UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-1 REGISTRATION STATEMENT

Under
The Securities Act of 1933

ZAFGEN, INC.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization) 2834 (Primary Standard Industrial Classification Code Number) 20-3857670 (I.R.S. Employer Identification Number)

One Broadway, 8th Floor Cambridge, Massachusetts 02139 (617) 401-3041

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Thomas E. Hughes Chief Executive Officer Zafgen, Inc. One Broadway, 8th Floor Cambridge, Massachusetts 02139 (617) 401-3041

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Mitchell S. Bloom, Esq. Michael J. Minahan, Esq. Goodwin Procter LLP Exchange Place 53 State Street Boston, MA 02109 (617) 570-1000 Thomas E. Hughes Chief Executive Officer Zafgen, Inc. One Broadway, 8th Floor Cambridge, Massachusetts 02139 (617) 401-3041 Patrick O'Brien, Esq. Ropes & Gray LLP Prudential Tower 800 Boylston Street Boston, Massachusetts 02199-3600 (617) 951-7000

| Approximate date of commencement of | proposed sale to the p | ublic: As soon as practicable a t | fter the effective date of thi | is registration statement. |
|-------------------------------------|------------------------|--|--------------------------------|----------------------------|
|-------------------------------------|------------------------|--|--------------------------------|----------------------------|

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended, check the following box. \Box

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. \Box

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. \Box

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large Accelerated Filer
☐ Accelerated Filer ☐

CALCULATION OF REGISTRATION FEE

| | Amount | Proposed Maximum | Proposed Maximum | |
|---|---------------|--------------------|------------------|---------------------|
| Title of Each Class of | to be | Aggregate Offering | Aggregate | Amount of |
| Securities to be Registered | Registered(1) | Price Per Share | Offering Price | Registration Fee(2) |
| Common stock, \$0.001 par value per share | 1,150,000 | \$16.00 | \$18,400,000 | \$2,370 |

- Represents only the additional number of shares being registered and includes shares of common stock issuable upon exercise of the underwriters' option to purchase additional shares. Does not include the securities that the Registrant previously registered on the Registration Statement on Form S-1 (File No. 333-195391).
- The registration fee is calculated in accordance with Rule 457(o) under the Securities Act of 1933, as amended, based on the proposed maximum aggregate offering price. The registrant previously registered securities at an aggregate offering price not to exceed \$92,000,000 on a Registration Statement on Form S-1 (File No. 333-195391), which was declared effective by the Securities and Exchange Commission on June 18, 2014. In accordance with Rule 462(b) under the Securities Act, an additional amount of securities having a proposed maximum aggregate offering price of \$18,400,000 is hereby registered, which includes shares issuable upon the exercise of the underwriters' option to purchase additional shares.

The Registration Statement shall become effective upon filing in accordance with Rule 462(b) promulgated under the Securities Act of 1933, as amended.

Explanatory Note and Incorporation by Reference

This Registration Statement is being filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended (the "Securities Act"). The contents of the Registration Statement on Form S-1 (File No. 333-195391) filed by Zafgen, Inc. with the Securities and Exchange Commission (the "Commission") pursuant to the Securities Act, which was declared effective by the Commission on June 18, 2014, are incorporated by reference into this Registration Statement.

The required opinion and consents are listed on an Exhibit Index attached hereto and filed herewith.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this Registration Statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on the 18th day of June, 2014

ZAFGEN, INC.

By: /s/ Thomas E. Hughes, Ph.D.

Thomas E. Hughes, Ph.D.

Chief Executive Officer and Director

Pursuant to the requirements of the Securities Act, this Registration Statement on Form S-1 has been signed by the following persons in the capacities and on the dates indicated.

| Name | Title | Date |
|---|--|---------------|
| /s/ Thomas E. Hughes, Ph.D. Thomas E. Hughes, Ph.D. | Chief Executive Officer and Director (Principal Executive Officer) | June 18, 2014 |
| * Patricia L. Allen | Chief Financial Officer (Principal Financial and Accounting Officer) | June 18, 2014 |
| * Peter Barrett, Ph.D. | Chairman of the Board of Directors | June 18, 2014 |
| * Bruce Booth, Ph.D. | Director | June 18, 2014 |
| * Avi Goldberg | Director | June 18, 2014 |
| * John L. LaMattina, Ph.D. | Director | June 18, 2014 |
| * Kevin P. Starr | Director | June 18, 2014 |
| * Frank Thomas | Director | June 18, 2014 |

^{*} Pursuant to Power of Attorney

By: /s/ Thomas E. Hughes, Ph.D.

Thomas E. Hughes, Ph.D. Attorney-in-Fact

EXHIBIT INDEX

| Exhibit No. | Exhibit Index |
|-------------|--|
| 5.1 | Opinion of Goodwin Procter LLP |
| 23.1 | Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm |
| 23.2 | Consent of Goodwin Procter LLP (included in Exhibit 5.1) |
| 24.1* | Power of Attorney |

^{*} Previously filed on the signature page to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-195391), filed with the Securities and Exchange Commission on April 18, 2014 and incorporated by reference herein.

Zafgen, Inc. One Broadway, 8th Floor Cambridge, MA 02142

Re: Securities Registered under Registration Statement on Form S-1

Ladies and Gentlemen:

We have acted as counsel to you in connection with your filing of a Registration Statement on Form S-1 (File No. 333-195391) (the "Initial Registration Statement") pursuant to the Securities Act of 1933, as amended (the "Securities Act") and (ii) a second Registration Statement on Form S-1 filed pursuant to Rule 462(b) promulgated under the Securities Act (the "462(b) Registration Statement", and together with the Initial Registration Statement, the "Registration Statement"). This opinion letter is furnished to you in connection with your filing of the 462(b) Registration Statement, relating to the registration of the offering by Zafgen, Inc., a Delaware corporation (the "Company"), of up to 1,150,000 shares (the "Shares") of the Company's Common Stock, \$0.001 par value per share, including Shares purchasable by the underwriters upon their exercise of an over-allotment option granted to the underwriters by the Company. The Shares are being sold to the several underwriters named in, and pursuant to, an underwriting agreement among the Company and such underwriters (the "Underwriting Agreement").

We have reviewed such documents and made such examination of law as we have deemed appropriate to give the opinions set forth below. We have relied, without independent verification, on certificates of public officials and, as to matters of fact material to the opinions set forth below, on certificates of officers of the Company.

The opinion set forth below is limited to the Delaware General Corporation Law (which includes reported judicial decisions interpreting the Delaware General Corporation Law).

Based on the foregoing, we are of the opinion that the Shares have been duly authorized and, when the Shares have been issued and delivered against payment in accordance with the terms approved by the Board of Directors, the Shares will be validly issued, fully paid and non-assessable.

We hereby consent to the inclusion of this opinion as Exhibit 5.1 to the 462(b) Registration Statement and to the references to our firm under the caption "Legal Matters" in the Initial Registration Statement. In giving our consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations thereunder.

Very truly yours,

/s/ Goodwin Procter LLP

GOODWIN PROCTER LLP

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-1 of Zafgen, Inc., filed pursuant to Rule 462(b) of the Securities Act of 1933, of our report dated March 14, 2014, except for Note 17, as to which the date is June 5, 2014, relating to the consolidated financial statements of Zafgen, Inc., which appears in Amendment No. 4 to the Registration Statement on Form S-1 (No. 333-195391). We also consent to the reference to us under the heading "Experts" in Amendment No. 4 to the Registration Statement filed on Form S-1 as incorporated by reference in this Registration Statement.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts June 18, 2014