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March 23, 2015

VIA EDGAR AND FEDERAL EXPRESS

United States Securities and Exchange Commission
Division of Corporation Finance
100 F Street, N.E.
Washington, D.C. 20549
Attention: Jeffrey P. Riedler

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

Dear Mr. Riedler:

This letter is submitted on behalf of Blueprint Medicines Corporation (the "**Company**") in response to comments 1-17 of the staff of the Division of Corporation Finance (the "**Staff**") of the U.S. Securities and Exchange Commission (the "**Commission**") as set forth in the Staff's letter dated March 19, 2015 addressed to Jeffrey W. Albers, President, Chief Executive Officer and Director of the Company (the "**Comment Letter**"), with respect to the Company's Draft Registration Statement on Form S-1, filed on February 19, 2015 (the "**Initial Registration Statement**"). The Company is concurrently publicly filing the Registration Statement on Form S-1 (the "**Registration Statement**"), which includes changes to reflect responses to the Staff's comments.

For reference purposes, the text of comments 1-17 of the Comment Letter has been reproduced herein with responses below each numbered comment. For your convenience, we have italicized the reproduced Staff comments from the Comment Letter. All capitalized terms used and not otherwise defined herein shall have the meanings set forth in the Registration Statement. The responses provided herein are based upon information provided to Goodwin Procter LLP by the Company. Unless otherwise indicated, page references in the descriptions of the Staff's comments refer to the Initial Registration Statement, and page references in the responses refer to the Registration Statement.

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.

RESPONSE: The Initial Registration Statement has been revised in response to the Staff's comment. In addition to the terms identified by the Staff, we have also added definitions for sarcoma, paralog, mastocytoma and target engagement. Please see revisions on pages 1, 2, 3, 4, 66, 81, 82 and 83 of the Registration Statement.

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.*

RESPONSE: The Initial Registration Statement has been revised in response to the Staff's comment. Please see revisions on pages 2, 81, 85 and 86 of the Registration Statement.

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.

RESPONSE: The Initial Registration Statement has been revised in response to the Staff's comment. Please see revisions on page 56 of the Registration Statement.

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.*

RESPONSE: The Company acknowledges the Staff's comment.

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.

RESPONSE: The Company respectfully advises the Staff that as collaboration agreements are entered into by the Company in the ordinary course of business, the Company has analyzed whether the agreements with Massachusetts General Hospital Cancer Center ("MGH"), Wellcome Trust Sanger Institute ("Sanger"), Person Genome Diagnostics ("PGDx"), and Alexion Pharma Holding ("Alexion") should be filed in accordance with Item 601(b)(10)(ii)(B) of Regulation S-K. This Item provides that a registrant must file "any contract upon which the registrant's business is *substantially dependent* as in the case of continuing contracts to sell the major part of registrant's products or services or to purchase the major part of registrant's requirements of goods, services or raw materials or any franchise or license or other agreement to use a patent, formula, trade secret, process or trade name upon which registrant's business depends to a material extent." Based on this review, the Company has concluded that of such agreements, only its research, development and commercialization agreement with Alexion (the "Alexion Agreement"), is a material agreement in accordance with Item 601(b)(10)(ii)(B) of Regulation S-K.

The Company advises the Staff that it is not substantially dependent on the material transfer agreement among the Company, MGH and Sanger (the "Sanger/MGH Agreement"). The Sanger/MGH Agreement covers a screening project where the Company provided MGH and Sanger the limited right to screen the Company's compounds against the MGH and Sanger human cancer cell line panel. The Company is not obligated to make any payments to either MGH or Sanger under the Sanger/MGH Agreement, and neither Sanger nor MGH is obligated to make any payments to the Company under the Sanger/MGH Agreement. The Company has the right, but not the obligation, to negotiate a license to any intellectual property rights that may result from the work conducted under the Sanger/MGH Agreement, but no intellectual property has been generated to date. The term of the Sanger/MGH Agreement is set to expire on January 9, 2017, and it can be terminated upon 60 days' written notice by any party's notice.

The Company advises the Staff that it is not materially dependent on its collaboration agreement with PGDx (the "PGDx Agreement"). The PGDx Agreement is a master services agreement setting forth the overarching terms that govern any projects to be engaged in by the parties under individual work plans mutually agreed upon by the parties. There is no requirement that the Company and PGDx enter into any number of

work plans. Under the inaugural work plan, the Company agreed to provide samples to PGDx and PGDx agreed to perform sequencing of the samples. The Company paid PGDx for the sequencing services upon receipt of an invoice from PGDx. Although the PGDx Agreement has no set term, it can be terminated by either party by providing 30 days written notice to the other party.

The Company advises the Staff that it has removed the references to MGH, Sanger and PGDx from its website to avoid any investor confusion as to the significance of these collaborations. Furthermore, the Initial Registration Statement has been revised to include a description of the material terms of the Alexion Agreement. Please see revisions on pages 102 and F-24 of the Registration Statement. In addition, the Alexion Agreement has been filed as Exhibit 10.10 to the Registration Statement.

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.*

RESPONSE: The Initial Registration Statement has been revised in response to the Staff's comment. Please see revisions on page 91 of the Registration Statement.

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.*

RESPONSE: The Initial Registration Statement has been revised in response to the Staff's comment. Please see revisions on page 91 of the Registration Statement.

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.*

RESPONSE: The Initial Registration Statement has been revised in response to the Staff's comment. Please see revisions on page 91 of the Registration Statement.

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.*

RESPONSE: The Initial Registration Statement has been revised in response to the Staff's comment. Please see revisions on page 98 of the Registration Statement.

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.*

RESPONSE: The Initial Registration Statement has been revised in response to the Staff's comment. Please see revisions on page 98 of the Registration Statement.

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.*

RESPONSE: The Initial Registration Statement has been revised in response to the Staff's comment. Please see revisions on pages 39 and 103 of the Registration Statement.

Executive Compensation, page 127

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

RESPONSE: Based on discussion with the Staff, the Company has not revised the executive compensation table in the Registration Statement 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.*

RESPONSE: The Company respectfully advises the Staff that the Company does not have a written agreement in place with Third Rock Ventures for the provision of consulting and management services provided by Third Rock Ventures. The Initial Registration Statement has been revised in

response to the Staff's comment to provide further information regarding the services provided by Third Rock Ventures. Please see revisions on page 141 and 142 of the Registration Statement.

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.*

RESPONSE: The Company has filed the forms of indemnification agreements to be entered into with the Company's directors and executive officers, respectively, in connection with this offering as Exhibits 10.11 and 10.12 to the Registration Statement.

Other Comments

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

RESPONSE: The Company acknowledges the Staff's comment and confirms that it will submit all exhibits as soon as practicable.

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.*

RESPONSE: The Company respectfully advises the Staff that the graphics included in the Initial Registration Statement are the only graphic, visual or photographic information that the Company intends to use in its prospectus.

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.*

RESPONSE: The Company respectfully advises the Staff that as of the date hereof no written communications have been presented to investors in reliance on Section 5(d) of the Securities Act. The Company will supplementally provide the Staff with any written communications that are presented to investors in reliance on Section 5(d) of the Securities Act that occur after the date hereof.

* * *

If you should have any questions concerning the enclosed matters, please contact the undersigned at (617) 570-1033.

Sincerely,

/s/ Michael J. Minahan

Michael J. Minahan, Esq.

Enclosures

cc: Jeffrey P. Riedler, *United States Securities and Exchange Commission*
Rolf Sundwall, *United States Securities and Exchange Commission*
James Rosenberg, *United States Securities and Exchange Commission*
Alla Berenshteyn, *United States Securities and Exchange Commission*
Dan Greenspan, *United States Securities and Exchange Commission*
Jeffrey W. Albers, President & Chief Executive Officer, *Blueprint Medicines Corporation*
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