UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM S-8

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

PRELUDE THERAPEUTICS INCORPORATED

Delaware

(State or other jurisdiction of incorporation or organization)

(Exact name of Registrant as specified in its charter)

81-1384762

(I.R.S. Employer Identification Number)

> 200 Powder Mill Road Wilmington, Delaware 19803 (302) 467-1280

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

2020 Equity Incentive Plan

2020 Employee Stock Purchase Plan

(Full title of the plans)

Kris Vaddi, Ph.D. Chief Executive Officer Prelude Therapeutics Holdings 200 Powder Mill Road Wilmington, Delaware 19803 (302)467-1280

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Please send copies of all communications to:

Effie Toshav, Esq. Robert Freedman, Esq. Julia Forbess, Esq. Fenwick & West LLP 555 California Street, 12th Floor San Francisco, California 94104 (415) 875-2300

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definition of "large accelerated filer", "accelerated filer", "smaller reporting company", and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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Large accelerated filer		Accelerated filer	
Non-accelerated filer	\boxtimes	Smaller reporting company	\boxtimes
		Emerging growth company	\boxtimes

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. \square

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price Per Share	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Common Stock, par value \$0.0001 per				
share				
2020 Equity Incentive Plan	2,185,283 (2)	\$57.28 (3)	\$125,173,011	\$13,657
2020 Employee Stock Purchase Plan	437,056 (4)	\$48.68 (5)	\$21,275,887	\$2,322
Total	2,622,339		\$146,448,898	\$15,979

- (1) Pursuant to Rule 416(a) under the Securities Act of 1933, as amended (the "Securities Act"), this Registration Statement shall also cover any additional shares of the Registrant's common stock that becomes issuable in respect of the securities identified in the above table by reason of any stock dividend, stock split, recapitalization or other similar transaction effected without the receipt of consideration that increases the number of the Registrant's outstanding shares of common stock.
- (2) Represents additional shares to be registered and available for grant under the 2020 Equity Incentive Plan ("2020 EIP") resulting from the annual 5% automatic increase in the number of authorized shares available for issuance under the 2020 EIP.
- (3) Estimated in accordance with Rules 457(c) and 457(h) of the Securities Act solely for the purpose of calculating the registration fee. The proposed maximum offering price per share of \$57.28 was computed by averaging the high and low prices of a share of Registrant's common stock as reported on The Nasdaq Stock Market LLC on March 12, 2021.
- (4) Represents additional shares to be registered and available for grant under the 2020 Employee Stock Purchase Plan ("2020 ESPP") resulting from the annual 1% automatic increase in the number of authorized shares available for issuance under the 2020 ESPP.
- (5) Estimated in accordance with Rules 457(c) and 457(h) of the Securities Act solely for the purpose of calculating the registration fee. The proposed maximum offering price per share of \$48.68 was computed by averaging the high and low prices of a share of Registrant's common stock as reported on The Nasdaq Stock Market LLC on March 12, 2021, multiplied by 85%, which is the percentage of the trading price per share applicable to purchasers under the 2020 ESPP.

REGISTRATION OF ADDITIONAL SHARES PURSUANT TO GENERAL INSTRUCTION E

Prelude Therapeutics Incorporated (the "*Registrant*") is filing this Registration Statement with the Securities and Exchange Commission (the "*Commission*") to register (a) 2,185,283 additional shares of common stock available for issuance under the Registrant's 2020 EIP, pursuant to the provision of the 2020 EIP providing for an annual 5% automatic increase in the number of shares reserved for issuance and (b) 437,056 additional shares of common stock available for issuance under the Registrant's 2020 ESPP, pursuant to the provision of the 2020 ESPP providing for an annual 1% automatic increase in the number of shares reserved for issuance.

ESPP, this Registration Statement hereby incorporates by reference the contents of the Registrant's Registration Statement on Form S-8 filed with the	
Commission on September 25, 2020 (Registration No. 333-249032), to the extent not superseded hereby.	

In accordance with General Instruction E of Form S-8, and only with respect to the common stock issuable under the 2020 EIP and 2020

PART II INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

Item 3. Incorporation of Documents by Reference.

The following documents filed by the Registrant with the Commission pursuant to the Securities Act and the Securities Exchange Act of 1934, as amended (the "Exchange Act") are incorporated herein by reference:

- (a) the Registrant's Annual Report on Form 10-K for the year ended December 31, 2020, filed with the Commission on March 16, 2021 pursuant to Section 13 of the Exchange Act;
- (b) the Registrant's Current Reports on Form 8-K filed with the Commission on <u>January 28, 2021</u> and <u>March 8, 2021</u>;
- (c) all other reports filed pursuant to Section 13(a) or 15(d) of the Exchange Act since the end of the fiscal year covered by the Registrant's Annual Report on Form 10-K referred to in (a) above; and
- (d) the description of the Registrant's common stock contained in the Registrant's registration statement on Form 8-A (File No. 001-39527) filed on September 16, 2020 under Section 12(b) of the Exchange Act, including any amendment or report filed for the purpose of updating such description.

All documents filed by the Registrant pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act subsequent to the filing of this Registration Statement and prior to the filing of a post-effective amendment which indicates that all securities offered hereby have been sold or which deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference into this Registration Statement and to be a part hereof from the date of filing such documents, except as to specific sections of such documents as set forth therein. Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes of this Registration Statement to the extent that a statement contained in any subsequently filed document which also is deemed to be incorporated by reference herein modifies or supersedes such statement.

Item 5. Interests of Named Experts and Counsel.

Not applicable.

Item 8. Exhibits.

The following exhibits are filed herewith:

Exhibit	Incorporated by Reference			Filed		
<u>Number</u>	Exhibit Description	<u>Form</u>	<u>File No.</u>	<u>Exhibit</u>	Filing Date	Herewith
4.1	Restated Certificate of Incorporation of the Registrant	10-Q	001-39527	3.1	11/10/2020	
4.2	Restated Bylaws of the Registrant	10-Q	001-39527	3.2	11/10/2020	
4.3	Form of Registrants Common Stock Certificate	S-1/A	333-248628	4.1	9/16/2020	
5.1	Opinion of Fenwick & West LLP					X
23.1	Consent of Fenwick & West LLP (contained in Exhibit 5.1)					X

23.2	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm					X
24.1	Power of Attorney (included on the signature page to this Registration Statement)					X
99.1	2020 Equity Incentive Plan and forms of award agreements thereunder	S-1/A	333-248628	10.3	9/21/2020	
99.2	2020 Employee Stock Purchase Plan and forms of award agreements thereunder	S-1/A	333-248628	10.4	9/21/2020	

SIGNATURES

Pursuant to the requirements of the Securities Act, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Wilmington, State of Delaware, on this 16th day of March, 2021.

PRELUDE THERAPEUTICS INCORPORATED

By: /s/ Krishna Vaddi
Krishna Vaddi
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Kris Vaddi and Brian Piper, and each of them, as his or her true and lawful attorney-in-fact and agent with full power of substitution, for him or her in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement on Form S-8, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his or her substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this Registration Statement has been signed by the following persons in the capacities and on the date indicated.

Name	Title	Date
/s/ Krishna Vaddi Krishna Vaddi, Ph.D.	Chief Executive Officer and Director (Principal Executive Officer)	March 16, 2021
/s/ Brian Piper Brian Piper, M.B.A.	Chief Financial Officer (Principal Financial and Accounting Officer)	March 16, 2021
/s/ Paul A. Friedman Paul A. Friedman	Director	March 16, 2021
/s/ David Bonita David Bonita, M.D.	Director	March 16, 2021
/s/ Mardi C. Dier Mardi C. Dier	Director	March 16, 2021
/s/ Julian Baker Julian Baker	Director	March 16, 2021
/s/ Victor Sandor Victor Sandor, M.D.C.M.	Director	March 16, 2021

March 16, 2021

Prelude Therapeutics Incorporated 200 Powder Mill Road Wilmington, Delaware 19803

Ladies and Gentlemen:

At your request, as your counsel, we have examined the Registration Statement on Form S-8 (the "Registration Statement") to be filed by Prelude Therapeutics Incorporated, a Delaware corporation (the "Company") with the Securities and Exchange Commission (the "Commission") on or about March 16, 2021 in connection with the registration under the Securities Act of 1933, as amended (the "Securities Act"), of an aggregate of 2,622,339 shares (the "Shares") of the Company's Common Stock, \$0.0001 par value per share (the "Common Stock"), subject to issuance by the Company (a) upon the exercise or settlement of awards granted or to be granted under the 2020 Equity Incentive Plan (the "2020 Plan") pursuant to the provision of the 2020 Plan providing for an annual 5% automatic increase in the number of shares reserved for issuance under the 2020 Plan and (b) pursuant to purchase rights to acquire shares of Common Stock granted or to be granted under the Company's 2020 Employee Stock Purchase Plan (the "Purchase Plan") pursuant to the provision of the Purchase Plan providing for an annual 1% automatic increase in the number of shares reserved for issuance under the Purchase Plan. The 2020 Plan and the Purchase Plan are collectively referred to in this letter as the "Plans".

At your request we are providing this letter to express our opinion on the matters set forth below in this letter ("our opinion").

In connection with our opinion, we have examined such matters of fact as we have deemed necessary, which included examination of originals or copies of: the Company's current Restated Certificate of Incorporation and Restated Bylaws (collectively, the "Charter Documents"), the Plans, the Registration Statement and the exhibits thereto, the prospectuses relating to the Plans, certain corporate proceedings of the Company's Board of Directors (the "Board") and the Company's stockholders relating to adoption or approval of the Charter Documents, the Plans and related forms of Plan agreements for use thereunder, the reservation of the Shares for sale and issuance, the filing of the Registration Statement and the registration of the issuance of the Shares under the Securities Act, and documents (including a certificate from the Company's transfer agent) regarding the Company's outstanding and reserved capital stock and other securities and such other documents as we have deemed advisable, and we have examined such questions of law as we have considered necessary.

In our examination of documents for purposes of this opinion, we have assumed, and express no opinion as to, the authenticity and completeness of all documents submitted to us as originals, the genuineness of signatures on documents reviewed by us, the conformity to originals and the completeness of all documents submitted to us as copies, the legal capacity of all parties executing any documents (other than the Company), the lack of any undisclosed termination or modification or waiver of any document, the absence of any extrinsic agreements or documents that might change or affect the interpretation or terms of documents, and the due authorization, execution and delivery of all documents by each party thereto other than the Company. We have also assumed that any certificates or instruments

representing the Shares, when issued, will be executed by the Company and by officers of the Company duly authorized to do so. In rendering our opinion, we have also relied upon a Certificate of Good Standing dated March 15, 2021 issued by the Delaware Secretary of State with respect to the Company and representations and certifications made to us by the Company, including without limitation representations in a Management Certificate addressed to us of even date herewith that the Company has available a sufficient number of authorized shares of Common Stock that are not currently outstanding or reserved for issuance under other outstanding securities or plans of the Company, to enable the Company to issue and deliver all of the Shares as of the date of this letter.

We render this opinion only with respect to, and we express no opinion herein concerning the application or effect of the laws of any jurisdiction other than, the existing Delaware General Corporation Law now in effect. We express no opinion with respect to the securities or "blue sky" laws of any state.

Based upon, and subject to, the foregoing, it is our opinion that when the 2,622,339 Shares of Common Stock that may be issued and sold by the Company (a) upon the exercise or settlement of awards granted or to be granted under the 2020 Plan or (b) pursuant to purchase rights to acquire shares of Common Stock granted or to be granted under the Purchase Plan, have been issued and sold by the Company against the Company's receipt of payment therefor (in an amount and type of consideration not less than the par value per share of Common Stock) in accordance with the terms (including, without limitation, payment and authorization provisions) of the applicable Plan, and have been duly registered on the books of the transfer agent and registrar for the Shares in the name or on behalf of the holders thereof, such Shares will be validly issued, fully paid and non-assessable.

We consent to the use of this opinion as an exhibit to the Registration Statement and further consent to all references to us, if any, in the Registration Statement, the prospectuses constituting a part thereof and any amendments thereto. We do not thereby admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission thereunder. This opinion is intended solely for use in connection with issuance and sale of the Shares subject to the Registration Statement and is not to be relied upon for any other purpose. In providing this letter, we are opining only as to the specific legal issues expressly set forth above, and no opinion shall be inferred as to any other matter or matters. This opinion is rendered on, and speaks only as of, the date of this letter first written above, and does not address any potential change in facts or law that may occur after the date of this opinion letter. We assume no obligation to advise you of any fact, circumstance, event or change in the law or the facts that may hereafter be brought to our attention, whether or not such occurrence would affect or modify any of the opinions expressed herein.

Very truly yours,

/s/ Fenwick & West LLP

FENWICK & WEST LLP

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-8) pertaining to the 2020 Equity Incentive Plan and to the 2020 Employee Stock Purchase Plan of Prelude Therapeutics Incorporated of our report dated March 16, 2021, with respect to the financial statements of Prelude Therapeutics Incorporated included in its Annual Report (Form 10-K) for the year ended December 31, 2020, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Philadelphia, Pennsylvania March 16, 2021