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UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, DC 20549

SCHEDULE 13D  
(Rule 13d-102)

INFORMATION TO BE INCLUDED IN STATEMENTS FILED PURSUANT  
TO RULE 13d-1(a) AND AMENDMENTS THERETO FILED PURSUANT  
TO RULE 13d-2(a)

(Amendment No. 2)\*

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**Prelude Therapeutics Incorporated**

(Name of Issuer)

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**Common stock, par value \$0.0001 per share**

(Title of Class of Securities)

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**74065P101**

(CUSIP number)

Alexandra A. Toohey  
Chief Financial Officer  
Baker Bros. Advisors LP  
860 Washington Street, 3<sup>rd</sup> Floor  
New York, NY 10014  
(212) 339-5690

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(Name, address and telephone number of person authorized to receive notices and communications)

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May 18, 2023

(Date of event which requires filing of this statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of Rule 13d-1(e), 13d-1(f) or 13d-1(g), check the following box .

(Continued on the following pages)

(Page 1 of 9 Pages)

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\*The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

The information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act.

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1.	NAMES OF REPORTING PERSONS Baker Bros. Advisors LP		
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP*		(a) <input type="checkbox"/> (b) <input type="checkbox"/>
3.	SEC USE ONLY		
4.	SOURCE OF FUNDS* OO		
5.	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) <input type="checkbox"/>		
6.	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER: 10,219,080 (1)	
	8.	SHARED VOTING POWER: 0	
	9.	SOLE DISPOSITIVE POWER: 10,219,080 (1)	
	10.	SHARED DISPOSITIVE POWER: 0	
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 10,219,080 (1)		
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES* <input type="checkbox"/>		
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 19.5% (1)(2)		
14.	TYPE OF REPORTING PERSON* IA, PN		

- (1) Includes 95,256 shares of voting common stock ("Common Stock") of Prelude Therapeutics Incorporated (the "Issuer") underlying 95,256 options to purchase Common Stock of the Issuer ("Stock Options") and 5,188 shares of Common Stock directly held by Baker Bros. Advisors LP (the "Adviser") from Exercised Stock Options (as defined in Item 5).
- (2) Based on 52,412,999 shares of Common Stock of the Issuer outstanding as of May 22, 2023 as reported in the Issuer's Prospectus filed with the Securities and Exchange Commission ("SEC") on May 19, 2023.

1.	NAMES OF REPORTING PERSONS Baker Bros. Advisors (GP) LLC		
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP*		(a) <input type="checkbox"/> (b) <input type="checkbox"/>
3.	SEC USE ONLY		
4.	SOURCE OF FUNDS* OO		
5.	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) <input type="checkbox"/>		
6.	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER: 10,219,080 (1)	
	8.	SHARED VOTING POWER: 0	
	9.	SOLE DISPOSITIVE POWER: 10,219,080 (1)	
	10.	SHARED DISPOSITIVE POWER: 0	
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 10,219,080 (1)		
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES* <input type="checkbox"/>		
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 19.5% (1)(2)		
14.	TYPE OF REPORTING PERSON* HC, OO		

(1) Includes 95,256 shares of Common Stock of the Issuer underlying 95,256 Stock Options and 5,188 shares of Common Stock directly held by the Adviser from Exercised Stock Options (as defined in Item 5).

(2) Based on 52,412,999 shares of Common Stock of the Issuer outstanding as of May 22, 2023 as reported in the Issuer's Prospectus filed with the SEC on May 19, 2023.

1.	NAMES OF REPORTING PERSONS Felix J. Baker	
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3.	SEC USE ONLY	
4.	SOURCE OF FUNDS* OO	
5.	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) <input type="checkbox"/>	
6.	CITIZENSHIP OR PLACE OF ORGANIZATION United States	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER: 10,219,080 (1)
	8.	SHARED VOTING POWER:
	9.	SOLE DISPOSITIVE POWER: 10,219,080 (1)
	10.	SHARED DISPOSITIVE POWER:
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 10,219,080 (1)	
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES* <input type="checkbox"/>	
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 19.5% (1)(2)	
14.	TYPE OF REPORTING PERSON* IN, HC	

(1) Includes 95,256 shares of Common Stock of the Issuer underlying 95,256 Stock Options and 5,188 shares of Common Stock directly held by the Adviser from Exercised Stock Options (as defined in Item 5).

(2) Based on 52,412,999 shares of Common Stock of the Issuer outstanding as of May 22, 2023 as reported in the Issuer's Prospectus filed with the SEC on May 19, 2023.

1.	NAMES OF REPORTING PERSONS Julian C. Baker		
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP*		(a) <input type="checkbox"/> (b) <input type="checkbox"/>
3.	SEC USE ONLY		
4.	SOURCE OF FUNDS* OO		
5.	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) <input type="checkbox"/>		
6.	CITIZENSHIP OR PLACE OF ORGANIZATION United States		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER: 10,219,080 (1)	
	8.	SHARED VOTING POWER	
	9.	SOLE DISPOSITIVE POWER: 10,219,080 (1)	
	10.	SHARED DISPOSITIVE POWER:	
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 10,219,080 (1)		
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES* <input type="checkbox"/>		
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 19.5% (1)(2)		
14.	TYPE OF REPORTING PERSON* IN, HC		

(1) Includes 95,256 shares of Common Stock of the Issuer underlying 95,256 Stock Options and 5,188 shares of Common Stock directly held by the Adviser from Exercised Stock Options (as defined in Item 5).

(2) Based on 52,412,999 shares of Common Stock of the Issuer outstanding as of May 22, 2023 as reported in the Issuer's Prospectus filed with the SEC on May 19, 2023.

## **Amendment No. 2 to Schedule 13D**

This Amendment No. 2 to Schedule 13D amends and supplements the previously filed Schedules 13D filed by Baker Bros. Advisors LP (the “Adviser”), Baker Bros. Advisors (GP) LLC (the “Adviser GP”), Julian C. Baker, and Felix J. Baker (collectively the “Reporting Persons”). Except as supplemented herein, such statements, as heretofore amended and supplemented, remain in full force and effect.

The Adviser GP is the sole general partner of the Adviser. Pursuant to the management agreements, as amended, among the Adviser, Baker Brothers Life Sciences, L.P. (“Life Sciences”) and 667, L.P. (“667”, and together with Life Sciences, the “Funds”), and their respective general partners, the Funds’ respective general partners relinquished to the Adviser all discretion and authority with respect to the investment and voting power over securities held by the Funds, and thus the Adviser has complete and unlimited discretion and authority with respect to the Funds’ investments and voting power over investments.

All capitalized terms contained herein but not otherwise defined shall have the meanings ascribed to such terms in the Schedule 13D, as amended. Information given in response to each item shall be deemed incorporated by reference in all other items, as applicable.

### **Item 3. Source and Amount of Funds or Other Consideration**

Item 3 of this Schedule 13D is supplemented and superseded, as the case may be, as follows:

The disclosure in Item 4 below is incorporated herein by reference.

### **Item 4. Purpose of the Transaction**

Item 4 of this Schedule 13D is supplemented and superseded, as the case may be, as follows:

On May 18, 2023, Prelude Therapeutics Incorporated (the “Issuer”) entered into an underwriting agreement (the “Underwriting Agreement”) with Morgan Stanley & Co. LLC (the “Underwriter”), related to a public offering (the “Offering”) of 3,048,522 shares of Common Stock and 1,448,222 shares of non-voting common stock (“Non-Voting Common Stock”) of the Issuer at a price to the public of \$5.75 per share and prefunded warrants to purchase up to 12,895,256 shares of the Issuer’s Common Stock (the “Prefunded Warrants”), at a price to the public of \$5.7499 per warrant with an exercise price of \$0.0001 per share. In addition, the Issuer granted the Underwriter an option exercisable for 30 days from the date of the Underwriting Agreement to purchase, at the public offering price less any underwriting discounts and commissions, up to an additional 2,608,800 shares of Common Stock to cover overallotments, if any. The Offering closed on May 22, 2023.

Pursuant to the Offering, 667 and Life Sciences purchased 121,178 and 1,327,044 shares of Non-Voting Common Stock, respectively, at the offering price of \$5.75 per share, totaling 1,448,222 shares of Non-Voting Common Stock in the aggregate. Pursuant to the Offering, 667 and Life Sciences purchased 970,220 and 10,625,036 Prefunded Warrants, respectively, at the offering price of \$5.7499 per share, totaling 11,595,256 Prefunded Warrants in the aggregate. Each of 667 and Life Sciences purchased the shares of Non-Voting Common Stock and Prefunded Warrants with their working capital.

Shares of Non-Voting Common Stock are convertible on a 1-for-1 basis at any time at the election of the holder into shares of Common Stock subject to beneficial ownership limitations as described below. The shares of Non-Voting Common Stock are only convertible to the extent that after giving effect to such conversion the holders thereof, together with their affiliates and any members of a Section 13(d) group with such holders, would beneficially own, for purposes of Rule 13d-3 under the Securities Exchange Act of 1934, as amended, no more than 9.99% of the outstanding shares of Common Stock (the “Beneficial Ownership Limitation”). By written notice to the Issuer, the Funds may from time to time increase or decrease the Beneficial Ownership Limitation applicable to that Fund to any other percentage not in excess of 19.99%. Any such change will not be effective until the 61st day after such notice is delivered to the Issuer. As a result of this restriction, the number of shares that may be issued upon conversion of the Non-Voting Common Stock by the above holders may change depending upon changes in the number of outstanding shares of Common Stock. The Non-Voting Common Stock is not currently convertible due to the effect of the Beneficial Ownership Limitation.

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The Prefunded Warrants are exercisable on a 1-for-1 basis at any time at the election of the holder into shares of Common Stock subject to beneficial ownership limitations as described below. The Prefunded Warrants are only exercisable to the extent that after giving effect to such exercise the holders thereof, together with their affiliates and any members of a Section 13(d) group with such holders, would beneficially own, for purposes of Rule 13d-3 under the Securities Exchange Act of 1934, as amended, no more than 4.99% of the outstanding shares of Common Stock (the “Maximum Percentage”). By written notice to the Issuer, the Funds may from time to time increase or decrease the Maximum Percentage applicable to that Fund to any other percentage not in excess of 19.99%. Any such increase will not be effective until the 61st day after such notice is delivered to the Issuer. As a result of this restriction, the number of shares that may be issued upon exercise of the Prefunded Warrants by the above holders may change depending upon changes in the number of outstanding shares of Common Stock. The Prefunded Warrants are not currently exercisable due to the effect of the Maximum Percentage.

The Funds hold securities of the Issuer for investment purposes. The Reporting Persons or their affiliates may purchase additional securities or dispose of securities in varying amounts and at varying times depending upon the Reporting Persons’ continuing assessments of pertinent factors, including the availability of shares of Common Stock or other securities for purchase at particular price levels, the business prospects of the Issuer, other business investment opportunities, economic conditions, stock market conditions, money market conditions, the attitudes and actions of the board of directors of the Issuer (the “Board”) and management of the Issuer, the availability and nature of opportunities to dispose of securities of the Issuer and other plans and requirements of the particular entities. . The Reporting Persons may discuss items of mutual interest with the Issuer’s management, other members of the Board and other investors, which could include items in subparagraphs (a) through (j) of Item 4 Schedule 13D.

Depending upon their assessments of the above factors, the Reporting Persons or their affiliates may change their present intentions as stated above and they may assess whether to make suggestions to the management of the Issuer regarding financing, and whether to acquire additional securities of the Issuer (by means of open market purchases, privately negotiated purchases, conversion of some or all of the Non-Voting Common Stock, exercise of some or all of the Prefunded Warrants, or otherwise) or to dispose of some or all of the securities of the Issuer under their control.

Except as otherwise disclosed herein, at the present time, the Reporting Persons do not have any plans or proposals with respect to any extraordinary corporate transaction involving the Issuer including, without limitation, those matters described in subparagraphs (a) through (j) of Item 4 of Schedule 13D.

**Item 5. Interest in Securities of the Issuer**

(a) and (b) Items 7 through 11 and 13 of each of the cover pages of this Amendment No. 2 are incorporated herein by reference.

The information set forth in Item 4 is hereby incorporated by reference into this Item 5.

Set forth below is the aggregate number of shares of Common Stock directly held by each of the Funds, which may be deemed to be indirectly beneficially owned by the Reporting Persons, as well as the shares of Common Stock that may be acquired upon conversion of Non-Voting Common Stock or exercise of Prefunded Warrants by the Funds, subject to, respectively, the Beneficial Ownership Limitation and the Maximum Percentage.

<b>Holder</b>	<b>Common Stock</b>	<b>Non-Voting Common Stock</b>	<b>Prefunded Warrants</b>
667, L.P.	870,873	630,658	970,220
Baker Brothers Life Sciences, L.P.	9,247,763	6,539,415	10,625,036
<b>Total</b>	<b>10,118,636</b>	<b>7,170,073</b>	<b>11,595,256</b>

The Adviser has voting and investment power over the Common Stock, non-qualified options to purchase Common Stock (“Stock Options”), Common Stock underlying such Stock Options and Common Stock received from the exercise of Stock Options by Julian C. Baker as directors’ compensation. The Adviser GP, and Felix J. Baker and Julian C. Baker as managing members of the Adviser GP, may be deemed to have the power to vote or direct the vote of and the power to dispose or direct the disposition of the Common Stock, Stock Options, Common Stock received from the exercise of Stock Options and Common Stock underlying such Stock Options received by Julian C. Baker received as director’s compensation.

The Adviser GP, Felix J. Baker and Julian C. Baker as managing members of the Adviser GP, and the Adviser may be deemed to be beneficial owners of securities of the Issuer directly held by the Funds.

Dr. Kelvin M. Neu, a former full-time employee of the Adviser, holds 41,500 Stock Options, as compensation for his previous service on the Board, of which 37,612 are vested or will vest within 60 days hereof. The Stock Options held by Dr. Neu are exercisable at \$12.85 per share and expire on September 1, 2030. Dr. Neu previously served, and Julian C. Baker currently serves, on the Board, each as a representative of the Funds. Vesting of the Stock Options held by Dr. Neu is subject to Julian C. Baker’s continuing service on the Board on each vesting date.

Julian C. Baker, a managing member of the Adviser GP, serves on the Board as a Class II Director and also serves on the Issuer’s compensation committee and acts as chairman of the Issuer’s nominating and governance committee. Julian C. Baker holds 23,344 Stock Options with an exercise price of \$31.02 per share and an expiration date of June 17, 2031 and 34,300 Stock Options with an exercise price of \$4.74 expiring on June 16, 2032. The abovementioned Stock Options held by Julian C. Baker are vested or will vest within 60 days hereof.

The Adviser holds 5,188 shares of Common Stock of the Issuer, as a result of the exercise of 5,188 of the Stock Options (the “Exercised Stock Options”) previously held directly by Dr. Neu. The policy of the Funds and the Adviser does not permit managing members of the Adviser GP or full-time employees of the Adviser to receive compensation for serving as directors of the Issuer, and the Funds are instead entitled to the pecuniary interest in the Exercised Stock Options. Dr. Neu, as a former full-time employee of the Adviser and former director of the Issuer, 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, the Exercised Stock Options and the Common Stock received as a result of the exercise of the Exercised Stock Options, the Adviser will have dispositive power as well as the ability to control the timing of exercise of the Exercised 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. Other than through their control of the Adviser, Felix J. Baker and Julian C. Baker have neither voting nor dispositive power and have no direct pecuniary interest in the Exercised Stock Options or the Common Stock.

(c) The information set forth in Items 3 and 4 is hereby incorporated by reference into this Item 5(c). Except as disclosed herein, none of the Reporting Persons or their affiliates has effected any other transactions in securities of the Issuer during the past 60 days.

(d) Certain securities of the Issuer are held directly by 667, a limited partnership the sole general partner of which is Baker Biotech Capital, L.P., a limited partnership the sole general partner of which is Baker Biotech Capital (GP), LLC. Julian C. Baker and Felix J. Baker are the controlling members of Baker Biotech Capital (GP), LLC.

Certain securities of the Issuer are held directly by Life Sciences, a limited partnership the sole general partner of which is Baker Brothers Life Sciences Capital, L.P., a limited partnership the sole general partner of which is Baker Brothers Life Sciences Capital (GP), LLC. Julian C. Baker and Felix J. Baker are the controlling members of Baker Brothers Life Sciences Capital (GP), LLC.

(e) Not applicable.

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**Item 6. Contracts, Arrangements, Understandings or Relationships with Respect to the Securities**

The disclosure in Item 4 regarding the Prefunded Warrants is incorporated herein by reference.

The foregoing description of the Prefunded Warrants does not purport to be complete and is qualified in its entirety by reference to the full text of the form of the Prefunded Warrants, which is incorporated by reference as Exhibit 99.1 hereto and is incorporated herein by reference.

**Item 7. Materials to be filed as Exhibits**

**Exhibit Description**

99.1 [Form of Prefunded Warrant \(incorporated by reference to Exhibit 4.1 to the Issuer's Current Report on Form 8-K, filed with the SEC on May 19, 2023\).](#)

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**SIGNATURE**

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

May 24, 2023

**BAKER BROS. ADVISORS LP**

By: Baker Bros. Advisors (GP) LLC, its general partner

By: /s/ Scott L. Lessing

Name: Scott L. Lessing

Title: President

**BAKER BROS. ADVISORS (GP) LLC**

By: /s/ Scott L. Lessing

Name: Scott L. Lessing

Title: President

/s/ Julian C. Baker

Julian C. Baker

/s/ Felix J. Baker

Felix J. Baker

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