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Zafgen Announces Initial Results from Phase 2a Study of Beloranib in Patients with Prader-Willi Syndrome

Beloranib trial demonstrates improvements in body composition and cardiovascular risk factors in the largest placebo-controlled, double-blind, randomized multiple dose trial performed for obesity to date in patients with Prader-Willi syndrome

CAMBRIDGE, Mass – January 15, 2014 -- Zafgen, Inc., a leading biopharmaceutical company dedicated to addressing the unmet needs of severely obese patients, today announced initial results from its Phase 2a study of beloranib, a selective inhibitor of methionine aminopeptidase 2 (MetAP2), in patients with Prader-Willi syndrome (PWS), a severe form of genetic obesity. These results showed improvements in body weight, hunger-related behaviors, and body composition, including reductions in body fat content and preserved lean body mass following four weeks of treatment.

These changes were observed despite the increased caloric intake that was a component of this trial. Known markers of beloranib response including those associated with cardiovascular disease risk were also improved, demonstrating that PWS patients responded to the molecular mechanism of beloranib.

“The results of this short-term proof-of-concept study are very promising and underscore our belief that beloranib has the potential to successfully treat this severe form of obesity. To our knowledge, this study represents the largest placebo-controlled, randomized, multiple dose trial to date for obesity in this patient population, and these results bode well for further study of beloranib in patients with this devastating condition,” said Thomas Hughes, Ph.D., President and Chief Executive Officer of Zafgen.

Similar to results seen in non-PWS obese patient populations, beloranib treatment in this study reduced body fat content by 8.1% vs. placebo in four weeks of treatment at the highest study dose of 1.8 mg, despite a 50% increased daily caloric allowance. Hunger-related behaviors improved, and a trend towards overall improvement in body weight was seen, although this did not reach statistical significance, in part due to the fact that study was not powered to demonstrate these differences. Key hormones, including adiponectin and leptin, also showed changes characteristic of non-PWS obese patients, demonstrating that the drug was highly active in these patients and had a similar effect to that seen in non-PWS patients.

“These results are very exciting for the treatment of PWS, as most patients showed improvements in body weight, hunger-related behaviors, and body fat content, despite the increased food intake included in the trial design,” explained Dr. Jennifer Miller, Associate Professor of Pediatric Endocrinology, University of Florida, and Principal Investigator for the study. “PWS is a complex genetic disease that is difficult to treat and the results of this trial demonstrate that beloranib has a beneficial impact on this underserved patient population. Notably, we were encouraged by reports of fullness, a first-time occurrence for PWS patients who otherwise lack the capacity to feel sated after meals.”

“PWS patients remain severely impacted by their disease and are not treatable with other anti-obesity agents,” added Janalee Heinemann, Director of Research & Medical Affairs for the Prader-Willi Syndrome Association (USA). “PWS represents one of the most severe forms of genetic obesity and we welcome these results, which are a significant step towards finding a treatment for those suffering from this life threatening condition.”

Beloranib, a novel obesity therapy that utilizes a unique mechanism of action, is being studied for its ability to reduce body weight and improve cardiometabolic risk factors in obese patients with and without PWS. This study was a randomized, double-blind, placebo-controlled trial to evaluate the safety and tolerability of a dose range of beloranib administered as twice-weekly subcutaneous injections for four weeks. The randomized treatment part of the study was followed by an additional four weeks of open label treatment, the results of which are not yet available. The trial enrolled 17 patients with genetically confirmed PWS, including 11 women and 6 men, with a mean age of 33.9 years, and mean body mass index (BMI) of 31.4 kg/m^2. Beloranib appeared to be safe and very well-tolerated. All 17 patients completed the randomized treatment part of the trial and all opted to continue into and completed the four-week open label extension.

About Prader-Willi Syndrome

Prader-Willi syndrome (PWS), the most common known genetic cause of life-threatening obesity, causes constant hunger that drives PWS patients to gain more weight on fewer calories than the average person. As a result, many of those affected become morbidly obese before the age of five. There is currently no cure for this disease. Although the cause is complex, it results from a deletion or loss of function of a cluster of genes on the 15th chromosome. PWS typically causes low muscle

mass and function, short stature, incomplete sexual development, and a chronic feeling of hunger that, coupled with a metabolism that utilizes drastically fewer calories than normal, can lead to excessive eating and life-threatening obesity. PWS occurs in males and females equally and in all races, with the same incidence around the world. Prevalence estimates have ranged from 1:8,000 to 1:50,000 with the most likely figure being approximately 1:40,000. To the best of our knowledge, prevalence is about 5,000-7,000 people in the United States needing treatment. You can learn more through the Prader-Willi Syndrome Association website at www.pwsausa.org.

About Beloranib

Beloranib is the first compound in its class that works by targeting a key enzyme called MetAP2 that controls the production and utilization of fatty acids. Inhibitors of MetAP2 reduce the production of new fatty acid molecules by the liver and help to convert stored fats into useful energy. Beloranib is being developed as a twice-weekly subcutaneous injection for severe obesity. Zafgen holds exclusive worldwide rights (exclusive of Korea) for development and commercialization of beloranib. The company licensed beloranib from CKD Pharma in Korea.

About Zafgen, Inc.

Zafgen is an innovative company dedicated to addressing the unmet need of severely obese patients and related orphan indications by bringing beloranib, a first-in-class novel medicine, to market. Founded in 2005 as a virtual company, Zafgen brings together leading experts in obesity and metabolic disease to address the underserved and growing population of patients who are severely obese. Zafgen's singular focus is on advancing novel therapeutics for patients suffering from severe obesity and obesity-related disorders including Prader-Willi syndrome and patients with hypothalamic obesity, including obesity resulting from surgical treatment of craniopharyngioma. The company is located in Cambridge, MA.