Spruce Biosciences Reports Baseline Characteristics from CAHmelia-203 and CAHmelia-204 Studies in Adult Classic CAH

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Baseline Characteristics Reinforce Study Enrichment Strategy in Adult Classic Congenital Adrenal Hyperplasia (CAH) Program

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jan. 5, 2024-- Spruce Biosciences, Inc. (Nasdaq: SPRB), a late-stage biopharmaceutical company focused on developing and commercializing novel therapies for rare endocrine disorders with significant unmet medical need, today reported baseline characteristics of patients enrolled in the CAHmelia-203 and CAHmelia-204 clinical studies of tildacerfont for the treatment of adult classic congenital adrenal hyperplasia (CAH).

“The baseline characteristics of patients enrolled in our CAHmelia-203 and CAHmelia-204 studies reinforce our adult CAH program enrichment strategy and underscore the clinical significance of both hyperandrogenemia and hypercortisolemia within this patient population,” said Javier Szwarcberg, M.D., M.P.H., Chief Executive Officer of Spruce Biosciences. “In particular, patients in CAHmelia-203, which is assessing the change in androstenedione (A4) from baseline at week 12, enrolled with mean baseline A4 levels nearly six times above the upper limit of normal on a mean baseline daily glucocorticoid (GC) dose of 27 mg hydrocortisone equivalents (HCe).”

Dr. Szwarcberg continued: “By contrast, patients in CAHmelia-204, which is assessing the absolute change in GC dose from baseline at week 24, enrolled with a mean baseline daily GC dose of 35 mg HCe and suppressed levels of A4. Collectively, we are encouraged by these baseline characteristics and look forward to reporting topline results from CAHmelia-203 in March, followed by CAHmelia-204 in the third quarter.”

CAHmelia Adult Classic CAH Program Baseline Characteristics

Study Characteristics	CAHmelia-203 (N = 96)	CAHmelia-204 (N = 98)[1]
Male/Female (Proportion of Total Subjects)	47% Male 53% Female	47% Male 53% Female
Average Age Age Ranges	32 Years Old (18 – 65 Years Old)	33 Years Old (18 – 64 Years Old)
Average Baseline Glucocorticoid (GC) Dose[2]	27 mg/day (14 mg/m^2/day)	35 mg/day (19 mg/m^2/day)
Average Baseline Androstenedione (A4) Level[3]	1,149 ng/dL	214 ng/dL
Body Mass Index (BMI)	50% Obese (BMI ≥ 30 kg/m^2)	53% Obese (BMI ≥ 30 kg/m^2)

[1] Patients enrolled as of December 20, 2023. Final enrollment is anticipated to be completed in January 2024 and projected between 98 and 100 patients.

[2] In hydrocortisone equivalents (HCe)

[3] Pre-GC dose.

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 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 glucocorticoids, 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 CRF1 receptor, which is the receptor for corticotropin-releasing factor (CRF), a hormone that is secreted by the hypothalamus. The CRF1 receptor is abundantly expressed in the pituitary gland where it is the primary regulator of the HPA axis. By blocking the CRF1 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 glucocorticoid doses given to CAH patients to near physiologic levels. Tildacerfont has been evaluated in over 200 subjects across nine completed clinical trials in which it has been generally well tolerated. No drug-related serious adverse events have been reported related to tildacerfont treatment in completed

studies.

About CAHmelia-203

CAHmelia-203 is a randomized, double-blind, placebo-controlled, dose ranging Phase 2b clinical trial evaluating the safety and efficacy of tildacerfont in adults with classic CAH and highly elevated levels of A4 at baseline while on stable glucocorticoid dosing. This clinical trial enrolled 96 subjects with elevated levels of A4. For the first six weeks, patients will receive blinded placebo to assess their adherence to their existing glucocorticoid therapy. Patients who continue to meet all eligibility criteria at the end of this period will enter a three-part treatment period. During the placebo-controlled treatment period, patients will be randomized in a blinded manner to receive placebo, 50mg, 100mg, or 200mg tildacerfont once daily. Dosing in the placebo-controlled treatment period will continue for 12 weeks. The primary endpoint of the clinical trial is the percentage change in A4 from baseline to week 12 with secondary endpoints including the proportion of patients with levels of 17-OHP and A4 within the target and normal range, respectively, and change in lesion volume of TARTs in men. Following the placebo-controlled treatment period, all patients will receive tildacerfont following a dose-escalation protocol that allows dose increase to 200mg once daily over 12 weeks. Following the 12-week dose-escalation period, all patients will continue receiving tildacerfont at 200mg once daily for an additional 46 weeks. Patients who achieve control of A4 while on supraphysiologic glucocorticoid treatment will have the opportunity to reduce their glucocorticoid dosing in the open-label period according to a pre-specified algorithm in the protocol. Additional endpoints include clinical outcomes and patient and clinician reported outcomes. For more information about the CAHmelia program, please visit https://www.sprucebio.com/cahmelia.

About CAHmelia-204

CAHmelia-204 is a randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of tildacerfont in reducing supraphysiologic glucocorticoid usage in approximately 90 adults with classic CAH in patients on supraphysiologic doses of glucocorticoids with normal or near normal levels of A4 at baseline. This clinical trial is designed in two parts. In the first part of the clinical trial, patients will be randomized to receive 200mg tildacerfont once daily or placebo for 24 weeks. During the second part of the clinical trial, all patients will receive open-label 200mg tildacerfont once daily for 52 weeks. Throughout the trial, tapering of glucocorticoids will be guided according to a pre-specified algorithm and continue to the lowest level possible (physiologic replacement levels), as long as patients remain well controlled based on standard biomarkers and clinical assessments. The primary endpoint of this clinical trial is the absolute change in daily glucocorticoid dose in hydrocortisone equivalents (HCe) from baseline at week 24. The percent change in glucocorticoid dose from baseline to week 24 will be assessed as a secondary endpoint. Median total cumulative GC dose (HCe) at week 24, change from baseline in insulin resistance at week 24, and percent change from baseline in weight at week 24 and after 52 weeks of tildacerfont treatment will also be assessed as secondary endpoints. Effects on insulin resistance, weight, waist circumference, bone mineral density after 52 weeks of tildacerfont treatment will be assessed as exploratory endpoints. For more information about the CAHmelia program, please visit https://www.sprucebio.com/cahmelia.

About Spruce Biosciences

Spruce Biosciences is a late-stage biopharmaceutical company focused on developing and commercializing novel therapies for rare endocrine disorders with significant unmet medical need. Spruce is initially developing its wholly-owned product candidate, tildacerfont, as the potential first non-steroidal, once-daily therapy for patients suffering from classic congenital adrenal hyperplasia (CAH) and other endocrine disorders. 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 results, conduct, progress and timing of Spruce’s clinical trials. 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” 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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