Spruce Biosciences Announces Topline Results from CAHmelia-203 in Adult Classic CAH and CAHptain-205 in Pediatric Classic CAH

March 13, 2024

CAHmelia-203 Study of Tildacerfont in Adult Classic Congenital Adrenal Hyperplasia (CAH) with Severe Hyperandrogenemia Did Not Meet Primary Efficacy Endpoint

Positive Data from CAHptain-205 Study of Tildacerfont in Pediatric Classic CAH Supports Further Dose-Ranging Across Additional Dosing Cohorts

Topline Results from CAHmelia-204 Study of Tildacerfont in Adult Classic CAH Evaluating Glucocorticoid (GC) Reduction Anticipated in Third Quarter of 2024

Resource Prioritization and Cost Reductions Extend Cash Runway Through End of 2025

Conference Call Today at 4:30 p.m. ET

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Mar. 13, 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 announced topline results from its CAHmelia-203 study of tildacerfont in adult classic congenital adrenal hyperplasia (CAH) and its CAHptain-205 study of tildacerfont in pediatric classic CAH.

Spruce is investigating tildacerfont, a second generation, once-daily oral antagonist of the CRF1 receptor, for the treatment of classic CAH. The global CAHmelia program in adult classic CAH is comprised of two Phase 2b studies designed to address the unmet medical needs of two distinct populations of adult CAH patients. CAHmelia-203 assesses androstenedione (A4) reduction in adult CAH patients with severe hyperandrogenemia, while CAHmelia-204 assesses glucocorticoid (GC) reduction, a potentially registrational endpoint, in adult CAH patients on supraphysiologic GC doses with normal or near normal levels of A4.

The Phase 2 CAHptain-205 study is focused on addressing the unmet medical need in pediatric CAH patients, which represents approximately 25% of the total patient population. The CAHmelia and CAHptain programs seek to address the unmet medical need across the entire spectrum of the CAH patient community, which has not seen a new standard of care since GCs were introduced in the 1950s.

CAHmelia-203 Study of Tildacerfont in Adult Classic CAH

CAHmelia-203 enrolled 96 subjects with a mean baseline A4 level of 1,151 ng/dL, which is more than five times above the upper limit of normal (ULN).

Data Highlights

- The clinical trial did not achieve the primary efficacy endpoint of the assessment of dose response for the change in A4 from baseline to week 12.
- 200mg QD of tildacerfont demonstrated a placebo-adjusted reduction from baseline in A4 of -2.6% at week 12 with a non-significant p-value.
- Compliance with study medication and GC was low with approximately 50% of patients reporting 80% or greater compliance, resulting in lower-than-expected tildacerfont exposure.
- Tildacerfont was generally safe and well tolerated at all doses with no treatment-related serious adverse events (SAEs). Most adverse events were reported as mild to moderate.

“We are grateful to all the patients, families, study team and investigators who supported the CAHmelia-203 clinical trial,” said Javier Szwarcberg, M.D., M.P.H., Chief Executive Officer, Spruce Biosciences. “CAHmelia-203 is the first study of its kind to address a difficult-to-treat CAH patient population with severe and more refractory hyperandrogenemia, which is often attributed to challenging real-life compliance with daily GCs. We garnered important data from this study which will inform ongoing development of tildacerfont in adult classic CAH.”

Dr. Szwarcberg added, “Looking ahead to the third quarter of 2024, we are eager to report topline results from CAHmelia-204, which is focused on assessing GC reduction, a potentially registrational endpoint, in a different population of adult CAH patients with relatively controlled A4 levels and historically better adherence to GC therapy. Assuming positive results from CAHmelia-204 and CAHptain-205, we plan to meet with the U.S. Food and Drug Administration (FDA) and comparable foreign regulatory authorities to outline the design of a registrational clinical program in adult and pediatric classic CAH.”

CAHmelia-203 and 204 Baseline Characteristics Highlight Two Distinct Patient Populations in Adult CAH with Differing Disease Status and Treatment Goals

Patients in CAHmelia-203 enrolled with severe hyperandrogenemia, as indicated with mean baseline A4 levels more than five times above the ULN. By contrast, patients in CAHmelia-204 enrolled with a mean baseline A4 value of 224 ng/dL, which is approximately the ULN, with 66% of patients enrolled with androgenic control, which is defined as having A4 values below the ULN at baseline.

Study Characteristics	CAHmelia-203	CAHmelia-204

	(N = 96)	(N = 100)
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[1]	27 mg/day (14 mg/m^2/day)	37 mg/day (20 mg/m^2/day)
Average Baseline Androstenedione (A4) Level[2]	1,151 ng/dL (>5x ULN)	224 ng/dL (~ULN)
Average Baseline 17-Hydroxyprogesterone (17-OHP) Level[2]	16,653 ng/dL (>80x ULN)	5,675 ng/dL (>28x ULN)
Average Baseline Adrenocorticotropic (ACTH) Level[2]	435 pg/dL (>6x ULN)	168 pg/dL (>2x ULN)
Body Mass Index (BMI)	50% Obese (BMI ≥ 30 kg/m^2)	53% Obese (BMI ≥ 30 kg/m^2)

[1] In hydrocortisone equivalents (HCe)

[2] Pre-GC dose.

“The CAHmelia-203 results underscore the complexities inherent in managing a patient group with challenges related to androgenic control and GC compliance,” said Irina Bancos, M.D., Principal Investigator and Associate Professor of Medicine and Endocrinologist at the Mayo Clinic. “Based on my clinical experience, patients within this group may face difficulties adhering to any therapeutic interventions, potentially impacting treatment outcomes.”

Dr. Bancos continued, “Patients with higher glucocorticoid doses and normal or near normal androgen levels, such as those enrolled in CAHmelia-204, are generally more consistent with GC therapy and easier to manage due to lower ACTH overdrive of the adrenal gland but carry higher risk of glucocorticoid-associated comorbidities. I look forward to reviewing results from CAHmelia-204, which will provide a more complete picture into the therapeutic potential of tildacerfont.”

CAHptain-205 Study of Tildacerfont in Pediatric Classic CAH

CAHptain-205 enrolled 30 children between two and 17 years of age with a mean baseline GC dose of 14 mg/m^2/day and mean baseline A4 level of 372 ng/dL. The study characterized the safety and pharmacokinetic profiles of tildacerfont, as well as changes in androgen levels over 12 weeks of treatment, and the ability to reduce daily GC dose upon A4 normalization.

Data Highlights

- Tildacerfont was generally safe and well tolerated at all dose ranges with no treatment-related SAEs reported.
- Preliminary pharmacokinetic analysis suggests that tildacerfont is cleared more rapidly in children than in adult CAH patients.
- 73% of all patients (22 of 30 patients) met the efficacy endpoint of A4 or GC reduction from baseline at 12 weeks of treatment with tildacerfont.
- 70% of patients with elevated baseline A4 values (16 of 23 patients) demonstrated an A4 reduction at week 4.

“As a pediatric endocrinologist, I’ve witnessed first-hand the significant unmet medical need and lack of treatment options for children and adolescents living with CAH,” said Will Charlton, M.D., M.A.S., Chief Medical Officer, Spruce Biosciences. “The CAHptain-205 study results demonstrate safety and tolerability in pediatric CAH patients with weight-adjusted tildacerfont doses up to 200mg daily. While we are encouraged by the therapeutic activity of doses investigated in the study, we plan to continue dose-ranging across additional cohorts to evaluate dose selection to inform our registrational program. We anticipate topline results in the fourth quarter of 2024.”

“I’m encouraged by the initial results from the CAHptain-205 study and the potential of tildacerfont to shift the treatment paradigm for pediatric classic CAH to a more balanced approach between androgens and GCs,” said Paul Thornton, M.B.B.S., Principal Investigator and Medical Director of the Endocrine and Diabetes Program at a CAH Center of Excellence. “These data suggest that tildacerfont may enable clinically meaningful reduction of A4 and GC levels in children and adolescents. This may improve long-term clinical outcomes, such as short stature and obesity, which are related to both androgen excess and exposure to chronic supraphysiologic GC doses.”

Business and Financial Update

The company intends to implement cost savings initiatives, including termination of the CAHmelia-203 study and a workforce reduction of approximately 21%. The company currently has over $81 million in cash and cash equivalents, which is anticipated to fund its current operating plan through the end of 2025, including through the CAHmelia-204 topline results and CAHptain-205 topline results from additional dosing cohorts.

Conference Call Details

Spruce’s management team and key study investigators will host a conference call today at 4:30 p.m. ET to discuss the topline results of the CAHmelia-203 and CAHptain-205 clinical studies. Analysts and investors can participate in the conference call by registering here or dialing (866) 777-2509.

An archived copy of the call will be available on the events section of the company’s investor relations website for approximately 90 days.

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 96 adults with classic CAH and highly elevated levels of A4 at baseline while on stable glucocorticoid dosing. For the first six weeks, patients received blinded placebo to assess their adherence to their existing glucocorticoid therapy. Patients who continued to meet all eligibility criteria at the end of this period and where compliant with therapy entered a three-part treatment period. During the placebo-controlled treatment period, patients randomized in a blinded manner to receive placebo, 50mg, 100mg, or 200mg tildacerfont once daily. Dosing in the placebo-controlled treatment period continued for 12 weeks. The primary endpoint of the clinical trial was the assessment of dose response for the change in A4 from baseline to week 12. Following the placebo-controlled treatment period, all patients received tildacerfont following a dose-escalation protocol that allowed dose increase to 200mg once daily over 12 weeks. Following the 12-week dose-escalation period, all patients continued receiving tildacerfont at 200mg once daily for an additional 46 weeks. Patients who achieved control of A4 while on supraphysiologic glucocorticoid treatment had the opportunity to reduce their glucocorticoid dosing in the open-label period according to a pre-specified algorithm in the protocol. 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 Phase 2b clinical trial to evaluate the safety and efficacy of tildacerfont in reducing glucocorticoid usage in 100 adults with classic CAH 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 from baseline at week 24. 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 utilized 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 enrolled five participants between the ages of 11 and 17 years of age, who received a weight-adjusted, adult dose equivalent of 50mg QD of tildacerfont. Cohort 2 enrolled seven participants between the ages of 11 and 17 years of age, who received a weight-adjusted, adult dose equivalent of 200mg QD of tildacerfont. Cohort 3 enrolled 18 participants between the ages of two and 10 years of age, who received 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 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 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. 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, 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 design, results, conduct, progress and timing of Spruce’s clinical trials; tildacerfont’s potential to be a novel treatment option that improves long-term health outcomes for patients with CAH; the implications of the different patient population in CAHmelia-204 compared with CAHmelia-203; Spruce’s expectations regarding reporting results of its clinical trials in 2024; Spruce’s plans to meet with the FDA and comparable foreign regulatory authorities to discuss the potential registrational path forward of tildacerfont for adult and pediatric classic CAH; the impact of cost savings initiatives and the length of Spruce’s anticipated cash runway; and Spruce’s product candidate, strategy and regulatory matters. 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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