February 18, 2016

Zafgen's Phase 2b Trial of Beloranib in Severe Obesity Complicated by Type 2 Diabetes Achieves Primary Efficacy Endpoint

- Beloranib demonstrates statistically and clinically significant improvements in body weight and glycemic control over six months of randomized treatment —

-Conference call scheduled for 8:30 AM Eastern Time-

BOSTON, Feb. 18, 2016 (GLOBE NEWSWIRE) -- Zafgen (Nasdaq:ZFGN), a biopharmaceutical company dedicated to significantly improving the health and well-being of patients affected by obesity and complex metabolic disorders, announced today positive efficacy results from its Phase 2b ZAF-203 clinical trial evaluating beloranib, a MetAP2 inhibitor, in the treatment of severe obesity complicated by type 2 diabetes. The clinical trial achieved its primary efficacy endpoint, as treatment with the 1.8 mg and the 1.2 mg doses of beloranib resulted in 12.7 percent ($p<0.0001$) and 13.5 percent ($p<0.0001$) reductions in body weight, respectively, compared with a reduction of 3.1 percent for 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 of 2.0 percent compared to a reduction of 0.6 percent for placebo.

"These results reinforce the strong efficacy profile of beloranib and further inform the potential of our MetAP2 inhibitor platform to impact metabolic disorders," stated Thomas Hughes, Ph.D., Chief Executive Officer of Zafgen. "In addition to the recent positive efficacy data from our bestPWS clinical trial, these data provide additional context regarding beloranib's benefit-risk profile in the treatment of severe forms of obesity. We look forward to discussing these results with the FDA as we work to establish a path forward for beloranib in Prader-Willi syndrome and other orphan obesity indications."

On January 20, 2016, Zafgen announced that the pivotal bestPWS ZAF-311 Phase 3 clinical trial of beloranib in Prader-Willi syndrome (PWS) had achieved its co-primary endpoints, demonstrating statistically significant and clinically meaningful weight loss and improvement in hyperphagia-related behaviors at both the 2.4 mg and 1.8 mg dose levels. Zafgen plans to present to the FDA the data from the ZAF-311 clinical trial, data from this ZAF-203 Phase 2b clinical trial, and a proposal for a risk mitigation strategy for beloranib in PWS in an effort to resolve the complete clinical hold the FDA placed on the beloranib IND in December 2015.

Dr. Hughes added, "We are actively working to better understand the mechanisms and incidence of underlying thromboembolic disease in PWS and severe obesity, as well as the potential impact of beloranib treatment on thrombosis in order to develop a strategy for risk mitigation."

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 of the partial clinical hold in October 2015.

	Average Weight at Baseline (kg)	*Change in Body Weight (kg)	*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 Squared 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

Beloranib treatment was associated with statistically significant and clinically meaningful reductions in HbA1c.

	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 Squared 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.*

- 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

"Obesity complicated by type 2 diabetes represents a serious public health concern with limited treatment success," said Dr. Joseph Proietto, Professor Emeritus at the University of Melbourne. "The compelling and clinically meaningful efficacy results of this long-term study demonstrate beloranib's unique mechanism of action and further validate investigation of MetAP2 inhibition as a potential treatment for obesity disorders and related co-morbidities, particularly in this difficult-to-treat population."

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 of 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.

Zafgen plans to present further data from the ZAF-203 Phase 2b trial at upcoming medical meetings.

Conference Call Information

Zafgen will host an investor conference call today, February 18, 2016 at 8:30 a.m., Eastern Time, to discuss the trial results in more detail. Investors and other interested parties may participate by dialing (844) 824-7428 in the United States or (973) 500-2177 outside the United States and referencing conference ID number 52656958. The call will also be webcast live on the Company's website at http://ir.zafgen.com/events.cfm. You can access the replay for seven days following the call by dialing (855) 859-2056 in the United States or (404) 537-3406 outside the United States and referencing conference ID number 52656958.

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. 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, obesity caused by hypothalamic injury, including craniopharyngioma-associated obesity, and other forms of severe obesity, including severe obesity in patients with type 2 diabetes, 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 preclinical 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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