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

DIVISION OF
CORPORATION FINANCE

March 19, 2015

Via E-mail
Jeffrey W. Albers
President and Chief Executive Officer
Blueprint Medicines Corporation
215 First Street
Cambridge, Massachusetts 02142

Re: Blueprint Medicines Corporation
Draft Registration Statement on Form S-1
Submitted February 19, 2015
CIK No. 0001597264

Dear Mr. Albers:

We have reviewed your draft registration statement and have the following 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 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 draft registration statement or filed registration statement, we may have additional comments.

Prospectus Summary

1. Please clarify the meaning of any significant scientific or technical terms the first time they are used in your prospectus summary in order to ensure that lay readers will understand the disclosure. For example, please define each of the following at their first use in this section:

    - KIT Exon 17;
    - PDGFRα D842V;
    - Systemic mastocytosis (SM);
    - Gastrointestinal stromal tumors (GIST);
    - FGFR4;
    - Hepatocellular carcinoma; and

- RET

Similarly, please revise your prospectus as necessary to explain the meaning of any important scientific terms or concepts in your Business section that are reasonably likely to be unfamiliar to lay readers.

Our Approach and Platform, page 2

2. Please disclose whether your discovery engine and proprietary compound library were developed by third parties or developed entirely in-house. To the extent developed by third parties, please discuss the relevant terms of any material collaboration or license agreements in the Business section and file these agreements as exhibits pursuant to Item 601 of Regulation S-K.

Use of Proceeds, page 55

3. We note that you have allocated proceeds to fund your planned Phase 1 clinical trials of BLU-285 and BLU-554. Please expand your disclosure to clarify whether the allocated proceeds will likely be sufficient to fund the indicated Phase 1 clinical trials to completion. If, in your view, they will likely not be sufficient, please estimate how far in each of the trials you are likely to progress with available proceeds.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Critical Accounting Policies and Estimates
Common Stock Valuation, page 70

4. We may have additional comments on your accounting for equity issuances including stock compensation and beneficial conversion features. Once you have an estimated offering price, please provide us an analysis explaining the reasons for the differences between recent valuations of your common stock leading up to the IPO and the estimated offering price.

Business, page 80

5. We note that your corporate website references collaborations with the following entities: Massachusetts General Hospital Cancer Center; Wellcome Trust Sanger Institute; Personal Genome Diagnostics; and Alexion Pharmaceuticals. In an appropriately titled subsection, please expand your disclosure in your Business section to include a discussion of all of your material collaboration agreements, including the specified collaborations on your website. In your description of each of these agreements you should summarize the arrangement with the collaborator and specifically identify, to the extent material and applicable:

- Nature and scope of intellectual property transferred if the agreement involves a license;
- Each party's rights and obligations;
- Duration of agreement and royalty term;
- Termination provisions;
- Investment features or share purchases;
- Payment provisions, which may include the following:

    - Up-front or execution payments received or paid;
    - Aggregate amounts paid or received to date under agreement;
    - Aggregate future potential milestone payments to be paid or received;
    - Royalty rates; and
    - Profit or revenue-sharing provisions

In addition, if you have not already done so, please file the agreements as exhibits to your registration statement as required under Item 601(b)(10) of Regulation S-K.

Systemic Mastocytosis (SM)
BLU-285 Pre-clinical Development in SM, page 89

6. In your discussion regarding the selectivity evaluation of BLU-285, please explain what constitutes "exquisite selectivity." If practicable, please disclose the number of kinases inhibited by BLU-285 as compared to midostaurin.

7. Please provide clarifying disclosure regarding the graphic at the bottom of page 89 so that it is sufficiently clear to readers what the illustration represents. For example, please explain the significance of the number and size of the dots in the graphic with respect to kinome selectivity. If individual kinases are identified, please specify.

8. Please include a brief discussion on page 89 explaining why midostaurin, rather than imantib or another kinase inhibitor, was the drug chosen for the comparative selectivity evaluation of BLU-285, particularly where imantib was used in your potency comparison.

BLU-554 Pre-clinical Development in HCC, pages 95-96

9. In your discussion regarding the selectivity evaluation of BLU-554, please explain what constitutes "high selectivity." If practicable, please disclose the number of kinases inhibited by BLU-554 as compared to BGJ-398.

10. As with our comment to your discussion of BLU-285, please provide clarifying disclosure regarding the graphic at the top of page 96. For example, please explain the significance of the number and size of the dots in the graphic with respect to kinome selectivity. If individual kinases are identified, please specify.

Intellectual Property, page 99

11. We note your disclosure regarding your patents and patent applications. For each of your most advanced drug candidates, please provide expected expiration dates for your issued patents and applications in each of (1) the U.S. and (2) foreign jurisdictions, as a group.

Executive Compensation, page 127

12. Please revise your executive compensation table to include compensation information for the fiscal year ended December 31, 2013.

Certain Relationships and Related Party Transactions
Agreements with Stockholders, page 136

13. Please describe the consulting and management services provided by Third Rock Ventures LLC in greater detail. If there is a consulting agreement or other agreement in place, please disclose the material terms of the agreement including the parties' rights and obligations, payment terms and termination provisions. In addition, please file the agreement as an exhibit to your registration statement as required under Item 601(b)(10) of Regulation S-K.

Indemnification Agreements and Directors' and Officers' Liability Insurance

14. You disclose that you entered into indemnification agreements with each of your current directors and executive officers. Please file a copy of the form of indemnification agreement as an exhibit to this registration statement as required under Item 601(b)(10) of Regulation S-K.

Other Comments

15. Please submit all outstanding exhibits as soon as practicable. We may have further comments upon examination of these exhibits.

16. Please provide us proofs of all graphic, visual or photographic information you will provide in the printed prospectus prior to its use, for example in a preliminary prospectus. Please note that we may have comments regarding this material.

17. Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your behalf, present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications.

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 Rolf Sundwall at (202) 551-3105 or James Rosenberg at (202) 551-3679 if you have questions regarding comments on the financial statements and related matters. Please contact Alla Berenshteyn at (202) 551-4325, 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
Kingsley L. Taft, Esq.
Goodwin Proctor LLP