UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-1 REGISTRATION STATEMENT

UNDER THE SECURITIES ACT OF 1933

PRELUDE THERAPEUTICS INCORPORATED

(Exact name of Registrant as specified in its charter)

Delaware (State of incorporation or organization) 2834 (Primary Standard Industrial Classification Code Number) 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)

Kris Vaddi, Ph.D. Chief Executive Officer Prelude Therapeutics Incorporated 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)

Copies to:

Effie Toshav, Esq. Robert A. Freedman, Esq. Julia Forbess, Esq. Fenwick & West LLP 555 California Street San Francisco, California 94104 (415) 875-2300 Richard C. Segal Brent B. Siler Divakar Gupta Cooley LLP 500 Boylston Street, 14th Floor Boston, Massachusetts 02116 (617) 937-2300

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities	urities
Act of 1933 check the following box. □	

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

333-251874

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. \Box

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration number of the earlier effective registration statement for the same offering. \Box

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 definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act:

Larg	ge accelerated filer		Accelerated fi	ler	
Non-accelerated filer ⊠			Smaller reporting company		\boxtimes
			Emerging gro	wth company	\boxtimes
any		th company, indicate by check mark if the registrant has elected not to use the extendal accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Accounting Standards provided pursuant to Section 7(a)(2)(B) of the Securities Accounting Standards provided pursuant to Section 7(a)(2)(B) of the Securities Accounting Standards provided pursuant to Section 7(a)(2)(B) of the Securities Accounting Standards provided pursuant to Section 7(a)(2)(B) of the Securities Accounting Standards provided pursuant to Section 7(a)(2)(B) of the Securities Accounting Standards provided pursuant to Section 7(a)(2)(B) of the Securities Accounting Standards provided pursuant to Section 7(a)(2)(B) of the Securities Accounting Standards provided pursuant to Section 7(a)(2)(B) of the Securities Accounting Standards provided pursuant to Section 7(a)(2)(B) of the Securities Accounting Standards provided pursuant to Section 7(a)(2)(B) of the Securities Accounting Standards provided pursuant to Section 7(a)(2)(B) of the Securities Accounting Standards provided pursuant to Section 7(a)(2)(B) of the Securities Accounting Standards provided pursuant to Section 7(a)(2)(B) of the Securities Standards provided pursuant to Section 7(a)(2)(B) of the Securities Standards provided pursuant to Section 7(a)(B) of the Securities Standards provided pursuant to Section 7(a)(B) of the Securities Standards provided pursuant to Section 7(a)(B) of the Securities Standards provided pursuant to Section 7(a)(B) of the Securities Standards provided pursuant to Section 7(a)(B) of the Securities Standards provided pursuant to Section 7(a)(B) of the Securities Standards provided pursuant to Section 7(a)(B) of the Securities Standards provided pursuant to Section 7(a)(B) of the Securities Standards provided pursuant to Section 7(a)(B) of the Securities Standards provided pursuant to Section 7(a)(B) of the Securities Standards provided pursuant to Section 7(a)(B) of the Securities Standards provided pursuant to Section 7(a)(B) of the Securities Sta		For complying w	<i>r</i> ith
		Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price(1)(2)	Amount of Registration I	
Con	ımon Stock, par value	\$0.0001 per share	\$28,505,625	\$3,110	
(2)	\$143,994,375 on a Registration Statement on Form S-1 (File No. 333-251874), which was declared effective by the Securities and Exchange Commission on January 6, 2021. In accordance with Rule 462(b) under the Securities Act, an additional amount of shares having a proposed maximum aggregate offering price of \$28,505,625 are hereby registered, which includes the additional shares that the underwriters have the option to purchase. To the extent shares of common stock are purchased by certain existing stockholders, the common stock will initially be issued in the form of non-voting common stock, \$0.0001 par value per share. The Proposed Maximum Aggregate Offering Price includes such shares of non-voting common stock, and this registration statement registers the offer and sale of such non-voting common stock and an equivalent number of shares of voting common stock, \$0.0001 par value per share into which such non-voting common stock is convertible at the option of the holder thereof.				
	This Registration S	tatement shall become effective upon filing in accordance with Rule 462(b) und	er the Securities Act	· .	

EXPLANATORY NOTE AND INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

Pursuant to Rule 462(b) under the Securities Act of 1933, as amended, Prelude Therapeutics Incorporated ("**Registrant**") is filing this Registration Statement on Form S-1 (this "**Registration Statement**") with the Securities and Exchange Commission ("**Commission**"). This Registration Statement relates to the public offering of securities contemplated by the Registration Statement on Form S-1 (File No. 333-251874) (the "**Prior Registration Statement**"), which the Registrant originally filed with the Commission on January 4, 2021, which the Commission declared effective on January 6, 2021.

The Registrant is filing this Registration Statement for the sole purpose of increasing the aggregate offering price of shares to be offered in the public offering by \$28,505,625, including the offering price of shares that may be sold upon exercise of the underwriters' option to purchase additional shares of the Registrant's common stock. The additional securities that are being registered for sale represent no more than 20% of the maximum aggregate offering price set forth in the Calculation of Registration Fee table contained in the Prior Registration Statement. The information set forth in the Prior Registration Statement and all exhibits to the Prior Registration Statement are incorporated by reference into this Registration Statement.

The required opinions and consents are listed on the Exhibit Index attached hereto and filed herewith.

EXHIBIT INDEX

Exhibit Number	Description
5.1	Opinion of Fenwick & West LLP
23.1	Consent of Independent Registered Public Accounting Firm
23.2	Consent of Fenwick & West LLP (included in Exhibit 5.1)
2/1	Power of Attorney (incorporated by reference to Eyhibit 24.1 to the Registration Statement on Form S-1 (Registration No. 333-251874))

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this registration statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Wilmington, State of Delaware, on this 6th day of January, 2021.

PRELUDE THERAPEUTICS INCORPORATED

By: /s/ Krishna Vaddi Krishna Vaddi, Ph.D. Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement on Form S-1 has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Krishna Vaddi	Chief Executive Officer and Director	January 6, 2021
Krishna Vaddi, Ph.D.	(Principal Executive Officer)	
	Chief Financial Officer	January 6, 2021
/s/ Brian Piper	(Principal Accounting and Financial Officer)	
Brian Piper, M.B.A.		
		January 6, 2021
*	Director	•
Paul A. Friedman, M.D.		
*	Director	January 6, 2021
David Bonita, M.D.	_	J
		I C 2021
*	Director	January 6, 2021
Mardi C. Dier	_	
		I C 2021
*	Director	January 6, 2021
Kelvin Neu, M.D.	_	
		January 6, 2021
*	Director	January 0, 2021
Victor Sandor, M.D.C.M.		
*By /s/ Krishna Vaddi		
Krishna Vaddi		
Attorney-in-fact		



555 California Street 12th Floor San Francisco, CA 9410 415,875,2300 Ferwick com

January 6, 2021

Prelude Therapeutics Incorporated 200 Powder Mill Road Wilmington, Delaware 19803

Ladies and Gentlemen:

At your request, we have examined the Registration Statement on Form S-1 (the "*Registration Statement*") filed by Prelude Therapeutics Incorporated, a Delaware corporation (the "*Company*"), with the Securities and Exchange Commission (the "*Commission*") on January 6, 2021, pursuant to Rule 462(b) of the Securities Act of 1933, as amended ("*Securities Act*"), in connection with the registration of an aggregate of 862,500 shares of the Company's common stock (the "*Shares*"), consisting of the Company's voting common stock, par value \$0.0001 per share (the "*Common Stock*"), and, to the extent Shares are purchased by certain existing stockholders of the Company, including by entities affiliated with certain of the Company's directors, the Company's non-voting common stock, par value \$0.0001 per share (the "*Non-Voting Common Stock*").

In connection with our opinion expressed below we have examined originals or copies of the underwriting agreement pursuant to which the Shares will be sold to the underwriters, the Registration Statement, the prospectus prepared in connection with the Registration Statement (the "*Prospectus*"), the Company's Restated Certificate of Incorporation (the "*Certificate*"), and the Company's Restated Bylaws (the "*Bylaws*"), certain minutes and consents of the Company's board of directors (the "*Board*") or a committee or committees thereof and the Company's stockholders relating to the Registration Statement, the Certificate and the Bylaws, and such other agreements, documents, certificates and statements of the Company, its transfer agent and public or government officials, as we have deemed advisable, and have examined such questions of law as we have considered necessary. In giving our opinion, we have also relied upon a good standing certificate regarding the Company issued by the Delaware Secretary of State and a management certificate addressed to us and dated of even date herewith executed by the Company containing certain factual representations by the Company.

In our examination of documents for purposes of this opinion, we have assumed, and express no opinion as to, the genuineness of all signatures on original documents, the authenticity and completeness of all documents submitted to us as originals, the conformity to originals and completeness of all documents submitted to us as copies, the legal capacity of all persons or entities executing the same (other than the Company), the lack of any undisclosed termination, modification, waiver or amendment to any document reviewed by us.

We render this opinion only with respect to, and express no opinion herein concerning the application or effect of the laws of any jurisdiction other than, the existing Delaware General Corporation Law.

In connection with our opinion expressed below, we have assumed that, at or prior to the time of the delivery of any shares of Shares, the Registration Statement will have been declared effective under the Securities Act that the registration will apply to the offer and sale of such shares of Shares and will not have been modified or rescinded and that there will not have occurred any change in law affecting the validity of the issuance of such shares of Shares.

Based upon the foregoing, we are of the opinion that the up to 862,500 Shares that may be issued and sold by the Company, when issued, sold and delivered in the manner and for the consideration stated in the Registration Statement and the Prospectus and in accordance with the resolutions adopted by the Board and by the Pricing Committee of the Board, will be validly issued, fully paid and nonassessable.

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 Prospectus constituting a part thereof and any amendments thereto.

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. This opinion is rendered as of the date first written above and is based solely on our understanding of facts in existence as of such date after the aforementioned examination. In rendering the opinions above, we are opining only as to the specific legal issues expressly set forth therein, and no opinion shall be inferred as to any other matter or matters. 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 on Form S-1 filed pursuant to Rule 462(b) of the Securities Act of 1933 of the reference to our firm under the caption "Experts" and to the incorporation by reference of our report dated July 23, 2020 (except for the reverse stock split described in Note 11, as to which the date is September 21, 2020), with respect to the financial statements of Prelude Therapeutics Incorporated included in the Registration Statement (Form S-1 No. 333-251874) and related Prospectus of Prelude Therapeutics Incorporated for the registration of its common stock.

/s/ Ernst & Young LLP

Philadelphia, Pennsylvania January 6, 2021