



Zafgen Reports Strong Clinical Progress and Updates Outlook for 2018

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ZGN-1061 Phase 2 trial fully enrolled with type 2 diabetes patients; topline data expected mid-year

Company returning to rare disorders with ZGN-1258; Prader-Willi syndrome expected as first indication

Increased cash position will fuel programs through multiple key milestones

BOSTON, Jan. 05, 2018 (GLOBE NEWSWIRE) -- Zafgen, Inc. (Nasdaq:ZFGN), a clinical-stage biopharmaceutical company leveraging its proprietary knowledge of MetAP2 systems biology to develop novel therapies for patients affected by a range of metabolic diseases, today announced strong clinical progress with its lead ZGN-1061 program currently in development for patients with complex type 2 diabetes. Additionally, the company unveiled plans to return to the rare metabolic disease space in 2018, with a second highly optimized MetAP2 development candidate, ZGN-1258, targeting an initial indication in Prader-Willi syndrome (PWS).

Zafgen also announced today that it increased its cash position during the fourth quarter of 2017 and expects to end calendar year 2017 with just over \$100 million in cash, cash equivalents and marketable securities. The company is well-capitalized to support its clinical-stage development programs beyond the first half of 2019, a period that will include multiple data readouts and other program milestones.

"Zafgen has deep proprietary knowledge of MetAP2 systems biology, and has significantly improved the translation of that biology with new insights, chemistries and product candidates that we believe will provide safe and effective treatment options for patients affected by a range of serious, metabolically driven conditions," said Jeffrey Hatfield, Chief Executive Officer, Zafgen. "We enter 2018 gaining momentum across the company, and have a clear vision in place for advancing our programs efficiently to drive shareholder value and ultimately deliver potentially transformative therapies to patients most in need."

Zafgen has undertaken extensive efforts to further characterize the MetAP2 pathway and its effects in various systems, and to optimize the profile of its development candidates to reflect this increased understanding. Each of Zafgen's current development candidates has been designed to preferentially distribute to specific target tissue systems relating directly to the indication being pursued, while reducing significantly the exposure to other tissue systems reached by its first MetAP2 inhibitor. As a result, the company expects that the current development candidates will have a substantial safety advantage over its first MetAP2 inhibitor.

"We are excited about the strong progress we have made throughout our development portfolio, particularly in our extended, company-wide effort to guide our return to clinical development for PWS," said Thomas Hughes, Ph.D., President and Chief Scientific Officer, Zafgen. "We are proceeding with a mix of purpose, care and transparency to translate the insights we have gained into investigational therapies with the efficacy and safety profile needed to meet the unique needs of patients affected by a range of diseases, including PWS."

Key updates and milestones in 2018 across each program include:

ZGN-1061 for Type 2 Diabetes

- Enrollment is complete in Zafgen's Phase 2 clinical trial of ZGN-1061, its investigational MetAP2 inhibitor for the treatment of type 2 diabetes, with 137 patients participating versus 120 planned (+14%) due to accelerated participation interest in the final weeks of the enrollment period. The Phase 2 trial is designed to evaluate safety, tolerability and glucose-lowering efficacy in diabetes patients who are also obese.
- Topline data are expected mid-year 2018.

ZGN-1258 for Prader-Willi Syndrome and Additional Rare Disorders

- Zafgen has selected ZGN-1258 as its development candidate for treating rare or orphan metabolic diseases, beginning with PWS, following extensive optimization and preclinical safety and efficacy profiling.
- Zafgen is beginning investigational new drug (IND) application-enabling work in the first quarter of 2018 in preparation for filing an IND with the U.S. Food and Drug Administration (FDA) and beginning Phase 1 clinical development by the end of the year.
- ZGN-1258 is designed to change the way the body metabolizes fat, reduce fat mass and decrease hyperphagia in PWS, a rare genetic form of life-threatening obesity characterized by unrelenting pathologic hunger (hyperphagia) leading to dangerous food-seeking behavior.

- ZGN-1258 exhibits an expanded ability to act on hunger control centers, in addition to peripheral adipose tissue, differentiating it from ZGN-1061. Based on preclinical studies, the efficacy profile of ZGN-1258 closely aligns with data seen in previous trials with the company's first MetAP2 inhibitor, but, importantly, the new compound appears to have no activity in endothelial cells *in vitro*, which is critical to reduce risk of thrombosis and thrombotic events in this patient population.
- As part of its commitment to the PWS community, Zafgen will also be developing and launching a global PWS natural history study mid-year. This study will inform Zafgen's development program, and will provide first-ever insights into the medical and clinical history in people with PWS.

Financial

- Zafgen entered into a \$20 million venture debt financing agreement with Silicon Valley Bank on December 29, 2017, adding non-dilutive capital to its balance sheet and extending its expected cash runway beyond the first half of 2019.

About Zafgen

Zafgen (Nasdaq:ZFGN) is a clinical-stage biopharmaceutical company leveraging its proprietary knowledge of MetAP2 systems biology to develop novel therapies for patients affected by a range of complex metabolic diseases. Zafgen has pioneered the study of MetAP2 inhibitors in both common and rare metabolic disorders, and its current disease areas of focus are type 2 diabetes, Prader-Willi syndrome and liver diseases. The company's lead product candidate is ZGN-1061, a MetAP2 inhibitor in Phase 2 clinical development with unique properties that maximize impact on metabolic parameters relevant to the treatment of type 2 diabetes and other related metabolic disorders. In 2018, Zafgen plans to file an investigational new drug (IND) application with the U.S. FDA and initiate Phase 1 clinical trials for ZGN-1258, its new molecule for the treatment of Prader-Willi syndrome and potential other rare and serious forms of obesity. 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 and obesity and Zafgen's expectations with respect to the timing and success of its preclinical studies and clinical trials of ZGN-1258, ZGN-1061 and its other product candidates, Zafgen's expected cash, cash equivalents and marketable securities balance as of December 31, 2017, and Zafgen's expectations regarding the length of its cash runway, 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 belorانب, the preclinical 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 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, 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 Contacts:

Zafgen, Inc.
Patricia Allen
Chief Financial Officer
617-648-9792

Media
Krystle Gibbs
Ten Bridge Communications
krystle@tenbridgecommunications.com
508-479-6358

Investors
Laura Perry or Mary Jenkins
Argot Partners
laura@argotpartners.com
mary@argotpartners.com
212-600-1902



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