Spruce Biosciences Completes Target Enrollment of CAHmelia-203 Study in Adult Classic Congenital Adrenal Hyperplasia

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Final Enrollment in CAHmelia-203 to Exceed Target Due to Substantial Patient Interest

CAHmelia-203 Topline Results Anticipated in the First Quarter of 2024

CAHmelia-204 Completion of Enrollment Anticipated in Early First Quarter of 2024

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Oct. 18, 2023-- 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 announced completion of target enrollment of 72 patients and closure of screening in the CAHmelia-203 clinical trial evaluating tildacerfont for the treatment of adult classic congenital adrenal hyperplasia (CAH) and provided updated anticipated milestones.

“Completing target enrollment in the CAHmelia-203 study is a significant milestone for our CAH program and reflects the continued strong enthusiasm from patients and study investigators alike, evidences the large unmet medical need in the CAH community, and reinforces the momentum within our broader tildacerfont program,” said Javier Szwarcberg, M.D., M.P.H., Chief Executive Officer of Spruce Biosciences. “Due to substantial patient interest in CAHmelia-203, eligible adult patients currently in screening will be allowed to enter the trial. As a result, we anticipate that final enrollment will exceed our original target of 72 patients, and project topline results from this study along with the topline results from all cohorts in our CAHptain clinical trial in pediatric classic CAH in the first quarter of 2024.”

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 androstenedione (A4) at baseline while on stable glucocorticoid dosing. Tildacerfont is a once-daily, potent and highly selective, non-steroidal, oral antagonist of the corticotropin-releasing factor (CRF) 1 receptor. 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-hydroxyprogesterone (17-OHP) and A4 within the target and normal range, respectively, and change in lesion volume of testicular adrenal rest tumors (TARTs) in men. Additional endpoints include clinical outcomes and patient and clinician reported outcomes.

Anticipated Upcoming Milestones

Spruce has updated its anticipated upcoming milestones as follows:

- Completion of enrollment in the CAHmelia-204 clinical trial in adult classic CAH patients on supraphysiologic doses of glucocorticoids with normal or near normal levels of A4 in early first quarter of 2024
- Topline results from all cohorts in the Phase 2 CAHptain clinical trial in pediatric classic CAH patients in the first quarter of 2024
- Topline results from the CAHmelia-203 clinical trial in adult classic CAH patients with highly elevated levels of A4 in the first quarter of 2024
- Topline results from the CAHmelia-204 clinical trial in adult classic CAH patients on supraphysiologic doses of glucocorticoids with normal or near normal levels of A4 in the third quarter of 2024

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 targets enrollment of approximately 72 patients 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 at week zero 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 to increase dosage 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 (replacement levels only), as long as patients remain well controlled based on standard biomarkers and clinical assessments. The primary endpoint of this clinical trial is the proportion of patients with reduction of glucocorticoid dose greater than or equal to 5 mg/day of hydrocortisone equivalent (HCe) 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 CAHptain-205

CAHptain-205 is a Phase 2 open-label clinical trial, which will utilize a sequential three cohort design, to evaluate the safety, efficacy, and pharmacokinetics of tildacerfont in children two to 17 years of age. The study will also characterize changes in androgen levels over 12 weeks of treatment, and the ability to reduce daily glucocorticoid dose based on A4 normalization. An optional open-label extension period will provide additional open-label treatment with tildacerfont to provide long-term safety data for up to two years. Cohort 1 will enroll up to five participants between the ages of 11 and 17 years of age, who will receive a weight-adjusted, adult dose equivalent of 50mg QD of tildacerfont. Cohort 2 will enroll up to five participants between the ages of 11 and 17 years of age, who will receive a weight-adjusted, adult dose equivalent of 200mg QD of tildacerfont. Cohort 3 will enroll up to 10 participants between the ages of two and 10 years of age, who will receive a weight-adjusted, adult dose equivalent of 200mg QD of tildacerfont. The primary endpoint of this clinical trial is safety. Additional secondary endpoints include the proportion of subjects who achieve reduction in A4 or daily glucocorticoid dosing at week 12 and the proportion of subjects with elevated A4 at baseline who achieve a reduction in A4 at week 4. For more information about the CAHptain program, please visit https://www.sprucebio.com/cahptain.

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 endogenous 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, 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 patients 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 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 therapy for patients suffering from classic congenital adrenal hyperplasia (CAH). Spruce is also developing tildacerfont for women suffering from polycystic ovary syndrome (PCOS). To learn more, visit www.sprucebiosciences.com and follow us on X, formerly known as Twitter, 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 enrollment, results, conduct, progress and timing of Spruce’s clinical trials; and the receipt and presentation of topline results from the same. 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”, “enable,” “expect”, “will”, “believe”, “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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