



Zafgen Presents New Data Highlighting Potential of ZGN-1061 for the Treatment of Type 2 Diabetes and Obesity at the American Diabetes Association's 77th Annual Scientific Sessions

-Successful Phase 1 Clinical Trial Garner's Late-Breaking ADA Presentation and Supports Advancement to Phase 2 Development-

-ZGN-1061 Treatment Improves Glycemic Control and Body Weight in Preclinical Models-

-Data Highlight Favorable Safety and Tolerability Profile-

BOSTON, June 10, 2017 -- Zafgen, Inc. (Nasdaq:ZFGN) today announced the presentation of new data for ZGN-1061, the Company's second-generation MetAP2 inhibitor, in two late-breaking posters at the American Diabetes Association's 77th Annual Scientific Sessions (ADA). The data show that ZGN-1061 treatment causes improvements across multiple metabolic measures consistent with MetAP2 inhibition, demonstrates rapid drug absorption and clearance, and has a favorable safety profile with no evidence of prothrombotic effects. The poster presentations, numbers 143-LB and 144-LB, are available on the ["Events & Presentations"](#) section of the Zafgen website.

"The results presented at ADA highlight the favorable safety and pharmacokinetic profile of ZGN-1061 and demonstrate its potential to positively impact glycemic control, weight loss and other metabolic parameters," stated Thomas Hughes, Ph.D., President and Chief Executive Officer of Zafgen. "Based on the data generated to date, as well as our deep experience with MetAP2 inhibition, we believe ZGN-1061 offers a novel opportunity to address the unmet medical need of patients failing other therapies and who are at the challenging interface of type 2 diabetes and obesity."

Phase 1 Clinical Trial Data

Poster 144-LB, "Single and Multiple Dose Evaluation of a Novel MetAP2 Inhibitor: Results of a Randomized, Double-Blind, Placebo-Controlled Clinical Trial," details the full results from the Phase 1 clinical trial of ZGN-1061, including new efficacy data related to secondary endpoints. The multiple ascending dose (MAD) phase evaluated twice-weekly administration of ZGN-1061 in overweight or obese patients (ZGN-1061 N=22, placebo N=7; average BMI of 33 kg/m²). Patients in the MAD phase were domiciled while receiving treatment and were subjected to inpatient safety monitoring for most of the clinical trial's 28-day duration. Data from the clinical trial are highlighted below:

- As previously reported, on average, patients treated with ZGN-1061 for four weeks lost weight relative to placebo-treated patients (-4.6 lbs, -2.2 lbs, and -3.8 lbs for 0.2 mg, 0.6 mg, and 1.8 mg, respectively vs. -0.51 lbs for placebo).
- Body weight loss was steady and progressive during treatment with ZGN-1061 and rebounded post-treatment, supporting a drug effect.
- ZGN-1061 produced improvements in waist circumference relative to placebo. In addition, treatment with ZGN-1061 resulted in a trend for reduced food intake relative to placebo.
- The clinical trial demonstrated trends for reductions in LDL-cholesterol, and high-sensitivity C-reactive protein (hsCRP). Notably, there were greater reductions in mean LDL-cholesterol and hsCRP in ZGN-1061-treated subjects with abnormally elevated LDL or hsCRP at baseline.

- The clinical trial also showed a trend for reductions in leptin and increases in adiponectin with ZGN-1061 compared to placebo, reflective of favorable changes in adipose function and signaling.
- ZGN-1061 is rapidly metabolized and cleared following administration, with a much shorter half-life than beloranib, minimizing exposure to the compound while driving desired metabolic effects.
- Single and repeat doses of ZGN-1061 were generally safe and well tolerated. There were no severe adverse events (AEs), no serious AEs (SAEs), and no AEs leading to early withdrawal from the clinical trial.
- As previously reported, there was no prothrombotic effect observed with ZGN-1061. No treatment emergent venous thromboembolisms (VTEs), no clinically meaningful D-dimer elevations indicative of thrombosis and no elevations in mean D-dimer levels were observed in the dosing groups compared to baseline or placebo. There were no clinically significant changes in coagulation laboratory parameters or other key biomarkers of interest, including von Willebrand factor and soluble thrombomodulin.

“The data emerging from our ZGN-1061 program are quite encouraging, and reinforce our confidence in the candidate as we advance toward initiating our Phase 2 clinical trial in patients with type 2 diabetes who are obese, in the second half of 2017,” said Dennis Kim, M.D., Chief Medical Officer of Zafgen. “We are particularly impressed with the optimized safety profile of ZGN-1061, as well as new preclinical data supporting the potential to impact both glycemic control and insulin resistance, consistent with MetAP2 inhibition.”

Preclinical Efficacy and Safety Differentiation Data

Preclinical data presented at the meeting demonstrated that ZGN-1061 showed similar effects on diabetes, obesity, and other metabolic endpoints, but with a greatly improved safety profile in comparison to the Company’s prior development compound, beloranib. In poster 143-LB, “The MetAP2 Inhibitor ZGN-1061 Improves Glycemia and has Weight Loss Efficacy with an Improved Safety Profile in Preclinical Models,” Zafgen presented results from a study comparing ZGN-1061, beloranib and vehicle in a mouse model of obesity and insulin resistance, as well as *in vitro* and *in vivo* data demonstrating the impact of ZGN-1061 versus beloranib on multiple thrombotic markers. Highlights of the data include:

- ZGN-1061 showed statistically significant improvements in glycemic control, insulin sensitivity, body weight, body fat, lipids and cardiometabolic biomarkers compared to vehicle, and these improvements were comparable to those seen for beloranib.
- ZGN-1061 is rapidly metabolized and cleared following administration, with a much shorter half-life than beloranib, minimizing exposure to the compound while driving desired metabolic effects.
- ZGN-1061 displays a reduced impact on endothelial cells compared to beloranib, and on several thrombotic markers, including P21, thrombomodulin, and plasminogen activator inhibitor-1 (PAI-1), *in vitro*, as well as thrombin time and D-dimer *in vivo*.
- ZGN-1061 has improved safety margins for morbidity and coagulopathy, with a 200-fold margin for ZGN-1061 compared to approximately 4-fold for a clinically equivalent dose of beloranib.

About ZGN-1061

ZGN-1061 is a fumagillin-class, injectable small molecule second generation MetAP2 inhibitor that was advanced into development due to its unique properties that maximize impact on metabolic parameters

relevant to the treatment of type 2 diabetes and other related metabolic disorders. In preclinical studies, ZGN-1061 has demonstrated promising efficacy in animal models of type 2 diabetes and obesity, with an improved pharmacokinetic profile and safety margin relative to previous molecules in the MetAP2 class. As demonstrated clinically for MetAP2 inhibitors, ZGN-1061 is anticipated to improve glycemic control while also helping to restore balance to fat metabolism, enabling calories to once again be used as a productive energy source, leading to improved metabolic control and long-term weight loss. Zafgen recently completed its first Phase 1 clinical trial of ZGN-1061, and is planning to advance the compound to Phase 2 clinical testing in patients with type 2 diabetes who are overweight or obese. Zafgen holds exclusive worldwide rights for the development and commercialization of ZGN-1061.

About Zafgen

Zafgen (Nasdaq:ZFGN) is a biopharmaceutical company dedicated to significantly improving the health and well-being of patients affected by metabolic diseases including type 2 diabetes and obesity. Zafgen is focused on developing novel therapeutics that treat the underlying biological mechanisms of metabolic diseases through the MetAP2 pathway. Zafgen has pioneered the study of MetAP2 inhibitors in both common and rare forms of obesity, and in patients affected by type 2 diabetes. Zafgen's lead product candidate is ZGN-1061, which is a novel, first-in-class, subcutaneous injection. Zafgen aspires to improve the lives of patients through targeted treatments and has assembled a team accomplished in bringing therapies to patients affected by 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 the use of ZGN-1061 and other MetAP2 inhibitors as treatments for metabolic diseases including type 2 diabetes and obesity, ZGN-1061's improved safety margin, including as it relates to pro-thrombotic characteristics, compared to first generation MetAP2 inhibitors, such as over beloranib, and Zafgen's expectations with respect to the timing and success of its preclinical studies and clinical trials of ZGN-1061 and its other product candidates, 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 ZGN-1061 and its other product candidates and to differentiate ZGN-1061 and its other product candidates from first generation MetAP2 inhibitors, such as beloranib, the preclinical and clinical results for ZGN-1061 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 of its product candidates, 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 when needed, Zafgen's dependence on third parties for development, manufacture, marketing, sales and distribution of product candidates, 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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