

May 5, 2017

DEAR STOCKHOLDERS



Zafgen's mission is to leverage our expertise to address the significant unmet medical needs at the intersection of type 2 diabetes, obesity and other major metabolic diseases. Our unique approach is focused on developing novel therapeutics that treat the underlying biological mechanisms of metabolic diseases through the MetAP2 pathway.

In July, we made a strategic decision to suspend development of beloranib in favor of second generation candidates, like our lead candidate ZGN-1061, that mirrored the weight loss and glucose lowering effects seen for our first generation candidate but with substantially increased safety margins that would support development in more prevalent indications. We moved quickly to advance ZGN-1061 into development, initiating a Phase 1 clinical trial in the fall. The clinical program is highly informed by our prior work with MetAP2 inhibitors, which provides us with a very clear view of what we need to see early-on in development in terms of pharmacokinetics, efficacy and safety.

We have been working assiduously to identify and understand the drivers of the thrombotic imbalance that we saw with beloranib, in order to advance our understanding of how ZGN-1061 and other second generation candidates may avoid these same effects. In collaboration with a range of experts, we conducted numerous studies to evaluate the impact of beloranib on a variety of prothrombotic activities, and have arrived at a clear understanding of why we believe it potentiates thrombosis. This knowledge increases our confidence in the potential of our ZGN-1061 program in specific, and our MetAP2 inhibitor platform in general.

We recently reported positive topline data from our Phase 1 clinical trial of ZGN-1061. ZGN-1061 demonstrated rapid drug absorption and clearance in line with pre-specified criteria established for the molecule, and was well-tolerated and safe, with no evidence of prothrombotic effects. Patients in the clinical trial experienced mean weight loss of up to approximately one pound per week. The results support advancement to initiate a Phase 2 clinical trial in patients with type 2 diabetes who are overweight or obese in the second half of this year.

Over the course of the coming year, our strategic focus is to establish a path forward for ZGN-1061 in commercially-relevant populations. We believe ZGN-1061 affords us a wealth of opportunities for development in both type 2 diabetes and obesity, where there exists a large and diverse patient population with substantial clinical needs. We are advancing our discussions with regulators and experts, with a goal to determine the specific populations we plan to target in later stage clinical trials. In addition to our primary focus on ZGN-1061, we will also continue to invest in our research and discovery platform in order to identify additional MetAP2 candidates for development.

We are very fortunate to have a strong cash position to support our research and development efforts. We ended 2016 with \$129M in cash, cash equivalents and marketable securities and continue to expect that our cash resources will take us through the end of 2018, by which time we expect to have data from a Phase 2a clinical trial of ZGN-1061.

ZGN-1061 represents a unique opportunity for Zafgen, with the chance to develop a second-generation candidate in a well-informed manner, yet without any meaningful competition. It's been a challenging time and we are still in the early stages of clinical development, but it's been a time of great excitement for our team. As we look to Zafgen's future, we remain grateful for our stockholders and employees and thank you for your continued support.

Sincerely,

A handwritten signature in blue ink, appearing to read "TEH", written over a light blue horizontal line.

Thomas E. Hughes, Ph.D.  
President and Chief Executive Officer