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

DIVISION OF
CORPORATION FINANCE

September 24, 2020

Mark C. McKenna
President and Chief Executive Officer
Prometheus Biosciences, Inc.
9410 Carroll Park Drive
San Diego, California 92121

Re: Prometheus Biosciences, Inc.
Draft Registration Statement on Form S-1
Submitted August 28, 2020
CIK No.0001718852

Dear Mr. McKenna:

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.

Draft Registration Statement on Form S-1

Prospectus Summary, page 1

1. We note your disclosure regarding the size of the IBD market in the United States and globally. To the extent such data is available, please indicate on page 1 your estimate of the portion of the IBD population that are relevant to your product candidates, for example with respect to PRA023 those predisposed to increased TL1A expression.

2. Please include the indication for each program in the pipeline table on pages 2, 92 and 111.

3. On page 3, please revise the disclosure to specifically describe what you mean by "clinically-validated" and the basis for that claim. Here or in the Business section, include

a brief overview of the Phase 2a clinical trial, including indication tested, enrollment and endpoints.

4. Please briefly clarify how PR600 is distinct from the anti-TNF agents mentioned on page 1.

5. Please revise the references on page 4 and elsewhere to "rapidly advancing PRA023 into the clinic" to avoid any implication that you have the ability to accelerate FDA approvals and commercialization of your product.

6. On pages 3 and 112, please clarify whether you are collaborating with Takeda in co-development of a drug or producing a companion diagnostic for a drug Takeda is developing.

The Offering, page 8

7. We note that you intend to affect a split of your common stock prior to the effectiveness of the offering. We remind you that in accordance with SAB Topic 4:C, you will need to revise your financial statements and your disclosures throughout the filing to give effect to the expected stock split. A signed, dated, and unrestricted auditor´s report must be included in the filing prior to effectiveness. See Rule 2-02 of Regulation S-X.

Use of Proceeds, page 83

8. Please revise page 83 to disclose how far you expect to proceed in your trials of PRA023 for the treatment of ulcerative colitis and Crohn’s disease and in the development of each of your other programs. Also, to the extent material amounts of other funds are necessary to accomplish your specified purposes, state the amounts of such other funds and the sources.

Management’s Discussion and Analysis of Financial Condition and Results of Operations, page 92

9. Please further describe the terms of the December 2019 services agreement with Takeda on page 95 and tell us why you believe it is not required to be filed as an exhibit pursuant to Item 601(b)(10) of Regulation S-K.

Business, page 110

10. On page 114 you state: “For our PRA023 program, we intend to retain worldwide development and commercialization rights.” Please revise to state the extent to which this ability is dependent on technology you in-licensed.

11. Please provide more detail about the oral S1P modulators mentioned on page 118 and how their mechanism of action differs from the standard of care described here and your product candidates.

12. We note the following statement on page 120: “the potential for TL1A as a therapeutic target in intestinal fibrosis was demonstrated in a study conducted by Cedars-Sinai evaluating the effect of anti-TL1A antibodies in mouse models of IBD. In these studies, treatment with a neutralizing TL1A mAb attenuated disease and reversed colonic fibrosis.” Please provide further details concerning these studies and the Cedars-Sinai study evaluating the effect of anti-TL1A antibodies in mouse models of IBD, if separate, including treatment mechanism, sample size and results.

13. With respect to the Pfizer study on page 120, please provide the number of participants and further describe the meaning of endoscopic improvement, clinical remission and the substantial decrease in disease biomarkers. Additionally, you state “treatment was generally safe and well-tolerated.” While we would not object if you state that the treatment was well-tolerated, please revise to avoid the implication that products that act on this target, like your product candidates, are safe as that determination is solely within the authority of the U.S. Food and Drug Administration and comparable regulatory bodies. Please also describe any serious adverse events reported.

14. On page 121 you state: “Across multiple patient cohorts, our companion diagnostic captured approximately 30% of the IBD population and showed about a 4-times greater probability of identifying patients predisposed to increased TL1A expression over IBD patients predisposed to lowered TL1A expression.” Please explain what capturing 30% of the IBD population means, and what the 4-times greater statement is a comparison to.

15. Please clarify which US and non-US patents and patent applications you own and which you license on page 125. Please also state the amount of the cited "subset" of the US patents and patent applications that you are pursuing in other countries.

16. Please revise to specify the LDT diagnostic products for which patent protection expired in 2020 as noted on page 126.

17. On page 130 you state the following with respect to the Falk Agreement: “In the event of such termination, all licenses granted to the terminating party will cease and be transferred to the non-terminating party, and such non-terminating party will have access to the terminating party’s technology, subject to the obligation to pay the applicable royalties to the terminating party.” Please clarify the meaning of access to technology and the contractual duration for such access.

18. On page 130 please provide the amount of the annual maintenance fee under the license agreement with Alloy Therapeutics, LLC.

19. We note when describing the royalty term for the collaboration and license agreements described on pages 127 - 130, you note that the term will expire on the latest to occur of several events, including the expiration date of the last valid claim on a country-by-country basis. Please revise to clarify the types of claims this refers to and when these claims are expected to expire.

Executive and Director Compensation, page 166

20. On page 169, please revise to explain the perquisites or personal benefits to your named executive officers that have or will be provided and the limited circumstances in which they have or will be provided.

4. Balance Sheet Details
Accrued Rebates and Sales Returns, page F-18

21. We note your disclosure that as a result of the PLI acquisition, the Company assumed a liability of approximately $9.0 million related to state government rebates for pharmaceutical products previously divested by PLI and recorded a corresponding indemnification asset of approximately $7.0 million for the expected reimbursement to be received from Nestlé as rebates are settled by the Company. We further note your statement that the Company plans to dispute a portion of this liability with state governments and if the Company is successful, this could have a material impact on the consolidated statements of operations in the future. Finally, we note your disclosure in your subsequent events footnote on page F-34 that as a result of the Amendment to the PLI Acquisition Agreement, Nestlé agreed to reimburse the Company for 77.5% of a pre-acquisition rebate liability of $9.0 million and 50% of any amounts settled by the Company that are above $9.0 million. As such, please confirm whether the only expected exposure and related impact to the Company's consolidated statements of operations in the future is approximately $1 million, otherwise please clarify the accounting guidance the Company is relying on, such that the Company is expecting a material impact on its consolidated statements of operations. Please update your disclosures to clarify accordingly.

You may contact Ameen Hamady at 202-551-3891 or Daniel Gordon at 202-551-3486 if you have questions regarding comments on the financial statements and related matters. Please contact Margaret Schwartz at 202-551-7153 or Mary Beth Breslin at 202-551-3625 with any other questions.

Sincerely,

Division of Corporation Finance
Office of Life Sciences

cc: Matthew T. Bush