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Zafgen Announces New Body Weight Loss and Cardiometabolic Data from Phase 2 Study of Beloranib in Obesity at American Diabetes Association's 73rd Scientific Sessions®

Interim Results Show Treatment with Beloranib Resulted in Clinically Meaningful Body Weight Loss and Improvements in Multiple Cardiometabolic Risk Factors in Severely Obese Subjects

CHICAGO – June 22, 2013 – Zafgen, Inc. today announced new data from an interim analysis conducted from an ongoing Phase 2 study of beloranib, a selective methionine aminopeptidase 2 (MetAP2) inhibitor. The 12-week study interim results showed rapid, progressive, and sustained clinically meaningful body weight loss of up to ~10 kg, improvements in cardiovascular risk factors and an encouraging tolerability and safety profile.

These findings were demonstrated in a 12-week study, which is the longest duration of treatment in humans with beloranib to date. The data will be presented in a late-breaking poster session at the American Diabetes Association's 73rd Scientific Sessions in Chicago at noon CST on Sunday, June 23, 2013.

Beloranib, a novel obesity therapy that restores the balance and utilization of fat, is being studied for its ability to treat obesity. These interim results of the 12-week Phase 2 trial follow the completion of three consecutive 4-week Phase 1b studies demonstrating rapid and significant weight loss, reductions in body fat, improvements in cardiovascular risk factors, and an encouraging tolerability and safety profile.

This double-blind, placebo-controlled study investigated the safety, tolerability, pharmacokinetics and metabolic effects of beloranib in obese men and women. Patients received beloranib or placebo administered through subcutaneous injections given twice-weekly over a 12-week period. Patients were allowed to eat normally and were not counseled to change their exercise habits.

Patients had a mean age of 40.3 years, with body weight of 101.2 kg, and a body mass index (BMI) of 37.9 kg/m^2. Patients receiving 12 weeks of treatment in the full trial were randomized to 0.6 mg (n = 37), 1.2 mg (n = 37), or 2.4 mg (n = 36) of subcutaneous beloranib vs. placebo (n = 38). The pre-specified interim analysis reflects results obtained in the first 19 patients completing 12 weeks of treatment with 0.6 mg (n = 5), 1.2 mg (n = 6), or 2.4 mg (n = 3) of subcutaneous beloranib vs. placebo (n = 5) as an initial dose-selection cohort that preceded enrollment of the complete Phase 2 study, for which results are expected in summer, 2013.

Beloranib appeared safe and showed dose responsive weight loss. After 12 weeks, subjects on 0.6 mg, 1.2 mg, or 2.4 mg lost an average of (± SEM) -3.8 ± 0.8 kg, -6.1 ± 1.5 kg, and -9.9 ± 2.3 kg, respectively, vs. +1.8 ± 0.4 kg for placebo (all $p<0.005$ vs. placebo). Additionally, patients treated with beloranib showed improvements in cardiometabolic risk factors including reduced triglycerides, LDL cholesterol and C-reactive protein (an inflammatory marker) vs. placebo. Sense of hunger also was reduced significantly.

Beloranib treatment for 12 weeks generally was well-tolerated by subcutaneous administration. The most common adverse effects with higher incidence during beloranib treatment were nausea, vomiting, and sleep disturbance. There were no severe or serious adverse events or deaths.

"We are encouraged to see such promising results with our longest duration of treatment to date," said Thomas E. Hughes Ph.D., President and CEO of Zafgen. "The results mark a major milestone for Zafgen and set the stage for advancement to more comprehensive trials to establish safety and efficacy of beloranib."

"The need for new options for severely obese patients has never been greater," said Caroline Apovian, M.D., F.A.C.N., professor of Medicine and Pediatrics, in the section of Endocrinology, Diabetes, and Nutrition, at Boston University School of Medicine. "Beloranib is showing promise as a novel approach in this field, and the dramatic weight loss seen after only 12 weeks is very impressive." Dr. Apovian is also director of the Center for Nutrition and Weight Management at Boston Medical Center and serves on the Zafgen Clinical Advisory Board.

Results from the complete Phase 2 study are expected in summer, 2013. More information about the study is available at ClinicalTrials.gov.

About Fat Metabolism and Beloranib

Research continues to show that obese and lean individuals metabolize fat differently. Studies indicate that once a person becomes obese, the body undergoes certain metabolic changes and is “programmed” to make and store more fat, making it much more difficult to reduce body weight. These metabolic adaptations that take place in obese people impair the normal release and breakdown of fatty acids from adipose tissue. Simultaneously, the body becomes much more efficient in diverting calories from food and storing them as fat.

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 by bringing beloranib, a first-in-class novel medicine, to market. Founded in 2005 as a capital efficient 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. The company is located in Cambridge, MA.