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Zafgen Initiates Multiple Ascending Dose Cohorts in Phase 1 Clinical Trial of ZGN-1061

Company Expects to Report Data by End of First Quarter 2017

BOSTON, Sept. 20, 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 that the Company has recently initiated dosing in the multiple ascending dose (MAD) cohorts of its ongoing Phase 1 clinical trial of ZGN-1061. The initiation of the MAD portion was triggered following a review of the initial safety and tolerability data from the first two cohorts of the single ascending dose (SAD) portion of the clinical trial. ZGN-1061 is a second-generation, differentiated MetAP2 inhibitor in development for severe and complicated obesity indications.

"For the last decade Zafgen has been studying the MetAP2 pathway to inform the development of molecules that will leverage the powerful benefits of MetAP2 inhibition, while minimizing off-target effects. Based on this work we have optimized ZGN-1061 to deliver an efficacy and safety profile appropriate for development in prevalent obesity-related disorders," said Thomas Hughes, Ph.D., President and Chief Executive Officer of Zafgen. "This clinical trial is an important first step as we look to validate the clinical profile of ZGN-1061. Initial results show ZGN-1061 exhibits pharmacokinetic properties in humans within our specified target range, translating to encouraging early safety and tolerability that support our plans for continued development of this promising candidate."

The Phase 1 clinical trial is evaluating safety, tolerability, and weight loss efficacy over four weeks of treatment. The clinical trial includes a SAD portion, which will enroll up to 48 healthy subjects across up to six cohorts of single escalating doses of ZGN-1061. The clinical trial also includes a MAD portion, which is evaluating twice-weekly ZGN-1061 over four weeks in up to 24 obese subjects. Key elements of the clinical trial involve evaluation of the uptake and elimination of ZGN-1061, or pharmacokinetics, and evaluation of endpoints related to blood coagulation. The Company continues to expect top-line data from the clinical trial by the end of the first quarter of 2017.

ZGN-1061, is a fumagillin-class MetAP2 inhibitor that originated from Zafgen's discovery program as part of a multi-year campaign to identify novel compounds that avoided limiting preclinical safety concerns observed with its first-generation MetAP2 inhibitor, beloranib, including teratogenicity and adverse effects on testicular function. The compound has metabolic efficacy, potency, and range of activity in animal models of obesity similar to beloranib, but displays highly differentiated safety properties and a reduced potential to impact thrombosis, supporting the value of the compound as a more highly optimized MetAP2 inhibitor.

"The clinical trial is progressing well, and we are particularly encouraged that there have been no significant safety signals or tolerability concerns observed in patients treated to date," stated Dennis Kim, M.D., Chief Medical Officer of Zafgen. "We look forward to further advancing this clinical trial, the results of which will provide us with important insights on the potential of ZGN-1061 in severe and complicated obesity, and help inform the doses, design, and patient population for our Phase 2 program."

About ZGN-1061

ZGN-1061 is a fumagillin-class, injectable small molecule second generation MetAP2 inhibitor that modulates the activity of key cellular processes that control the body's ability to make and store fat, and utilize fat and glucose as an energy source. In preclinical studies, ZGN-1061 has demonstrated promising efficacy and potency in animal models of obesity, with an improved pharmacokinetic profile and safety margin relative to previous molecules in the MetAP2 class. ZGN-1061 is anticipated to help reduce hunger and restore balance to fat metabolism, enabling calories to once again be used as a productive energy source, leading to weight loss and improved metabolic control. ZGN-1061 is currently in Phase 1 clinical development. 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 obesity and complex metabolic disorders. Zafgen is focused on developing novel therapeutics that treat the underlying biological mechanisms of severe and complicated obesity through the MetAP2 pathway. Zafgen has pioneered the study of MetAP2 inhibitors in both common and rare forms of obesity. Zafgen's lead product candidate is ZGN-1061, which is a novel, first-in-class, twice-weekly subcutaneous injection. Zafgen is also developing ZGN-839, a liver-targeted MetAP2 inhibitor, for the treatment of nonalcoholic steatohepatitis, or NASH, and abdominal obesity. 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 severe and complicated obesity 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, including timing of reporting results from such clinical trials 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, 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 when needed 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 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.

Media/Investor Relations Contact:

Zafgen, Inc.

Patricia Allen

Chief Financial Officer

617-648-9792

Argot Partners

Investor Relations

Laura Perry or Glenn Garmont

212-600-1902

laura@argotpartners.com

glenn@argotpartners.com

Spectrum Science

Media Relations

Michelle Strier

202-587-2582

mstrier@spectrumspace.com

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