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Via EDGAR and Courier

September 18, 2020

U.S. Securities and Exchange Commission
Division of Corporation Finance
100 F Street, N.E.
Washington, D.C. 20549

Attn: Jessica Livingston
David Lin
Eric Atallah
Angela Connell

Re: Spruce Biosciences, Inc.
Draft Registration Statement on Form S-1
Submitted August 7, 2020
CIK No. 0001683553

Ladies and Gentlemen:

On behalf of Spruce Biosciences, Inc. (the "***Company***"), we submit this letter in response to comments received from the staff (the "***Staff***") of the U.S. Securities and Exchange Commission (the "***Commission***") by letter dated September 3, 2020 (the "***Comment Letter***") with respect to the Company's draft Registration Statement on Form S-1 confidentially submitted to the Commission on August 7, 2020. Concurrently with the submission of this response letter, the Company is filing its Registration Statement on Form S-1 (the "***Registration Statement***") with the Commission. In addition to addressing the comments raised by the Staff in the Comment Letter, the Company has included other revisions and updates to its disclosure in the Registration Statement.

For the convenience of the Staff, the numbering of the paragraphs below corresponds to the numbering of the comment in the Comment Letter, the text of which we have incorporated into this response letter for convenience in italicized type and which is followed by the Company's response. Page references in the text of this response letter correspond to the page numbers of the Registration Statement.

Prospectus Summary, page 1

1. *Please ensure that the information you include in your summary is balanced. For example, we note the risk disclosure on pages 6 and 13 that you have a limited operating history, have incurred significant net losses since inception, anticipate that you will continue to do so for the foreseeable future and expect these losses to increase as you continue clinical development and seek regulatory approvals. Please provide a more detailed and prominent discussion of the most material risks you face.*

   Response: In response to the Staff's comment, the Company has revised the disclosure on pages 6 and 7 of the Registration Statement to provide an expanded, a more detailed and prominent discussion of the most material risks the Company faces.

2. *On page 5, please revise the table to disclose all remaining stages you must successfully complete before you could seek FDA approval. For example, please revise to reference Phase 3 trials and any estimated timetable. In this regard, we note your disclosure on pages 132 - 133 regarding Phase 1, Phase 2, and Phase 3 clinical trials.*

   Response: In response to the Staff's comment, the Company has revised the disclosure on pages 5, 15, and 112 of the Registration Statement to reference the possibility that the Company may be required by the U.S. Food and Drug Administration ("***FDA***") and comparable foreign regulatory authorities to initiate one or more additional clinical trials, including a Phase 3 clinical trial or trials. However, the Company advises the Staff that the estimated timing or scope of any such future clinical trials is not currently ascertainable, as the design, duration, and scope of such clinical trials will be decided upon after further discussions with the FDA or comparable foreign regulatory authorities. The Company has expanded the disclosure on page 15 of the Registration Statement to more clearly address this uncertainty.

Risk Factors

Our amended and restated certificate of incorporation and amended and restated bylaws will provide that..., page 76

3. *Please revise your disclosure on pages 76 and 185 regarding choice of forum for consistency. In particular, please revise the first sentence under "Choice of Forum" on page 185 to clarify that both your amended and restated bylaws and amended and restated certificate of incorporation include such provision, and similarly, revise the second paragraph of the risk factor to clarify that both documents provide that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.*

   Response: In response to the Staff's comment, the Company has revised the disclosure on pages 77, 78, and 188 of the Registration Statement.

Management's Discussion and Analysis of Financial Condition and Results of Operations

License Agreement with Eli Lilly and Company, page 92

4. *You disclose on pages 92 and F-44 that in May 2016, you entered into a License Agreement with Lilly, which could require you to pay Lilly up to an aggregate of $23.0 million upon the achievement of certain clinical and commercialization milestones. Please revise to describe such milestones in greater detail, including how they will be calculated and any timeframe, as applicable.*

   Response: In response to the Staff's comment, the Company has revised the disclosure on pages 94, 129, F-21, and F-45 of the Registration Statement.

Loan Agreement, page 97

5. *Please expand to provide more detailed disclosure of any material financial covenants contained in your Loan Agreement, including quantifying any ratios, as applicable. If any of such covenants could materially impact your ability to obtain additional debt financing, please revise your "Funding Requirements" disclosure on page 98 to disclose the same, and expand your risk factor disclosure as appropriate.*

Response: The Company respectfully acknowledges the Staff's comment and advises the Staff that the Loan and Security Agreement, dated September 23, 2019, between the Company and Silicon Valley Bank (the "***Loan Agreement***"), contains a negative covenant impacting the Company's ability to obtain additional debt financing and certain remedies that Silicon Valley Bank may pursue upon the occurrence of an Event of Default (as defined in the Loan Agreement), including a material adverse change in the Company's business, operations, or condition (financial or otherwise). However, the Loan Agreement does not contain any material financial covenants, including financial ratios. Accordingly, in response to the Staff's comment, the Company has revised the disclosure on pages 41, and 99 of the Registration Statement to reference the aforementioned negative covenant regarding the Company's ability to obtain additional debt financing and that a material adverse change in the Company's business constitutes an Event of Default under the Loan Agreement.

Management's Discussion and Analysis of Financial Condition and Results of Operations Critical Accounting Policies, Significant Judgments and Use of Estimates

Stock-Based Compensation Expense, page 103

6. *Once you have an estimated offering price or range, please explain to us how you determined the fair value of the common stock underlying your equity issuances and the reasons for any differences between the recent valuations of your common stock leading up to the IPO and the estimated offering price. This information will help facilitate our review of your accounting for equity issuances including stock-based compensation.*

Response: Following the submission of this response letter, the Company will provide the Staff with the requested information.

Internal Control Over Financial Reporting, page 106

7. *We note from your disclosures on page 71 that you identified a material weakness in internal control over financial reporting primarily related to a lack of timely review over the financial statement close process and you were unable to adequately conduct review and analysis of certain routine transactions. Additionally you disclose that the measures you have taken to date may not be sufficient to remediate the material weakness in your internal control over financial reporting. Please revise to clarify what remains to be completed in your remediation plan, if anything. Also, if the material weakness has not been fully remediated, please revise to disclose how long you estimate it will take to complete your plan and disclose any material costs you have, or expect to be, incurred.*

Response: In response to the Staff's comment, the Company has revised the disclosure on page 73 of the Registration Statement.

General

8. *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. Please contact the staff member associated with the review of this submission to discuss how to submit the materials, if any, to us for our review.*

Response: The Company is providing to the Staff, on a supplemental basis, copies of the written communications, as defined in Rule 405 under the Securities Act of 1933, as amended (the "***Securities Act***"), that have been used in meetings with potential investors in reliance on Section 5(d) of the Securities Act. These materials were only made available for viewing by potential investors during the Company's presentations, and no copies were retained by any potential investor. Pursuant to Rule 418 under the Securities Act, the copies supplementally provided shall not be deemed to be filed with, or a part of, or included in, the Registration Statement.

To the extent the Company conducts additional meetings, it expects to use the same or similar materials, and the Company undertakes to provide the Staff with copies of any additional written communications that are presented to potential investors in the future by it or anyone authorized to do so on its behalf in reliance on Section 5(d) of the Securities Act, whether or not such potential investors retain copies of such communications.

Please contact me at (415) 693-2097 or Alexa Ekman at (858) 550-6183 with any questions or further comments regarding the Company's response to the Staff's comments.

Sincerely,

/s/ Kristin VanderPas
Kristin VanderPas
Cooley LLP

cc: Richard King, Spruce Biosciences, Inc.
Samir Gharib, Spruce Biosciences, Inc.
Alexa Ekman, Cooley LLP
Brian J. Cuneo, Latham & Watkins LLP
Drew Capurro, Latham & Watkins LLP