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

DIVISION OF
CORPORATION FINANCE

February 17, 2022

Keith Gottesdiener, M.D.
President and Chief Executive Officer
Prime Medicine, Inc.
21 Erie Street
Cambridge, MA 02139

Re: Prime Medicine, Inc.
Amendment No. 2 to Draft Registration Statement on Form S-1
Submitted February 4, 2022
CIK No. 0001894562

Dear Dr. Gottesdiener:

We have reviewed your amended 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.

Amendment No. 2 to Draft Registration Statement on Form S-1

Our Prime Editing Platform, page 1

1. Although we note your response to prior comment 2 and your revisions on page 45, we continue to believe that your disclosure in this section that your Prime Editing technology has the theoretical potential for repairing approximately 90 percent of known disease-causing mutations across many organisms, organs and cell types should be balanced with disclosure that your licenses from the Broad Institute are subject to an inclusive innovation model, are subject to march-in-licenses, and that the Broad Institute may terminate your license with respect to gene targets under the terms of the Broad License Agreement. Please revise your disclosure to make investors aware of these arrangements in your prospectus summary.

Overview, page 1

2. We note your response to comment 5 and re-issue. Given your prominent disclosure on the first page that you have "proprietary Prime Editing technology[,]" please provide balancing disclosure on this same page that you do not currently own any issued patents. If the term "proprietary" is referring to another method of IP protection, please so advise and update this page accordingly. Your disclosure should also address the technology that is proprietary, or company-developed, versus the technology developed at Broad Institute which you have in-licensed.

3. We note your response to comment 6 as it concerns our request that you disclose that Dr. Liu will not be an officer or director of your company and will work in the capacity as a consultant to your company and will retain his positions and affiliations with the Broad Institute, Harvard University and the Howard Hughes Medical Institute. Given your prominent disclosure on page 1 that "Prime Medicine was co-founded by a world-renowned leader in the field of gene editing, David Liu, Ph.D.[,]" there should be balancing disclosure in this same section that Dr. Liu will not be an officer or director of your company, will solely work in the capacity as a consultant to your company under a consulting agreement the current term of which runs through September 2025, and will retain his positions and affiliations with the Broad Institute, Harvard University and the Howard Hughes Medical Institute. If there is uncertainty to whether Dr. Liu will or will not be an officer or director of the Company, this uncertainty should also be disclosed in this section.

4. We note your response to comment 6 as it concerns our request that you briefly indicate Dr. Liu's involvement with other gene editing companies, including Editas Medicine, Inc. and Beam Therapeutics, Inc., and the potential for conflicts of interest. While we are satisfied with your response as it concerns Editas Medicine, it does not appear that you have responded to our request that you briefly indicate Dr. Liu's involvement with Beam Therapeutics, Inc. Please so indicate this involvement and address any conflicts of interest in the prospectus summary.

5. We note your amended disclosure on page 120 that you "have also licensed certain improvements to Prime Editing from Dr. Liu's laboratory at Broad Institute and Dr. Liu has entered into an agreement with us pursuant to which he is obligated to assign to us any inventions with respect to the services he performs for us. However, such obligations are subject to limitations and do not extend to his work in other fields or to the intellectual property arising from his employment with Harvard, HHMI and Broad Institute. To obtain such intellectual property rights, we would need to enter into license agreements with such institutions, including negotiations under the Broad Option Agreement, which may expire in November 2022, and such license agreements may not be available on commercially reasonable terms or at all." Please address this specific risk in your risk factor section and cross-reference this risk factor in your prospectus summary. We do not believe that the current risk factor on page 25 entitled "[t]he gene editing field is relatively

new and is evolving rapidly" adequately addresses this specific risk. Ensure that this revised risk factor addresses whether you would need to enter into new license agreements to obtain the rights to the "engineered pegRNAs″ that you mention on page 137.

Pipeline Table, page 5

6. We note your response to comment 5. Please provide two separate columns for your phase 1 and phase 2 trials or, alternatively, disclose the basis for your belief that you will have a phase 1/2 trial for every indication listed in the pipeline table.

Summary Financial Data, page 13

7. Please provide us with your calculation of pro forma net loss per share attributable to common stockholders. Based on the description included in footnote 4 for the numerator, it would appear the amount is $0.82.

Risk Factors, page 15

8. We note your response to comment 12. While you adequately addressed our repricing concerns about the 2022 plan on page 224, it appears that these concerns may still apply to the 2019 plan. On page 222 you state "[t]he administrator of the 2019 Plan is specifically authorized to exercise its discretion to reduce the exercise price of outstanding stock options or effect the repricing of such awards through cancellation and re-grants." As such, please include appropriate risk factor disclosure, including whether proxy advisory firms could find such repricing without stockholder approval contrary to a performance-based pay philosophy, or tell us why such disclosure would not be appropriate.

Our rights to develop and commercialize our Prime Editing platform technology and product candidates are subject to the terms..., page 45

9. We note your response to comment 13 but we cannot locate responsive revisions on page 45 or in the cross-referenced section which appears to refer to your disclosure starting on page 178. As such, we re-issue the comment. Please revise this risk factor to identify the product candidates that are or may be subject to the Broad march-in-license. If all gene targets are subject to the march-in-license, please make that clear.

Business

Overview, page 117

10. Although we note your response to prior comment 19, with respect to your disclosure that more than 1,500 laboratories have requested the reagents to perform Prime Editing in their laboratories, please disclose if those requests have made to you or to Broad Institute. Please also disclose if those requests are part of Broad Institute’s inclusive innovation model pursuant to which Broad Institute retains the right, under specified circumstances, to grant to third parties (other than specified competitors of yours) licenses under the licensed patent rights that would otherwise fall within the scope of the exclusive license

granted to you. Include risk factor disclosure as appropriate. Please also clarify what "reagents" encompasses in this context.

11. We note your response to comment 20 that "the *Nature* publication in December 2019 did not disclose any pegRNA, ngRNA or Prime Editor protein sequences that are used in your current programs." Please so indicate this on this page of the filing. If your Prime Editors were not used in the cited studies and papers, please qualify your statement, as appropriate, that "Prime Editing technology has been extensively validated *in vitro* and in animal studies."

12. With respect to your disclosure that "[a]lthough Prime Editing technology is not yet validated in clinical studies, as first described in a Nature publication in December 2019, Prime Editing technology has been extensively validated in vitro and in animal studies with over 50 papers published in the primary scientific literature to date," we continue to believe that you should balance your disclosure to indicate the developing nature of this technology. As requested by our prior comment 20, please indicate the publication in the science journal *Cell* in October 2021 co-authored by one of your founders which indicated that while prime editing enables precise sequence changes in DNA, cellular determinants of prime editing remain poorly understood and that DNA mismatch repair (MMR) impedes prime editing and promotes undesired indels and that new prime editing systems were recently developed in an attempt to overcome these limitations. In this regard, although we note your response that the company has recently developed new Prime Editing systems to overcome limitations such as MMR, we note your disclosure on page 139 that you are developing approaches to transiently modify MMR so that desired Prime Edits are favored, and any undesired by-products are minimized, and that you are evaluating several different approaches to modulating the MMR response including active pharmaceutical ingredients, such as siRNA, or small interfering RNA, or other approaches that transiently modulate MMR activity which could be co-administered with a Prime Editor. Please indicate these developments and disclose to what extent the new Prime Editing systems and your approaches to transiently modify MMR have been validated.

Scientific Advisory Board, page 121

13. We note your response to comment 30 and your amendment on page 121. In addition to the "focal points" already listed, as requested by our prior comment please disclose if there are any rules or procedures governing your Scientific Advisory Board.

Our Prime Editing Platform, page 126

14. We note your response to comment 21. Given your disclosure on page 126 that this table is not derived from head-to-head comparison studies, we do not object to the inclusion of this table in the filing; however, we request that you explicitly disclose the "publicly available data" underlying the conclusions in this table. We also note that your February 4, 2022 correspondence states that "the Company’s own data, form the basis for these assessments." If true, please amend the filing to disclose that the conclusions in this table

are also derived from your own data.

Pledge to Broad Institute and Harvard, page 182

15. We note your response to comment 27. We do not agree that the written agreement underlying your Pledge to donate $5 million to the Broad Institute and Harvard University annually for 14 years is not a material contract in amount or in effect. In amount, this contract is worth a potential aggregate amount of $70 million over 14 years. In effect, it appears that you are using this Pledge as a form of consideration in order to have continued access to the intellectual property owned by the Broad Institute and Harvard University. For example, you have an executed option agreement with Broad Institute connected to your patent rights and, in evaluating and approving the Pledge annually, you "will consider if the previous year's grant was used for the intended purpose." Moreover, Dr. Liu is employed at Harvard and you will consider whether Dr. Liu "has continued in good standing on his active agreements with Prime Medicine" in determining whether to renew the annual pledge. Accordingly, we believe this is a material contract. Please file it as an exhibit pursuant to Item 601(b)(10) of Regulation S-K.

Research Collaboration, Option and License Agreement with Myeloid, page 182

16. We note your disclosure on this page that Myeloid is a related party and your disclosure on page 230 that Newpath Partners, L.P. holds more than 5 percent of your voting securities, and holds more than 5 percent of Myeloid's voting securities. As such, it appears this agreement should be filed as an exhibit under Item 601(b)(10)(ii)(A) of Regulation S-K. Please file your Research Collaboration, Option and License Agreement with Myeloid as an exhibit or tell us why you do not believe you are required to file this agreement.

Executive Compensation, page 216

17. We note your response to comment 32. We also note your disclosure that Dr. Anzalone was a co-founder of the company. Please tell us why Dr. Anzalone would not be considered a promoter for purposes of Securities Act Rule 405 and Regulation S-K Item 601(b)(10)(ii)(A) and whether you should file the Employment Agreement and the Employee Confidentiality, Assignment and Nonsolicitation Agreement with Dr. Anzalone as exhibits, or file those agreements as appropriate.

11. License and Collaboration Agreements
Related Party Beam Collaboration Agreement, page F-40

18. We note your response to comment 35 in which you note that you evaluated the protected product option and the collaboration product option under the guidance in ASC 606-10-55-41 through 55-43. Please tell us how you concluded that these options represent options for additional goods or services rather than a material right that you would not receive without entering into that contract. In this regard, clarify whether these options

offer a future discount that is incremental to the range of discounts typically given to the same class of customer. Please also tell us whether you will receive any further consideration for the license granted to Beam for products in which an IND is filed but Beam does not exercise the protected product option and you do not exercise the collaboration product option and how this consideration differs whether either of these options are exercised. For example, you disclose that the the sickle cell disease product is a licensed product under the Beam Collaboration and that Beam has not designated this product as a protected product and you therefore have not received any development or sales-based milestones in relation to this product. To the extent that neither option is ultimately exercised in relation to this sickle cell product, clarify whether you are entitled to any further consideration in the form of milestones or royalties.

You may contact Tracey Houser at 202-551-3736 or Angela Connell at 202-551-3426 if you have questions regarding comments on the financial statements and related matters. Please contact Dillon Hagius at 202-551-7967 or Tim Buchmiller at 202-551-3635 with any other questions.

Sincerely,

Division of Corporation Finance
Office of Life Sciences

cc: Marishka DeToy, Esq.