UNITED STATES SECURITIES AND EXCHANGE COMMISSION Washington, D.C. 20549

SCHEDULE 13D

Under the Securities Exchange Act of 1934 (Amendment No. 2)*

Prelude Therapeutics Incorporated

(Name of Issuer)

COMMON STOCK

(Title of Class of Securities)

74065P101

(CUSIP Number)

OrbiMed Advisors LLC OrbiMed Capital GP VI LLC OrbiMed Capital LLC

601 Lexington Avenue, 54th Floor New York, NY 10022 Telephone: (212) 739-6400

(Name, Address and Telephone Number of Person Authorized to Receive Notices and Communications)

May 22, 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 §§240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box.

Note: Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See §240.13d-7(b) for other parties to whom copies are to be sent.

* 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 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

CUSIP No. 74065P101

| 1 | Names of Reporting Persons. OrbiMed Advisors LLC | | | |
|-----|--|--|--|--|
| 2 | Check the Appropriate Box if a Member of a Group (See Instructions). (a) o (b) o | | | |
| 3 | SEC Use Only | | | |
| 4 | Source of Funds (See Instructions) AF | | | |
| 5 | Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e) 0 | | | |
| 6 | Citizenship or Place of Organization Delaware | | | |
| | NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH | | Sole Voting Power 0 | |
| BEN | | | Shared Voting Power 10,119,756 (1) | |
| RE | | | Sole Dispositive Power 0 | |
| F | | | Shared Dispositive Power 15,716,642 (1) | |
| 11 | Aggregate Amount Beneficially Owned by Each Reporting Person 15,716,642 (1) | | | |
| 12 | Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions) 0 | | 0 | |
| 13 | Percent of Class Represented by Amount in Row (11) 28.6% (2) | | | |
| 14 | Type of Reporting Person (See Instructions) IA | | | |

(1) Includes 10,119,756 voting shares of common stock of Prelude Therapeutics Incorporated (the "Issuer") and 5,596,886 non-voting shares of common stock of the Issuer. Each share of the Issuer's non-voting common stock at the holder's election, provided that as a result of such conversion, such holder, together with its affiliates and any members of a Schedule 13(d) group with such holder, would not beneficially own in excess of 9.99% of the Issuer's common stock immediately prior to and following such conversion, unless otherwise as expressly provided for in the Issuer's restated certificate of incorporation. However, this ownership limitation may be increased (not to exceed 19.99%) or decreased to any other percentage designated by the holder of non-voting common stock upon 61 days' notice to the Issuer.

(2) This percentage is calculated based upon 55,021,799 shares of common stock outstanding of the Issuer following the closing of an underwritten public offering of shares (assuming the underwriters of the offer exercise their option to purchase additional shares of common stock in full), as set forth in the Issuer's Rule 424(b)(5) Prospectus filed with the Securities and Exchange Commission on May 19, 2023.

CUSIP No. 74065P101

| 1 | Names of Reporting Persons. OrbiMed Capital GP VI LLC | | | |
|------|--|--|--|--|
| 2 | Check the Appropriate Box if a Member of a Group (See Instructions). (a) o (b) o | | | |
| 3 | SEC Use Only | | | |
| 4 | Source of Funds (See Instructions) AF | | | |
| 5 | Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e) 0 | | | |
| 6 | Citizenship or Place of Organization Delaware | | | |
| - | NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH | | Sole Voting Power 0 | |
| BENI | | | Shared Voting Power 10,119,756 (1) | |
| REI | | | Sole Dispositive Power 0 | |
| | | | Shared Dispositive Power 15,716,642 (1) | |
| 11 | Aggregate Amount Beneficially Owned by Each Reporting Person 15,716,642 (1) | | | |
| 12 | Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions) 0 | | 0 | |
| 13 | Percent of Class Represented by Amount in Row (11) 28.6% (2) | | | |
| 14 | Type of Reporting Person (See Instructions) OO | | | |

- (1) Includes 10,119,756 voting shares of common stock of Prelude Therapeutics Incorporated (the "Issuer") and 5,596,886 non-voting shares of common stock of the Issuer. Each share of the Issuer's non-voting common stock is convertible into one share of the Issuer's voting common stock at the holder's election, provided that as a result of such conversion, such holder, together with its affiliates and any members of a Schedule 13(d) group with such holder, would not beneficially own in excess of 9.99% of the Issuer's common stock immediately prior to and following such conversion, unless otherwise as expressly provided for in the Issuer's restated certificate of incorporation. However, this ownership limitation may be increased (not to exceed 19.99%) or decreased to any other percentage designated by the holder of non-voting common stock upon 61 days' notice to the Issuer.
- (2) This percentage is calculated based upon 55,021,799 shares of common stock outstanding of the Issuer following the closing of an underwritten public offering of shares (assuming the underwriters of the offer exercise their option to purchase additional shares of common stock in full), as set forth in the Issuer's Rule 424(b)(5) Prospectus filed with the Securities and Exchange Commission on May 19, 2023.

CUSIP No. 74065P101

| 1 | Names of Reporting Persons. OrbiMed Capital LLC | | | |
|-----|--|--------------|-----------------------------------|--|
| 2 | Check the Appropriate Box if a Member of a Group (See Instructions). (a) o (b) o | | | |
| 3 | SEC Use Only | SEC Use Only | | |
| 4 | Source of Funds (See Instructions) AF | | | |
| 5 | Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e) 0 | | | |
| 6 | Citizenship or Place of Organization Delaware | | | |
| - | NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH | | Sole Voting Power 789,500 | |
| BEN | | | Shared Voting Power 0 | |
| | | | Sole Dispositive Power 872,800 | |
| | | | Shared Dispositive Power 0 | |
| 11 | Aggregate Amount Beneficially Owned by Each Reporting Person 872,800 | | | |
| 12 | Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions) 0 | | | |
| 13 | Percent of Class Represented by Amount in Row (11) 1.6%* | | | |
| 14 | Type of Reporting Person (See Instructions) IA | | | |

(1) Includes 789,500 voting shares of common stock of Prelude Therapeutics Incorporated (the "Issuer") and 83,300 non-voting shares of common stock of the Issuer. Each share of the Issuer's non-voting common stock is convertible into one share of the Issuer's voting common stock at the holder's election, provided that as a result of such conversion, such holder, together with its affiliates and any members of a Schedule 13(d) group with such holder, would not beneficially own in excess of 9.99% of the Issuer's common stock immediately prior to and following such conversion, unless otherwise as expressly provided for in the Issuer's restated certificate of incorporation. However, this ownership limitation may be increased (not to exceed 19.99%) or decreased to any other percentage designated by the holder of non-voting common stock upon 61 days' notice to the Issuer.

(2) This percentage is calculated based upon 55,021,799 shares of common stock outstanding of the Issuer following the closing of an underwritten public offering of shares (assuming the underwriters of the offer exercise their option to purchase additional shares of common stock in full), as set forth in the Issuer's Rule 424(b)(5) Prospectus filed with the Securities and Exchange Commission on May 19, 2023.

Item 1. Security and Issuer

This Amendment No. 2 ("<u>Amendment No. 2</u>") to Schedule 13D supplements and amends the statement on Schedule 13D filed by OrbiMed Advisors LLC, OrbiMed Capital GP VI LLC, and OrbiMed Capital LLC originally filed with the Securities and Exchange Commission (the "<u>SEC</u>") on April 17, 2020, as amended by Amendment No. 1 filed with the SEC on January 14, 2021. The Statement relates to the common stock, par value \$0.0001 per share (the "<u>Shares</u>") of Prelude Therapeutics Incorporated, a corporation organized under the laws of Delaware (the "<u>Issuer</u>"), with its principal executive offices located at 200 Powder Mill Road, Wilmington, Delaware 19803. The Shares are listed on the NASDAQ Global Select Market under the ticker symbol "PRLD". Information given in response to each item shall be deemed incorporated by reference in all other items, as applicable.

On May 22, 2023, the Issuer completed an underwritten public offering of 4,496,744 Shares at a price to the public of \$5.75 per Share (the "<u>Offering</u>") and of 12,895,256 warrants to purchase Shares at a price to the public of \$5.7499 per warrant. In addition, the Issuer granted the underwriters of the Offering an option exercisable for 30 days to purchase, at the public offering price less any underwriting discounts and commissions, up to an additional 2,608,800 Shares (the "<u>Underwriter Option</u>"). As a result of the Offering, and notwithstanding the participation of OrbiMed Private Investments VI, LP ("<u>OPI VI</u>") in the Offering, the Issuer's total number of outstanding Shares increased, and the percentage of outstanding Shares that the Reporting Persons may be deemed to beneficially own was reduced by more than 1% since the last filing.

Item 2. Identity and Background

(a) This Schedule 13D is being filed by OrbiMed Advisors LLC ("OrbiMed Advisors"), OrbiMed Capital GP VI LLC ("OrbiMed GP"), and OrbiMed Capital LLC ("OrbiMed Capital") (collectively, the "Reporting Persons").

(b) — (c), (f) OrbiMed Advisors, a limited liability company organized under the laws of Delaware and a registered investment adviser under the Investment Advisers Act of 1940, as amended, is the managing member or general partner of certain entities as more particularly described in Item 6 below. OrbiMed Advisors has its principal offices at 601 Lexington Avenue, 54th Floor, New York, New York 10022.

OrbiMed GP, a limited liability company organized under the laws of Delaware, is the general partner of a limited partnership as more particularly described in Item 6 below. OrbiMed GP has its principal offices at 601 Lexington Avenue, 54th Floor, New York, New York 10022.

OrbiMed Capital, a limited liability company organized under the laws of Delaware and a registered investment adviser under the Investment Advisers Act of 1940, as amended, is the investment adviser of certain entities as more particularly described in Item 6 below. OrbiMed Capital has its principal offices at 601 Lexington Avenue, 54th Floor, New York, New York 10022.

The directors and executive officers of OrbiMed Advisors, OrbiMed Capital, and OrbiMed GP are set forth on Schedules I, II, and III, respectively, attached hereto. Schedules I, II and III set forth the following information with respect to each such person:

- (i) name;
- (ii) business address;

(iii) present principal occupation of employment and the name, principal business and address of any corporation or other organization in which such employment is conducted; and

(iv) citizenship.

(d) — (e) During the last five years, neither the Reporting Persons nor any Person named in Schedules I through III 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.

Item 3. Source and Amount of Funds or Other Consideration

On and prior to the close of the Offering on May 22, 2023, OrbiMed Advisors and OrbiMed GP, pursuant to their authority under the limited partnership agreement of OPI VI, as more particularly referred to in Item 6 below, caused OPI VI to purchase 869,565 Shares in the Offering. The source of funds for such purchases was the working capital of OPI VI.

As a result of the transactions described in this Item 3, OrbiMed GP, as the general partner of OPI VI, and OrbiMed Advisors, as the managing member of OrbiMed GP, may each be deemed to be the beneficial owners of approximately 28.6% of the outstanding Shares.

Item 4. Purpose of Transaction

This Amendment No. 2 relates to the acquisition of Shares by the Reporting Persons. The Shares acquired by the Reporting Persons were acquired for the purpose of making an investment in the Issuer and not with the intention of acquiring control of the Issuer's business on behalf of the Reporting Persons' respective advisory clients.

The Reporting Persons from time to time intend to review their investment in the Issuer on the basis of various factors, including the Issuer's business, financial condition, results of operations and prospects, general economic and industry conditions, the securities markets in general and those for the Issuer's Shares in particular, as well as other developments and other investment opportunities. Based upon such review, the Reporting Persons will take such actions in the future as the Reporting Persons may deem appropriate in light of the circumstances existing from time to time. If the Reporting Persons believe that further investment in the Issuer is attractive, whether because of the market price of Shares or otherwise, they may acquire Shares or other securities of the Issuer either in the open market or in privately negotiated transactions. Similarly, depending on market and other factors, the Reporting Persons may determine to dispose of some or all of the Shares currently owned by the Reporting Persons or otherwise acquired by the Reporting Persons either in the open market or in privately negotiated transactions.

Except as set forth in this Schedule 13D, the Reporting Persons have not formulated any plans or proposals which relate to or would result in: (a) the acquisition by any person of additional securities of the Issuer or the disposition of securities of the Issuer, (b) an extraordinary corporate transaction, such as a merger, reorganization or liquidation, involving the Issuer or any of its subsidiaries, (c) a sale or transfer of a material amount of the assets of the Issuer or any of its subsidiaries, (d) any change in the present Board of Directors or management of the Issuer's capitalization or dividend policy of the Issuer, (f) any other material change in the Issuer's business or corporate structure, (g) any change in the Issuer's charter or bylaws or other instrument corresponding thereto or other action which may impede the acquisition of control of the Issuer by any person, (h) causing a class of the Issuer's securities to be deregistered or delisted from a national securities exchange or to cease to be authorized to be quoted in an inter-dealer quotation system of a registered national securities association, (i) a class of equity securities of the Issuer becoming eligible for termination of registration pursuant to Section 12(g)(4) of the Act or (j) any action similar to any of those enumerated above.

Item 5. Interest in Securities of the Issuer

(a) — (b) The following disclosure is based upon 55,021,799 Shares outstanding of the Issuer following the closing of the Offering (assuming the Underwriter Option is exercised in full), 42,171,540 of which are voting Shares and 12,850,259 are non-voting Shares, as set forth in the Issuer's Rule 424(b)(5) Prospectus filed with the SEC on May 19, 2023.

Each non-voting Share is convertible into one voting Share at the holder's election, provided that as a result of such conversion, such holder, together with its affiliates and any members of a Schedule 13(d) group with such holder, would not beneficially own in excess of 9.99% of the Issuer's Shares immediately prior to and following such conversion, unless otherwise as expressly provided for in the Issuer's restated certificate of incorporation. However, this ownership limitation may be increased (not to exceed 19.99%) or decreased to any other percentage designated by the holder of non-voting Shares upon 61 days' notice to the Issuer.

As of the date of this filing, OPI VI, a limited partnership organized under the laws of Delaware, holds 15,716,642 Shares, which amount includes 10,119,756 voting Shares and 5,596,886 non-voting Shares, constituting approximately 28.6% of the issued and outstanding Shares. OrbiMed GP is the general partner of OPI VI, pursuant to the terms of the limited partnership agreement of OPI VI, and OrbiMed Advisors is the managing member of OrbiMed GP, pursuant to the terms of the limited liability company agreement of OrbiMed GP. As a result, OrbiMed Advisors and OrbiMed GP share power to direct the vote and disposition of the Shares held by OPI VI and may be deemed directly or indirectly, including by reason of their mutual affiliation, to be the beneficial owners of the Shares held by OPI VI. OrbiMed Advisors exercises this investment and voting power through a management committee comprised of Carl L. Gordon, Sven H. Borho, and W. Carter Neild, each of whom disclaims beneficial ownership of the Shares held by OPI VI.

In addition, OrbiMed Advisors and OrbiMed GP, pursuant to their authority under the limited partnership agreement of OPI VI, caused OPI VI to enter into the agreements referred to in Item 6 below.

As of the date of this filing, The Biotech Growth Trust PLC ("<u>BIOG</u>"), a publicly-listed investment trust organized under the laws of England, holds 346,500 Shares, which amount includes 263,200 voting Shares and 83,300 non-voting Shares, constituting approximately 0.6% of the issued and outstanding Shares. OrbiMed Capital is the investment advisor of BIOG. As a result, OrbiMed Capital has the power to direct the vote and disposition of the Shares held by BIOG and may be deemed directly or indirectly, including by reason of mutual affiliation, to be the beneficial owner of the Shares held by BIOG. OrbiMed Capital disclaims any beneficial ownership over the shares of the other Reporting Persons. OrbiMed Capital exercises this investment and voting power through a management committee comprised of Carl L. Gordon, Sven H. Borho, and W. Carter Neild, each of whom disclaims beneficial ownership of the Shares held by BIOG.

As of the date of this filing, OrbiMed Partners Master Fund Limited ("<u>OPM</u>"), an exempted company organized under the laws of Bermuda, holds 526,300 voting Shares constituting approximately 1.0% of the issued and outstanding Shares. OrbiMed Capital is the investment advisor of OPM. As a result, OrbiMed Capital has the power to direct the vote and disposition of the Shares held by OPM and may be deemed directly or indirectly, including by reason of mutual affiliation, to be the beneficial owner of the Shares held by OPM. OrbiMed Capital disclaims any beneficial ownership over the shares of the other Reporting Persons. OrbiMed Capital exercises this investment and voting power through a management committee comprised of Carl L. Gordon, Sven H. Borho, and W. Carter Neild, each of whom disclaims beneficial ownership of the Shares held by OPM.

(c) Except as disclosed in Item 3, the Reporting Persons have not effected any transactions during the past sixty (60) days in any Shares.

(d) Not applicable.

(e) Not applicable.

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

In addition to the relationships between the Reporting Persons described in Items 2 and 5 above, OrbiMed GP is the general partner of OPI VI, pursuant to the terms of the limited partnership agreement of OPI VI. Pursuant to this agreement and relationship, OrbiMed GP has discretionary investment management authority with respect to the assets of OPI VI. Such authority includes the power to vote and otherwise dispose of securities held by OPI VI. The number of outstanding Shares of the Issuer attributable to OPI VI is 15,716,642 Shares. OrbiMed GP, pursuant to its authority under the limited partnership agreement of OPI VI, may be considered to hold indirectly 15,716,642 Shares.

OrbiMed Advisors is the managing member of OrbiMed GP, pursuant to the terms of the limited liability company agreement of OrbiMed GP. Pursuant to these agreements and relationships, OrbiMed Advisors and OrbiMed GP have discretionary investment management authority with respect to the assets of OPI VI. Such authority includes the power of OrbiMed GP to vote and otherwise dispose of securities held by OPI VI. The number of outstanding Shares attributable to OPI VI is 15,716,642 Shares. OrbiMed Advisors, pursuant to its authority under the terms of the limited liability company agreement of OrbiMed GP, may also be considered to hold indirectly 15,716,642 Shares. OrbiMed Capital is the investment advisor to OPM and BIOG. OrbiMed Capital may be deemed to have voting and investment power over the securities held by OPM and BIOG. Such authority includes the power of OrbiMed Capital to vote and otherwise dispose of securities held by OPM and BIOG. The number of outstanding Shares attributable to OPM is 526,300 Shares and to BIOG is 346,500 Shares. OrbiMed Capital, as the investment advisor to OPM and BIOG, may also be considered to hold indirectly 872,800 Shares.

David Bonita ("<u>Bonita</u>"), a member of OrbiMed Advisors, is a member of the Board of Directors of the Issuer and, accordingly, OrbiMed Advisors and OrbiMed GP may have the ability to affect and influence control of the Issuer. From time to time, Bonita may receive stock options or other awards of equity-based compensation pursuant to the Issuer's compensation arrangements for non-employee directors. Pursuant to an agreement with OrbiMed Advisors and OrbiMed GP, Bonita is obligated to transfer any securities issued under any such stock options or other awards, or the economic benefit thereof, to OrbiMed Advisors and OrbiMed GP, which will in turn ensure that such securities or economic benefits are provided to OPI VI.

Investors' Rights Agreement

In addition, OPI VI and certain other stockholders of the Issuer entered into an Amended and Restated Investors' Rights Agreement with the Issuer (the "<u>Investors' Rights Agreement</u>"), dated as of August 21, 2020. Pursuant to the Investors' Rights Agreement and subject to the terms and conditions therein, the parties agreed that:

Demand Registration Rights

At any time beginning six months following the date of the effective date of the registration statement of the Issuer's initial public offering, the holders of at least 50% of the registrable securities then outstanding of the Issuer may make a written request that the Issuer register some or all of their registrable securities, subject to certain specified conditions and exceptions, including that the aggregated gross offering price of such offering must exceed \$10 million. The Issuer is required to use commercially reasonable efforts to effect the registration and will pay all registration expenses, other than underwriting discounts and commissions, related to any demand registration. The Issuer is not obligated to effect more than two of these registrations.

Piggyback Registration Rights

Whenever the Issuer proposes to file a registration statement under the Securities Act of 1933, as amended (the "Securities Act"), including a registration statement on Form S-3 as discussed below, other than with respect to certain excluded registrations, OPI VI will be entitled to notice of the registration and have the right, subject to limitations that the underwriters may impose on the number of Shares included in the registration, to include the Shares held by OPI VI in the registration.

Form S-3 Registration Rights

At any time after the Issuer is qualified to file a registration statement on Form S-3 under the Securities Act, and subject to limitations and conditions specified in the Investors' Rights Agreement, holders of at least 25% of the registrable securities then outstanding may make a written request that the Issuer prepare and file a registration statement on Form S-3 covering their Shares, so long as the aggregate price to the public equals or exceeds \$5 million. The Issuer is not obligated to effect more than two of these Form S-3 registrations in any 12-month period.

Lock-Up Agreement

Pursuant to a lock-up agreement entered into in connection with the Offering (the "Lock-Up Agreement"), each of OPI VI, OPM, BIOG, and Bonita agreed that he or it will not, during the period ending 90 days after the date of the Offering (the "Lock-Up Period"), directly or indirectly (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of any Shares or securities convertible into or exercisable or exchangeable for Shares with respect to which OPI VI, OPM, BIOG, or Bonita, as applicable, has beneficial ownership or (2) enter into any swap or other agreement that transfers, in whole or in part, the economic consequences of ownership of any such Shares.

After the Lock-Up Period expires, OPI VI's, OPM's, BIOG's, and Bonita's Shares will be eligible for sale in the public market, subject to any applicable limitations under Rule 144 under the Securities Act, and other applicable U.S. securities laws.

The foregoing descriptions of the Investors' Rights Agreement and the Lock-Up Agreement do not purport to be complete and are qualified in their entirety by reference to the full texts of the Investors' Rights Agreement and the Lock-Up Agreement, which are filed as Exhibits 2 and 3 and incorporated herein by reference.

Item 7. Material to Be Filed as Exhibits

| Exhibit | Description |
|---------|--|
| 1. | Joint Filing Agreement among OrbiMed Advisors LLC, OrbiMed Capital LLC, and OrbiMed Capital GP VI LLC. |
| 2. | Amended and Restated Investors' Rights Agreement by and among the Issuer and certain of its stockholders, dated as of August 21, 2020 (incorporated by reference to Exhibit 4.2 to the Issuer's Registration Statement on Form S-1/A (File No. 333-248628), filed with the SEC on September 16, 2020). |
| 3. | Form of Lock-Up Agreement (incorporated by reference to Exhibit A of Exhibit 1.1 to the Issuer's Current Report on Form 8-K (File No. 001-39527), filed with the SEC on May 19, 2023. |

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.

Dated: May 24, 2023

ORBIMED ADVISORS LLC

By: <u>/s/ Carl L. Gordon</u> Name: Carl L. Gordon Title: Member

ORBIMED CAPITAL GP VI LLC

- By: ORBIMED ADVISORS LLC, its managing member
- By: <u>/s/ Carl L. Gordon</u> Name: Carl L. Gordon Title: Member of OrbiMed Advisors LLC

ORBIMED CAPITAL LLC

By: <u>s/ Carl L. Gordon</u> Name: Carl L. Gordon Title: Member

SCHEDULE I

The names and present principal occupations of each of the executive officers and directors of OrbiMed Advisors LLC are set forth below. Unless otherwise noted, each of these persons is a United States citizen and has a business address of 601 Lexington Avenue, 54th Floor, New York, NY 10022.

| Name | Position with Reporting Person | Principal Occupation |
|---|--------------------------------|---|
| Carl L. Gordon | Member | Member OrbiMed Advisors LLC |
| Sven H. Borho German and Swedish Citizen | Member | Member OrbiMed Advisors LLC |
| W. Carter Neild | Member | Member OrbiMed Advisors LLC |
| Geoffrey C. Hsu | Member | Member OrbiMed Advisors LLC |
| C. Scotland Stevens | Member | Member OrbiMed Advisors LLC |
| David P. Bonita | Member | Member OrbiMed Advisors LLC |
| Peter A. Thompson | Member | Member OrbiMed Advisors LLC |
| Matthew S. Rizzo | Member | Member OrbiMed Advisors LLC |
| Trey Block | Chief Financial Officer | Chief Financial Officer OrbiMed Advisors LLC |

SCHEDULE II

The names and present principal occupations of each of the executive officers and directors of OrbiMed Capital LLC are set forth below. Unless otherwise noted, each of these persons is a United States citizen and has a business address of 601 Lexington Avenue, 54th Floor, New York, NY 10022.

| Name | Position with Reporting Person | Principal Occupation |
|---|--------------------------------|--|
| Carl L. Gordon | Member | Member OrbiMed Capital LLC |
| Sven H. Borho German and Swedish Citizen | Member | Member OrbiMed Capital LLC |
| W. Carter Neild | Member | Member OrbiMed Capital LLC |
| Geoffrey C. Hsu | Member | Member OrbiMed Capital LLC |
| C. Scotland Stevens | Member | Member OrbiMed Capital LLC |
| David P. Bonita | Member | Member OrbiMed Capital LLC |
| Peter A. Thompson | Member | Member OrbiMed Capital LLC |
| Matthew S. Rizzo | Member | Member OrbiMed Capital LLC |
| Trey Block | Chief Financial Officer | Chief Financial Officer OrbiMed Capital LLC |

SCHEDULE III

The business and operations of OrbiMed Capital GP VI LLC are managed by the executive officers and directors of its managing member, OrbiMed Advisors LLC, set forth in Schedule I attached hereto.

EXHIBIT INDEX

| Exhibit | Description |
|---------|--|
| 1. | Joint Filing Agreement among OrbiMed Advisors LLC, OrbiMed Capital LLC, and OrbiMed Capital GP VI LLC. |
| 2. | Amended and Restated Investors' Rights Agreement by and among the Issuer and certain of its stockholders, dated as of August 21, 2020 (incorporated by reference to Exhibit 4.2 to the Issuer's Registration Statement on Form S-1/A (File No. 333-248628), filed with the SEC on September 16, 2020). |
| 3. | Form of Lock-Up Agreement (incorporated by reference to Exhibit A of Exhibit 1.1 to the Issuer's Current Report on Form 8-K (File No. 001-39527), filed with the SEC on May 19, 2023. |

JOINT FILING AGREEMENT

The undersigned hereby agree that Amendment No. 2 to the Statement on Schedule 13D, dated May 22, 2023, with respect to the common stock of Prelude Therapeutics Incorporated is filed on behalf of each of us pursuant to and in accordance with the provisions of Rule 13d-1(k) under the Securities Exchange Act of 1934, as amended. Each of the undersigned agrees to be responsible for the timely filing of this Statement, and for the completeness and accuracy of the information concerning itself contained therein. This Agreement may be executed in any number of counterparts, all of which taken together shall constitute one and the same instrument.

IN WITNESS WHEREOF, the undersigned have executed this Agreement as of the 24th day of May 2023.

ORBIMED ADVISORS LLC

By: <u>/s/ Carl L. Gordon</u> Name: Carl L. Gordon Title: Member

ORBIMED CAPITAL GP VI LLC

- By: ORBIMED ADVISORS LLC, its managing member
- By: <u>/s/ Carl L. Gordon</u> Name: Carl L. Gordon Title: Member of OrbiMed Advisors LLC

ORBIMED CAPITAL LLC

By: <u>s/ Carl L. Gordon</u> Name: Carl L. Gordon Title: Member