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Zafgen Announces Additional Weight Loss and Cardiometabolic Data from Phase 1 Studies of Beloranib in Obesity at American Diabetes Association's 72nd Scientific Sessions®

Results Show Treatment with Beloranib Resulted in Weight Loss and Corresponding Reductions in Multiple Cardiometabolic Risk Factors in Severely Obese Subjects

PHILADELPHIA, June 10, 2012 – Zafgen, Inc., the world's first biopharmaceutical company dedicated to addressing the unmet need of severely obese patients, today announced new data from two Phase 1 studies of beloranib, a selective methionine aminopeptidase 2 inhibitor (MetAP2), which showed significant weight loss and improvements in cardiometabolic risk markers in severely obese women. Treatment with beloranib was associated with improvements in weight loss and triglycerides, LDL cholesterol, waist circumference and diastolic blood pressure, with no evidence of major tolerability or safety issues. Body composition measured in one study indicated a reduction in fat mass with beloranib. The data will be presented in a poster session at the American Diabetes Association's 72nd Annual Scientific Sessions in Philadelphia on June 10th at noon EST.

Beloranib, a novel obesity therapy that utilizes a unique mechanism of action, is being studied for its ability to restore balance to the production and utilization of fat. The Phase 1 trials were randomized, double-blind, placebocontrolled studies to evaluate the safety, tolerability and efficacy of twice-weekly intravenously administered beloranib in severely obese women with a body mass index (BMI) of 39.1±3.7 BMI kg/m2. Individuals received 0.9 mg/m², 3 or 6 mg beloranib (beloranib N=17) or placebo (N=11) twice weekly over a 25-day period (7 doses). Patients were allowed to eat normally and were not counseled to change their exercise habits. The trial enrolled 34subjects of which 28 completed the study.

After 25 days of treatment, subjects treated with beloranib had lost significantly more weight (mean±SE: 4.3±0.4 kg; $p<0.001$, paired t test for change from baseline) versus the group that received placebo (-0.6±0.5 kg, NS).

Additionally, subjects treated with beloranib showed improvements in cardiometabolic risk factors including reduced triglycerides (mean±SE: -34.4±8.8 mg/dL), LDL cholesterol (-34.1±8.0 mg/dL), waist circumference (3.9±0.9 cm), and diastolic blood pressure (-4.5±2.1 mmHg; all $p<0.05$, paired t test for change from baseline), and C-reactive protein (-64%, $p<0.001$) whereas there was no change with placebo.

There was a trend for beloranib to be associated with a reduction in the percentage of subjects with metabolic syndrome that did not reach statistical significance. Body composition, measured in one study by bioelectric impedance, (N=9 beloranib 3 and 6 mg, N=8 placebo) indicated expected reduction in fat mass with beloranib.

The most common adverse events were nausea, infusion site injury and headache. Most events were of mild/moderate intensity and tended to be self-limiting.

"The need for new, effective agents for the treatment of obesity has never been greater," said Tom Hughes, president and CEO of Zafgen. "Options for people suffering from severe obesity are particularly limited because these patients are often beyond reach of other agents and have co-morbidities that put them at higher risk of serious, costly complications and death. We look forward to progressing clinical studies with beloranib, which is a promising new option for those with the most severe form of this disease."

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.

About Beloranib
Beloranib is the first compound in its class that works by targeting a key enzyme called methionine aminopeptidase 2 (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.

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 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. The company is located in Cambridge, MA.