

| OMB APPROVAL | |
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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>Mauro David J</u> (Last) (First) (Middle) <u>C/O PRELUDE THERAPEUTICS INCORPORATED</u> <u>200 POWDER MILL ROAD</u> (Street) <u>WILMINGTON DE 19803</u> (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) Director 10% Owner <input checked="" type="checkbox"/> Officer (give title below) Other (specify below) <p style="text-align:center">Chief Medical Officer</p> |
| | 3. Date of Earliest Transaction (Month/Day/Year) <u>09/07/2021</u> | |
| | 4. If Amendment, Date of Original Filed (Month/Day/Year) | |

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 | 09/07/2021 | | M | | 15,000 | A | \$1.89 | 15,000 | D | |
| Common Stock | 09/07/2021 | | s ⁽¹⁾ | | 7,487 | D | \$35.9112 ⁽²⁾ | 7,513 | D | |
| Common Stock | 09/07/2021 | | s ⁽¹⁾ | | 2,873 | D | \$36.9234 ⁽³⁾ | 4,640 | D | |
| Common Stock | 09/07/2021 | | s ⁽¹⁾ | | 4,640 | D | \$37.7876 ⁽⁴⁾ | 0 | D | |

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 |
| Employee Stock Option (Right to Buy) | \$1.89 | 09/07/2021 | | M | | | 15,000 | (5) | 07/17/2029 | Common Stock | 15,000 | \$0.00 | 167,610 | D | |

Explanation of Responses:

- The transactions reported on this Form 4 were effected pursuant to a Rule 10b5-1 trading plan adopted by the reporting person.
- The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$35.50 to \$36.49, inclusive. The reporting person undertakes to provide to the Issuer, any security holder of the Issuer, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the ranges set forth herein.
- The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$36.50 to \$37.48, inclusive. The reporting person undertakes to provide to the Issuer, any security holder of the Issuer, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the ranges set forth herein.
- The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$37.50 to \$38.18, inclusive. The reporting person undertakes to provide to the Issuer, any security holder of the Issuer, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the ranges set forth herein.
- The stock option vested as to 25% of the total shares monthly on May 1, 2020, and thereafter vests as to 1/48 of the total shares monthly until fully vested, subject to the Reporting Person's provision of service to the Issuer on the vesting date.

Remarks:

/s/ Brian Piper, Attorney-in-Fact 09/09/2021

** 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.