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

DIVISION OF
CORPORATION FINANCE

January 18, 2022

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

Re: Prime Medicine, Inc.
Draft Registration Statement on Form S-1
Submitted December 20, 2021
CIK No. 0001894562

Dear Dr. Gottesdiener:

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

Our Prime Editing Platform, page 1

1. In an appropriate location in your prospectus, please briefly provide support for your disclosure that your Prime Editing technology is capable of repairing approximately 90 percent of known disease-causing mutations across many organisms, organs and cell types, or revise this claim as appropriate. Given that you are in the research stage for most of your targeted indications in humans, please balance this disclosure with any known problems in editing genes that cause human disease in various tissue types. As one example only, we note your disclosure on page 143 that in the second most common form of CGD, the NCF1 gene location is complex. If the location of the gene in the chromosome and/or its complex location could impact your ability to edit a targeted gene

please make that clear and provide other balancing disclosure as appropriate as to the 90 percent claim. We also note your disclosure that a significant portion of your studies to date have been *in vitro* or *ex vivo*, if cautionary disclosure about this claim for *in vivo* gene editing is warranted, please include appropriate balancing disclosure.

2. Please balance your disclosure that your Prime Editing technology has broad therapeutic applications and is capable of repairing approximately 90 percent of known disease-causing mutations across many organisms, organs and cell types with disclosure regarding the potential impact of the march-in-license under the Broad License Agreement that is described on page 166.

Prospectus Summary
Overview, page 1

3. Please remove the statement that your Prime Editing Technology is "effective." Efficacy determinations are in the exclusive purview of the FDA or other regulators. In this regard, we note your statements on page 20 that "[g]ene editing, including platforms such as Prime Editing, is a novel technology that is not yet clinically validated for human therapeutic use" and that "[t]he approach we are taking to discover and develop novel therapeutics is unproven and may never lead to marketable products." Ensure that similar efficacy language, which we note is present throughout the filing, is also removed.

4. You state that Prime Editing is your "versatile, precise" and "broad next generation gene editing technology." Please clarify that this is your belief and provide balancing language that gene editing, including your Prime Editing platform, is a novel technology that has not been FDA approved for any indication. We note risk factor disclosures to this effect on pages 20 and 25.

5. We note your disclosure on this page that your Prime Editing technology is "proprietary." Please provide balancing disclosure that you do not currently own any issued patents. We note your risk factor disclosure to this effect on pages 45 and 47.

6. With regard to your disclosure that Prime Medicine was co-founded by David Liu, Ph.D., please also 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. Please also 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. We also note your disclosure that if nuclease gene editing approaches are "scissors" for the genome, and base editors are "pencils," erasing and rewriting a subset of single letters in the gene, then Prime Editing is a "word processor." To the extent there may be future improvements or enhancements to Prime Editing, or next-generation gene editing technologies, developed by Dr. Liu or his group at the Broad Institute, Harvard or HHMI, please caution investors, if true, that the related intellectual property rights may not necessarily be assigned to your company and would have to be

negotiated for under the Broad Option Agreement which may expire in November 2022 and is also subject to the policies and regulations of certain institutions and certain agreements between Dr. Liu and certain third parties, including Editas Medicine and Beam Therapeutics, and may not be available on commercially reasonable terms or at all. In this regard, we also note your disclosure under "Engineered pegRNAs" on page 134 that Dr. Liu's laboratory at the Broad Institute has recently developed engineered pegRNAs that can improve Prime Editing efficiency by 3-fold or more in multiple human cell types and is an enhancement that is now being incorporated into your research activities. In an appropriate location, please disclose whether you have exclusively in-licensed the intellectual property rights to the epegRNAs and include risk factor disclosure, if appropriate.

Our strategy, page 4

7. We note your disclosure on this page and on page 118 that you intend to de-risk your Prime Editing platform. Please explain what you mean by de-risk. It is not appropriate to convey that your candidates are without development risk. If necessary, please revise this language.

Pipeline Table, page 5

8. Include all clinical stages that must be completed before commercialization (i.e., add columns for Phases 1, 2 and 3).

9. Please explain what is involved in "lead optimization" and why you believe this is a separate and distinct development phase, as opposed to part of the discovery phases. While we will consider your response, we do not currently believe that the lead optimization is distinct from the discovery phase and should thus be depicted under the discovery column. A textual discussion of the program is likely a more appropriate place to make distinctions regarding different segments within a particular phase.

10. We note the pipeline table has seven "undisclosed" indications that are only discussed briefly in the business section on pages 153 (two hearing loss indications) and 160 (three neuromuscular indications, a muscular dystrophy indication, and a progressive lung disease indication). To the extent these are material programs, disclose the specific targets and provide more fulsome descriptions of these programs. Otherwise, please remove them from the table or explain the basis for your belief that they are material and should be included in your pipeline table.

Summary Financial Data, page 13

11. Please revise your calculation of pro forma weighted-average common shares outstanding to reflect the conversion of preferred stock outstanding at each period end. In this respect, it appears that your calculation of weighted-average common shares outstanding as of December 31, 2020 includes the conversion of preferred shares that were not yet issued.

Risk Factors, page 15

12. We note your disclosure on page 207 that the administrator of the 2022 Plan is specifically authorized to exercise its discretion to reduce the exercise price of outstanding stock options and stock appreciation rights or effect the repricing of such awards through cancellation and re-grants without stockholder consent. 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.

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

13. Please revise to identify the product candidates that are or may be subject to march-in rights.

We are an "emerging growth company"..., page 74

14. We note your disclosure that you have irrevocably elected not to avail yourselves of the extended transition period for complying with new or revised accounting standards, which is inconsistent with the disclosures you have provided on the cover sheet and pages 10 and 113. Please revise your disclosures to remedy this inconsistency.

Use of Proceeds, page 82

15. We note your disclosure that you intend to use the proceeds from the offering to achieve "preclinical proof-of-concept in several programs." Please identify these programs. To the extent that you plan to use a material portion of the proceeds to fund the development of a specific pipeline candidate, please separately quantify the amounts you expect to allocate to each product candidate and specify how far in the clinical development for each of these product candidates you expect to reach with the proceeds of this offering.

Dilution, page 86

16. We note that your calculations of historical and pro forma net tangible book (deficit) per share assumes 100,768, 255 shares of common stock outstanding as of September 30, 2021. Please tell us how you determined to include any unvested restricted shares in this calculation given that such shares are not included in your calculation of basic and diluted earnings per share. Expand your disclosures to clarify the number of shares used in the calculation. Refer to ASC 260-10-45-13.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Critical Accounting Policies and Significant Judgments and Estimates
Stock-Based Compensation Expense, page 109

17. Please expand your disclosures regarding your estimated enterprise value to provide the specific valuation methods under the market approach used, along with the corresponding

material estimates and assumptions used in each method to estimate the enterprise value that is being allocated to your various equity instruments.

18. Please expand the table included on page 111 to include all equity-based grants for fiscal year 2020.

Business
Overview, page 114

19. Please qualify your statement on this page and other locations that "Prime Editing has been extensively validated with over 50 papers published in primary scientific literature" by indicating, as you disclose on page 20, that "[g]ene editing, including platforms such as Prime Editing, is a novel technology that is not yet clinically validated for human therapeutic use." We also note your disclosure here that "more than 1,500 laboratories have requested the reagents to perform Prime Editing in their laboratories." Please clarify what type of validation this is intended to convey to investors and clarify if distributing your reagents could allow competitors to reverse-engineer or improve your technology in ways that could circumvent your intellectual property.

20. You note that Prime Editing was "[f]irst described in a Nature publication in December 2019[.]" Please clarify whether this publication specifically concerned any of your current product candidates. We also understand that there was a 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. Please update your disclosure for the findings in this publication that would be material to investors.

Our Prime Editing Platform, page 122

21. We note the table on page 124, which contains head-to-head comparisons between Prime Editing and three other methods of gene editing. Please disclose the sources for these comparisons. For instance, did you conduct your own head-to-head study or are you relying on a third-party comparison? If these methods have not been directly compared and studied, please remove this table.

22. Please remove the "effectiveness" section of the table on page 124. As Prime Editing has not been FDA approved - nor does it appear that any of the gene editing methodologies mentioned in this table have been FDA approved - the inclusion of this section is not appropriate.

Our License and Collaboration Agreements
Strategic relationship with Beam Therapeutics, page 161

23. Please revise the description of the Beam Collaboration Agreement to:

- disclose the the maximum aggregate milestones you may receive under the agreement for both protected and collaboration products;
- narrow the disclosure of the sales royalty provision range to a range that does not exceed ten percentage points; and
- state when the royalty provisions expire.

As it concerns the aggregate milestones, we do not believe your use of the terms "low-eight figures," "mid eight figures," or "high-eight figures" is sufficient, and, as it concerns the royalty range, we do not believe your reference to a "low-double-digit" royalty narrowed the range to 10 percentage points.

24. Please provide more specific disclosure about the material terms of the collaboration with Beam as it concerns the Sickle Cell product that is listed on your pipeline table. This disclosure should:
- quantify milestone payments received to date;
- narrow the disclosure of the sales royalty provision range to a range that does not exceed ten percentage points; and
- state when the royalty provisions expire.

License agreement with The Broad Institute, page 164

25. Please revise the description of the Broad Institute License Agreement to disclose:
- the the maximum aggregate milestones you may receive under the agreement for both protected and collaboration products;
- the expected expiry of the last-to-expire ending patent application licensed under the agreement; and
- when the royalty provisions expire.

As it concerns the aggregate milestones, we do not believe your use of the terms "low-eight figures" or "mid- eight figures" is sufficient.

Option Agreement with Broad Institute, page 167

26. Please file your option agreement with Broad Institute as an exhibit pursuant to Item 601(b)(10) of Regulation S-K or tell us why you do not believe you are required to file this agreement.

Pledge to the Broad Institute and Harvard University, page 168

27. If there is a written agreement underlying the Pledge to donate $5,000,000 to Broad Institute and Harvard University annually for 14 years, please file it as an exhibit pursuant to Item 601(b)(10) of Regulation S-K or tell us why you do not believe you are required to file this agreement.

Facilities, page 190

28. We note that you lease three different properties. Please file your lease agreements as exhibits pursuant to Item 601(b)(10) of Regulation S-K or tell us why you do not believe

you are required to file them.

Management, page 191

29. Please identify and provide disclosure regarding any significant employees who are not executive officers but who have made or are expected to make significant contributions to the business of the company. For example, we note your disclosure regarding Dr. Andrew Anzalone on page 116 but do not see disclosure in accordance with Item 401(c) of Regulation S-K.

30. We note your disclosure on page 212 that Dr. Liu will serve as Chairman of your Scientific Advisory Board. In an appropriate location in your prospectus, please identify any other members of your advisory board and describe the role or function of the scientific advisory board and whether there are any rules or procedures governing such board.

Non-Employee Directors, page 192

31. Please clarify that John Evans is serving as a director pursuant to the Beam Collaboration Agreement, which we note you disclose on page 163. Review Item 401(a) of Regulation S-K.

Executive Compensation, page 200

32. Please file the Employment Agreement and the Employee Confidentiality, Assignment and Nonsolicitation Agreement with Andrew V. Anzalone as exhibits pursuant to Item 601(b)(10) of Regulation S-K or tell us why you do not believe you are required to file them.

Policies for Approval of Related Party Transactions, page 213

33. Please disclose the standards that will be applied in determining whether to approve any of the transactions described in this section. Refer to Item 404(b)(1)(ii) of Regulation S-K.

2. Summary of Significant Accounting Policies, page F-11

34. Please revise your Summary of Significant Accounting Policies to describe your accounting policy for research and development expenses, including the type of costs included in this line item and when costs are accrued and/or recognized. In this respect, we note that your current disclosures only describe your accounting policy for acquired IPR&D. Refer to ASC 730-10-25-2 and ASC 730-20-35-1 for guidance.

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

35. You disclose that there is no variable consideration under the Beam Collaboration

Agreement despite your assertion that you are entitled to receive development payments from Beam on Beams' development of licensed products. You also disclose that upon Beam's opt in, which appears to have occurred in September 2020, you are entitled to development, regulatory and sales milestones as well as royalties. Please explain how you determined that such potential milestone payments are not considered variable consideration under the agreement. Please also disclose how you are accounting for any sales-based milestones and royalties.

15. Subsequent Events, page F-45

36. Please expand your disclosures for the grant of performance-based options to list the three separate milestones that need to be met for vesting, including whether it was probable that the milestones would be met.

General

37. 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.

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.