UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

DIVISION OF
CORPORATION FINANCE

March 27, 2014

Via E-mail
Thomas E. Hughes, Ph.D.
President and Chief Executive Officer
Zafgen, Inc.
One Broadway, 8th Floor
Cambridge, MA 02142

Re: Zafgen, Inc.
Amendment No. 1 to Draft Registration Statement on Form S-1
Confidentially Submitted March 14, 2014
CIK No. 0001374690

Dear Dr. Hughes:

We have reviewed your amended confidential draft registration statement and have the following additional comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by providing the requested information and either submitting an amended confidential draft registration statement or publicly filing your registration statement on EDGAR. If you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing the information you provide in response to these comments and your amended confidential draft registration statement or filed registration statement, we may have additional comments.

Business, page 73
Clinical Trials, page 80

1. We note your response to our prior comment 6 and associated revisions to your draft registration statement. In addition to these revisions, please address, at the bottom of page 73 and in your discussion of clinical trials as appropriate, the import of the data you have presented from your trials that relate to the potential efficacy of beloranib. If, as you state, none of the five clinical trials you completed was designed to demonstrate efficacy, please make clear to investors the limitations inherent in such trial design, the consequent value of any clinical observations from these trials that bear on efficacy and the extent to which you may rely on these results in your future regulatory filings with the FDA to support claims of efficacy.

2. We note your response to our prior comment 7 and associated revision on page 82 of your draft registration statement. Please also clarify here the importance of statistical significance to the FDA's (and comparable regulatory authorities') approval process.

Phase 2a Clinical Trials, pages 85-88

3. We note your response to our prior comment 9 and the revisions to the description of your ZAF-201 trial, in which you discuss levels of C-reactive protein and triglycerides. In particular, we note your revised disclosure that C-reactive protein is a cardiovascular risk marker. However, you should correlate your discussion of such results to the goals and endpoints of the trial. For example, why are markers of cardiovascular risk, such as C-reactive protein and triglyceride levels, significant to your trial results, and what do such data suggest about beloranib?

4. We note your response to our prior comment 11 and associated revisions. You discuss levels of high- and low-density lipoprotein cholesterol in patients treated with beloranib in this trial and your ZAF-201 Phase 2a trial. Again, in each instance, you should correlate your discussion of such results to the goals and endpoints of the trial. Specifically, you state that data relating to LDL cholesterol levels indicate that the livers of PWS patients respond to beloranib treatment in a similar fashion as livers of otherwise conventionally obese patients. Please explain how liver function is significant in this regard. In your revised disclosure, please avoid overly-complex scientific terminology that could be confusing to a reasonable investor.

Clinical Trial Summary and Next Steps, pages 88-89

5. We note your response to our prior comment 13 and acknowledge your statement that many details of the planned Phase 3 trial, including expected patient enrollment numbers, are still being negotiated with the FDA. However, you should provide expanded disclosure in your next amendment regarding your strategy for patient enrollment that includes a discussion of how you expect to find and enroll PWS patients and any difficulties you anticipate given the rarity of the disease.

6. Please include the specific details from your response to our prior comment 14 regarding your communications with the FDA in your disclosure and disclose whether you expect that your current discussions with the FDA to result in a Special Protocol Assessment for the planned Phase 3 trial.

Children's License, page 91

7. We note your response to our prior comment 16 and revised disclosure indicating that the patents licensed under this agreement relate to decreasing the growth of fat tissue. Please expand your disclosure to indicate how the intellectual property licensed under this

agreement relates to beloranib, if at all, and how it is different from the intellectual property licensed under the CKD agreement.

If you intend to respond to these comments with an amended draft registration statement, please submit it and any associated correspondence in accordance with the guidance we provide in the Division's October 11, 2012 announcement on the SEC website at http://www.sec.gov/divisions/corpfin/cfannouncements/drsfilingprocedures101512.htm.

Please keep in mind that we may publicly post filing review correspondence in accordance with our December 1, 2011 policy (http://www.sec.gov/divisions/corpfin/cfannouncements/edgarcorrespondence.htm). If you intend to use Rule 83 (17 CFR 200.83) to request confidential treatment of information in the correspondence you submit on EDGAR, please properly mark that information in each of your confidential submissions to us so we do not repeat or refer to that information in our comment letters to you.

You may contact Christine Torney at (202) 551-3652 or Jim Rosenberg at (202) 551-3679 if you have questions regarding comments on the financial statements and related matters. Please contact Austin Stephenson at (202) 551-3192, Dan Greenspan at (202) 551-3623, or me at (202) 551-3715 with any other questions.

Sincerely,

/s/ *Daniel Greenspan for*

Jeffrey P. Riedler
Assistant Director

cc: Via E-mail
Michael J. Minahan, Esq.
Goodwin Procter LLP