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Zafgen Refocuses Resources on Development of Differentiated Second-Generation MetAP2 Inhibitor ZGN-1061

-ZGN-1061 in Phase I Development for Severe and Complicated Obesity Indications-

- Suspending Development of Beloranib; Implementing Strategic Restructuring to Align Operations with Clinical Development Priorities-

-Strong Cash Position Sufficient to Fund Operations through Phase 2a Clinical Trials for ZGN-1061-

-Company to Host Conference Call at 5:00 PM Eastern Time-

BOSTON, July 19, 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, announced today that, following a comprehensive review of its assets and clinical programs, as well as feedback from regulatory authorities, the Company is refocusing its resources on development of a differentiated second-generation MetAP2 inhibitor, ZGN-1061, in severe and complicated obesity.

"As the leader of the MetAP2 inhibitor field, we have spent many years validating the tremendous potential of this pathway for the treatment of complicated obesity with beloranib, which in multiple clinical trials demonstrated robust reductions in body weight, improvements in glycemic control, and other benefits related to cardiovascular disease risk," said Thomas Hughes, Ph.D., President and Chief Executive Officer of Zafgen. "However, given the heightened complexity and future cost of beloranib development, balanced against the emerging product profile of ZGN-1061, we believe that the long-term opportunity for ZGN-1061 is more robust than for beloranib. Given our deep knowledge of this new and exciting drug class, and our strong cash position, we believe we are well-positioned to advance ZGN-1061 as a potential new treatment for prevalent obesity-related indications."

The beloranib Investigational New Drug (IND) application was placed on full clinical hold in December 2015 by the U.S. Food and Drug Administration (FDA). To address the clinical hold, Zafgen recently held a Type A meeting with the FDA to discuss the clinical and preclinical data for beloranib as well as a proposed risk mitigation strategy for beloranib in Prader-Willi syndrome (PWS). Following its discussions with the FDA and review of other considerations, Zafgen has determined that the obstacles, costs and development timelines to obtain marketing approval for beloranib are too great to justify additional investment in the program, particularly given the promising emerging profile of ZGN-1061. The Company is therefore suspending further development of beloranib in order to focus its resources on ZGN-1061.

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

Zafgen is currently screening patients to initiate a Phase 1 clinical trial evaluating ZGN-1061 for safety, tolerability, and weight loss efficacy over four weeks of treatment, and currently expects Phase 1 clinical data by the end of the first quarter of 2017. Based on the clinical data demonstrating beloranib's significant effect on body weight and glycemic control in patients with severe obesity complicated by type 2 diabetes, Zafgen plans to focus later-stage development of ZGN-1061 in severe and complicated obesity.

As part of the strategic restructuring, the Company plans to reorganize its operations to align with its new priorities focused on ZGN-1061 development. Zafgen's workforce is being reduced by approximately 34%, to a total of 31 employees, by December 2016. Zafgen expects the restructuring to result in approximately \$4.8 million in reduced annualized workforce expenses once the plan is fully implemented. The Company also expects to incur a non-recurring charge of approximately \$2.4 million in the third quarter of 2016 related to the restructuring.

In addition, both Patrick Loustau, President, and Alicia Secor, Chief Commercial Officer, will be leaving the Company to pursue other opportunities.

"We would like to thank Patrick, Alicia, and all of our employees for their hard work and dedication over the past several months as we explored every reasonable path to remove the full clinical hold on the beloranib IND and advance beloranib development," continued Dr. Hughes. "We would also like to express our deepest gratitude to the investigators, patients and families who participated in our beloranib trials. While we are disappointed that we could not see beloranib through to approval, we are excited about the potential of ZGN-1061, and look forward to advancing this high-value candidate in the clinic."

Zafgen ended June 30, 2016 with approximately \$150.5 million in cash and cash equivalents and now expects to end 2016 with greater than \$125 million. The Company believes that its current cash balance is sufficient to fund operations through the end of 2018, at which time it expects to have completed a Phase 2a clinical trial for ZGN-1061.

Conference Call and Webcast

Zafgen will host an investor conference call today, July 19, 2016 at 5:00 p.m., Eastern Time, to discuss its strategic focus on ZGN-1061 and corporate restructuring. 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 52579673. 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 52579673.

About ZGN-1061

ZGN-1061 is a fumagillin-class, injectable small molecule second generation MetAP2 inhibitor that was discovered by Zafgen's researchers and has been shown to have an improved profile relative to previous inhibitors in the class. Like other MetAP2 inhibitors that have shown promise in the treatment of metabolic diseases including severe and complicated obesity, ZGN-1061 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. ZGN-1061 is also 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 has an emerging safety profile and dosage form that are believed to be appropriate for the treatment of prevalent forms of severe and complicated obesity, and 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 which is being developed for the treatment of severe and complicated obesity. 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 forms of severe and complicated obesity, Zafgen's expectations with respect to the timing and success of its non-clinical studies and clinical trials of ZGN-1061 and its other product candidates, and Zafgen's expected cash and cash equivalents balance as of December 31, 2016, 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 pre-clinical 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 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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