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Zafgen Announces New Weight Loss and Safety Data from Phase 2 Trial of Beloranib in Hypothalamic Injury Associated Obesity at ENDO 2015

Beloranib Treatment Led to Rapid and Significant Weight Loss and Improvements in Cardiometabolic Biomarkers, Similar to Results Seen in Conventional Obesity Patients

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SAN DIEGO, March 7, 2015 (GLOBE NEWSWIRE) -- Zafgen, Inc., 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 a recently completed Phase 2 trial of beloranib, a MetAP2 inhibitor, in patients with hypothalamic injury associated obesity (HIAO). These findings, presented for the first time at the Endocrine Society Annual Meeting (ENDO) on March 7, 2015, demonstrated meaningful and statistically significant weight loss and improvement in cardiometabolic biomarkers.

"We are very pleased with the results from this latest study of patients with HIAO, which demonstrated proof of concept for both the safety and effectiveness of beloranib on body weight and cardiovascular risk markers in this patient population," said Thomas Hughes, Ph.D., Chief Executive Officer of Zafgen. "These positive results also indicate that the efficacy of beloranib in HIAO patients is similar to that observed in conventionally obese patients, as beloranib treatment leads to meaningful and statistically significant weight loss in both patient populations."

HIAO is a rare form of medically induced obesity resulting from damage to the hypothalamus following resection of central nervous system tumors such as craniopharyngiomas. The hypothalamus is a homeostatic control center in the brain that provides oversight of multiple hormonal systems, metabolic rate, hunger, and satiety. Patients affected by HIAO fail to regulate metabolism and food intake normally, resulting in rapid and intractable weight gain, treatment resistant severe obesity, and associated co-morbidities.

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.

This Phase 2 randomized, double-blind, placebo-controlled trial evaluated the efficacy, safety and tolerability of beloranib 1.8 mg administered as twice-weekly subcutaneous injections for four weeks followed by an optional 4-week, open-label extension. The trial enrolled 14 patients who were mostly women with a mean age of 31.9 years, mean body mass index (BMI) of 42.9 kg/m² and mean body weight (BW) of 126.4 kg. All patients had radiographic evidence of hypothalamic damage with documentation of subsequent rapid and significant BW gain. Patients were not counseled to adhere to any diet or exercise regimens as part of the trial.

Results from this trial showed that after four weeks of treatment, patients randomized to beloranib lost on average (\pm standard error of mean) -3.40 ± 0.6 kg of BW vs. -0.25 ± 0.8 kg for placebo ($p=0.01$). Results from the open-label extension suggested no apparent waning of the effect of beloranib within eight weeks of treatment. Furthermore, known markers of beloranib response, including major cardiovascular risk factors such as lipid parameters and markers of inflammation, were also improved at both four and eight weeks of treatment, corresponding with beloranib treatment.

In this Phase 2 trial, there were no early discontinuations due to adverse events (AEs), severe AEs or serious AEs in patients receiving beloranib. In addition, no clinically significant abnormal laboratory measures, vital signs, or electrocardiography (ECG) findings were observed. The most common AEs occurring in more than one patient treated with beloranib were dizziness, headache, and nasopharyngitis. These AEs were generally mild and transient in nature.

"The results of this proof of concept study are important, as they show that beloranib has a unique mechanism of action which mediates weight loss through actions independent from a fully functional hypothalamus," said Ashley H. Shoemaker, M.D., M.S.C.I., Assistant Professor of Pediatric Endocrinology and Diabetes at Vanderbilt University. "Beloranib continues to demonstrate promising results, and results from this study support its potential as a safe and effective treatment option for this unique patient population."

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 Hypothalamic Injury-Associated Obesity (HIAO)

HIAO is most commonly caused by damage incurred during removal of a central nervous system tumor called craniopharyngioma but it can also result from less common types of hypothalamic injury such as strokes, brain trauma, or radiation therapy to the brain. Craniopharyngioma is a rare form of benign brain tumor that occurs most commonly during childhood and infiltrates near the optic nerve, pituitary gland and the hypothalamus. Treatment of these tumors commonly involves surgical removal of the tumor mass, followed by radiation treatment, which results in disruption or removal of neighboring structures including the hypothalamus. Post-treatment hypothalamic dysfunction results in hyperphagia and significant obesity in up to 50% of these patients, resulting in a variety of co-morbid conditions and a deteriorated quality of life. Craniopharyngioma-associated obesity occurs in males and females equally and in all races, with the same incidence around the world. The incidence estimates have ranged from 0.13 to 0.17 per 100,000 per year, or approximately 400 to 500 new cases per year in the United States and 650 to 850 new cases per year in the European Union.

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 Quarterly Report on Form 10-Q 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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