Zafgen Announces Positive Full Results in Phase 2 Proof-of-Concept Trial of ZGN-1061 in Patients with Difficult-to-Control Type 2 Diabetes

June 23, 2018

Trial met all primary objectives, demonstrated efficacy and safety and established minimally effective dose of 0.9 mg for ZGN-1061

Patient dosing recently initiated for the 1.8 mg dose cohort

Zafgen presenting the Phase 2 clinical data and data from two supportive nonclinical studies at the American Diabetes Association 78th Scientific Sessions

Company to hold conference call on Monday, June 25, 2018 at 8:00 a.m. ET

BOSTON, June 23, 2018 (GLOBE NEWSWIRE) -- Zafgen, Inc., (Nasdaq:ZFGN), a clinical-stage biopharmaceutical company using its proprietary knowledge of MetAP2 systems biology to help patients affected by a range of metabolic diseases, announced today positive full results from the Company's Phase 2 clinical trial of ZGN-1061, designed to demonstrate proof-of-concept efficacy and safety in patients with type 2 diabetes and establish a minimally effective dose. The trial met all of its primary endpoints at the 0.9 mg dose, and 12-week data demonstrated a favorable safety and tolerability profile, with no treatment-related serious adverse events and no CV safety signals observed. Data for this trial and two supportive nonclinical studies for ZGN-1061 are being presented as late-breaker abstracts at the American Diabetes Association (ADA) 78th Scientific Sessions in Orlando, Florida.

"These positive Phase 2 data show clinically relevant efficacy, favorable safety profile and dose responsive results in line with our expectations for this proof-of-concept trial in patients with type 2 diabetes," said Thomas E. Hughes, Ph.D., President and Chief Scientific Officer, Zafgen. "Statistically significant lowering of glucose levels and A1C was observed, with a curve continuing to show potential for A1C lowering beyond 12 weeks. Of particular interest, the safety data in this clinical trial were unremarkable and highly differentiated from our first generation MetAP2 inhibitor, with no CV safety signals observed."

ZGN-1061 demonstrated a statistically significant reduction in A1C at 0.9 mg versus placebo at Week 8 ($p<0.01$) and Week 12 ($p<0.001$). A1C lowering results from the trial establishes the 0.9 mg dose as a minimally effective dose, with progressive A1C lowering to 12 weeks with no signs of waning of effect. The 0.9 mg dose in this trial represents approximately 50% target engagement of MetAP2. These results were well-supported by several relevant metabolic biomarkers, including postprandial and fasting plasma glucose, FGF21, adiponectin and leptin. ZGN-1061 was generally safe and well-tolerated, with primarily mild to moderate adverse events (AEs) and an overall high study completion rate (95%). The most frequent AEs were injection site bruising, upper respiratory infection, and diarrhea that was mild and self-limiting. Serious adverse events – upper abdominal pain and skin ulcer – were reported by two patients on treatment and deemed not related to study drug by the principal investigator. Importantly, there were no elevations in D-dimer concentrations across the dosing groups as compared to baseline or placebo and no CV safety signals observed.

In addition to the Phase 2 clinical data for ZGN-1061, Zafgen is also reporting supportive nonclinical data for ZGN-1061, including data on combination treatment with ZGN-1061 and liraglutide, and data on treatment with ZGN-1061 in nonalcoholic steatohepatitis (NASH). Nonclinical data on treatment with both ZGN-1061 and liraglutide suggest that combination therapy with these glucose-lowering agents may yield additive improvement in glycemic control and weight loss, demonstrating the effect of two complementary mechanisms – MetAP2 and GLP-1. From nonclinical data in a NASH model, we observed that ZGN-1061 markedly reduced liver weight, NAS score and markers of liver damage (ALT and AST). These NASH-related data, combined with previous gene expression data with ZGN-1061 and clinical liver fat content data from Zafgen's first generation MetAP2 inhibitor, suggest potential clinical value in treating liver-specific metabolic conditions. It is estimated that up to 70 percent of people with type 2 diabetes have concomitant NASH.

"The clinical data announced today for ZGN-1061 reinforce our excitement about the potential of our second-generation MetAP2 inhibition platform to address advanced, complex type 2 diabetes, while also providing a potential safety read-through to our rare disease programs with high unmet medical need, starting with Prader-Willi syndrome," said Jeffrey Hatfield, Chief Executive Officer, Zafgen. "Zafgen's MetAP2 inhibition platform approach is also supported by the combination therapy and NASH nonclinical studies for ZGN-1061, opening the door for potential additional value in the treatment of type 2 diabetes."

As previously announced, based on the safety and tolerability results of the interim analysis for the ZGN-1061 Phase 2 proof-of-concept trial detailed in March 2018, Zafgen opted to explore the higher end of the potential therapeutic range of ZGN-1061 by adding a 1.8 mg dose arm to the trial. Patient dosing was recently initiated and will run in parallel with completion of long-term toxicology studies for ZGN-1061. Results are expected in early 2019.

"The results of the Phase 2 trial announced today, together with the data we expect to generate at the higher 1.8 mg dose, further strengthen ZGN-1061's position as one of the most attractive and innovative clinical stage programs for the treatment of type 2 diabetes in the industry," said Brian McVeigh, Chief Business Officer, Zafgen. "We look forward to continuing discussions with potential development and commercialization partners with a focus on type 2 diabetes. This is an incredibly exciting time for Zafgen as we deliver on our strategy of advancing our second-generation MetAP2 inhibitors for the treatment of metabolic disorders, with an increasing focus on rare disorders such as Prader-Willi syndrome which we intend to commercialize ourselves, while also adding value for prevalent diseases such as type 2 diabetes which we intend to partner."

Full data for these studies are available in the posters being presented at the ADA meeting and will be discussed in a conference call on Monday, June 25, 2018 at 8:00 a.m. See details below.

Conference Call Information
Zafgen will host an investor conference call Monday, June 25, 2018 at 8:00 a.m., Eastern Time, to discuss the ZGN-1061 Phase 2 data and clinical development plans, nonclinical studies for ZGN-1061 as well as other forward-looking information about Zafgen's business. 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 7568645. The call will also be webcast live on the company's website at https://zafgen.gcs-web.com/events-and-presentations. A replay of this conference call will be available beginning at 11:00 am ET on June 25, 2018 through July 2, 2018 by dialing (855) 859-2056 in the United States or (404) 537-3406 outside the United States. To access the replay please provide Conference ID number 7568645.

Poster Information: American Diabetes Association 78th Scientific Sessions
Poster Hall, Monday, June 25, 2018, 12:00 p.m. ET

105-LB: Results of an Interim Analysis of a Phase 2, Randomized, Double-Blind, Placebo-Controlled Clinical Trial of ZGN-1061 in Patients with Type 2 Diabetes and Obesity: Update with Full Results
Authors: T. Kim, D. Zhuang, T. E. Hughes, D. D. Kim, K. Taylor

108-LB: ZGN-1061, a Novel MetAP2 Inhibitor, and Liraglutide Combine to Improve Glycemic Control and Reduce Body Weight in a Rat Model of Diet-Induced Obesity
Authors: B.F. Burkey, P.J. Pedersen, T.X. Pedersen, M. Feigh, J. Vath, T.E. Hughes

107-LB: ZGN-1061 Improves Metabolic Parameters and Hepatic Pathology in an Obese Mouse Model of Diet-Induced and Biopsy-Confirmed Nonalcoholic Steatohepatitis
Authors: B.F. Burkey, M. Illemann, S. Veidal, M. Feigh, J. Vath, T.E. Hughes

About Zafgen
Zafgen (Nasdaq:ZFGN) is a clinical-stage biopharmaceutical company leveraging its proprietary MetAP2 biology platform to develop novel therapies for patients affected by complex metabolic diseases. Zafgen has pioneered the study of MetAP2 inhibitors in both common and rare metabolic disorders and is currently advancing programs for type 2 diabetes, Prader-Willi syndrome and liver diseases. The Company's lead product candidate, ZGN-1061, a MetAP2 inhibitor for difficult-to-control type 2 diabetes, has successfully completed a Phase 2 clinical trial. Learn more at www.zafgen.com.

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-1258, ZGN-1061 and other second-generation MetAP2 inhibitors as treatments for metabolic diseases including Prader-Willi syndrome, type 2 diabetes, liver diseases and obesity and Zafgen's expectations with respect to the timing and success of its nonclinical studies and clinical trials of ZGN-1258, 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-1258, ZGN-1061 and its other product candidates and to differentiate ZGN-1258, ZGN-1061 and its other product candidates from first generation MetAP2 inhibitors, such as beloranib, the nonclinical and clinical results for ZGN-1258, 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 nonclinical 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, 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, including without limitation Zafgen's Quarterly Reports on Form 10-Q, 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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