



NEWS RELEASE

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**Zafgen Inc. Appoints Industry Veteran and Recognized Metabolic Disorders Expert
Thomas Hughes, Ph.D., as Company's First Chief Executive Officer**

*Former Head of Diabetes Research at Novartis Will Lead Company in Development of Novel
Therapies to Treat Obesity*

CAMBRIDGE, Mass., September 9, 2008 – Zafgen Inc., a private venture-backed biopharmaceutical company focused on developing novel obesity therapeutics today announced that Thomas Hughes, Ph.D., has been named the company's first chief executive officer. Dr. Hughes was formerly vice president and global head, cardiovascular and metabolism disease area, at the Novartis Institutes for BioMedical Research, Inc. in Cambridge, where he directed drug discovery research teams specializing in cardiovascular disease, type 2 diabetes and related metabolic disorders.

A rapidly growing epidemic, obesity currently affects an estimated 400 million people worldwide and drives an expanding prevalence of obesity-related co-morbidities including type 2 diabetes, which is anticipated to affect 380 million people by 2025. Zafgen has developed a novel approach to treat obesity based on preclinical research around vascular targeting in adipose tissue. Fat tissue is exceptional for its plasticity, its high degree of vascularization, and its ability to continuously remodel and grow new blood vessels as it expands. Zafgen's lead molecules directly target this ability to remodel and expand, causing the fat tissue to shrink, ultimately leading to reduction in weight.

"While the currently available treatments for obesity can be effective in the short term, long-term efficacy has not been consistent with patient and health care provider expectations. Many existing and emerging agents also have tolerability or safety limitations that reduce their overall effectiveness or restrict their use," stated Dr. Hughes. "Vascular targeting of adipose tissue addresses the fundamental biology of obesity in an entirely new way and may provide a more effective means to achieve sustainable weight loss. Zafgen's orally active lead molecules have demonstrated compelling and durable efficacy and a promising early tolerability profile in numerous gold-standard obesity models. A unique and powerful peripheral mechanism not only differentiates these compounds from marketed and investigational obesity therapeutics, but also is potentially well-suited to combination with existing and emerging therapies impacting weight

and metabolic control. As weight loss, diet, and exercise are the cornerstones of therapy for type 2 diabetes, hypertension, and hypercholesterolemia, well-tolerated agents leading to significant and sustained weight loss are desperately needed and of potentially great medical value. I believe Zafgen's near-term product development opportunities are extraordinarily promising."

"We are very pleased to appoint a recognized scientific expert and seasoned drug development executive to lead Zafgen, and Tom's decision to join our organization is a testament to the paradigm-shifting approach we are pursuing," stated Peter Barrett, Ph.D., chairman of Zafgen's board of directors and partner, Atlas Venture. "Tom's experience is ideally suited to lead Zafgen through our next stage of growth as we prepare to enter the clinic with our first drug candidate in 2009. His move to join Zafgen is further validation of this disruptive approach to treating obesity."

During his 20-year tenure at Novartis, Dr. Hughes has been involved in a wide range of drug discovery efforts in the metabolic and cardiovascular disease area, focusing on glucose homeostasis, diabetic complications, lipid metabolism, aging biology, and the control of blood clotting. In addition to serving as head of cardiovascular and metabolism research, Dr. Hughes also served as the vice president and global head of the diabetes and metabolism disease areas. From 1995 to 2002, Dr. Hughes was responsible for the conception and leadership of the dipeptidyl peptidase IV (DPP4) inhibitor program within Novartis research, leading to the discovery of the marketed antidiabetic compound vildagliptin, for which he was recognized with the Novartis Distinguished Scientist Award in 2000. Dr. Hughes earned his Ph.D. in nutritional biochemistry from Tufts University and received an M.S. in Zoology from Virginia Polytechnic Institute & State University. He graduated with a B.A. in biology from Franklin and Marshall College.

Kevin Starr, former interim chief executive officer, Zafgen Inc. and partner, Third Rock Ventures added, "Tom represents a key element in our strategy to grow a truly outstanding company. In addition to a clear vision, great corporate culture, and first-rate science is – importantly – leadership. Tom's leadership is a perfect complement to the exceptional team that we are assembling at Zafgen. We are at the forefront of a major therapeutic advance in obesity."

Also supporting the company's efforts is a scientific advisory board comprised of several renowned experts in the fields of obesity and other metabolic disorders, including Lou Tartaglia, Ph.D., chairman of the Zafgen scientific advisory board, partner, Third Rock Ventures; Maria Rupnick, M.D., co-founder of Zafgen, instructor in medicine, Children's Hospital Boston and acute/critical care cardiologist, Brigham and Women's Hospital; Randy Seeley, Ph.D., professor, psychiatry and associate director, the Obesity Research Center, the University of Cincinnati College of Medicine; Steven Smith, M.D., assistant executive director, clinical research, the Pennington Biomedical Research Center; and Lou Aronne, M.D., clinical professor of medicine, Weill Medical College of Cornell University, adjunct clinical associate professor of medicine, Columbia University and assistant attending physician, New York Presbyterian Hospital.

About Zafgen Inc.

Zafgen Inc. is the first biopharmaceutical company dedicated to developing novel obesity therapeutics based on vascular targeting in adipose tissue (fat). Zafgen's groundbreaking approach directly targets adipose vasculature to shrink fat cells and help the body sustain a lean, healthy state. Adipose tissue is unique among all tissues in the body for its capacity to expand and contract based on nutritional and metabolic requirements, and this plasticity is acutely dependent upon an ability to remodel and grow new blood vessels. Zafgen's leadership and scientific advisors include the leading experts in obesity, metabolic disorders and medicinal chemistry. Founded in 2005, the company is located in Cambridge, Massachusetts. For more information, visit www.zafgen.com.

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