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# Zafgen Presents Positive Safety and Efficacy Data From Phase 2 Trial of Beloranib in Severe Obesity and Proof of Concept Trial in Prader-Willi Syndrome at ECO 2015

**Poster Numbers: PO.111, PO.112**

*Beloranib Treatment Led to Rapid and Significant Weight Loss and Improvements in Cardiometabolic Biomarkers, Supports Potential to Improve Common Co-Morbid Conditions*

PRAGUE, Czech Republic, May 8, 2015 (GLOBE NEWSWIRE) -- Zafgen, Inc. (Nasdaq:ZFGN), a biopharmaceutical company dedicated to significantly improving the health and well-being of patients affected by obesity and complex metabolic disorders, today announced positive efficacy and safety data from its ZAF-201 Phase 2 trial of beloranib, a MetAP2 inhibitor, in obese patients. The Company also announced efficacy and safety data from ZAF-211, a proof of concept study of beloranib in patients with Prader-Willi syndrome (PWS). These findings, presented at the 22$^{nd}$ European Congress on Obesity (ECO) on May 7-8, 2015 in Prague, Czech Republic, demonstrated meaningful weight loss and improvement in cardiometabolic biomarkers.

"We are very pleased to present these results to the European obesity research community from our trials in patients with severe obesity and PWS, which demonstrated that treatment with beloranib is not only safe, but also showed meaningful improvements in body weight in obese patients," said Thomas Hughes, Ph.D., Chief Executive Officer of Zafgen. "In both trials, beloranib treatment also improved a variety of biomarkers associated with cardiovascular disease risk and inflammation, supporting its potential to improve common co-morbid conditions affecting patients with obesity and PWS."

Beloranib is a novel, first-in-class injectable small molecule therapy with a unique mechanism of action that reduces drive to eat while stimulating the use of stored fat as an energy source.

**Severe Obesity Results (ZAF-201)**

ZAF-201, a Phase 2 randomized, double-blind, placebo-controlled trial evaluated the efficacy, safety and tolerability of beloranib 0.6 mg, 1.2 mg or 2.4 mg administered as twice-weekly subcutaneous injections for 12 weeks in patients with severe obesity. The trial enrolled 147 men and women, of which 117 completed the study. The mean age of patients was 48.4 years, and body mass index (BMI) and body weight (BW) was consistent with Class 2 obesity (approximately 38 kg/m$^2$ and 100 kg, respectively). Patients were not counseled to adhere to any diet or exercise regimens as part of the trial.

Results from this trial showed that 12 weeks of treatment with beloranib led to sustained, progressive, and dose-dependent weight loss of up to ~11 kg from baseline. Additionally, beloranib treatment significantly reduced sense of hunger and prospective food intake, and known markers of beloranib response, including major cardiovascular risk factors and markers of inflammation, were also improved at 12 weeks.

Significant reductions in total and LDL cholesterol and triglyceride levels and an increase in HDL cholesterol were noted in the beloranib 2.4 mg group. A significant increase in HDL cholesterol and decrease in triglyceride levels was observed with beloranib 1.2 mg. Consistent with reduced fat mass and improved adipose tissue function and inflammation, significant ($p < 0.001$) changes in adiponectin, leptin, and hs-CRP were observed with beloranib.

**PWS Results (ZAF-211)**

PWS is the most common known genetic cause of life-threatening obesity and results in constant and unrelenting hunger that drives patients with PWS to engage in problematic hunger-related behaviors and gain excessive weight. As a result, many of those affected become morbidly obese and suffer significant mortality.

The proof of concept study with beloranib enrolled adult patients with PWS and started with a two-week, single-blind, placebo lead-in period followed by a four-week, double-blind, randomized, treatment period of beloranib 1.2 mg, 1.8 mg, or placebo administered as twice-weekly subcutaneous injections. An optional four-week, open-label extension phase was also offered to patients. The trial enrolled 17 patients with confirmed PWS, all of whom completed the study, with a mean age of 33.5 years, mean BMI of 31.4 kg/m$^2$ and mean BW of 71.8 kg. The study design allowed for a 50% increase in calorie intake for the duration of the study to account for stringent calorie restriction being enforced at the group home where these patients were housed.

Results from this trial showed that beloranib appeared safe and well-tolerated, and led to dose-dependent body and total fat mass reductions despite 50% increase in total daily calorie intake. Treatment with beloranib also reduced hyperphagia-related behaviors typical of patients with PWS, and improved biomarkers associated with cardiovascular disease risk and adipose tissue function. The effects of beloranib treatment on body mass and total fat mass in this trial were similar to those seen in non-PWS obese patients, indicating that beloranib effects are evident in PWS as well.

"The results of this proof of concept study are important, as treatment with beloranib reduced hyperphagia-related (compulsive overeating) problem behaviors typical of PWS," said Dennis Kim, M.D., Chief Medical Officer at Zafgen. "Beloranib continues to demonstrate promising results, and this study supports its potential as a safe and effective treatment option for this unique patient population. Based on these study results, Zafgen has moved forth with the program in PWS and is currently conducting a Phase 3 clinical trial in the United States that we refer to as the *bestPWS* trial."

**Safety and Tolerability**

In both trials, there were no reports of severe adverse events (SAEs) or AEs leading to early study withdrawal in patients receiving beloranib; the most common AE was injection site bruising of mild intensity comparable between beloranib and placebo groups. In the Phase 2 trial of beloranib in severe obesity, the most common cause for early study withdrawal was sleep-related, mainly a delay of onset of sleep.

Other commonly reported AEs included nausea, diarrhea and headache. These AEs were generally mild and transient in nature. In addition, no clinically significant abnormal laboratory measures, vital signs, or electrocardiography (ECG) findings were observed in either trial.

**About Beloranib**

Beloranib is a novel, first-in-class injectable small molecule therapy with a unique mechanism of action that reduces hunger while stimulating the use of stored fat as an energy source. Beloranib is a potent inhibitor of methionine aminopeptidase 2, or MetAP2, an enzyme that modulates the activity of key cellular processes that control metabolism. MetAP2 inhibitors work, at least in part, by directing MetAP2 binding to cellular stress mediators, and, thus, reducing the tone of signals that drive lipid synthesis by the liver and fat storage throughout the body. In this manner, MetAP2 inhibition increases metabolism of fat as an energy source. Zafgen holds exclusive worldwide rights (exclusive of South Korea) for the development and commercialization of beloranib. Zafgen exclusively licensed beloranib from Chong Kun Dang (CKD) Pharmaceutical Corp. of South Korea.

**About Severe Obesity**

Severely obese people are among the most medically underserved populations globally, beyond reach of currently approved therapies and are at increased risk for serious health issues and premature death. According to the Centers for Disease Control and Prevention, more than one-third of U.S. adults are obese, and for those who are severely obese, getting to a healthier state is especially difficult because their bodies become "programmed" to create and store more fat. There currently are no approved medical therapies that fully address the biological mechanisms of obesity, and many patients are still beyond reach of meaningful treatment with current therapies.

**About Prader-Willi Syndrome (PWS)**

Prader-Willi syndrome (PWS), the most common known genetic cause of life-threatening obesity, results in constant and unrelenting hunger that drives patients with PWS to engage in problematic hunger-related behaviors and gain excessive weight. As a result, many of those affected become morbidly obese and suffer significant mortality. 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.

**About Zafgen**

Zafgen (Nasdaq:ZFGN) is a biopharmaceutical company dedicated to significantly improving the health and well-being of patients affected by obesity and complex metabolic disorders. Zafgen is focused on developing novel therapeutics that treat the underlying biological mechanisms through the MetAP2 pathway. Beloranib, Zafgen's lead product candidate, is a novel, first-in-class, twice-weekly subcutaneous injection being developed for the treatment of multiple indications, including severe obesity in two rare diseases, Prader-Willi syndrome and obesity caused by hypothalamic injury, including craniopharyngioma-associated obesity; and severe obesity in the general population. Zafgen aspires to improve the lives of patients through targeted treatments and has assembled a team accomplished in bringing therapies to patients with both rare and prevalent metabolic diseases.

**Safe Harbor Statement**

Various statements in this release concerning Zafgen's future expectations, plans and prospects, including without limitation, Zafgen's expectations regarding beloranib as a treatment for HIAO, Prader-Willi syndrome, and severe obesity in the general population, its expectations with respect to the timing and success of its clinical trials, the expected requirements and timing of additional clinical trials and pre-clinical studies, and its plans regarding commercialization of beloranib may constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995 and other federal securities laws. Forward-looking statements can be identified by terminology such as "anticipate," "believe," "could," "could increase the likelihood," "estimate," "expect," "intend," "is planned," "may," "should," "will," "will enable," "would be expected," "look forward," "may provide," "would" or similar terms, variations of such terms or the negative of those terms. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including, without limitation, Zafgen's ability to successfully demonstrate the efficacy and safety of its product candidates, the pre-clinical and clinical results for its product candidates, which may not support further development, actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials, obtaining, maintaining and protecting its intellectual property, Zafgen's ability to enforce its patents against infringers and defend its patent portfolio against challenges from third parties, competition from others developing products for similar uses, Zafgen's ability to manage operating expenses, Zafgen's ability to obtain additional funding to support its business activities and establish and maintain strategic business alliances and new business initiatives, Zafgen's dependence on third parties for development, manufacture, marketing, sales and distribution of products, the outcome of litigation, and unexpected expenditures, as well as those risks more fully discussed in the section entitled "Risk Factors" in Zafgen's most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission, as well as discussions of potential risks, uncertainties, and other important factors in Zafgen's subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent Zafgen's views only as of today and should not be relied upon as representing its views as of any subsequent date. Zafgen explicitly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

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