Free Writing Prospectus Filed Pursuant to Rule 433 To Prospectus dated November 24, 2021 Preliminary Prospectus Supplement dated May 17, 2023 Registration Statement File No. 333- 261019 May 18, 2023

Prelude Therapeutics Incorporated

This free writing prospectus relates to the offering of shares of common stock and pre-funded warrants to purchase shares of common stock of Prelude Therapeutics Incorporated (the "Company") and should be read together with the preliminary prospectus supplement dated May 17, 2023 (the "Preliminary Prospectus"), which supplements the prospectus included in the Company's Registration Statement on Form S-3 (File No. 333-261019), relating to the offering of such securities. Capitalized and other terms used but not defined herein have the meaning as set forth in the Preliminary Prospectus.

The following information supplements and updates the information contained in the Preliminary Prospectus.

Issuer: Prelude Therapeutics Incorporated

Trade Date: May 18, 2023 May 22, 2023 **Expected Settlement Date:**

by the Company:

Shares of Common Stock offered 4,496,744 shares of common stock (1,448,222 of which are non-voting common stock)

Common Stock offered by the Company:

Pre-Funded Warrants to purchase Pre-funded warrants to purchase up to an aggregate of 12,895,256 shares of our common stock, Each pre-funded warrant will have an exercise price of \$0.0001 per share, will be exercisable upon issuance and does not expire.

Option to Purchase Additional Shares of Common Stock offered

2,608,800 shares of common stock

by the Company:

Public Offering Price:

\$5.75 per share of our common stock and \$5.7499 per pre-funded warrant (which equals the public offering price of

the common stock less the \$0.0001 per share exercise price of each such pre-funded warrant).

Listing:

The shares of voting common stock are listed on the Nasdaq Global Select Market under the symbol "PRLD." Our non-voting common stock is not listed for trading on any securities exchange. We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market, any other nationally recognized securities exchange or any other

nationally recognized trading system.

Indications of Interest:

Investment entities affiliated with our 5% stockholders affiliated with our directors have expressed an interest in purchasing an aggregate of \$80.0 million of our securities in this offering at the public offering price. Although we anticipate that these entities will purchase, and that the underwriter will sell to these entities, all of these securities, indications of interest are not binding agreements or commitments to purchase, the underwriter could determine to sell more, less or no shares of common stock or pre-funded warrants to purchase shares of common stock to these entities and these entities could determine to purchase more, less or no securities in this offering.

Underwriter: Morgan Stanley & Co. LLC

The Company has filed a registration statement and a Preliminary Prospectus and accompanying prospectus with the U.S. Securities and Exchange Commission (the "SEC") for the offering to which this communication relates. Before you invest, you should read the Preliminary Prospectus and accompanying prospectus and the documents incorporated by reference therein that the Company has filed with the SEC for more complete information about the Company and this offering. You may get these documents, including the Preliminary Prospectus and accompanying prospectus, for free by visiting EDGAR on the SEC website at http://www.sec.gov. Alternatively, the Company, any underwriter or any dealer participating in the offering will arrange to send you the Preliminary Prospectus and accompanying prospectus if you request it by contacting Morgan Stanley & Co. LLC, 180 Varick St, 2nd Floor, New York, NY 10014.