Spruce Biosciences Provides Clinical Program Updates and Outlines Anticipated Milestones for 2023

January 9, 2023

Topline Results from CAHmelia-203 in Adult Classic Congenital Adrenal Hyperplasia (CAH) Anticipated in 2H 2023

Amendment to Phase 2 CAHptain Clinical Trial in Pediatric Classic CAH Enhances Study Design; Topline Data from Adolescents Anticipated in 2H 2023

Topline Data in Phase 2 P.O.W.E.R. Study in Polycystic Ovary Syndrome Anticipated in 1H 2023

Entered Exclusive Licensing Agreement with Kaken Pharmaceutical to Develop and Commercialize Tildacerfont for CAH in Japan

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jan. 9, 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 provided an update on its clinical programs, anticipated upcoming milestones and strategic priorities for advancing tildacerfont in classic congenital adrenal hyperplasia (CAH) and polycystic ovary syndrome (PCOS).

“As we enter 2023, we are pleased to have recently announced our strategic partnership with Kaken Pharmaceutical to develop and commercialize tildacerfont in Japan,” said Javier Szwarcberg, M.D., MPH, Chief Executive Officer of Spruce Biosciences. “2022 was a year of clinical execution across the board, which puts us in a strong position to report topline data for a number of our clinical programs this year, particularly our CAHmelia-203 study for adult classic CAH in the second half of 2023. We also continue to make progress in our Phase 2 P.O.W.E.R. study for the treatment of PCOS and anticipate reporting topline proof-of-concept data in the first half of 2023.”

Dr. Szwarcberg continued, “Children represent the greatest unmet medical need in classic CAH, with urgent necessity for androgen-lowering and glucocorticoid-sparing therapies to reduce the risk of premature puberty and adverse effects, both of which have the potential to be addressed by tildacerfont, if approved. To that end, we’ve identified opportunities to enhance our CAHptain pediatric classic CAH clinical trial, by lowering the minimum age requirement from 6 years to 2 years of age and increasing the study length from 2 weeks to 12 weeks, with an additional 2-year extension option. We expect these enhancements will expand the amount of informative data that can be generated from the program and increase attractiveness for patients and families to participate.”

Clinical Programs

Late-Stage CAHmelia Program in Adult Classic CAH

- **CAHmelia-203 Study for Adult Classic CAH:** CAHmelia-203 is a randomized, double-blind, placebo-controlled, dose-ranging study evaluating the safety and efficacy of tildacerfont in adult patients with classic CAH and is designed to enroll approximately 72 patients with high levels of androstenedione (A4) while on their current glucocorticoid regimen. Enrollment in the clinical trial is approaching 50%.
  - **Anticipated Upcoming Milestone:** Topline results in the second half of 2023
- **CAHmelia-204 Study for Adult Classic CAH:** CAHmelia-204 is a randomized, double-blind, placebo-controlled study evaluating the safety and efficacy of tildacerfont in adult patients with classic CAH. The study is designed to enroll approximately 90 patients on supraphysiologic doses of glucocorticoids at or above 30 mg/d hydrocortisone equivalent with normal or near normal levels of A4. Enrollment in the clinical trial recently surpassed 25%.
  - **Anticipated Upcoming Milestone:** Topline results in the second half of 2024

Pediatric Classic CAH Program

Phase 2 CAHptain Clinical Study in Pediatric Classic CAH: Spruce is investigating tildacerfont for the treatment of classic CAH in children. There is a significant medical need to bring androgen-lowering and glucocorticoid-sparing therapies to pediatric classic CAH patients to reduce the risk of premature puberty and the adverse effects of glucocorticoids, including stunted growth resulting in short stature as adults. The Phase 2 open-label clinical trial utilizes a sequential 3 cohort design (cohorts 1 and 2 comprising of adolescent patients 11 to 17 years of age, and cohort 3 comprising of children 2 to 10 years of age) to evaluate the safety, pharmacokinetics (PK), and exploratory pharmacodynamics (PD) of tildacerfont in children 2 to 17 years of age with classic CAH. Spruce implemented key protocol changes to enhance the study design and gather additional data to inform future clinical development:

- Increasing the Study Length, Lowering Age Eligibility, and Adding an Open-Label Extension to Make the Trial More Accessible to Patients and Families
  - Spruce amended the study length from a 2-week PK and exploratory PD study to a 12-week study. The company plans to also offer a 2-year open-label extension to the 12-week study. These changes are designed to enable

patients to retain access to the study drug for up to 2 years following completion of the study, and provide for observation of clinical outcomes, such as bone age and predicted adult height.
    - The company is lowering the minimum age requirement from 6 years to 2 years of age. Given the significant growth and development that occurs in children between the ages of 2 years and 5 years of age, this change is designed to provide important data on the impact of reductions in androgen levels and glucocorticoids (GC) in younger children.

- Increasing the Amount of Data That Can Be Extrapolated from Program
    - The following additional data will be collected to inform a potential Phase 3 registrational clinical trial, while allowing for observation of key clinical outcomes:
        - 2 weeks of pediatric tildacerfont PK exposure data at two weight adjusted doses (50mg and 200mg) to inform a dose for the Phase 3 registrational program;
        - 4 weeks of PD data to potentially show reduction in androstenedione (A4) and establish dose-response (day 1-28);
        - A4 reduction data and GC reduction based on a protocol-specified algorithm (day 28-90); and
        - sub-chronic safety data at 12 weeks.

- **Anticipated Upcoming Milestone:** Topline data from adolescents (cohorts 1 and 2) in the second half of 2023

Polycystic Ovary Syndrome (PCOS) Program

Phase 2 P.O.W.E.R. Clinical Study in PCOS: Spruce is conducting the P.O.W.E.R. study, a randomized, placebo-controlled, dose escalation study which will evaluate the safety and efficacy of tildacerfont titrated to 200 mg once daily compared to placebo at 12 weeks in subjects with PCOS and elevated adrenal androgens as measured by dehydroepiandrosterone sulfate (DHEAS) levels at baseline. PCOS is a hormonal disorder common among females of reproductive age characterized by hirsutism, irregular periods, infertility, and ovarian cysts. Adrenal androgen overproduction is thought to contribute to the clinical manifestations of PCOS in some patients. By reducing ACTH-stimulated adrenal androgen production, tildacerfont has the potential to treat the clinical sequelae of PCOS.

- **Anticipated Upcoming Milestone:** Topline results in the first half of 2023

Financial Update

The company estimates that its cash, cash equivalents, and investments were approximately $79 million as of December 31, 2022. This amount is unaudited and preliminary and is subject to completion of financial closing procedures. Additional information and disclosure would be required for a more complete understanding of the company's financial position and results of operations as of December 31, 2022.

With the anticipated receipt of the $15.0 million upfront payment from the company's license agreement with Kaken Pharmaceutical, Spruce's cash runway is expected to extend into the first half of 2024.

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 a rare form of polycystic ovary syndrome (PCOS) with primary adrenal androgen excess. To learn more, visit www.sprucebiosciences.com and follow us on Twitter @Spruce_Bio, 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, including the timing of reporting topline data and the impact of the strategies to enhance the design of the CAHmelia studies and the resulting informative data that may be generated, the fulfillment of Spruce's strategic business objectives, the advancement of Spruce's drug development pipeline, and Spruce's expectations regarding its extended cash runway. 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 "anticipated," "expects," "intended," "plans", "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 macroeconomic and geopolitical events, including the COVID-19 pandemic, 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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