



Spruce Biosciences Achieves Proof of Concept in Phase 2 Study of Tildacerfont in Congenital Adrenal Hyperplasia

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-Tildacerfont demonstrates meaningful reduction in key disease biomarkers adrenocorticotrophic hormone (ACTH), 17-hydroxyprogesterone (17-OHP) and androstenedione (A4)

-Well-tolerated and safe, tildacerfont holds potential as a treatment for patients with congenital adrenal hyperplasia, a rare endocrine disorder

San Francisco – March 25, 2019 – [Spruce Biosciences](http://www.sprucebiosciences.com), a clinical-stage biotechnology company developing novel therapies for rare endocrine disorders, today reported positive proof of concept data from a Phase 2 multicenter, multiple-dose, dose-escalation trial of tildacerfont, an oral corticotropin-releasing factor type-1 (CRF₁) receptor antagonist, for the treatment of patients with congenital adrenal hyperplasia (CAH). The Phase 2 results were presented in a late-breaking poster presentation at the Annual Meeting of the Endocrine Society (ENDO 2019), the premier conference for endocrine science and medicine.

Spruce's Phase 2 trial involved 18 patients with uncontrolled classic CAH. Ten patients in Cohort A received two weeks of treatment at each of three doses: 200, 600 and 1,000 mg tildacerfont once per day (QD) for a total of six weeks of treatment. Eight patients in Cohort B were treated for two weeks with 400 mg per day (200 mg twice per day [BID]). The study was designed to assess safety, tolerability, pharmacokinetics and the ability of tildacerfont to reduce adrenal androgens (androstenedione [A4]), progestins (17-hydroxyprogesterone [17-OHP]) and adrenocorticotrophic hormone (ACTH), the primary driver of adrenal tissue hyperplasia.

Across both cohorts, tildacerfont was well-tolerated, exhibited a predictable, dose-dependent pharmacokinetic profile and was effective in reducing excess A4, 17-OHP and ACTH. There were no serious AEs and no AEs leading to withdrawal.

In Cohort A, improvements in A4 were demonstrated in 10 of 10 patients (100 percent), and 17-OHP and ACTH were both improved in 8 of 10 patients (80 percent). In Cohort B, improvements in A4 were demonstrated in 6 of 8 patients (75 percent), 17-OHP in 6 of 7 patients (86 percent) and ACTH in 5 of 7 patients (71 percent).

Additionally, after six weeks of treatment with tildacerfont, the one male patient with confirmed testicular adrenal rest tumors (TARTs) at baseline saw a notable reduction in tumor size after 6 weeks of therapy. TARTs are ACTH-responsive, space-occupying lesions of the testes that lead to pain and infertility in men and boys as young as four years old, and represent a meaningful unmet need in males with CAH.

"These results demonstrate that a targeted therapy like tildacerfont, capable of treating the underlying disease is on the horizon for patients with CAH" said Kyriakie Sarafoglou, M.D., associate professor, department of pediatrics at the University of Minnesota and first author of the poster.

Alexis Howerton, Ph.D., CEO at Spruce Biosciences, added: "We are excited to be able to share these data with the clinical community at ENDO 2019, which reveal that the majority of patients treated with tildacerfont achieved meaningful reductions across the three key biomarkers for CAH. We are highly motivated by the potential to fulfill a therapeutic void for patients living with CAH and are optimistic that a CRF₁ receptor antagonist such as tildacerfont will be the right treatment solution for this rare disease."

CAH is a rare endocrine disease of impaired cortisol synthesis coupled with adrenal androgen excess. Although CAH is a part of the nationwide newborn screening program, there are currently no FDA-approved therapies. Patients are often prescribed supraphysiologic doses of steroids to suppress androgen production, yet the vast majority of patients continue to suffer from poorly controlled disease, along with the adverse effects associated with high dose steroids.

For more information on Spruce, please visit www.sprucebiosciences.com.

About Spruce Biosciences

Spruce Biosciences is a clinical-stage biotechnology company developing novel therapies for rare endocrine disorders. Spruce's lead program, tildacerfont (formerly SPR001), is an oral, non-steroidal small molecule with the potential to be the first FDA-approved therapy for CAH. For more information on Spruce Biosciences and its lead clinical program for CAH, please visit www.sprucebiosciences.com.

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