

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden hours per response:	0.5

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Reporting Person* <u>BAKER BROS. ADVISORS LP</u> (Last) (First) (Middle) 860 WASHINGTON STREET 3RD FLOOR (Street) NEW YORK NY 10014 (City) (State) (Zip)	2. Issuer Name and Ticker or Trading Symbol <u>Prelude Therapeutics Inc [PRLD]</u>	5. Relationship of Reporting Person(s) to Issuer (Check all applicable) <input checked="" type="checkbox"/> Director <input checked="" type="checkbox"/> 10% Owner Officer (give title below) Other (specify below)
	3. Date of Earliest Transaction (Month/Day/Year) 01/27/2021	
4. If Amendment, Date of Original Filed (Month/Day/Year)		6. Individual or Joint/Group Filing (Check Applicable Line) Form filed by One Reporting Person <input checked="" type="checkbox"/> Form filed by More than One Reporting Person

Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned

1. Title of Security (Instr. 3)	2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any (Month/Day/Year)	3. Transaction Code (Instr. 8)		4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5)			5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4)	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial Ownership (Instr. 4)
			Code	V	Amount	(A) or (D)	Price			
Common Stock	01/27/2021		M		5,188	A	\$12.85	876,061	I ⁽³⁾	See Footnotes ⁽¹⁾⁽²⁾⁽³⁾⁽⁶⁾⁽⁷⁾⁽⁸⁾⁽⁹⁾⁽¹¹⁾⁽¹²⁾
Common Stock	01/27/2021		M		5,188	A	\$12.85	9,252,951	I ⁽⁵⁾	See Footnotes ⁽¹⁾⁽²⁾⁽⁵⁾⁽⁶⁾⁽⁷⁾⁽⁸⁾⁽⁹⁾⁽¹¹⁾⁽¹²⁾

Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transaction Code (Instr. 8)		5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)		6. Date Exercisable and Expiration Date (Month/Day/Year)		7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4)	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)	
				Code	V	(A)	(D)	Date Exercisable	Expiration Date						Title
Non-Qualified Stock Options (right to buy)	\$12.85	01/27/2021		M		5,188		(1)(2)	09/01/2030	Common Stock	5,188	(10)	41,500	I	See Footnotes ⁽³⁾⁽⁴⁾⁽⁶⁾⁽⁷⁾⁽⁸⁾⁽⁹⁾⁽¹¹⁾⁽¹²⁾
Non-Qualified Stock Options (right to buy)	\$12.85	01/27/2021		M		5,188		(1)(2)	09/01/2030	Common Stock	5,188	(10)	41,500	I	See Footnotes ⁽⁴⁾⁽⁵⁾⁽⁶⁾⁽⁷⁾⁽⁸⁾⁽⁹⁾⁽¹¹⁾⁽¹²⁾

1. Name and Address of Reporting Person*
BAKER BROS. ADVISORS LP
 (Last) (First) (Middle)
 860 WASHINGTON STREET
 3RD FLOOR
 (Street)
 NEW YORK NY 10014
 (City) (State) (Zip)

1. Name and Address of Reporting Person*
667, L.P.
 (Last) (First) (Middle)
 860 WASHINGTON STREET, 3RD FLOOR
 (Street)
 NEW YORK NY 10014
 (City) (State) (Zip)

1. Name and Address of Reporting Person*
Baker Bros. Advisors (GP) LLC
 (Last) (First) (Middle)

860 WASHINGTON STREET
3RD FLOOR

(Street)
NEW YORK NY 10014
(City) (State) (Zip)

1. Name and Address of Reporting Person*

[Baker Brothers Life Sciences LP](#)

(Last) (First) (Middle)
860 WASHINGTON STREET
3RD FLOOR

(Street)
NEW YORK NY 10014
(City) (State) (Zip)

1. Name and Address of Reporting Person*

[BAKER FELIX](#)

(Last) (First) (Middle)
860 WASHINGTON STREET
3RD FLOOR

(Street)
NEW YORK NY 10014
(City) (State) (Zip)

1. Name and Address of Reporting Person*

[BAKER JULIAN](#)

(Last) (First) (Middle)
860 WASHINGTON STREET, 3RD FLOOR

(Street)
NEW YORK NY 10014
(City) (State) (Zip)

Explanation of Responses:

1. Common stock ("Common Stock") of Prelude Therapeutics Incorporated (the "Issuer") received upon exercise of 5,188 non-qualified stock options exercisable into Common Stock on a 1-for-1 basis ("Stock Options") that were issued to Dr. Kelvin M. Neu, a former employee of Baker Bros. Advisors LP (the "Adviser") and former director of the board of directors of the Issuer (the "Board"), in his capacity as a former director of the Issuer are reflected in the ownership of each of the Funds (as defined below). The Stock Options with a strike price of \$12.85 per share, vested in 36 equal monthly installments beginning on October 24, 2020, subject to an individual designated by the Adviser continuing to serve on the Board.
2. Dr. Neu and Julian C. Baker, a managing member of Baker Bros. Advisors (GP) LLC (the "Adviser GP") and current director of the Issuer pursuant to the policies of the Adviser, do not have any right to the pecuniary interest in the Stock Options issued or the Common Stock received upon exercise of such Stock Options for either Dr. Neu's past service on the the Board or Julian C. Baker's current service on the Board Each of the Funds owns an indirect proportionate pecuniary interest in the Common Stock received upon exercise of the Stock Options issued in connection with Dr. Neu's past service on the Board and Julian C. Baker's current service on the Board, less the exercise cost of those options.
3. After giving effect to the transaction reported herein and as a result of their ownership interest in (i) Baker Biotech Capital, L.P. and (ii) 667, L.P. ("667"), Julian C. Baker and Felix J. Baker each may be deemed to have an indirect pecuniary interest in 870,873 shares of Common Stock reported in column 5 of Table I directly held by 667, a limited partnership of which the sole general partner is Baker Biotech Capital, L.P., a limited partnership of which the sole general partner is Baker Biotech Capital (GP),LLC, due to their interest in 667 and Baker Biotech Capital, L.P.'s right to receive an allocation of a portion of the profits from 667 and the 5,188 shares of Common Stock reported in column 5 of Table I held directly by the Adviser.
4. In addition, each of the Funds has the right to receive a portion of the 41,500 options reported in column 9 of Table II held directly by Dr. Neu.
5. After giving effect to the transaction reported herein and as a result of their ownership interest in (i) Baker Brothers Life Sciences Capital, L.P. and (ii) Baker Brothers Life Sciences, L.P. ("Life Sciences", and together with 667, the "Funds"), Julian C. Baker and Felix J. Baker each may be deemed to have an indirect pecuniary interest in 9,247,763 shares of Common Stock reported in column 5 of Table I directly held by Life Sciences, a limited partnership of which the sole general partner is Baker Brothers Life Sciences Capital, L.P., a limited partnership of which the sole general partner is Baker Brothers Life Sciences Capital (GP),LLC, due to their interest in Life Sciences and Baker Brothers Life Sciences Capital, L.P.'s right to receive an allocation of a portion of the profits from Life Sciences and the 5,188 shares of Common Stock reported in column 5 of Table I held directly by the Adviser.
6. The Adviser serves as the investment adviser to the Funds. In connection with the services provided by the Adviser, the Adviser receives an asset-based management fee that does not confer any pecuniary interest in the securities held by the Funds. The Adviser GP is the Adviser's sole general partner. Julian C. Baker and Felix J. Baker are managing members of the Adviser GP. The Adviser has complete and unlimited discretion and authority with respect to the investment and voting power of the securities held by the Funds. The general partners of the Funds relinquished to the Adviser all discretion and authority with respect to the investment and voting power of the securities held by the Funds.
7. Julian C. Baker, Felix J. Baker, the Adviser GP and the Adviser disclaim beneficial ownership of the securities held directly by the Funds except to the extent of their pecuniary interest therein, and this report shall not be deemed an admission that any of Julian C. Baker, Felix J. Baker, the Adviser GP or the Adviser is a beneficial owner of such securities for purposes of Section 16 or any other purpose.
8. The policy of the Funds and the Adviser, and the Nominee Agreement (as defined below) do not permit former employees of the Adviser or managing members of the Adviser GP to receive compensation for serving as a director of the Issuer, and the Funds are instead entitled to the pecuniary interest in the Common Stock received from the exercise of the Stock Options.
9. Solely as a result of their ownership interest in (i) the general partners of the Funds and (ii) the Funds as limited partners, Felix J. Baker and Julian C. Baker may be deemed to have an indirect pecuniary interest in the shares issued upon exercise of the Stock Options (i.e. no direct pecuniary interest).
10. These non-qualified stock options are not priced.
11. The disclosure of the exercise of Stock Options for Common Stock reported on this form is a single exercise of 5,188 shares. The 5,188 shares are reported for each of the Funds as each has an indirect pecuniary interest.
12. Dr. Neu entered into a Nominee Agreement (the "Nominee Agreement") with the Adviser on January 23, 2021. Pursuant to the Nominee Agreement, Dr. Neu agreed that, with respect to the Stock Options and Common Stock from the exercise of Stock Options, the Adviser will have dispositive power as well as the ability to control the timing of exercise of the Stock Options and that any proceeds from the sale of the Common Stock will be remitted to the Adviser net of brokerage commissions consistent with the policies of the Adviser for current employees.

Remarks:

Effective January 25, 2021, Dr. Kelvin M. Neu, a former employee of Baker Bros. Advisors LP resigned from the board of directors (the "Board") of Prelude Therapeutics Incorporated (the "Issuer"). Effective on January 25, 2021, the Board appointed Julian C. Baker, a managing member of Baker Bros. Advisors (GP) LLC (the "Adviser GP") to fill the vacancy on the Board as a Class II Director. Julian C. Baker shall hold office for a term expiring at the 2022 Annual Meeting of the Issuer's stockholders. By virtue of their representation on the Board of Directors of the Issuer, for purposes of Section 16 of the Securities Exchange Act of 1934, as amended, the reporting persons are deemed directors by deputization of the Issuer.

[By: Baker Bros. Advisors LP,](#)
[Name: Scott L. Lessing, Title: 01/29/2021](#)
[President /s/ Scott L. Lessing](#)
[Baker Bros. Advisors LP, Mgmt. 01/29/2021](#)
[Co. and Inv. Adviser to 667, L.P.,](#)
[pursuant to authority granted by,](#)
[Baker Biotech Capital, L.P., GP to](#)
[667, L.P. Name: Scott L. Lessing,](#)

<u>Title: President /s/ Scott L. Lessing</u>	
<u>By: Baker Bros. Advisors (GP) LLC, Name: Scott L. Lessing.</u>	<u>01/29/2021</u>
<u>Title: President /s/ Scott L. Lessing</u>	
<u>Baker Bros. Advisors LP, Mgmt. Co. and Inv. Adviser to BAKER BROTHERS LIFE SCIENCES, L.P., pursuant to authority granted by Baker Brothers Life Sciences Capital, L.P., GP to Baker Brothers Life Sciences, L.P.</u>	<u>01/29/2021</u>
<u>Name: Scott L. Lessing, Title: President /s/</u>	
<u>/s/ Felix J. Baker</u>	<u>01/29/2021</u>
<u>/s/ Julian C. Baker</u>	<u>01/29/2021</u>
** Signature of Reporting Person	Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.