### FORM 4

## **UNITED STATES SECURITIES AND EXCHANGE COMMISSION**

	Washington, D.C.

# STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

OMB APPROVAL

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

Section obligat	this box if no long 16. Form 4 or ions may contirtion 1(b).		STAT		ed purs	uant to	Section	on 16(a)	of the	Securitie	s Ex	xchange Ac y Act of 19	ct of 1934	ERSHIP	E	MB Number stimated ave ours per resp	rage burde	3235-0287 n 0.5
1. Name and Address of Reporting Person*  BAKER BROS. ADVISORS LP			2. Issuer Name <b>and</b> Ticker or Trading Symbol Prelude Therapeutics Inc [ PRLD ]															
(Last) 860 WAS	`	First) N STREET, 3RD	(Middle) FLOOR		3. Date of Earliest Transaction (Month/Day/Year) 06/17/2022						Officer (give ti below)	tle	Other below)	(specify				
(Street) NEW YO		NY State)	10014 (Zip)		4. If A	mendn	nent, D	Pate of O	riginal	Filed (M	lonth	h/Day/Year	)	6. Indivi	dual or Joint/Gro Form filed by Form filed by	One Repor	ting Persor	n ´
Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned																		
Date				saction 2A. Deemed Execution D if any (Month/Day/			Date,	Date, Transaction Disposed Of (D) (Instr. 3,		) or 4 and 5)	5. Amount of Securities Beneficially Ow Following Report Transaction(s)		nership : Direct Indirect str. 4)	Indirect				
					Code V Amount (A) or P				Price	(Instr. 3 and 4)			(111501. 4)					
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)		saction of Expiration Date (Month/Day/Year) Securities		of Securities D Underlying S		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4)	10. Ownershi Form: Direct (D) or Indirec (I) (Instr. 4	p Benefic (Instr. 4	ure of Indirect cial Ownership l)					
				Code	v	(A)	(D)	Date Exercis	sable	Expirati Date	on	Title	Amount or Number of Shares					
Non- Qualified Stock Options (right to buy)	\$4.74	06/17/2022		A		34,300	)	(1)		06/16/20	)32	Common Stock	34,300	\$0.00	34,300	I	See Foo (5)(6)	otnotes <sup>(1)(2)(3)(4)</sup>

1. Name and Address of Reporting Person* BAKER BROS. ADVISORS LP							
(Last) 860 WASHINGTO	(First) ON STREET, 3R	(Middle)					
(Street)							
NEW YORK	NY	10014					
(City)	(State)	(Zip)					
1. Name and Address 667, L.P.	of Reporting Perso	n*					
(Last) 860 WASHINGTO	(First) ON STREET, 3R	(Middle)					
(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)					
1. Name and Address of Reporting Person* BAKER FELIX							

(Last)	(First)	(Middle)						
860 WASHINGTO	N STREET, 3RD FLO	OR						
(Street)								
NEW YORK	NY	10014						
(City)	(State)	(Zip)						
Name and Address of Reporting Person*								
Baker Bros. Adv	Baker Bros. Advisors (GP) LLC							
(Last)	(First)	(Middle)						
860 WASHINGTON STREET, 3RD FLOOR								
(Street)								
NEW YORK	NY	10014						
(City)	(State)	(Zip)						
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)						

#### **Explanation of Responses:**

- 1. 34,300 non-qualified stock options ("Stock Options") exercisable solely into common stock ("Common Stock") of Prelude Therapeutics Incorporated (the "Issuer") were granted under the Issuer's 2020 Stock Incentive Plan, as Amended and Restated, to Julian C. Baker, a managing member of Baker Bros. Advisors (GP) LLC (the "Adviser GP"), in his capacity as a director of the Issuer. The Stock Options have a strike price of \$4.74 per share, and vest upon the earlier to occur of the first anniversary of the grant date or the date of the next annual general shareholders' meeting of the Issuer, subject to Julian C. Baker's continued service on the Board of Directors of the Issuer (the "Board") or an earlier change in control of the Issuer.
- 2. Julian C. Baker serves on the Board as a representative of Baker Brothers Life Sciences, L.P. ("Life Sciences") and 667, L.P. ("667", and together with Life Sciences, the "Funds").
- 3. Pursuant to the policies of Baker Bros. Advisors LP (the "Adviser"), Julian C. Baker does not have any right to any of the Issuer's securities issued as part of his service on the Board and the Funds are entitled to receive all of the pecuniary interest in the securities issued. The Funds each own an indirect proportionate pecuniary interest in the Stock Options. Solely as a result of Felix J. Baker's and Julian C. Baker's ownership interests in (i) the general partners of the Funds and (ii) the Funds, Felix J. Baker and Julian C. Baker may be deemed to have an indirect pecuniary interest in the Stock Options (i.e. no direct pecuniary interest).
- 4. 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.
- 5. 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.
- 6. Pursuant to agreements between Julian C. Baker and the Adviser and the policies of the Adviser, the Adviser has voting and dispositive power over the Stock Options and any Common Stock received as a result of the exercise of Stock Options.

### Remarks

Julian C. Baker, a managing member of Baker Bros. Advisors (GP) LLC, the sole general partner of Baker Bros. Advisors LP, is a director of Prelude Therapeutics Incorporated (the "Issuer"). 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: 06/22/2022 President /s/ Scott L. Lessing Baker Bros. Advisors LP, Mgmt. Co. and Inv. Adviser to 667, L.P. pursuant to authority granted by Baker Biotech Capital, L.P., GP 06/22/2022 to 667, L.P. Name: Scott L. Lessing, Title: President /s/ Scott L. Lessing /s/ Julian C. Baker 06/22/2022 06/22/2022 /s/ Felix J. Baker By: Baker Bros. Advisors (GP) LLC, Name: Scott L. Lessing, 06/22/2022 Title: President /s/ Scott L. Lessing Baker Bros. Advisors LP, Mgmt. Co. and Inv. Adviser to BAKER BROTHERS LIFE SCIENCES, L.P., pursuant to authority 06/22/2022 granted by Baker Brothers Life Sciences Capital, L.P., GP to Baker Brothers Life Sciences, L.P., Name: Scott L. Lessing, Title: President /s/ \*\* Signature of Reporting Person

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

- $^{\star}$  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.