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Zafgen Presents New Data from the Phase 2b Clinical Trial Evaluating Beloranib in Severe Obesity Complicated by Type 2 Diabetes at the American Diabetes Association's 76th Scientific Sessions

Beloranib demonstrates statistically and clinically significant improvements in body weight, body composition, and glycemic control in ZAF-203 clinical trial

NEW ORLEANS, June 11, 2016 (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 new data from the ZAF-203 clinical trial evaluating beloranib, a MetAP2 inhibitor, for the treatment of severe obesity complicated by type 2 diabetes. Data presented today during the American Diabetes Association's 76th Scientific Sessions showed that beloranib was associated with improvement in body composition, including a significant decrease in body weight, fat mass, reduction in waist and hip circumference, and improvements in liver fat, as well as glycemic control parameters including HbA1c, fasting plasma glucose (FPG), post-prandial glucose, beta-cell function, and insulin sensitivity, when compared to placebo.

As previously reported, the ZAF-203 clinical trial achieved its primary efficacy endpoint, as beloranib demonstrated a statistically significant reduction in body weight compared to placebo. Patients enrolled in both the 1.8 mg and 1.2 mg treatment arms also met a key secondary endpoint, with patients in each dose arm achieving, on average, an absolute reduction in HbA1c following six months of treatment of 2.0 percent compared to a reduction of 0.6 percent for placebo.

"These results reinforce the potential of MetAP2 inhibition as an approach to treating metabolic disorders associated with obesity, and point to potential improvements in both pancreatic function and insulin sensitivity as contributors to improved glycemic control," stated Thomas Hughes, Ph.D., Chief Executive Officer of Zafgen. "Additionally, these data add to the compelling and consistent efficacy data that have emerged across our beloranib clinical trials, while offering greater perspective on its benefit-risk profile."

ZAF-203 Efficacy and Safety Results

In the ZAF-203 clinical trial, 152 patients were randomized and received twice-weekly subcutaneous injections of either 1.8 mg or 1.2 mg of beloranib or placebo, in addition to a diet and exercise regimen. Sixty-six patients comprised the pre-specified primary analysis population, completing six months of treatment in compliance with the protocol prior to the Company's suspension of dosing in the trial at the time the FDA placed a partial clinical hold on the beloranib IND in October 2015.

The primary analysis population were a mean age of 55, had a body mass index (BMI) of 39.0 kg/m^2, fat mass of 36-42 percent, and average HbA1c levels of 8.3 percent at baseline.

Primary Endpoint

	Average Weight at Baseline (kg)	*Change in Body Weight	*Percent Change in Body Weight	*p-value
1.8 mg beloranib (n=19)	109.1	-14.2	-12.7	<0.0001
1.2 mg beloranib (n=25)	120.4	-15.0	-13.5	<0.0001
Placebo (n=22)	103.2	-3.8	-3.1	

**Endpoint results shown are Least Squares mean values. p-value is the test of the difference from placebo. Similar results were obtained for the 152-patient intent to treat (ITT) population using a mixed-model repeated measures (MMRM) statistical method.*

- 95% (p<0.0001) and 92% (p<0.0001) of patients enrolled in the 1.8 mg and 1.2 mg treatment arms achieved a 5% reduction in body weight, versus 27% of placebo-treated patients
- 74% (p<0.0001) and 64% (p<0.0001) of patients enrolled in the 1.8 mg and 1.2 mg treatment arms achieved a 10%

reduction in body weight, versus 5% of placebo-treated patients

Secondary Endpoints
Beloranib treatment was associated with statistically significant and clinically meaningful reductions in HbA1c and several other glycemic control parameters.

	Average HbA1c at Baseline	*Average HbA1c at Week 26	*Absolute Change in HbA1c	*p-value
1.8 mg beloranib (n=19)	8.2%	6.3%	-2.0%	<0.0001
1.2 mg beloranib (n=25)	8.5%	6.3%	-2.0%	<0.0001
Placebo (n=22)	8.1%	7.7%	-0.6%	

**Endpoint results shown are Least Squares mean values. p-value is the test of the difference from placebo.*

- 74% (p<0.01) and 72% (p<0.01) of patients enrolled in the 1.8 mg and 1.2 mg treatment arms achieved the treatment goal of <7% HbA1c at six months, versus 23% of placebo-treated patients
- 63% (p<0.01) and 68% (p <0.01) of patients enrolled in the 1.8 mg and 1.2 mg treatment arms achieved the treatment goal of ≤6.5% HbA1c at six months, versus 18% of placebo-treated patients
- At Week 26, least squares mean HbA1c in beloranib-treated patients was 6.3%.

Patients treated with beloranib demonstrated statistically significant decreases from baseline in fasting plasma glucose compared to placebo at all time points (p<0.01 for both doses). Clinically meaningful reductions from baseline in mean postprandial plasma glucose concentrations were observed with both beloranib doses compared to placebo. The overall area under the curve for postprandial plasma glucose was decreased at all post-baseline assessments with either 1.8 or 1.2 mg of beloranib versus placebo. In addition, after 26 weeks, there was a significant improvement in β-cell function (HOMA2 %B) with both doses of beloranib compared to placebo. Furthermore, insulin sensitivity (HOMA2 %S) was significantly improved in patients that received the 1.2 mg dose of beloranib compared to placebo.

These observed improvements in HbA1c and improvements in other markers of glycemic control, including reduced fasting plasma glucose, reduced postprandial glucose, improved β-cell function, and improved insulin sensitivity, occurred without any attendant increase in the risk of hypoglycemia.

In this clinical trial, beloranib treatment was also associated with statistically significant improvements in body composition which was measured using bioimpedance.

Patients treated with 1.8 mg and 1.2 mg beloranib had consistent reduction in fat mass that was statistically significant compared to placebo at Week 12 and Week 26. Furthermore, in those treated with beloranib, fat mass accounted for approximately 75 percent of weight loss, which is consistent with that observed with other interventions including diet and exercise. In this clinical trial, there was also a small but significant reduction in lean mass in beloranib-treated subjects compared to no change in placebo-treated subjects.

	Change in Fat Mass	Change in Lean Mass
1.8 mg beloranib (n=19)	-21.7 % p<0.001	-5.7% p<0.05
1.2 mg beloranib (n=25)	-24.1% p<0.001	-5.0% p<0.05
Placebo (n=22)	-7.4%	0.6%

Beloranib-treated patients also had improvements in waist and hip circumference, liver fat, leptin, and adiponectin compared with placebo (p<0.05).

The most common adverse events (AEs) in the clinical trial were upper respiratory tract infection, diarrhea, and injection site bruising. These were generally mild and transient in nature and occurred at comparable incidence rates between beloranib and placebo treated patients. Ten patients in the beloranib groups (five in each of the 1.8 mg and 1.2 mg groups) withdrew due to AEs compared to two patients in the placebo group. Consistent with prior beloranib clinical trials in conventional obesity, the most common causes of AEs leading to early withdrawal were sleep related, leading to four withdrawals from the clinical trial. In the clinical trial, there were a total of nine serious adverse events (SAEs) identified in eight patients, one in the 1.8 mg group, six in the 1.2 mg group, and two in the placebo group. As previously disclosed, one of the SAEs was a

pulmonary embolism in the 1.2 mg treatment group. During the VTE screening process that followed the FDA's partial clinical hold on the beloranib IND in October 2015, two additional VTEs were identified in patients in this clinical trial: deep vein thrombosis in a patient who had received 1.8 mg of beloranib, and superficial thrombophlebitis in a patient who had received 1.2 mg of beloranib.

The FDA placed a full clinical hold on the beloranib IND in December 2015.

About Beloranib
Beloranib is a novel, first-in-class injectable small molecule therapy that works by inhibiting MetAP2, an enzyme that modulates the activity of key cellular processes that control metabolism. Once a person becomes obese, the body undergoes certain metabolic changes and becomes "programmed" to create and store more fat, making it much more difficult to reduce body weight. Beloranib is believed to help reduce hunger and restore balance to fat metabolism, enabling calories to once again be used as a productive energy source. Because beloranib works beyond just regulating hunger through the hypothalamus, it has the potential to be used in a variety of complex metabolic disorders such as Prader-Willi syndrome and hypothalamic injury associated obesity. Zafgen holds exclusive worldwide rights (exclusive of South Korea) for the development and commercialization of beloranib. Zafgen exclusively licensed beloranib from Chong Kun Dang Pharmaceutical Corporation (CKD Pharma) of South Korea.

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 is also developing ZGN-839, a liver-targeted MetAP2 inhibitor, for the treatment of nonalcoholic steatohepatitis, or NASH, and abdominal obesity, as well as second-generation MetAP2 inhibitors, which may be developed for the treatment of 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 PWS and obesity caused by hypothalamic injury, including craniopharyngioma-associated obesity, Zafgen's expectations regarding the use of other MetAP2 inhibitors as treatments for other forms of severe obesity, including severe obesity in the general population, Zafgen's expectations with respect to the timing and success of its non-clinical studies and clinical trials of beloranib and its other product candidates, the expected requirements and timing of additional requirements for planned clinical trials, and the need for additional clinical trials and pre-clinical studies, and Zafgen's 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 obtain a release of the full clinical hold that the FDA placed on the investigational new drug application for beloranib, Zafgen's ability to successfully demonstrate the efficacy and safety of beloranib and its other product candidates, the pre-clinical and clinical results for beloranib and its other product candidates, which may not support further development and marketing approval, actions of regulatory agencies, which may affect the initiation, timing and progress of pre-clinical studies and clinical trials, Zafgen's ability to obtain, maintain and protect 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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