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

DIVISION OF
CORPORATION FINANCE

August 19, 2020

Kris Vaddi, Ph.D.
Chief Executive Officer
Prelude Therapeutics Incorporated
200 Powder Mill Road
Wilmington, DE 19803

Re: Prelude Therapeutics Incorporated
Draft Registration Statement on Form S-1
Submitted July 23, 2020
CIK No. 0001678660

Dear Dr. Vaddi:

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

Overview, page 2

1. Given the status of your development of your product candidates, please tell us the basis for your claims on page 1 and throughout the registration statement that your product candidates are potent and selective.

2. Please revise your pipeline tables on pages 2 and 93 to include columns depicting each of Phase 1, Phase 2, and Phase 3 to ensure that all stages in the clinical trial process prior to seeking FDA approval are shown. In addition, please remove the "Pivotal" label, as it is premature to suggest that the completion of the Phase 1/2 clinical trials will lead to a

pivotal Phase 3 trial for the products listed. Note that the arrows for each listed program should be accurately drawn to show the precise phase of development after the table has been revised.

Implications of Being an Emerging Growth Company and a Smaller Reporting Company, page 5

3. Please 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.

Use of Proceeds, page 72

4. Please revise the discussion to identify the stage of clinical development you expect to achieve with the proceeds of the offering for PRT543, PRT811, and PRT1419. To the extent you expect to begin a particular stage of development but do not expect to complete it, please indicate that you will need to raise additional funding to complete that stage of development.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Critical Accounting Policies
Stock-Based Compensation, page 88

5. 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 compensation and beneficial conversion features.

Target Selection, page 99

6. We note your statements regarding your framework for optimizing your drug discovery and development efforts that you believe "increases the probability of clinical and regulatory success...." We also note your statements that you believe your approach "will result in better targeted and more effective cancer therapies" and that you have observed "promising clinical activity" to date. Please revise the prospectus to remove any statements, such as these, that imply forthcoming regulatory approval of you product candidates or the safety and efficacy of your candidates, as these determinations are the exclusive authority of the FDA or other regulators.

Our Product Candidates, page 101

7. Revise to explain briefly key measures you cite throughout your Business section, including terms such as “complete response” and “stable disease.” Also, please ensure that you provide a balanced presentation of clinical results. In this regard, we note that

your discussion of the interim and preliminary efficacy data for your PRT543 Phase 1 trial where you highlight a patient with a confirmed complete response but you do not provide interim data for the other 25 patients. Please revise or advise.

8. Please revise the discussion that accompanies Tables 2, 3, and 5 to clarify how these results demonstrate the relative inhibitory potency of your product candidates and also discuss why the levels achieved support continued clinical development.

Group A (Solid Tumors), page 111

9. Please revise your disclosure to briefly explain the parameters "Tmax" and "AUC0-T" listed in the tables on pages 111, 112 and 119.

Employment Arrangements with our Named Executive Officers, page 153

10. Please file your employment agreements with each of your executive officers as exhibits to the registration statement, as required by Item 601(b)(10) of Regulation S-K.

Audited Financial Statemetns as of December 31, 2018 and 2019 and for the Years then Ended
Note 1 Net Loss Per Share and Unaudited Pro Forma Net Loss Per Share, page F-11

11. Your pro forma net loss per share calculation appears to assume that the 8,823,529 shares of Series B convertible preferred stock issued in May 2019 converted at the beginning of the period rather than at their date of issuance. Please refer to ASC 260-10-45-40(c) and advise or revise your pro forma information accordingly. Also, once you update your financial statements for the six months ended June 30, 2020, please address this comment as it relates to the 8,823,529 shares of Series B convertible preferred stock issued in March 2020.

You may contact Rolf Sundwall at 202-551-3105 or Jeanne Baker at 202-551-3691 if you have questions regarding comments on the financial statements and related matters. Please contact Jeffrey Gabor at 202-551-2544 or Laura Crotty at 202-551-7614 with any other questions.

Sincerely,

Division of Corporation Finance
Office of Life Sciences

cc: Rob Freedman, Esq.