in the pituitary, limiting the amount of androgen produced downstream from the adrenal gland. By controlling excess adrenal androgens through an independent mechanism, tildacerfont has the potential to reduce the unwanted clinical symptoms associated with high androgen exposure and could also enable treating physicians to lower the supraphysiologic GC doses given to CAH patients to near physiologic levels. No drug-related serious adverse events have been reported related to tildacerfont treatment in completed studies.

About Spruce Biosciences

Spruce Biosciences is a late-stage biopharmaceutical company focused on developing and commercializing novel therapies for neurological and endocrine disorders with significant unmet medical need. To learn more, visit www.sprucebio.com and follow us on X, LinkedIn, Facebook and YouTube.

Forward-Looking Statements

Statements contained in this press release regarding matters that are not historical facts are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements include statements regarding, among other things, the Company’s plans to evaluate a full range of strategic options, the discontinuance of the CAHmelia-204 and CAHptain-205 clinical trials, and the wind-down of the Company’s investment in tildacerfont for the treatment of CAH. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Words such as “anticipate”, “will”, “potential”, “plan” and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Spruce’s current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, risks and uncertainties associated with Spruce’s business in general, the impact of geopolitical and macroeconomic events, and the other risks described in Spruce’s filings with the U.S. Securities and Exchange Commission. All forward-looking statements contained in this press release speak only as of the date on which they were made and are based on management’s assumptions and estimates as of such date. Spruce undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

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