
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.)*

Prelude Therapeutics Incorporated

(Name of Issuer)

Common stock, par value \$0.0001 per share

(Title of Class of Securities)

74065P101

(CUSIP number)

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

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

September 24, 2020

(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 11 Pages)

*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.

1.	NAMES OF REPORTING PERSONS Baker Bros. Advisors LP		
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) <input type="checkbox"/> p (b) <input type="checkbox"/> p		
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) o		
6.	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER: 10,121,228 (1)	
	8.	SHARED VOTING POWER: 0	
	9.	SOLE DISPOSITIVE POWER: 10,121,228 (1)	
	10.	SHARED DISPOSITIVE POWER: 0	
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 10,121,228 (1)		
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES* <input type="checkbox"/> p		
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 31.1% (1)(2)		
14.	TYPE OF REPORTING PERSON* IA, PN		

- (1) Includes 2,592 shares of voting common stock ("Common Stock") of Prelude Therapeutics Incorporated (the "Issuer") underlying options to purchase Common Stock of the Issuer ("Stock Options").
- (2) Based on 32,593,010 of Common Stock of the Issuer outstanding as the close of the initial public offering of the Issuer (the "IPO") according to information received from the Issuer.

1.	NAMES OF REPORTING PERSONS Baker Bros. Advisors (GP) LLC		
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) p (b) p		
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) o		
6.	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER: 10,121,228 (1)	
	8.	SHARED VOTING POWER: 0	
	9.	SOLE DISPOSITIVE POWER: 10,121,228 (1)	
	10.	SHARED DISPOSITIVE POWER: 0	
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 10,121,228 (1)		
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES* p		
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 31.1% (2)		
14.	TYPE OF REPORTING PERSON* HC, OO		

(1) Includes 2,592 shares of Common Stock of the Issuer underlying Stock Options.

(2) Based on 32,593,010 shares of Common Stock of the Issuer outstanding as the close of the IPO according to information received from the Issuer.

1.	NAMES OF REPORTING PERSONS Felix J. Baker		
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) p (b) p		
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) o		
6.	CITIZENSHIP OR PLACE OF ORGANIZATION United States		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER: 10,121,228 (1)	
	8.	SHARED VOTING POWER:	
	9.	SOLE DISPOSITIVE POWER: 10,121,228 (1)	
	10.	SHARED DISPOSITIVE POWER:	
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 10,121,228 (1)		
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES* p		
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 31.1% (2)		
14.	TYPE OF REPORTING PERSON* IN, HC		

(1) Includes 2,592 shares of Common Stock of the Issuer underlying Stock Options.

(2) Based on 32,593,010 shares of Common Stock of the Issuer outstanding as the close of the IPO according to information received from the Issuer.

1.	NAMES OF REPORTING PERSONS Julian C. Baker		
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) p (b) p		
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) o		
6.	CITIZENSHIP OR PLACE OF ORGANIZATION United States		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER: 10,121,228 (1)	
	8.	SHARED VOTING POWER	
	9.	SOLE DISPOSITIVE POWER: 10,121,228 (1)	
	10.	SHARED DISPOSITIVE POWER:	
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 10,121,228 (1)		
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES* p		
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 31.1% (2)		
14.	TYPE OF REPORTING PERSON* IN, HC		

(1) Includes 2,592 shares of Common Stock of the Issuer underlying Stock Options.

(2) Based on 32,593,010 shares of Common Stock of the Issuer outstanding as the close of the IPO according to information received from the Issuer.

Schedule 13D

ITEM 1. Security and Issuer.

The class of equity securities to which this statement on Schedule 13D relates is the common stock, par value \$0.0001 per share (the "Common Stock") of Prelude Therapeutics Incorporated (the "Issuer"), a corporation organized under the laws of Delaware. The address of the principal executive offices of the Issuer is 200 Powder Mill Road, Wilmington, DE 19803. Information given in response to each item shall be deemed incorporated by reference in all other items, as applicable.

ITEM 2. Identity and Background.

(a) The Reporting Persons are:

1. Baker Bros. Advisors LP (the "Adviser")
2. Baker Bros. Advisors (GP) LLC (the "Adviser GP")
3. Felix J. Baker
4. Julian C. Baker

(b) The business address of each of the Reporting Persons is:

c/o Baker Bros. Advisors LP
860 Washington Street, 3rd Floor
New York, NY 10014
(212) 339-5690

(c) The Adviser is an entity engaged in investment activities, and the Adviser GP is in the business of acting as its general partner and, through the Adviser, investment activities. The principal business of each of Julian C. Baker and Felix J. Baker is to serve as a managing member of the Adviser GP.

(d) and (e) During the past five years, none of the Reporting Persons nor any of the Funds (as defined below) has been (i) convicted in a criminal proceeding (excluding traffic violations or similar misdemeanors) or (ii) a party to a civil proceeding of a judicial or administrative body of competent jurisdiction and as a result of such proceeding was or is subject to a judgment, decree or final order enjoining future violations of, or prohibiting or mandating activities subject to, federal or state securities laws or finding any violation with respect to such laws.

(f) The Adviser GP is a limited liability company organized under the laws of the State of Delaware. The Adviser is a limited partnership organized under the laws of the State of Delaware. The citizenship of each of Julian C. Baker and Felix J. Baker is the United States of America.

Item 3. Source and Amount of Funds or Other Consideration

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

The securities of the Issuer reported herein were purchased by 667, L.P. ("667") and Baker Brothers Life Sciences, L.P. ("Life Sciences" and together with 667, the "Funds") with the working capital of the Funds both in transactions with the underwriters (as described below) and as a result of conversions of securities formerly acquired in private transactions directly with the Issuer. The aggregate purchase price of the securities of the Issuer directly held by the Funds was approximately \$90,457,100.

Item 4. Purpose of the Transaction.

On September 24, 2020, the Issuer entered into an underwriting agreement (the “Underwriting Agreement”) with Morgan Stanley & Co. LLC, Goldman Sachs & Co. LLC and BofA Securities (the “Underwriters”), related to an initial public offering (the “IPO”) of 8,325,000 shares of Common Stock at a price to the public of \$19.00 per share. In addition, the Issuer granted the Underwriters 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 1,248,750 shares of Common Stock to cover overallotments, if any. The IPO closed on September 29, 2020.

Pursuant to the IPO, 667 and Life Sciences purchased 104,628 and 1,474,319 shares of Common Stock, respectively, at the offering price of \$19.00 per share, totaling 1,578,947 shares of Common Stock in the aggregate. Each of 667 and Life Sciences purchased the shares of Common Stock with their working capital.

On September 29, 2020, 667 and Life Sciences acquired 219,653 and 1,976,841 shares of non-voting common stock of the Issuer (“Non-Voting Common Stock”), respectively, and acquired 329,478 and 2,965,263 shares of Common Stock, respectively, resulting from the automatic conversion immediately prior to the close of the IPO of shares of Series A Convertible Preferred Stock of the Issuer (“Series A Preferred”) on a 1 for 1 basis without additional consideration. The shares of Series A Preferred were convertible at any time, on a 1 for 1 basis, and automatically converted immediately prior to the closing of the IPO on a 1 for 1 basis.

Additionally, on September 29, 2020, 667 and Life Sciences acquired 247,034 and 2,698,424 shares of Non-Voting Common Stock, respectively, and acquired 370,552 and 4,047,634 shares of Common Stock, respectively, resulting from the automatic conversion immediately prior to the close of the IPO of shares of Series B Convertible Preferred Stock of the Issuer (“Series B Preferred”) on a 1 for 1 basis without additional consideration. The shares of Series B Preferred were convertible at any time, on a 1 for 1 basis, and automatically converted immediately prior to the closing of the IPO on a 1 for 1 basis.

Further, on September 29, 2020, 667 and Life Sciences acquired 30,349 and 382,884 shares of Non-Voting Common Stock, respectively, and acquired 45,524 and 574,327 shares of Common Stock, respectively, resulting from the automatic conversion immediately prior to the close of the IPO of shares of Series C Convertible Preferred Stock of the Issuer (“Series C Preferred”) on a 1 for 1 basis without additional consideration. The shares of Series C Preferred were convertible at any time, on a 1 for 1 basis, and automatically converted immediately prior to the closing of the IPO on a 1 for 1 basis.

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.

Dr. Kelvin M. Neu, a full-time employee of the Adviser, has served on the Board of Directors of the Issuer (the “Board”) since June 29, 2016. Dr. Neu serves on the Board as a representative of the Funds. Dr. Neu was granted 46,688 options to purchase Common Stock (“Stock Options”), adjusted for a 1.1566 for 1 reverse split on September 18, 2020, which has an exercise price of \$12.85 and vests in 36 equal monthly installments beginning on October 24, 2020, subject to Dr. Neu’s continuing service on the Board on each vesting date. The Stock Options expire on September 1, 2030.

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 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, which could include items in subparagraphs (a) through (j) of Item 4 of 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, 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 Schedule 13D 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 by the Funds, subject to the Beneficial Ownership Limitation.

Holder	Common Stock	Non-Voting Common Stock
667, L.P.	870,873	497,036
Baker Brothers Life Sciences, L.P.	9,247,763	5,058,149
Total	10,118,636	5,555,185

The Adviser GP is the sole general partner of the Adviser. Pursuant to management agreements, as amended, among the Adviser, 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 of the 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.

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.

(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.

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

None.

Item 7. Material to be Filed as Exhibits.

Exhibit	Description
99.1	Agreement Regarding the Joint Filing of Schedule 13D by and among the Reporting Persons.

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.

September 30, 2020

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

JOINT FILING AGREEMENT

Pursuant to Rule 13d-1(k)(1) under the Securities Exchange Act of 1934, as amended, the undersigned hereby agree that only one statement containing the information required by Schedule 13D need be filed with respect to the beneficial ownership by each of the undersigned of securities of Prelude Therapeutics Incorporated.

This Agreement may be executed in any number of counterparts, each of which shall be deemed an original.

EXECUTED as of this 30th day of September 2020

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
