As filed with the Securities and Exchange Commission on February 21, 2018

Registration No. 333-

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-8 REGISTRATION STATEMENT UNDER THE

SECURITIES ACT OF 1933

Blueprint Medicines Corporation

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation)

45 Sidney Street Cambridge, Massachusetts

(Address of principal executive offices)

Identification No.)

02139 (Zip Code)

26-3632015

(I.R.S. Employer

2015 Stock Option and Incentive Plan 2015 Employee Stock Purchase Plan (Full titles of the plans)

Jeffrey W. Albers President and Chief Executive Officer Blueprint Medicines Corporation

45 Sidney Street Cambridge, Massachusetts 02139 (Name and address of agent for service)

(617) 374-7580

(Telephone number, including area code, of agent for service) Please send copies of all communications to:

Kingsley L. Taft, Esq. Danielle M. Lauzon, Esq. Goodwin Procter LLP 100 Northern Avenue Boston, Massachusetts 02210 (617) 570-1000

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 definitions of "large accelerated filer," "accelerated filer," and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ☑ Non-accelerated filer □

(Do not check if a smaller reporting company)

Accelerated filer
Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

CALCULATION OF REGISTRATION FEE

Title of Securities to be Registered	Amount to be Registered (1)	Proposed Maximum Offering Price Per Share	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Common Stock, \$0.001 par value per share	1,743,101	\$ 74.27 (2)	\$ 129,451,395.77 (2)\$ 16,116.70
Common Stock, \$0.001 par value per share	435,775	\$ 63.13 (3)	\$ 27,510,475.75 (3	\$ 3,425.06
Total	2,178,876		\$ 156,961,871.52	\$ 19,541.76

(1) In accordance with Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), this registration statement shall be deemed to cover any additional shares of common stock that may from time to time be offered or issued under the above-named plans to prevent dilution resulting from stock splits, stock dividends, recapitalizations or similar transactions effected without the receipt of consideration which results in an increase in the number of the Registrant's outstanding shares of Common Stock. Pursuant to Rule 416(c) under the Securities Act, this Registration Statement shall also cover an indeterminate amount of interests to be offered or sold pursuant to the employee benefit plans described herein.

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rules 457(c) and 457(h) of the Securities Act and based upon the average of the high and low prices of the Registrant's Common Stock as reported on The Nasdaq Global Select Market on February 13, 2018.

(3) Estimated solely for the purpose of calculating the registration fee pursuant to Rules 457(c) and 457(h) of the Securities Act and based upon the average of the high and low prices of the Registrant's Common Stock as reported on The Nasdaq Global Select Market on February 13, 2018, multiplied by 85%, which is the percentage of the price per share applicable to purchasers under the 2015 Employee Stock Purchase Plan.

EXPLANATORY NOTE

This Registration Statement on Form S-8 relating to the 2015 Stock Option and Incentive Plan (the "2015 Plan") and the 2015 Employee Stock Purchase Plan (the "2015 ESPP") of Blueprint Medicines Corporation (the "Registrant") is being filed for the purpose of registering additional securities of the same class as other securities for which a Registration Statement on Form S-8 has previously been filed and is effective. Accordingly, this Registration Statement on Form S-8 incorporates by reference the contents of (i) the Registration Statement on Form S-8 (File No. 333-203749) filed with the Securities and Exchange Commission (the "SEC") on April 30, 2015 by the Registrant, relating to the 2015 Plan and the 2015 ESPP, (ii) the Registration Statement on Form S-8 (File No. 333-210125) filed with the SEC on March 11, 2016 by the Registrant, relating to the 2015 Plan and the 2015 ESPP and (iii) the Registration Statement on Form S-8 (File No. 333-216575) filed with the SEC on March 9, 2017 by the Registrant, relating to the 2015 ESPP, in each case, except for "Item 8. Exhibits" with respect to which the Exhibit Index set forth below is incorporated herein by reference.

EXHIBIT INDEX

		Incorporated by Reference		-	
Exhibit Number	Description of Exhibit	Form	File No.	Exhibit Number	Filing Date
3.1	Fifth Amended and Restated Certificate of Incorporation of	10-Q	001-37359	3.1	November 9, 2015
	<u>the Registrant</u>				
3.2	Amended and Restated Bylaws of the Registrant	10-Q	001-37359	3.2	November 9, 2015
4.1	Specimen Common Stock Certificate	S-1/A	333-202938	4.1	April 20, 2015
4.2	Second Amended and Restated Investors' Rights Agreement,	S-1	333-202938	4.4	March 23, 2015
	dated as of November 7, 2014, by and among the Registrant				
	and the Investors listed therein				
5.1	Opinion of Goodwin Procter LLP, counsel to the Registrant				*
23.1	Consent of Ernst & Young LLP, an independent registered				*
	<u>public accounting firm</u>				
23.2	Consent of Goodwin Procter LLP (included in Exhibit 5.1)				*
24.1	Power of attorney (included on the signature pages of this				*
	<u>registration statement)</u>				
99.1	2015 Stock Option and Incentive Plan	10-K	001-37359	10.2	March 11, 2016
99.2	2015 Employee Stock Purchase Plan	S-8	333-203749	99.3	April 30, 2015
	* Filed herewith.				

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on this 21st day of February, 2018.

BLUEPRINT MEDICINES CORPORATION

By: /s/ Jeffrey W.

Albers Jeffrey W. Albers President and Chief Executive Officer

POWER OF ATTORNEY AND SIGNATURES

We, the undersigned officers and directors of Blueprint Medicines Corporation, hereby severally constitute and appoint Jeffrey W. Albers and Michael Landsittel, and each of them singly, our true and lawful attorneys with full power to any of them, and to each of them singly, to sign for us and in our names in the capacities indicated below the Registration Statement on Form S-8 filed herewith and any and all amendments to said Registration Statement, and generally to do all such things in our name and on our behalf in our capacities as officers and directors to enable Blueprint Medicines Corporation to comply with the provisions of the Securities Act of 1933, as amended, and all requirements of the Securities and Exchange Commission, hereby ratifying and confirming our signatures as they may be signed by our said attorneys, or any of them, to said registration statement and any and all amendments thereto.

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Jeffrey W. Albers Jeffrey W. Albers	President, Chief Executive Officer and Director (<i>Principal Executive Officer</i>)	February 21, 2018
/s/ Michael Landsittel Michael Landsittel	Vice President of Finance (Principal Financial and Accounting Officer)	February 21, 2018
/s/ Daniel S. Lynch Daniel S. Lynch	Chairman of the Board	February 21, 2018
/s/ Nicholas Lydon Nicholas Lydon, Ph.D.	Director	February 21, 2018
/s/ Alexis Borisy Alexis Borisy	Director	February 21, 2018
/s/ Mark Goldberg Mark Goldberg, M.D.	Director	February 21, 2018
/s/ Charles A. Rowland, Jr. Charles A. Rowland, Jr.	Director	February 21, 2018
/s/ George Demetri George Demetri, M.D.	Director	February 21, 2018
/s/ Lonnel Coats Lonnel Coats	Director	February 21, 2018
/s/ Lynn Seely Lynn Seely, M.D.	Director	February 21, 2018

February 21, 2018

Blueprint Medicines Corporation 45 Sidney Street Cambridge, MA 02139

Re: Securities Being Registered under Registration Statement on Form S-8

Ladies and Gentlemen:

We have acted as counsel to you in connection with your filing of a Registration Statement on Form S-8 (the "Registration Statement") pursuant to the Securities Act of 1933, as amended (the "Securities Act"), on or about the date hereof relating to an aggregate of 2,178,876 shares (the "Shares") of Common Stock, \$0.001 par value per share, of Blueprint Medicines Corporation, a Delaware corporation (the "Company"), that may be issued pursuant to the Company's 2015 Stock Option and Incentive Plan and 2015 Employee Stock Purchase Plan (collectively, the "Plans").

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 opinion set forth below, on certificates of officers of the Company.

The opinion set forth below is limited to the Delaware General Corporation Law.

For purposes of the opinion set forth below, we have assumed that a sufficient number of authorized but unissued shares of the Company's Common Stock will be available for issuance when the Shares are issued.

Based on the foregoing, we are of the opinion that the Shares have been duly authorized and, upon issuance and delivery against payment therefor in accordance with the terms of the Plans, will be validly issued, fully paid and nonassessable.

We hereby consent to the inclusion of this opinion as Exhibit 5.1 to the 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 consent to the incorporation by reference in the Registration Statement (Form S-8) pertaining to the 2015 Stock Option and Incentive Plan and the 2015 Employee Stock Purchase Plan of Blueprint Medicines Corporation of our reports dated February 21, 2018, with respect to the consolidated financial statements of Blueprint Medicines Corporation and the effectiveness of internal control over financial reporting of Blueprint Medicines Corporation included in its Annual Report (Form 10-K) for the year ended December 31, 2017, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts February 21, 2018