



Spruce Biosciences Announces Positive Results from 12-week, Phase 2a Study of Tildacerfont in Adults with Congenital Adrenal Hyperplasia

September 19, 2019

– **Tildacerfont demonstrated maximum mean reductions of 84% adrenocorticotrophic hormone (ACTH), 82% 17-hydroxyprogesterone (17-OHP) and 79% androstenedione (A4), key disease biomarkers in CAH patients with elevated androgens**

– **The majority of tildacerfont-treated patients saw their ACTH levels normalize as a result of treatment**

– **Non-steroidal tildacerfont holds potential as a first-in-class treatment for patients with congenital adrenal hyperplasia**

San Francisco – September 19, 2019 – [Spruce Biosciences](#), a clinical-stage biotechnology company developing novel therapies for rare endocrine disorders, today announced positive results from a Phase 2a, multicenter, 12-week trial of tildacerfont, an investigational, oral, once-a-day corticotropin-releasing factor type-1 receptor antagonist, in development for the treatment of congenital adrenal hyperplasia (CAH).

The Phase 2a study enrolled patients with classic CAH accompanied by elevated androgens at baseline who were treated with tildacerfont once-daily over 12 weeks, resulting in clinically relevant reductions in key parameters. These included mean reductions from baseline of 74% for ACTH, 82% for 17-OHP and 55% for A4. ACTH is the direct target of tildacerfont, while A4 is the critical downstream biomarker used in clinical management of patients with CAH. Maximum mean reductions observed at any timepoint in the study were 84% for ACTH, 82% for 17-OHP and 79% for A4. In addition, 60% of patients with elevated, abnormal ACTH and 40% of patients with elevated A4 saw reductions to normalization by week 12. The primary endpoint of safety and tolerability was achieved, with no new safety signals observed in the study and the majority of adverse events classified as mild, not related to study drug and single event occurrences. No serious adverse events were observed.

“There is a significant and urgent need for new CAH treatments as there are currently no FDA-approved therapies,” said Richard Auchus, M.D., Ph.D., an investigator in the study and professor of internal medicine and pharmacology, division of metabolism, endocrinology & diabetes at University of Michigan, Ann Arbor. “The results of this study are encouraging as they demonstrate, for the first time, that a novel non-steroidal treatment can produce clinically meaningful reductions across key biomarkers over a period of 12 weeks. These data indicate tildacerfont could be a promising new treatment option for patients with CAH.”

Further, Richard King, chief executive officer at Spruce Biosciences, commented, “The magnitude of these reductions coupled with patients having been able to achieve normalization after only 12 weeks of treatment suggests that tildacerfont may provide a first-in-class option for patients to better manage their disease by reducing their exposure to elevated androgens and, potentially, their lifelong steroid burden.”

About Congenital Adrenal Hyperplasia (CAH)

Classic CAH is a rare genetic disorder affecting the ability of the adrenal glands to function properly. CAH results from a mutation in the gene that encodes the enzyme 21-hydroxylase, which is necessary for the synthesis of key adrenal hormones. As a result, people with CAH have an impaired ability to produce the hormone, cortisol, which can result in life-threatening adrenal crises. Cortisol is also known as “the stress hormone,” and is critical for the body’s response to stress, illness and injury.

In CAH, the adrenal glands often produce excessive levels of male sex hormones or androgens. While both sexes need androgens for proper growth and development, an excess can cause problems that may include precocious puberty, short stature, hirsutism, increased risk of testicular adrenal rest tumors (TART) in men, and virilization and menstrual dysfunction in women.

Although CAH testing is part of the newborn screening program, there are currently no FDA-approved therapies for CAH. Glucocorticoids (such as hydrocortisone, prednisone and dexamethasone) are commonly used to treat CAH but are associated with a wide-range of side effects, including weight gain, reduced bone mineral density, metabolic abnormalities and increased cardiovascular risk.

Tildacerfont Phase 2a Study Design

This phase 2a study was a U.S. multicenter, open-label, 12-week active treatment trial designed to evaluate the safety, tolerability and efficacy of once-daily 400 mg tildacerfont in adult subjects with classic CAH. Efficacy was characterized by tildacerfont’s ability to reduce key disease biomarkers over time in subjects with elevated baseline ACTH and adrenal hormones (17-OHP and A4). In addition, several clinical outcomes were also evaluated.

Full results of the study will be reported at an upcoming medical conference.

About Tildacerfont

Spruce’s investigational lead product candidate, tildacerfont (formerly SPR001) is a potent, highly selective, oral, small-molecule antagonist of the corticotropin-releasing factor type-1 (CRF1) receptor. Preclinical studies have shown that through targeted delivery, tildacerfont binds to CRF1 receptors to block CRF-stimulated receptor function, thereby decreasing the production of excess androgens (androstenedione [A4]), progestins (17-hydroxyprogesterone [17-OHP]) and adrenocorticotrophic hormone (ACTH), the primary driver of adrenal gland enlargement. This may allow physicians to reduce the chronic, high-dose steroids used to treat patients with congenital adrenal hyperplasia (CAH), potentially allowing physicians and patients complete control of CAH.

Tildacerfont has been granted orphan drug status by both the FDA and EMA. For more information on tildacerfont, please visit www.sprucebiosciences.com.

About Spruce Biosciences

Spruce Biosciences is a clinical-stage biotechnology company focused on developing and commercializing novel therapies for rare endocrine disorders. The company's lead product candidate, tildacerfont, is an investigational oral drug that is being evaluated in Phase 2 studies for the treatment of congenital adrenal hyperplasia (CAH). The company also plans to evaluate tildacerfont in other diseases impacted by elevated ACTH or adrenal androgens. Backed by investors including Novo Holdings and RiverVest Venture Partners, Spruce is committed to bringing new treatment options to patients with unmet needs. For more information, please visit sprucebiosciences.com.

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