UNITED STATES SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

SCHEDULE 14A

Proxy Statement Pursuant to Section 14(a) of the Securities Exchange Act of 1934 (Amendment No.)

Filed by the Registrant \boxtimes Filed by a Party other than the Registrant \square Check the appropriate box:

Preliminary Proxy Statement

□ Confidential, for Use of the Commission Only (as permitted by Rule 14a-6(e)(2))

□ Definitive Proxy Statement

□ Definitive Additional Materials

□ Soliciting Material Pursuant to §240.14a-12

PRELUDE THERAPEUTICS INCORPORATED

(Name of Registrant as Specified In Its Charter)

N/A

(Name of Person(s) Filing Proxy Statement, if other than the Registrant)

Payment of Filing Fee (Check all boxes that apply):

⊠ No fee required.

□ Fee paid previously with preliminary materials.

□ Fee computed on table in exhibit required by Item 25(b) per Exchange Act Rules 14a-6(i)(1) and 0-11

PRELUDE THERAPEUTICS INCORPORATED 200 Powder Mill Road Wilmington, Delaware 19803 NOTICE OF ANNUAL MEETING OF STOCKHOLDERS

To Be Held June 16, 2023

To Our Stockholders:

NOTICE IS HEREBY GIVEN that the 2023 Annual Meeting of Stockholders of Prelude Therapeutics Incorporated (the Company) will be held via a virtual meeting of stockholders. You will be able to participate in the 2023 Annual Meeting and vote during the 2023 Annual Meeting via live webcast by visiting www.virtualshareholdermeeting.com/PRLD2023 on Friday, June 16, 2023 at 1:00 p.m. (Eastern Time). It is important that you retain a copy of the control number found on the proxy card or voting instruction form, as such number will be required in order for stockholders to gain access to the virtual meeting.

We are holding the meeting for the following purposes, which are more fully described in the accompanying proxy statement:

- 1. To elect two Class III directors, each to serve a three-year term through the 2026 annual meeting of stockholders following this meeting and until a successor has been elected and qualified or until earlier resignation or removal.
- 2. To ratify the appointment of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2023.
- 3. To approve an amendment to our Restated Certificate of Incorporation to limit the liability of certain officers of the Company as permitted pursuant to recent amendments to Delaware General Corporation Law.

In addition, stockholders may be asked to consider and vote upon such other business as may properly come before the meeting or any adjournment or postponement thereof.

Only stockholders of record at the close of business on April 20, 2023 are entitled to receive notice of, and to vote at, the meeting and any adjournments thereof.

For a period of ten days prior to June 16, 2023, a complete list of the stockholders entitled to vote at the meeting will be available upon request by any stockholder for any purpose relating to the meeting. Stockholders can request the list of stockholders through our investor relations website at https://investors.preludetx.com/investor-relations.

Your vote as a stockholder of the Company is very important. Each share of common stock that you own represents one vote.

For questions regarding your stock ownership, you may contact our Investor Relations department at https://investors.preludetx.com/investor-relations or email Lindsey Trickett, Vice President of Investor Relations, at ltrickett@preludetx.com or, if you are a registered holder, our transfer agent, Computershare Trust Company, N.A. by email at shareholder@computershare.com or through their website at www.computershare.com. Whether or not you expect to attend the meeting, we encourage you to read the proxy statement and vote through the internet or by telephone, or to request, sign and return your proxy card as soon as possible, so that your shares may be represented at the meeting. For specific instructions on how to vote your shares, please refer to the section entitled "General Proxy Information" in the proxy statement.

By Order of the Board of Directors,

Krishna Vaddi, Ph.D. Chief Executive Officer

Wilmington, Delaware

Important Notice Regarding the Availability of Proxy Materials for the virtual Annual Meeting of Stockholders to be held on June 16, 2023: the Proxy Statement and our Annual Report on Form 10-K are available at <u>https://investors.preludetx.com/investor-relations</u>.

PRELUDE THERAPEUTICS INCORPORATED

PROXY STATEMENT FOR 2023 ANNUAL MEETING OF STOCKHOLDERS

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PRELUDE THERAPEUTICS INCORPORATED

200 Powder Mill Road

Wilmington, Delaware 19803

PROXY STATEMENT FOR THE 2023 ANNUAL MEETING OF STOCKHOLDERS

To Be Held on June 16, 2023

INFORMATION ABOUT SOLICITATION AND VOTING

The accompanying proxy is solicited on behalf of the Board of Directors (the Board) of Prelude Therapeutics Incorporated (the Company) for use at the Company's 2023 Annual Meeting of Stockholders (Annual Meeting) to be held via a virtual meeting of stockholders. You will be able to participate in the Annual Meeting and vote during the Annual Meeting via live webcast by visiting www.virtualshareholdermeeting.com/PRLD2023 on Friday, June 16, 2023 at 1:00 p.m. (Eastern Time), and any adjournment or postponement thereof. You will need the control number included on your proxy card or voting instruction form, or included in the e-mail to you if you received the proxy materials by e-mail, as such number will be required in order for stockholders to gain access to the virtual meeting.

INTERNET AVAILABILITY OF PROXY MATERIALS

Under rules adopted by the Securities and Exchange Commission (SEC), we are furnishing proxy materials to our stockholders primarily via the Internet, instead of mailing printed copies to each stockholder. On or about [•], 2023, we expect to send to our stockholders a Notice of Internet Availability of Proxy Materials (Notice of Internet Availability) containing instructions on how to access our proxy materials, including our proxy statement and our Annual Report on Form 10-K for the year ended December 31, 2022 (Form 10-K). The Notice of Internet Availability also provides instructions on how to vote and includes instructions on how to receive paper copies of the proxy materials by mail, or an electronic copy of the proxy materials by email.

This process is designed to reduce our environmental impact and lower the costs of printing and distributing our proxy materials while providing our stockholders timely access to this important information. If you would prefer to receive printed proxy materials, please follow the instructions included in the Notice of Internet Availability.

GENERAL INFORMATION ABOUT THE MEETING

Purpose of the Meeting

At the meeting, stockholders will act upon the proposals described in this proxy statement. In addition, we will consider any other matters that are properly presented for a vote at the meeting. We are not aware of any other matters to be submitted for consideration at the meeting. If any other matters are properly presented for a vote at the meeting, the persons named in the proxy, who are officers of the company, have the authority in their discretion to vote the shares represented by the proxy.

Record Date; Quorum

Only holders of record of common stock at the close of business on April 20, 2023, the record date, will be entitled to vote at the meeting. At the close of business on April 20, 2023, [•] shares of common stock were outstanding and entitled to vote.

The holders of a majority of the voting power of the shares of stock entitled to vote at the meeting as of the record date must be present or represented by proxy at the meeting in order to hold the meeting and conduct business. This presence is called a quorum. Your shares are counted as present at the meeting if you are present and vote online at the virtual meeting or if you have properly submitted a proxy.

GENERAL PROXY INFORMATION

Voting Rights; Required Vote

Each holder of shares of common stock is entitled to one vote for each share of common stock held as of the close of business on April 20, 2023, the record date. You may vote all shares owned by you at such date, including (1) shares held directly in your name as the stockholder of record and (2) shares held for you as the beneficial owner in street name through a broker, bank, trustee or other nominee. Dissenters' rights are not applicable to any of the matters being voted on.

Stockholder of Record: Shares Registered in Your Name. If on April 20, 2023, your shares were registered directly in your name with our transfer agent, Computershare Trust Company, N.A., then you are considered the stockholder of record with respect to those shares. As a stockholder of record, you may vote at the meeting, or vote in advance through the internet or by telephone, or if you request to receive paper proxy materials by mail, by filling out and returning the proxy card.

Beneficial Owner: Shares Registered in the Name of a Broker or Nominee. If on April 20, 2023, your shares were held in an account with a brokerage firm, bank or other nominee, then you are the beneficial owner of the shares held in street name. As a beneficial owner, you have the right to direct your broker on how to vote the shares held in your account, and your broker has enclosed or provided voting instructions for you to use in directing it on how to vote your shares. Because the brokerage firm, bank or other nominee that holds your shares is the stockholder of record, if you wish to attend the meeting and vote your shares, you must obtain a valid proxy from the firm that holds your shares giving you the right to vote the shares at the meeting.

Each director will be elected by a plurality of the votes cast at the meeting. This means that the two individuals nominated for election to the Board of Directors at the meeting receiving the highest number of "FOR" votes will be elected. You may either vote "FOR" one, two, or both of the nominees or "WITHHOLD" your vote with respect to one, two, or both of the nominees. You may not cumulate votes in the election of directors. Because directors are elected by a plurality of the votes received, only votes "FOR" will affect the outcome. If you "ABSTAIN" from voting, it will have the same effect as a "WITHHOLD" vote. Proposal No. 2 (Approval of the ratification of the appointment of our independent registered public accounting firm) will be obtained if the holders of a majority of shares present online at the meeting or represented by proxy and entitled to vote on the matter vote "FOR". If you "ABSTAIN" from voting, it will have the same effect as an "AGAINST" vote. Proposal No. 2 is considered a routine matter, and therefore no broker non-votes are expected to exist in connection with Proposal No. 2. Proposal No. 3 (Approval of an amendment to our Restated Certificate of Incorporation) will be obtained if the holders of a majority of shares outstanding and entitled to vote on the matter vote "FOR". Any broker non-vote or vote to "ABSTAIN" will have the same effect as an "AGAINST" vote.

A proxy submitted by a stockholder may indicate that the shares represented by the proxy are not being voted (stockholder withholding) with respect to a particular matter. In addition, a broker may not be permitted to vote on shares held in street name on a particular matter in the absence of instructions from the beneficial owner of the stock (broker non-vote). The shares subject to a proxy which are not being voted on a particular matter because of either stockholder withholding or broker non-votes will count for purposes of determining the presence of a quorum, but are not treated as votes cast.

Recommendations of the Board of Directors on Each of the Proposals Scheduled to be Voted on at the Meeting

The Board of Directors recommends that you vote **FOR** the election of each of the Class III directors named in this proxy statement (Proposal 1), **FOR** the ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2023 (Proposal 2), and **FOR** the proposed amendment to our Restated Certificate of Incorporation (Proposal 3).

None of the directors or executive officers has any substantial interest in any matter to be acted upon, other than elections to office with respect to the directors nominated in Proposal 1 and the executive officer exculpation provisions in Proposal 3.

Voting Instructions; Voting of Proxies

If you are a stockholder of record, you may:

- vote online at the Annual Meeting -attend the Annual Meeting online and follow the instructions posted at www.virtualshareholdermeeting.com/PRLD2023. You will need the control number included on your proxy card or voting instruction form, or included in the e-mail to you if you received the proxy materials by e-mail;
- vote through the internet or by telephone in order to do so, please follow the instructions shown on your proxy card; or
- vote by mail if you request or receive a paper proxy card and voting instructions by mail, simply complete, sign and date the proxy card and return it as soon as possible before the meeting in the envelope provided.

Votes submitted through the internet or by telephone must be received by 11:59 p.m. (Eastern Time), on June 15, 2023. Submitting your proxy, whether by telephone, through the internet or by mail if you requested or received a paper proxy card, will not affect your right to vote online should you decide to attend the virtual meeting. If you are not the stockholder of record, please refer to the voting instructions provided by your nominee to direct how to vote your shares. For Proposal 1, you may either vote "FOR" all of the nominees to the Board of Directors, or you may withhold your vote from any nominee you specify. For Proposal 2 and Proposal 3, you may vote "FOR" or "AGAINST" or "ABSTAIN" from voting. Your vote is important. Whether or not you plan to attend the meeting, we urge you to vote by proxy to ensure that your vote is counted.

All proxies will be voted in accordance with the instructions specified on the proxy card. If you sign a physical proxy card and return it without instructions as to how your shares should be voted on a particular proposal at the meeting, your shares will be voted in accordance with the recommendations of our Board of Directors stated above.

If you received a Notice of Internet Availability, please follow the instructions included on the notice on how to access and vote your proxy card. If you do not vote and you hold your shares in street name, and your broker does not have discretionary power to vote your shares, your shares may constitute "broker non-votes" (as described above) and will not be counted in determining the number of shares necessary for approval of the proposals. However, shares that constitute broker non-votes will be counted for the purpose of establishing a quorum for the meeting.

If you receive more than one proxy card or Notice of Internet Availability, your shares are registered in more than one name or are registered in different accounts. To make certain all of your shares are voted, please follow the instructions included on the Notice of Internet Availability on how to access and vote each proxy card. If you requested or received paper proxy materials by mail, please complete, sign, date and return each proxy card to ensure that all of your shares are voted.

Expenses of Soliciting Proxies

We will pay the expenses associated with soliciting proxies. Following the original distribution and mailing of the solicitation materials, we or our agents may solicit proxies by mail, email, telephone, facsimile, by other similar means, or in person. Our directors, officers and other employees, without additional compensation, may solicit proxies personally or in writing, by telephone, email or otherwise. Following the original distribution and mailing of the solicitation materials, we will request brokers, custodians, nominees and other record holders to forward copies of those materials to persons for whom they hold shares and to request authority for the exercise of proxies. In such cases, we, upon the request of the record holders, will reimburse such holders for their reasonable expenses. If you choose to access the proxy materials and/or vote through the internet, you are responsible for any internet access charges you may incur.

Revocability of Proxies

A stockholder of record who has given a proxy may revoke it at any time before the closing of the polls by the inspector of elections at the meeting by:

- delivering to our Corporate Secretary (by any means, including facsimile) a written notice stating that the proxy is revoked;
- signing and delivering a proxy bearing a later date;
- voting again through the internet or by telephone; or
- attending and voting online at the meeting by following the instructions posted at www.virtualshareholdermeeting.com/PRLD2023 (although attendance at the meeting will not, by itself, revoke a proxy).

Please note, however, that if your shares are held of record by a brokerage firm, bank or other nominee, and you wish to revoke a proxy, you must contact that firm to revoke or change any prior voting instructions.

Electronic Access to the Proxy Materials

The Notice of Internet Availability will provide you with instructions regarding how to:

- view our proxy materials for the meeting through the Internet;
- instruct us to mail paper copies of our future proxy materials to you; and
- instruct us to send our future proxy materials to you electronically by email.

Choosing to receive your future proxy materials by email will reduce the impact of our annual meetings of stockholders on the environment and lower the costs of printing and distributing our proxy materials. If you choose to receive future proxy materials by email, you will receive an email next year with instructions containing a link to those materials and a link to the proxy voting site. Your election to receive proxy materials by email will remain in effect until you terminate it.

Voting Results

Voting results will be tabulated and certified by the inspector of elections appointed for the meeting. The final results will be tallied by the inspector of elections and filed with the SEC in a Current Report on Form 8-K within four business days of the Annual Meeting.

Implications of Being an "Emerging Growth Company" and "Smaller Reporting Company"

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012, and a "smaller reporting company" as defined under Rule 405 of the Securities Act of 1933, as amended (the Securities Act), and, as such, have elected to comply with certain reduced public company reporting requirements. These reduced reporting requirements include reduced disclosure about the company's executive compensation arrangements and no requirement to have non-binding advisory votes on executive compensation.

CORPORATE GOVERNANCE STANDARDS AND DIRECTOR INDEPENDENCE

We are committed to good corporate governance practices. These practices provide an important framework within which our Board of Directors and management pursue our strategic objectives for the benefit of our stockholders.

Corporate Governance Guidelines

Our Board of Directors has adopted Corporate Governance Guidelines that set forth expectations for directors, director independence standards, Board committee structure and functions, and other policies for the governance of the company. Our Corporate Governance Guidelines are available without charge on the investor relations section of our website at https://investors.preludetx.com/investor-relations.

Board Composition and Leadership Structure

The positions of Chief Executive Officer and Chair of our Board of Directors are held by two different individuals, Krishna Vaddi and Paul A. Friedman, respectively. This structure allows our Chief Executive Officer to focus on our day-to-day business while our Chair leads our Board of Directors in its fundamental role of providing advice to and independent oversight of management. Our Board of Directors believes such separation is appropriate, as it enhances the accountability of the Chief Executive Officer to the Board of Directors and strengthens the independence of the Board of Directors from management.

Board's Role in Risk Oversight

Our Board of Directors believes that open communication between management and the Board of Directors is essential for effective risk management and oversight. Our Board of Directors meets with our Chief Executive Officer and other members of the senior management team at quarterly Board of Director meetings, where, among other topics, they discuss strategy and risks in the context of reports from the management team and evaluate the risks inherent in significant transactions. While our Board of Directors is ultimately responsible for risk oversight, our Board of Directors in fulfilling its oversight responsibilities in certain areas of risk. The Audit Committee assists our Board of Directors in fulfilling its oversight responsibilities with respect to risk management in the areas of internal control over financial reporting and disclosure controls and procedures. The Compensation Committee assists our Board of Directors in fulfilling its oversight responsibilities and corporate Governance Committee assists our Board of Directors in fulfilling its oversight responsibilities and corporate governance committee assists our Board of Directors in fulfilling its oversight responsibilities and corporate governance committee assists our Board of Directors in fulfilling its oversight responsibilities with respect to the management of corporate, legal and regulatory risk.

Director Independence

Our common stock is listed on the Nasdaq Global Select Market. Under the rules of the Nasdaq Stock Market, independent directors must constitute a majority of a listed company's Board of Directors. In addition, the rules of the Nasdaq Stock Market require that, subject to specified exceptions, each member of a listed company's Audit, Compensation and Nominating and Corporate Governance Committees must be an "independent director". Under the rules of the Nasdaq Stock Market, a director will only qualify as an "independent director" if, in the opinion of that company's Board of Directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. Additionally, Compensation Committee members must not have a relationship with the listed company that is material to the director's ability to be independent from management in connection with the duties of a Compensation Committee member.

Audit Committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended (Exchange Act). In order to be considered independent for purposes of Rule 10A-3, a member of an Audit Committee of a listed company may not, other than in his or her capacity as a member of the Audit Committee, the Board of Directors or any other Board committee: (i) accept, directly or indirectly, any consulting, advisory or other compensatory fee from the listed company or any of its subsidiaries or (ii) be an affiliated person of the listed company or any of its subsidiaries.

Our Board of Directors has undertaken a review of the independence of each director and considered whether each director has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. As a result of this review, our Board of Directors determined that Martin Babler, Julian C.

Baker, David P. Bonita, Mardi C. Dier, Paul A. Friedman and Victor Sandor, representing six of our seven incumbent directors, are "independent directors" as defined under the applicable rules and regulations of the SEC and the listing requirements and rules of the Nasdaq Stock Market. In making these determinations, our Board of Directors reviewed and discussed information provided by the directors and us with regard to each directors' business and personal activities and relationships as they may relate to us and our management, including the beneficial ownership of our capital stock by each non-employee director and any affiliates.

Committees of Our Board of Directors

Our Board of Directors has established an Audit Committee, a Compensation Committee and a Nominating and Corporate Governance Committee, each of which has the composition and responsibilities described below. Each of these committees has a written charter, copies of which are available without charge on the investor relations section of our website at https://investors.preludetx.com/investor-relations. Members serve on these committees until their resignation or until otherwise determined by our Board of Directors.

Audit Committee

Our Audit Committee is composed of Martin Babler, David P. Bonita and Mardi C. Dier. Mardi C. Dier is the Chair of our Audit Committee. The composition of our Audit Committee meets the requirements for independence under the current Nasdaq Stock Market and SEC rules and regulations. Each member of our Audit Committee is financially literate. In addition, our Board of Directors has determined that Mardi C. Dier is an "audit committee financial expert" as defined in Item 407(d)(5)(ii) of Regulation S-K promulgated under the Securities Act. This designation does not impose on her any duties, obligations or liabilities that are greater than are generally imposed on members of our Audit Committee and our Board of Directors. Our Audit Committee is directly responsible for, among other things:

- selecting and hiring our independent registered public accounting firm;
- the qualifications, independence and performance of our independent auditors;
- the preparation of the audit committee report to be included in our annual proxy statement;
- overseeing our compliance with legal and regulatory requirements;
- our accounting and financial reporting processes, including our financial statement audits and the integrity of our financial statements; and
- reviewing and approving related-person transactions.

Compensation Committee

Our Compensation Committee is composed of Julian C. Baker, David P. Bonita and Mardi C. Dier. David P. Bonita is the Chair of our Compensation Committee. The composition of our Compensation Committee meets the requirements for independence under the current Nasdaq Stock Market and SEC rules and regulations. Our Compensation Committee is responsible for, among other things:

- evaluating, recommending, approving and reviewing executive officer compensation arrangements, plans, policies and programs;
- evaluating and providing input for non-employee director compensation arrangements for determination by the management team;
- administering our cash-based and equity-based compensation plans; and
- overseeing our compliance with regulatory requirements associated with the compensation of directors, officers and employees.

The Compensation Committee has the sole authority and responsibility, subject to any approval by the Board of Directors which the Compensation Committee or legal counsel determines to be desirable or required by applicable law or the Nasdaq rules, to determine all aspects of executive compensation packages for the Chief Executive Officer and other executive officers. The Compensation Committee also makes recommendations to our Board of Directors regarding the form and amount of compensation of non-employee directors. The Compensation Committee may take into account the recommendations of the Chief Executive Officer with respect to compensation of the other executive officers, and the

recommendations of the Board of Directors or any member of the Board of Directors with respect to compensation of the Chief Executive Officer and other executive officers.

The Compensation Committee engaged an independent executive compensation consulting firm, Compensia, Inc. (Compensia), to evaluate our executive compensation and Board of Directors compensation program and practices and to provide advice and ongoing assistance on these matters for the fiscal year ended December 31, 2022. Specifically, Compensia was engaged to:

- provide compensation-related data for a peer group of companies to serve as a basis for assessing competitive compensation practices;
- review and assess our current Board of Directors, Chief Executive Officer and other executive officer compensation policies and practices and equity profile, relative to market practices;
- review and assess our current executive compensation program relative to market to identify any potential changes or enhancements to be brought to the attention of the Compensation Committee; and
- review market practices regarding base salary, bonus and equity programs.

Representatives of Compensia met informally with the Chair of the Compensation Committee and attended the regular meetings of the Compensation Committee during their respective periods of appointment during 2022, including executive sessions from time to time without any members of management present. During the fiscal year ended December 31, 2022, Compensia worked directly with the Compensation Committee (and not on behalf of management) to assist the committee in satisfying its responsibilities and undertook no projects for management without the committee's prior approval. The Compensation Committee has determined that none of the work performed by Compensia during the fiscal year ended December 31, 2022 raised any conflict of interest.

Nominating and Corporate Governance Committee

Our Nominating and Corporate Governance Committee is composed of Julian C. Baker, Paul A. Friedman and Victor Sandor. Julian C. Baker is the Chair of our Nominating and Corporate Governance Committee. Our Nominating and Corporate Governance Committee is responsible for, among other things:

- identifying, considering and recommending candidates for membership on our Board of Directors;
- overseeing the process of evaluating the performance of our Board of Directors; and
- advising our Board of Directors on other corporate governance matters.

Codes of Business Conduct and Ethics

Our Board of Directors has adopted a code of business conduct and ethics that applies to all of our employees, officers and directors, including our Chief Executive Officer, President, Chief Financial Officer and other executive and senior financial officers. We intend to disclose future amendments to certain provisions of our code of business conduct and ethics, or waivers of these provisions, on our website or in public filings. The full text of our code of business conduct and ethics section of our website at https://investors.preludetx.com/investor-relations.

Anti-hedging

We have adopted an Insider Trading Policy that that applies to all of our employees, officers and directors, including our Chief Executive Officer, President, Chief Financial Officer and other executive officers, which prohibits such individuals from engaging in hedging or monetization transactions involving our common stock, such as zero cost collars and forward sale contracts, or contributing our common stock to exchange funds in a manner that could be interpreted as hedging in our common stock.

Compensation Committee Interlocks and Insider Participation

During 2022, Julian C. Baker, David P. Bonita and Mardi C. Dier served on our Compensation Committee. None of our current executive officers has served as a member of the Board of Directors, or as a member of the Compensation or similar committee, of any entity that has one or more executive officers who served on our Board of Directors or Compensation Committee during the fiscal year ended December 31, 2022.

Board and Committee Meetings and Attendance

The Board of Directors and its committees meet regularly throughout the year and also hold special meetings and act by written consent from time to time. During 2022, the Board of Directors met six times, the Audit Committee met four times, and the Compensation Committee met six times. During 2022, none of the directors attended fewer than 75% of the aggregate of the total number of meetings held by the Board of Directors during his or her tenure and the total number of meetings held by all committees of the Board of Directors on which such director served during his or her tenure. The independent members of the Board of Directors also meet separately without management directors on a regular basis to discuss such matters as the independent directors consider appropriate.

Board Attendance at Annual Stockholders' Meeting

We invite and encourage each member of our Board of Directors to attend our Annual Meeting. We do not have a formal policy regarding attendance of our annual meetings of stockholders by the members of our Board of Directors.

Communication with Directors

Stockholders and interested parties who wish to communicate with our Board of Directors, non-management members of our Board of Directors as a group, a committee of the Board of Directors or a specific member of our Board of Directors (including our Chair) may do so by letters addressed to:

Prelude Therapeutics Incorporated c/o Corporate Secretary 200 Powder Mill Road Wilmington, Delaware 19803

All communications by letter addressed to the attention of our Corporate Secretary will be reviewed by the Corporate Secretary and provided to the members of the Board of Directors unless such communications are unsolicited items, sales materials and other routine items and items unrelated to the duties and responsibilities of the Board of Directors.

Considerations in Evaluating Director Nominees

The Nominating and Corporate Governance Committee is responsible for identifying, considering and recommending candidates to the Board of Directors for Board membership. A variety of methods are used to identify and evaluate director nominees, with the goal of maintaining and further developing a diverse, experienced and highly qualified Board of Directors. Candidates may come to our attention through current members of our Board of Directors, professional search firms, stockholders or other persons.

The Nominating and Corporate Governance Committee will recommend to the Board of Directors for selection all nominees to be proposed by the Board of Directors for election by the stockholders, including approval or recommendation of a slate of director nominees to be proposed by the Board of Directors for election at each annual meeting of stockholders, and will recommend all director nominees to be appointed by the Board of Directors to fill interim director vacancies.

Our Board of Directors encourages selection of directors who will contribute to the company's overall corporate goals. The Nominating and Corporate Governance Committee may from time to time review and recommend to the Board of Directors the desired qualifications, expertise and characteristics of directors, including such factors as business experience, diversity and personal skills in life sciences and biotechnology, finance, marketing, financial reporting and other areas that are expected to contribute to an effective Board of Directors. Exceptional candidates who do not meet all of these criteria may still be considered. In evaluating potential candidates for the Board of Directors, the Nominating and Corporate Governance Committee considers these factors in the light of the specific needs of the Board of Directors at that time.

In addition, under our Corporate Governance Guidelines, a director is expected to spend the time and effort necessary to properly discharge such director's responsibilities. Accordingly, a director is expected to regularly attend meetings of the Board of Directors and committees on which such director sits, and to review prior to meetings material distributed in advance for such meetings. Thus, the number of other public company boards and other boards (or comparable governing bodies) on which a prospective nominee is a member, as well as his or her other professional responsibilities, will be considered. Also, under our Corporate Governance Guidelines, there are no limits on the number of three-year terms that may be served by a director. However, in connection with evaluating recommendations for nomination for reelection, the

Nominating and Corporate Governance Committee considers director tenure. We value diversity on a company-wide basis but have not adopted a specific policy regarding Board diversity. For further information on the current composition of our board see "Board Diversity" under the section below entitled "Proposal No. 1 Election of Class III Directors — Non-Employee Director Compensation".

Stockholder Recommendations for Nominations to the Board of Directors

The Nominating and Corporate Governance Committee will consider properly submitted stockholder recommendations for candidates for our Board of Directors who meet the minimum qualifications as described above. The Nominating and Corporate Governance Committee does not intend to alter the manner in which it evaluates candidates, including the minimum criteria set forth above, based on whether or not the candidate was recommended by a stockholder. A stockholder of record can nominate a candidate for election to the Board of Directors by complying with the procedures in Article I, Section 1.12 of our amended and restated bylaws. Any eligible stockholder who wishes to submit a nomination should review the requirements in the amended and restated bylaws on nominations by stockholders. Any nomination should be sent in writing to our Corporate Secretary, Prelude Therapeutics Incorporated, 200 Powder Mill Road, Wilmington, Delaware 19803. Submissions must include the full name of the proposed nominee, complete biographical information, a description of the proposed nominee's qualifications as a director, other information specified in our amended and restated bylaws, and a representation that the nominating stockholder is a beneficial or record holder of our stock. Any such submission must be accompanied by the written consent of the proposed nominee to be named as a nominee and to serve as a director if elected. These candidates are evaluated at meetings of the Nominating and Corporate Governance Committee and may be considered at any point during the year. If any materials are provided by a stockholder in connection with the recommendation of a director candidate, such materials are forwarded to the Nominating and Corporate Governance Committee.

Additional information regarding the process for properly submitting stockholder nominations for candidates for membership on our Board of Directors is set forth below under "Stockholder Proposals to Be Presented at Next Annual Meeting."

PROPOSAL NO. 1 ELECTION OF CLASS III DIRECTORS

Our Board of Directors is divided into three classes. Each class serves for three years, with the terms of office of the respective classes expiring in successive years. Directors and director nominees in Class III will stand for election at this meeting. The terms of office of directors in Class I and Class II do not expire until the annual meetings of stockholders to be held in 2024 and 2025, respectively. Our Nominating and Corporate Governance Committee recommended to our Board of Directors, and our Board of Directors nominated Krishna Vaddi and Mardi C. Dier, each of whom is currently serving as a Class III director, for election as Class III directors at the Annual Meeting. At the recommendation of our Nominating and Corporate Governance Committee, our Board of Directors proposes that each of the Class III nominees be elected as a Class III director for a three-year term expiring at the annual meeting of stockholders to be held in 2026 and until such director's successor is duly elected and qualified or until such director's earlier resignation, removal, disqualification or removal.

Each director will be elected by a plurality of the votes present online at the virtual Annual Meeting or represented by proxy at the Annual Meeting and entitled to vote on the election of directors. This means that the two individuals nominated for election to the Board of Directors at the Annual Meeting receiving the highest number of "FOR" votes will be elected. You may either vote "FOR" one or multiple of the nominees or "WITHHOLD" your vote with respect to one or multiple of the nominees. Shares represented by proxies will be voted "FOR" the election of each of the Class III nominees, unless the proxy is marked to withhold authority to so vote. You may not cumulate votes in the election of directors. If any nominee for any reason is unable to serve, the proxies may be voted for such substitute nominee as the proxy holders, who are officers of our company, might determine. Each nominee has consented to being named in this proxy statement and to serve if elected. Proxies may not be voted for more than three directors.

Nominees to the Board of Directors

The nominees and their ages as of April 20, 2023 are provided in the table below. Additional biographical information for each nominee is set forth in the text below the table.

| Name | Age | Class |
|--|-----|-----------|
| Krishna Vaddi, Ph.D. | 57 | Class III |
| Mardi C. Dier ⁽¹⁾ | 59 | Class III |
| (1) Chair of our Audit Committee and member of our Compensation Committee 10 | e | |

Krishna ("Kris") Vaddi, Ph.D. has served as our Chief Executive Officer and a member of our Board of Directors since February 2016. From June 2014 to June 2016, Dr. Vaddi also served as Chief Executive Officer of Orsenix, LLC, a clinical stage biotechnology company. Dr. Vaddi previously held several roles at Incyte Corporation, most recently as Senior Advisor from June 2015 to June 2016 and Group Vice President from March 2010 to June 2015. Dr. Vaddi received a BVSc in Veterinary Medicine from Acharya N.G. Ranga Agricultural University in India and a Ph.D. in Pharmacology and Toxicology from the University of Florida. We believe that Dr. Vaddi's experience as our founder and Chief Executive Officer and history in the biopharmaceutical field qualifies him to serve on our Board of Directors.

Mardi C. Dier has served as a member of our Board of Directors since August 2020. Ms. Dier currently serves as the Chief Financial Officer and Chief Business Development Officer at privately held ACELYRIN, INC since November 2022. She previously served as the Executive Vice President and Chief Financial Officer of Ultragenyx Pharmaceutical Inc., a biotechnology company from October 2020 to November 2022. Ms. Dier served as Executive Vice President and Chief Financial Officer, and also as Chief Business Officer, of Portola Pharmaceuticals, Inc., a biopharmaceutical company, from November 2013 and October 2018, respectively, until its acquisition by Alexion Pharmaceuticals in July 2020, and as a Senior Vice President and Chief Financial Officer from August 2006 to November 2013. From 2003 to 2006, Ms. Dier served as Vice President of Investor Relations at Chiron Corporation, a biopharmaceutical company. From 1994 to 2001, Ms. Dier served as a Director, Investment Banking at Prudential Securities, Inc., a securities firm. Ms. Dier previously served as a director of Health Care Royalty and director and member of the audit committee, of ORIC Pharmaceuticals, Inc and Synthekine. Ms. Dier received a B.S. in Biology from Stanford University and an M.B.A. from the Anderson Graduate School of Management at the University of California, Los Angeles. We believe Ms. Dier is qualified to serve on our Board of Directors because of her experience in the biotechnology industry and her extensive experience in finance and accounting.

Continuing Directors

The directors who are serving for terms that end after the Annual Meeting and their ages as of April 20, 2023 are provided in the table below. Additional biographical information for each continuing director is set forth in the text below the table.

| Name | Age | Class |
|--|-----|----------|
| Paul A. Friedman, M.D. ⁽¹⁾ | 80 | Class I |
| David P. Bonita, M.D. ⁽²⁾ | 47 | Class I |
| Martin Babler ⁽³⁾ | 58 | Class II |
| Julian C. Baker ⁽⁴⁾ | 56 | Class II |
| Victor Sandor, M.D.C.M. ⁽⁵⁾ | 56 | Class II |
| | | |

(1) Member of our Nominating and Corporate Governance Committee

(2) Chair of our Compensation Committee and member of our Audit Committee

(3) Member of our Audit Committee

(4) Chair of our Nominating and Corporate Governance Committee and member of our Compensation Committee

(5) Member of our Nominating and Corporate Governance Committee

Paul A. Friedman, M.D. has served as a member of our Board of Directors since July 2016. Dr. Friedman has served as Chief Executive Officer and Chairman of the board of directors of Madrigal Pharmaceuticals, Inc., a biopharmaceutical company, since July 2016. Dr. Friedman previously served as the Chief Executive Officer of Incyte Corporation from November 2001 to January 2014. He has previously served on the boards of directors of Incyte Corporation, Alexion Pharmaceuticals, Cerulean Pharma Inc. and Verastem, Inc. Dr. Friedman received an A.B. in Biology from Princeton University and an M.D. from Harvard Medical School. We believe that Dr. Friedman's extensive experience in our business and on public company boards qualifies him to serve on our Board of Directors.

David P. Bonita, M.D. has served as a member of our Board of Directors since July 2016. Dr. Bonita is a member at OrbiMed Advisors LLC, an investment firm. Dr. Bonita currently serves on the boards of directors of Acutus Medical, Inc., Ikena Oncology, Inc., Repare Therapeutics Inc. and Third Harmonic Bio, Inc., as well as several private companies. Dr. Bonita also previously served on the boards of directors of Clementia Pharmaceuticals Inc., IMARA Inc., SI-BONE, Inc., Tricida Inc., and ViewRay Inc. Prior to OrbiMed, Dr. Bonita worked as a corporate finance analyst in the healthcare investment banking groups of Morgan Stanley and UBS. He received a B.A. in biology from Harvard University and a joint M.D./M.B.A. from Columbia University. We believe that Dr. Bonita is qualified to serve on our Board of Directors based



on his roles on several public and private boards of directors as well as his extensive experience in investing in healthcare companies.

Martin Babler has served as a member of our Board of Directors since July 2021. Mr. Babler serves as the President and Chief Executive Officer of Alumis Inc., a biopharmaceutical company since September 2021. Prior to his current role he was President and Chief Executive Officer at Principia Biopharma Inc., a biopharmaceutical company from April 2011 until its acquisition by Sanofi S.A. in October 2020. From December 2007 to April 2011, Mr. Babler served as President and Chief Executive Officer of Talima Therapeutics, Inc., a pharmaceutical company. From 1998 to 2007, Mr. Babler held several positions at Genentech, Inc., a biopharmaceutical company, most notably as Vice President, Immunology Sales and Marketing. While at Genentech he also helped to build and led the Commercial Development organization and led the Cardiovascular Marketing organization. Mr. Babler was previously employed at Eli Lilly and Company, a pharmaceutical company, in positions focused on sales, sales management, global marketing and business development. Mr. Babler presently serves on the Board of Directors of Neoleukin Therapeutics, Inc., Sardona Therapeutics Inc., and on the Emerging Companies Section Governing Board of the Biotechnology Innovation Organization, or BIO. Mr. Babler received a Swiss Federal Diploma in pharmacy from the Federal Institute of Technology in Zurich and completed the Executive Development Program at the Kellogg Graduate School of Management at Northwestern University. We believe Mr. Babler is qualified to serve on our Board of Directors because of his experience in the biotechnology industry and his extensive experience in finance and accounting.

Julian C. Baker has served as a member of our Board of Directors since January 2021. Mr. Baker is a Managing Member of Baker Bros. Advisors LP, which he and his brother, Felix Baker, Ph.D., founded in 2000. Mr. Baker's career as a fund-manager began in 1994 when he co-founded a biotechnology investing partnership with the Tisch Family. Previously, Mr. Baker was employed from 1988 to 1993 by the private equity investment arm of Credit Suisse First Boston Corporation. Mr. Baker holds an A.B. from Harvard University. Mr. Baker also serves on the boards of Incyte Corporation, Acadia Pharmaceuticals, Inc., Everyone Medicines Inc., and Alumis, Inc. We believe Mr. Baker is qualified to serve on our Board of Directors due to his experience investing in many life sciences companies.

Victor Sandor, M.D.C.M. has served as a member of our Board of Directors since May 2020. From September 2014 to December 2019, Dr. Sandor served as the Chief Medical Officer at Array BioPharma Inc., a pharmaceutical company. From September 2014 to June 2019, he served as the Senior Vice President for Global Clinical Development at Incyte Corporation, a pharmaceutical company. From February 2010 to September 2014, Dr. Sandor served as the Vice President and Chief Medical Officer for oncology at Biogen Idec and, from October 2009 to February 2010, held positions of increasing responsibility in oncology product development at AstraZeneca. Dr. Sandor has served on the Board of Directors of Kymera Therapeutics since November of 2022, ADC Therapeutics SA since April 2020, Istarti Oncology since July 2019, and Merus N.V. since June 2019. Dr. Sandor received a M.D.C.M. from McGill University in Montreal, Canada, and completed his Fellowship in Medical Oncology at the National Institutes of Health in Bethesda, Maryland. We believe that Dr. Sandor is qualified to serve on our Board of Directors due to his experience in the field of medicine, clinical drug development and scientific experience.

Board Diversity

Due to the complex nature of our business, the Board believes it is important to consider diversity of race, ethnicity, gender, sexual orientation, age, education, cultural background, and professional experiences in evaluating board candidates in order to provide practical insights and diverse perspectives.

| Board Diversity Mat | rix (As of April 20, 20 | 23) | | | | |
|---|-------------------------|-----|------------|-------------------------------|--|--|
| Total Number of Directors | 7 | | | | | |
| | Woman | Man | Non-Binary | Did Not Disclose Gender | | |
| Part I: Gender Identity | | | | | | |
| Directors | 1 | 6 | — | _ | | |
| Part II: Demographic Background | | | | | | |
| African American or Black | - | — | — | | | |
| Alaskan Native or Native American | _ | — | _ | | | |
| Asian | _ | 1 | — | | | |
| Hispanic or Latinx | _ | — | — | | | |
| Native Hawaiian or Pacific Islander | — | _ | — | _ | | |
| White | 1 | 5 | _ | | | |
| Two or More Races or Ethnicities | _ | _ | _ | | | |
| LGBTQ+ | | 1 | | | | |
| Did Not Disclose Demographic Background | | | | | | |

Family Relationships

There are no familial relationships among any of our directors and executive officers.

Non-Employee Director Compensation

Our current non-employee director program as approved by the Board of Directors is as follows:

Each non-employee director who is elected or appointed to our Board of Directors will be granted an option to purchase 68,600 shares of our common stock upon the director's initial appointment to our Board of Directors (an Initial Grant). The Initial Grant will vest in 36 monthly installments on each monthly anniversary of the date of grant, such that the Initial Grant will become fully vested and exercisable on the third anniversary of the date of grant, subject to the directors continued service on each applicable vesting date or an earlier change of control of Prelude. If the non-employee director's service ends on the date of vesting, then the vesting will be deemed to have occurred.

In addition, each non-employee director who continues to serve on our Board of Directors following our annual meeting of stockholders will be granted an option to purchase 34,300 shares of our common stock on the date of such annual meeting of stockholders, referred to as an Annual Grant. Each Annual Grant will vest on the earlier of (a) the next annual meeting of the Company's stockholders and (b) the one-year anniversary of the grant date of the Annual Grant, subject to the director's continued service on the applicable vesting date or an earlier change in control of Prelude. If the non-employee director's service ends on the date of vesting, then the vesting will be deemed to have occurred.

Non-employee directors are also reimbursed for reasonable expenses incurred in serving as a director, including travel expenses for attending meetings of our Board of Directors.

The following table sets forth the compensation earned by or paid to our non-employee directors for services provided during the year ended December 31, 2022. Our Chief Executive Officer, Dr. Vaddi, receives no compensation for his service as a director. Other than as described below, none of our non-employee directors received any fees or reimbursement of any expenses (other than customary expenses in connection with the attendance of meetings of our Board of Directors) or any equity or non-equity awards in the year ended December 31, 2022.

| Name | Fees Earned or Paid in Cash (\$) | Option Awards (\$) ⁽¹⁾ | Total (\$) |
|--------------------------------------|--|--------------------------------------|---------------|
| Martin Babler | 42,500 | 106,186 | 148,686 |
| Julian C. Baker ⁽²⁾ | 48,000 | 116,390 | 164,390 |
| David P. Bonita, M.D. ⁽³⁾ | 52,500 | 116,390 | 168,890 |
| Mardi C. Dier | 55,000 | 116,390 | 171,390 |
| Paul A. Friedman, M.D. | 69,000 | 116,390 | 185,390 |
| Victor Sandor, M.D.C.M. | 155,848 | 216,690 | 372,538 |

(1) The amounts reported in the Option Awards columns represent the aggregate grant date fair value of the awards granted under our 2020 Stock Incentive Plan, or the 2020 Plan, to the directors during the year ended December 31, 2022 as computed in accordance with FASB ASC Topic 718, or ASC 718. The assumptions used in calculating the grant date fair value of the awards reported in the Option Awards columns are set forth in Note 10 to our audited financial statements included in our Form 10-K. Note that the amounts reported in this column reflect the aggregate accounting cost for these options, and do not necessarily correspond to the actual economic value that may be received by the director from the options.

As of December 31, 2022, Mr. Bonita, Ms. Dier, and Mr. Friedman each held options to purchase 104,332 shares of our common stock, Mr. Babler held options to purchase 67,693 shares of our common stock, Mr. Baker held options to purchase 57,544 shares of our common stock, and Mr. Sandor held options to purchase 123,560 shares of our common stock.

- (2) Mr. Baker earned compensation under our Non-Employee Director Compensation Policy which was paid directly to Mr. Baker's employer.
- (3) Dr. Bonita earned compensation under our Non-Employee Director Compensation Policy which was paid directly to Dr. Bonita's employer.
- (4) From January 1, 2022 through July 31, 2022, Dr. Sandor was compensated for services on the Science and Technology Committee of the Board. Dr. Sandor was paid \$50,000 quarterly and a prorated amount for services rendered in the third quarter of 2022 resulting in \$116,848 earned in 2022.

OUR BOARD OF DIRECTORS RECOMMENDS A VOTE "FOR" THE ELECTION OF EACH OF THE NOMINATED CLASS III DIRECTORS.

PROPOSAL NO. 2 RATIFICATION OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Our Audit Committee has selected Ernst & Young LLP as our principal independent registered public accounting firm to perform the audit of our financial statements for the fiscal year ending December 31, 2023. Ernst & Young LLP audited our financial statements for the fiscal years ended December 31, 2022 and 2021. We expect that representatives of Ernst & Young LLP will be present at the Annual Meeting, will be able to make a statement if they so desire and will be available to respond to appropriate questions.

At the Annual Meeting, the stockholders are being asked to ratify the appointment of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2023. Although ratification by stockholders is not required by law, our Audit Committee is submitting the selection of Ernst & Young LLP to our stockholders because we value our stockholders' views on our independent registered public accounting firm and as a matter of good corporate governance. If this proposal does not receive the affirmative approval of a majority of the votes cast on the proposal, the Audit Committee would reconsider the appointment. Notwithstanding its selection and even if our stockholders ratify the selection, our Audit Committee, in its discretion, may appoint another independent registered public accounting firm at any time during the year if the Audit Committee believes that such a change would be in our best interests and the interests of our stockholders.

The following table presents fees for professional audit services rendered by Ernst & Young LLP for the audit of our annual financial statements for the years ended December 31, 2022 and 2021.

Principal Accountant Fees and Services

| Fees Billed | F | Fiscal Year 2022 | | scal Year 2021 |
|-----------------------------------|----|------------------|----|----------------|
| Audit fees ⁽¹⁾ | \$ | 475,000 | \$ | 454,000 |
| Audit-related fees ⁽²⁾ | | — | | — |
| Tax fees ⁽³⁾ | | 74,160 | | 20,940 |
| All other fees ⁽⁴⁾ | | 2,000 | | 2,000 |
| Total fees | \$ | 551,160 | \$ | 476,940 |

(1) "Audit fees" include fees for professional services provided by Ernst & Young LLP in connection with the audit of our financial statements, review of our quarterly financial statements, and related services that are typically provided in connection with registration statements.

- (2) "Audit-related fees" include fees billed for assurance and related services reasonably related to the performance of the audit or review of our financial statements for fiscal years 2022 and 2021.
- (3) "Tax fees" include fees for professional services rendered for tax compliance, advice and tax services.
- (4) All other fees for the years ended December 31, 2022 and 2021 were for expenses rendered in connection with software licensures fees.

Policy on Audit Committee Pre-Approval of Audit and Permissible Non-Audit Services of Independent Registered Public Accounting Firm

Our Audit Committee pre-approves all audit and permissible non-audit services provided by the independent registered public accounting firm. These services may include audit services, audit-related services, tax services and other services. Pre-approval is detailed as to the particular service or category of services and is generally subject to a specific budget. The independent registered public accounting firm and management are required to periodically report to the Audit Committee regarding the extent of services provided by the independent registered public accounting firm in accordance with this pre-approval, and the fees for the services performed to date. Our Audit Committee may also pre-approve particular services on a case-by-case basis. All of the services relating to the fees described in the table above were approved by our Audit Committee.

OUR BOARD OF DIRECTORS RECOMMENDS A VOTE "FOR" APPROVAL OF PROPOSAL NO. 2.

REPORT OF THE AUDIT COMMITTEE

The information contained in the following report of the Audit Committee is not considered to be "soliciting material," "filed" or incorporated by reference in any past or future filing by us under the Exchange Act or the Securities Act unless and only to the extent that we specifically incorporate it by reference.

The Audit Committee has reviewed and discussed with our management and Ernst & Young LLP our audited financial statements as of and for the year ended December 31, 2022. The Audit Committee has also discussed with Ernst & Young LLP the matters required to be discussed by the applicable requirements of the Public Company Accounting Oversight Board (United States) and the SEC.

The Audit Committee has received and reviewed the written disclosures and the letter from Ernst & Young LLP required by applicable requirements of the Public Company Accounting Oversight Board regarding the independent accountant's communications with the Audit Committee concerning independence, and has discussed with Ernst & Young LLP its independence.

Based on the review and discussions referred to above, the Audit Committee recommended to our Board of Directors that the audited financial statements as of and for the year ended December 31, 2022 be included in our Form 10-K for filing with the SEC.

Submitted by the Audit Committee Mardi C. Dier, Chair Martin Babler David P. Bonita 16

PROPOSAL NO. 3 APPROVAL OF AN AMENDMENT TO OUR RESTATED CERTIFICATE OF INCORPORATION

Our Board of Directors has unanimously adopted a resolution to amend our Restated Certificate of Incorporation, subject to stockholder approval, to exculpate the Company's officers from personal liability to the Company or its stockholders for monetary damages for breaches of fiduciary duty of care. Article VIII of our Restated Certificate of Incorporation currently provides for the Company to limit the monetary liability of directors in certain circumstances pursuant to and consistent with Section 102(b)(7) of the General Corporation Laws of Delaware (the DCGL). Effective August 1, 2022, Section 102(b)(7) of the DCGL was amended to permit a corporation's certificate of incorporation to include a provision eliminating or limiting monetary liability for officers for breach of the fiduciary duty (the Section 102(b)(7) Amendment).

If the stockholders approve this proposal at the Annual Meeting, the Company will file an Amended and Restated Certificate of Incorporation in the form attached hereto as Appendix A (the Charter Amendment). In accordance with the DGCL, however, our Board of Directors may elect to abandon the Charter Amendment without further action by the stockholders at any time prior to the effectiveness of the filing of the Charter Amendment with the Secretary of State of the State of Delaware, notwithstanding stockholder approval of the Charter Amendment.

Purpose and Possible Effects of the Proposed Charter Amendment

Our Board of Directors desires to amend our Restated Certificate of Incorporation to maintain provisions consistent with the governing statutes contained in the DCGL. Prior to the Section 102(b)(7) Amendment, the DGCL has permitted Delaware corporations to exculpate directors from personal liability for monetary damages associated with breaches of the duty of care, but that protection did not extend to a Delaware corporation's officers. Consequently, stockholder plaintiffs have employed a tactic of bringing certain claims that would otherwise be exculpated if brought against directors, against individual officers to avoid dismissal of such claims. The Section 102(b)(7) Amendment was adopted to address inconsistent treatment between officers and directors and address rising litigation and insurance costs for stockholders.

As is currently the case with directors under our Restated Certificate of Incorporation, this provision would not exculpate officers from liability for breach of the duty of loyalty, acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law, or any transaction in which the officer derived an improper personal benefit. Nor would this provision exculpate such officers from liability for claims brought by or in the right of the corporation, such as derivative claims. Our Board of Directors believes it is necessary to provide protection to officers to the fullest extent permitted by law in order to attract and retain top talent. This protection has long been afforded to directors, and accordingly, our Board of Directors believes that this Proposal No. 3, which would extend exculpation to officers, as specifically permitted by the Section 102(b)(7) Amendment, is fair and in the best interests of the Company and its stockholders.

The affirmative vote of the holders of a majority shares outstanding and entitled to vote at the Annual Meeting is required to approve the Charter Amendment. Any broker non-vote or vote to "ABSTAIN" will have the same effect as an "AGAINST" vote.

OUR BOARD OF DIRECTORS RECOMMENDS A VOTE "FOR" APPROVAL OF PROPOSAL NO. 3.

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth certain information with respect to the beneficial ownership of our common stock as of March 31, 2023, by:

- each stockholder known by us to be the beneficial owner of more than 5% of our common stock;
- each of our directors or director nominees;
- each of our named executive officers; and
- all of our directors and executive officers as a group.

Percentage ownership of our common stock is based on 47,916,255 shares of our common stock outstanding on March 31, 2023 (of which 11,402,037 shares are non-voting common stock). We have determined beneficial ownership in accordance with the rules of the SEC, and thus it represents sole or shared voting or investment power with respect to our securities, and the information is not necessarily indicative of beneficial ownership for any other purpose. Unless otherwise indicated below, to our knowledge, the persons and entities named in the table have sole voting and sole investment power with respect to all shares that they beneficially owned, subject to community property laws where applicable. We have deemed all shares of common stock subject to options or other convertible securities held by that person or entity that are currently exercisable or that will become exercisable within 60 days of March 31, 2023 to be outstanding and to be beneficially owned by the person or entity holding the option for the purpose of computing the percentage ownership of that person or entity but have not treated them as outstanding for the purpose of computing the percentage ownership of any other person or entity. Unless otherwise indicated, the address of each beneficial owner listed in the table below is c/o Prelude Therapeutics Incorporated, 200 Powder Mill Road, Wilmington, Delaware 19803.

| | Number of Beneficially | | Percentage of Shares Beneficially Owned | | |
|--|---------------------------|-------------------------------|--|-------------------------------|--|
| Name of Beneficial Owner | Voting Common Stock | Non-Voting Common Stock | Voting Common Stock | Non-Voting Common Stock | |
| Directors and Named Executive Officers: | | | | | |
| Krishna Vaddi ⁽¹⁾ | 4,442,366 | — | 11.6% | _ | |
| Jane Huang ⁽²⁾ | 162,083 | _ | * | | |
| Laurent Chardonnet ⁽³⁾ | 132,790 | — | * | _ | |
| Andrew Combs ⁽⁴⁾ | 492,201 | _ | 1.3 | | |
| Bryant D. Lim | — | — | * | — | |
| Peggy A. Scherle ⁽⁵⁾ | 478,318 | — | 1.3 | — | |
| Paul A. Friedman ⁽⁶⁾ | 564,946 | — | 1.5 | — | |
| David P. Bonita ⁽⁷⁾ | 10,104,539 | 5,680,186 | 27.6 | 49.8% | |
| Julian C. Baker ⁽⁸⁾ | 10,147,168 | 5,721,851 | 27.8 | 50.2 | |
| Victor Sandor ⁽⁹⁾ | 88,876 | — | * | — | |
| Mardi C. Dier ⁽¹⁰⁾ | 76,047 | — | * | — | |
| Martin Babler ⁽¹¹⁾ | 22,244 | — | * | — | |
| All executive officers and directors as a group (12 persons) $^{\#}$ | 26,711,578 | 11,402,037 | 67.9 | 100.0 | |
| Other 5% or Greater Stockholders: | | | | | |
| OrbiMed Entities ⁽¹²⁾ | 10,039,691 | 5,680,186 | 27.5 | 49.8 | |
| Baker Bros. Advisors LP and Affiliates ⁽¹³⁾ | 10,126,417 | 5,721,851 | 27.7 | 50.2 | |
| FMR LLC ⁽¹⁴⁾ | 4,878,551 | | 13.4 | | |
| UBS Group AB ⁽¹⁵⁾ | 2,325,935 | — | 6.4 | _ | |

* Represents beneficial ownership of less than one percent.

Includes directors, nominees and current executive officers.

(1) Consists of (i) 2,701,389 shares of voting common stock held by Dr. Vaddi, of which (a) 117,097 shares are unvested as of March 31, 2023 and subject to forfeiture to us if Dr. Vaddi ceases to provide service to us prior to the vesting of the shares and (b) 1,740,977 shares of voting common stock subject to options that are exercisable within 60 days of March 31, 2023, (ii) 120,665 shares of voting common stock held by Sidus Ventures, LLC, (iii) 423,655 shares of voting common stock held by Dolphin City Trust, (iv) 551,776 shares of voting common stock held by Blue Sky Trust and (v) 551,774 shares of voting common stock held by Brocade Trust. Dr. Vaddi is the manager of Sidus Ventures, LLC and may be deemed to have beneficial ownership over the securities held by Sidus Ventures, LLC. Dr. Vaddi is

the beneficiary of Dolphin City Trust and may be deemed to have beneficial ownership over the securities held by Dolphin City Trust. Dr. Vaddi is the investment advisor for each of the Blue Sky Trust and the Brocade Trust, and may be deemed to have beneficial ownership over the securities held by each of the Blue Sky Trust and the Brocade Trust.

- (2) Represents 162,083 shares of voting common stock that are subject to options that are exercisable within 60 days of March 31, 2023.
- (3) Represents 132,790 shares of voting common stock, of which 95,625 shares of voting common stock that are subject to options that are exercisable within 60 days of March 31, 2023.
- (4) Represents 492,201 shares of voting common stock, of which 184,994 shares of voting common stock that are subject to options that are exercisable within 60 days of March 31, 2023.
- (5) Represents 478,318 shares of voting common stock, of which 302,633 shares of voting common stock that are subject to options that are exercisable within 60 days of March 31, 2023.
- (6) Represents 564,946 shares of voting common stock, of which 64,848 shares of voting common stock that are subject to options that are exercisable within 60 days of March 31, 2023.
- (7) Represents (i) shares of common stock referenced in footnote (12) below and (ii) 64,848 shares of voting common stock that are subject to options that are exercisable within 60 days of March 31, 2023. For the common stock referenced in footnote (12) below, Dr. Bonita is a member of OrbiMed Advisors LLC, but he disclaims beneficial ownership of the shares held by the OrbiMed Entities, except to the extent of his pecuniary interest therein if any.
- (8) Represents shares of common stock referenced in footnote (13) below and (ii) 23,344 shares of voting common stock that are subject to options that are exercisable within 60 days of March 31, 2023. Mr. Baker disclaims beneficial ownership of all shares held by the Baker Funds, except to the extent of his indirect pecuniary interest therein.
- (9) Represents 88,876 shares of voting common stock that are subject to options that are exercisable within 60 days of March 31, 2023.
- (10) Represents 76,047 shares of voting common stock, of which 66,047 shares of voting common stock that are subject to options that are exercisable within 60 days of March 31, 2023.
- (11) Represents 22,244 shares of voting common stock that are subject to options that are exercisable within 60 days of March 31, 2023.
- (12) Represents (i) 526,300 shares of voting common stock purchased by OrbiMed Partners Master Fund Limited, or OPM, (ii) 9,250,191 shares of voting common stock purchased by OrbiMed Private Investments VI, LP, or OPI VI, (iii) 263,200 shares of voting common stock purchased by The Biotech Growth Trust PLC, or BIOG, and together with OPM and OPI VI, the OrbiMed Entities, (iv) 5,596,886 shares of non-voting common stock purchased by OPI VI and (v) 83,300 shares of non-voting common stock purchased by BIOG. OrbiMed Capital GP VI LLC, or OrbiMed GP VI, is the general partner of OPI VI and OrbiMed Advisors LLC, or OrbiMed Advisors, a registered investment advisor under the Investment Advisors Act of 1940, as amended, is the managing member of OrbiMed GP VI. By virtue of such relationships, OrbiMed GP VI and OrbiMed Advisors may be deemed to have voting and investment power over the securities held by OPI VI and as a result may be deemed to have beneficial ownership over such securities. David Bonita, a member of OrbiMed Advisors, is a member of our Board of Directors. Each of OrbiMed GP VI, OrbiMed Advisors, and David Bonita disclaims beneficial ownership of the shares held by OPI VI, except to the extent of its or his pecuniary interest therein if any. OrbiMed Capital LLC, or OrbiMed Capital, is the portfolio manager to BIOG and the investment advisor. OPM. By virtue of such relationships, OrbiMed Capital may be deemed to have voting and investment power over the securities held by BIOG and OPM, and as a result may be deemed to have beneficial ownership of the shares held by OPI VI, except to the extent of its or his pecuniary interest therein if any. OrbiMed Capital may be deemed to have voting and investment power over the securities held by BIOG and OPM, and as a result may be deemed to have beneficial ownership over such securities. OrbiMed Capital is a relying advisor of OrbiMed Advisors. OrbiMed Capital and OrbiMed Advisors exercise voting and investment power through a management committee comprised of C
- (13) Based on information contained on a Schedule 13D/A filed January 29, 2021. Represents (i) 2,593 shares of voting common stock subject to options that are exercisable within 60 days of March 31, 2023 and 5,188 shares of voting common stock from exercise of options, (ii) 870,873 shares of our voting common stock and 509,480 shares of our non-voting common stock held by 667, L.P. and (iii) 9,247,763 shares of our voting common stock and 5,212,371 shares of our non-voting common stock held by Baker Brothers Life Sciences, L.P., together with 667, L.P. (the Baker Funds). Baker Bros. Advisors LP, or the Advisor, serves as the investment advisor to the Baker Funds and has complete and unlimited discretion and authority with respect to their investments and voting power over the securities held by the Baker Funds. Baker Bros. Advisors (GP) LLC, or the Advisor GP, is the sole general partner of the

Advisor. Julian C. Baker and Felix J. Baker are the managing members of the Advisor GP. The shares of non-voting common stock are only convertible to voting common stock 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 Company, the Baker Funds may from time to time increase or decrease the Beneficial Ownership Limitation applicable to that Baker 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 Company. Julian C. Baker is also a member of our Board of Directors. Julian C. Baker, Felix J. Baker, the Advisor GP and the Advisor disclaim beneficial ownership of these securities held directly by the Baker Funds, except to the extent of their pecuniary interest therein. The address for the Advisor, the Advisor GP, Felix J. Baker and Julian C. Baker is c/o Baker Bros. Advisors LP, 860 Washington Street, 3rd Floor, New York, NY 10014.

- (14) Based solely on information contained on a Schedule 13G/A filed February 10, 2023.
- (15) Based solely on information contained on a Schedule 13G/A filed February 13, 2023.

EXECUTIVE OFFICERS

The following table provides information regarding our executive officers as of April 20, 2023:

| Name | Age | Position(s) |
|----------------------------|-----|--|
| Krishna Vaddi, Ph.D. | 57 | Chief Executive Officer and Director |
| Jane Huang, M.D. | 50 | President and Chief Medical Officer |
| Laurent Chardonnet, M.B.A. | 58 | Chief Financial Officer |
| Peggy A. Scherle, Ph.D. | 61 | Chief Scientific Officer |
| Andrew P. Combs, Ph.D. | 57 | Executive Vice President and Head of Chemistry |
| Bryant D. Lim, J.D. | 52 | Chief Legal Officer and Corporate Secretary |

Krishna ("Kris") Vaddi, Ph.D. has served as our Chief Executive Officer and a member of our Board of Directors since February 2016. Dr. Vaddi's biographical information is set forth above under the heading "Proposal No. 1 Election of Class III Directors – Continuing Directors."

Jane Huang, M.D. has served as our President and Chief Medical Officer since April 2022. Prior to joining the Company, Dr. Huang served as Chief Medical Officer, Hematology of BeiGene, Ltd., since September 2016. Prior to BeiGene, Dr. Huang served as the Vice President, Clinical Development at Acerta Pharma from April 2015 to September 2016. Previously, she worked at Genentech, Inc from 2005 to March 2015, serving most recently as Group Medical Director. Dr. Huang is an independent director for Protara Therapeutics since June 2021 and she currently serves as an Adjunct Clinical Assistant Professor in Oncology at Stanford University, specializing in thoracic oncology. Dr. Huang received her Bachelor of Science degree in Biological Sciences from Stanford University and her M.D. from University of Washington School of Medicine. She is board certified in hematology, oncology, and internal medicine, and she completed her residency in internal medicine and fellowships in hematology and oncology at Stanford University.

Laurent Chardonnet, M.B.A. has served as our Chief Financial Officer since November 2021. Mr. Chardonnet previously served as Senior Vice President and Chief Financial Officer of Axcella Health Inc. from November 2019 until November 2021. From 2004 to November 2019, Mr. Chardonnet served in various positions at Incyte Corporation, including Vice President, Treasurer and Principal Accounting Officer, Head of Finance and Administration for the Incyte's European division; and as Vice President of Alliances Prior to Incyte, Mr. Chardonnet served as Controller, Vice President of Finance and acting Chief Financial Officer of Drug Abuse Sciences, a privately held biotechnology company, and as a senior consultant at PricewaterhouseCoopers LLP. Mr. Chardonnet received his Master of Business Administration from Vanderbilt University and his initial business degree from the Institut Superieur de Gestion in Paris.

Peggy A. Scherle, Ph.D. has served as our Chief Scientific Officer since April 2018. Dr. Scherle previously held several roles at Incyte Corporation, a pharmaceutical company, most recently as Group Vice President, Discovery Biology and Preclinical Pharmacology from March 2017 until March 2018. Her prior roles at Incyte included Vice President, Preclinical Pharmacology from 2014 until 2017 and as Executive Director, In Vitro Biology from 2011 until 2014. Earlier in her career, Dr. Scherle held scientific research positions with DuPont Pharmaceuticals and Bristol-Myers Squibb. Dr. Scherle received a B.S. degree in Biochemistry from Michigan State University and a Ph.D. in Immunology from the University of Pennsylvania. She completed her postdoctoral training at the National Institutes of Health.

Andrew P. Combs, Ph.D. has served as our Executive Vice President and Head of Chemistry since April 2019. Dr. Combs previously held several roles at Incyte Corporation, a pharmaceutical company, most recently as Vice President of Discovery Chemistry where he led teams in medicinal chemistry, analytical chemistry, enabling technologies, computational design and informatics from January 2003 until February 2019. His prior roles at Incyte included as Senior Director from 2003 until 2006 and as Executive Director from 2006 until 2015 and Vice President from 2015 until 2019. Earlier in his career, Dr. Combs held positions of increasing responsibility, starting as a Senior Research Scientist and advancing to a Director of medicinal chemistry at DuPont-Merck, DuPont Pharmaceuticals and Bristol-Myers Squibb. Dr. Combs received B.S. degrees in Chemistry and Molecular Biology from the University of Wisconsin-Madison, a Ph.D. in Organic Chemistry from the University of California, Los Angeles, and completed his training as a Howard Hughes Medical Institute post-doctoral fellow at Harvard University.

Bryant D. Lim, J.D. has served as our Chief Legal Officer and Corporate Secretary since February 2023. Prior to joining the Company, Mr. Lim served as Senior Vice President, General Counsel and Chief Business Officer at Aceragen Inc. from September 2022 to February 2023 and Idera Pharmaceuticals from September 2018 to October 2022, where he instituted

and oversaw all legal, corporate governance and business development activities. Prior to Aceragen and Idera, Mr. Lim served as the Vice President of Legal at Incyte Corporation (Incyte) from May 2014 to September 2018, having served most recently as its Global Chief Compliance Officer. Prior to Incyte, Mr. Lim held roles of increasing responsibility at ViroPharma Incorporated, Merck & Co., Inc. and Morgan, Lewis & Bockius LLP. Mr. Lim began his legal career as a law clerk for a federal judge. Mr. Lim currently has served on the board of directors for Life Sciences of Pennsylvania, the statewide biotechnology industry association, since May 2019. Mr. Lim received a J.D. from Villanova University School of Law and a B.A. from the University of Rochester.

EXECUTIVE COMPENSATION

The following tables and accompanying narrative disclosure set forth information about the compensation provided to certain of our executive officers during the years ended December 31, 2022 and 2021. These executive officers, who include our principal executive officer, the two most highly-compensated executive officers (other than our principal executive officer) who were serving as executive officers at the end of the fiscal year ended December 31, 2022 were:

- Krishna Vaddi, Ph.D., Chief Executive Officer;
- Jane Huang, M.D., President and Chief Medical Officer; and
- Peggy A. Scherle, Ph.D., Chief Scientific Officer.

We refer to these individuals as our "named executive officers."

Summary Compensation Table

The following table presents summary information regarding the total compensation for services rendered in all capacities that was earned by our named executive officers during the years ended December 31, 2022 and 2021.

| Year | Salary (\$) | Bonus (\$) | Stock Awards (\$) ⁽¹⁾ | Option Awards (\$) ⁽¹⁾ | Non-Equity Incentive Plan Compensation (\$) ⁽²⁾ | All Other Compensatio n (\$) | Total (\$) |
|------|--|--|--|--|---|--|--|
| | | | | 2,498,24 | | 4 | |
| 2022 | 558,333 | | | 4 | 238,425 | 9,150 | 3,304,152 |
| | | | | 6,224,23 | | (| |
| 2021 | 544,192 | | | 4 | 265,688 | 8,700) | 7,042,814 |
| | | (| | 1,627,66 | | | |
| 2022 | 391,761 | 4,450) | 729,000 | 0 | 167,344 | — | 2,920,215 |
| 2021 | | — , | _ | _ | _ | — | _ |
| | | 300,00 (| | | | (| |
| 2022 | 416,667 | 0) | — | 761,865 | 142,800 | 9,150 | 1,630,482 |
| 2021 | 408,271 | _ | _ | 2,068,82 8 | 156,000 | (4 8,700 ⁾ | 2,641,799 |
| | 2022 2021 2022 2022 2021 2022 | 2022 558,333 2021 544,192 2022 391,761 2021 — 2022 416,667 | 2022 558,333 — 2021 544,192 — 2022 391,761 4,450 2021 — — 2022 391,761 $300,00$ 2022 416,667 0 | YearSalary (\$)Bonus (\$)Awards (\$) ⁽¹⁾ 2022558,3332021544,1922022391,761 $4,450$ $\stackrel{6}{)}$ 2021 $300,00$ $\stackrel{7}{7}$ 2022416,6670) | YearSalary (\$)Bonus (\$)Awards (\$)(1)Awards (\$)(1)2022558,3332,498,242022558,33342021544,19242022391,7614,450 $\stackrel{6}{)}$ 729,000202120212022391,7614,450 $\stackrel{6}{)}$ 729,000020212022416,6670 $\stackrel{7}{)}$ 761,8652,068,82 | YearSalary (\$)Bonus (\$)Stock Awards (\$)(1)Option Awards (\$)(1)Incentive Plan Compensation (\$)(2)2022558,333— $-$ 2,498,242021554,192—-6,224,232021544,192—-42022391,7614,450 $^{\circ}$ 1,627,662021—42022391,7614,450 $^{\circ}$ 729,00002021——2022391,7614,450 $^{\circ}$ 729,00002021————2022416,6670 $^{\circ}$ —2022416,6670 $^{\circ}$ —2024416,6670 $^{\circ}$ —2025416,6670 $^{\circ}$ —2026416,6670 $^{\circ}$ —2027416,6670 $^{\circ}$ —2028416,6670 $^{\circ}$ —2029416,6670 $^{\circ}$ —2020416,6670 $^{\circ}$ —2021————2022416,6670 $^{\circ}$ —2023416,6670 $^{\circ}$ —2024416,6670 $^{\circ}$ —2025416,6670 $^{\circ}$ —2026416,6670 $^{\circ}$ —2027416,6670 $^{\circ}$ —2028 | YearSalary (\$)Bonus (\$)Stock Awards (\$)(1)Option Awards (\$)(1)Incentive Plan Compensation (\$)(2)All Other Compensation n (\$)2022558,333——2,498,24(4)2021544,192——4238,4259,1502022391,7614,450729,0000167,344—2021————4265,6888,7002022391,7614,450729,0000167,344—2021——————2021——————2022391,7614,450729,0000167,344—2021——————2022416,6670————2022416,6670——761,865142,8009,1502,068,82—————4 |

(1) The amounts reported in the Stock Awards and Option Awards columns represent the aggregate grant date fair value of the awards granted under the 2016 Stock Incentive Plan and the 2020 Plan to the named executive officers during the years ended December 31, 2022 and December 31, 2021 as computed in accordance with FASB ASC Topic 718, or ASC 718. The assumptions used in calculating the grant date fair value of the awards reported in the Stock Awards and Option Awards columns are set forth in Note 10 to our audited financial statements included in our Annual Report on Form 10-K. Note that the amounts reported in this column reflect the aggregate accounting cost for these awards, and do not necessarily correspond to the actual economic value that may be received by the named executive officer from the awards.

(2) Represents cash bonus amounts for fiscal year 2022 awarded to our named executed officers which are awarded based on achievement of our corporate performance goals and individual achievement.

(3) Dr. Vaddi is also a member of our Board of Directors but does not receive any additional compensation in his capacity as a director.

(4) Amounts represent the employer matching contribution to the named executive officer's 401(k) plan contributions during the relevant year.

- (5) Dr. Huang's employment with us commenced on April 4, 2022.
- (6) Amount reflects sign-on bonus granted to Dr. Huang in 2022.
- (7) Amount represents retention bonus paid to Dr. Scherle in November 2022.

Non-Equity Incentive Plan Compensation

Annual bonuses for our executive officers are based on the achievement of corporate and, for all of the executive officers other than our Chief Executive Officer, individual performance objectives, as determined by our Board of Directors. For the 2022 bonuses, the Company's performance objectives included determination of program discontinuation with minimum impact for PRT543 and PRT811, completion of dose escalation for PRT1419, demonstrating objective responses to PRT2527, IND studies of PRT3645 and PRT3789, ensuring company-wide compliance and alignment with our budget and

culture objectives while strengthening our corporate function and capabilities. In February 2023, based on the achievement of these corporate performance objectives and satisfaction of individual performance goals, our Board of Directors determined to award bonuses equal to 85% of target.

2022 Outstanding Equity Awards at Fiscal Year-End Table

The following table presents, for each of our named executive officers, information regarding outstanding stock options held as of December 31, 2022.

| | | | Option A | wards | | Stock Awards | | |
|------------------|---------------|--|--|-------------------------------------|------------------------------|--|--|--|
| Name | Grant Date | Number of Securities Underlying Unexercised Options Exercisable | Number of Securities Underlying Unexercised Options Unexercisable | Option Exercise Price (\$) | Option Expiration Date | Number of Shares of Restricted Stock That Have Not Vested (#) | Market Value of Shares of Restricted Stock That Have Not Vested (\$) ⁽¹⁾ | |
| Krishna Vaddi, | 2/20/2015 | (2 | | 0.01 | 2/25/2025 | | | |
| Ph.D. | 2/28/2017 | 12,969) | (3 | 0.31 | 2/27/2027 | — | — | |
| | 6/17/2019 | 513,132 | 59,667 ⁾ | 1.89 | 6/16/2029 | — (4 | — | |
| | 6/17/2019 | — | — | — | — | 45,020) (4 | 271,921 | |
| | 3/26/2020 | — | (2 | — | — | 135,084 | 815,907 | |
| | 3/27/2020 | 393,800 | 178,998 | 1.89 | 3/26/2030 | _ | _ | |
| | 9/2/2020 | 405,184 | 315,143 | 12.85 | 9/1/2030 | _ | _ | |
| | 7/20/2021 | 101,220 | (3 184,580) | 31.23 | 7/19/2031 | _ | _ | |
| | 2/15/2022 | — | 327,900) (3 | 10.58 | 2/14/2032 | — | _ | |
| Jane Huang | 5/2/2022 | — | 460,000 | 4.86 | 4/20/2032 | (5 | | |
| | 5/2/2022 | — | (2 | — | — | 150,000 | 906,000 | |
| Peggy A. Scherle | 11/13/2018 | 27,018 |) | 1.43 | 11/13/2028 | — | _ | |
| | 2/13/2019 | 41,429 | 1,801) (3 | 1.43 | 2/13/2029 | — | — | |
| | 3/27/2020 | 29,163 | 13,509 | 1.89 | 3/26/2030 | — | | |
| | 9/2/2020 | 104,564 | 81,324) | 12.85 | 9/1/2030 | | _ | |
| | 7/20/2021 | 33,645 | 61,355) (3 | 31.23 | 7/19/2031 | _ | _ | |
| | 2/15/2022 | | 100,000 | 10.58 | 2/14/2032 | — | — | |

(1) Based on the closing price of our common stock on December 30, 2022.

(2) This option was 100% vested on the grant date.

(3) 1/4th of the option vested on the one-year anniversary of the vesting commencement date and an additional 1/48th vests monthly thereafter, subject to the executive's continued service to us. The options are also subject to acceleration of vesting upon a qualifying termination of employment, as described in greater detail in the "Employment Arrangements with our Named Executive Officers" section below.

(4) 1/4th of the restricted stock vested on the one-year anniversary of the vesting commencement date, and an additional 1/48th vests monthly thereafter for 36 months, subject to the executive's continued service to us. These shares would vest in full upon a qualifying termination of employment, as described in the "Employment Arrangements with our Named Executive Officers" section below.

(5) 1/4th of the restricted stock vested on the one-year anniversary of the vesting commencement date, and an additional 1/16th vests quarterly thereafter for 36 months, subject to the executive's continued service to us. These shares are also subject to acceleration of vesting upon a qualifying termination of employment, as described in the "Employment Arrangements with our Named Executive Officers" section below.

Employment Arrangements with our Named Executive Officers

We have entered into written employment agreements with each of our named executive officers, setting forth the terms and conditions of employment of each named executive officer, including his or her initial base salary, target bonus, equity awards and employee benefit plan participation, including the following base salaries and target bonus opportunities for each of our named executive officers: Krishna Vaddi: \$561,000 base salary and target bonus of 50% of base salary; Jane Huang: \$525,000 base salary and target bonus of 50% base salary; Peggy Scherle: \$420,000 base salary and target bonus of 40%.

Potential Payments upon Termination or Change in Control

Under the employment agreements with our named executive officers, in the event the named executive officer is terminated by the Company without "cause", he or she will be entitled to receive his or her base salary and we will directly pay or reimburse the named executive officer for the cost of continued healthcare coverage, in each case for 12 months in the case of Dr. Vaddi and for nine months in each case of Dr. Huang and Dr. Scherle. In addition, Dr. Huang will be eligible to receive her annual target bonus opportunity prorated based on date of termination and partial acceleration of her new hire equity awards. Dr. Vaddi will be eligible to receive a partial acceleration of his restricted stock awards.

In the event that the named executive officer is terminated without "cause" or he or she resigns for "good reason", in each case, within 12 months following a change in control of the company, in lieu of the foregoing, he or she will be entitled to receive (i) his or her base salary and we will directly pay or reimburse the named executive officer for the cost of continued healthcare coverage, in each case for 18 months in the case of Dr. Vaddi and for 12 months in each case for Dr. Huang and Dr. Scherle, (ii) a multiple of his or her annual target bonus opportunity equal to 150% for Dr. Vaddi and 100% for Dr. Huang and Dr. Scherle, and (iii) his or her equity awards will become fully vested and exercisable, as applicable.

The severance payments and benefits would be subject to the named executive officer's execution of a general release of claims against us, and his or her agreement to comply with the non-competition and non-solicitation provisions in his or her proprietary information and restrictive covenant agreement. To the extent such severance payments and benefits are payable in connection with a change in control and would result in excise taxes imposed by Section 4999 of the Internal Revenue Code of 1986, as amended, then each of the named executive officers would be entitled to receive (i) the full payment of such payments and benefits or (ii) such lesser amount as would result in no portion of those payments and benefits being subject to the excise tax, whichever results in the greater net after-tax position for the executive.



EQUITY COMPENSATION PLAN INFORMATION

The following table presents information as of December 31, 2022 with respect to compensation plans under which shares of our common stock may be issued.

| _Plan category | Number of securities to be issued upon exercise of outstanding options, warrants and rights (#) | exe outsta wa | ghted-average rcise price of anding options, arrants and ights (\$) ⁽¹⁾ | Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column a) (#) |
|---|---|---------------------|--|--|
| Equity compensation plans approved by security holders ⁽²⁾ | 9,390,930 | \$ | 12.08 | 6,449,187 ⁽³⁾ |
| Equity compensation plans not approved by security holders | | | | — |
| Total | 9,390,930 | \$ | 12.08 | 6,449,187 |

(1) The weighted-average exercise price does not reflect the shares that will be issued in connection with the settlement of restricted stock units (RSUs), since RSUs have no exercise price.

(2) Includes the 2016 Stock Incentive Plan, the 2020 Equity Incentive Plan, and excludes purchase rights accruing under the 2020 Employee Stock Purchase Plan.

(3) As of December 31, 2022, there were 5,139,028 shares of common stock available for issuance under the 2020 Equity Incentive Plan. The number of shares reserved for issuance under our 2020 Equity Incentive Plan increased automatically by 2,394,951 on January 1, 2023 and will increase automatically on the first day of January of each of 2021 through 2030 by the number of shares equal to the lesser of five percent (5%) of the total number of outstanding shares of all classes of the company's common stock outstanding on each December 31 immediately prior to the date of increase or a lower number approved by our board of directors. As of December 31, 2022, there were 1,310,159 shares of common stock available for issuance under the 2020 Employee Stock Purchase Plan. The number of shares reserved for issuance under our 2020 Employee Stock Purchase Plan increased automatically on the first day of January 1, 2023 and will increase automatically on the first day of January of each year during the term of the 2020 Employee Stock Purchase Plan by the number of shares equal to the lesser of one percent (1%) of the total outstanding shares of our common stock as of the immediately preceding December 31 or a lower number approved by our board of directors. As of December 31, 2022, there were no shares of common stock available for issuance under our 2016 Stock Incentive Plan. To the extent that outstanding awards under our 2016 Stock Incentive Plan are forfeited, awards lapse unexercised, or would otherwise have been returned to the share reserve under the 2016 Stock Incentive Plan.

CERTAIN RELATIONSHIPS AND RELATED-PARTY TRANSACTIONS

From January 1, 2022 to the present, there have been no transactions, and there are currently no proposed transactions, in which the amount involved exceeds \$120,000 to which we or any of our subsidiaries was (or is to be) a party and in which any director, director nominee, executive officer, holder of more than 5% of our capital stock, or any immediate family member of or person sharing the household with any of these individuals, had (or will have) a direct or indirect material interest, except for payments set forth under "Proposal No. 1 Election of Class III Directors" and "Executive Compensation" above.

Participation in Our Public Offering

OrbiMed Private Investments VI, LP and its affiliated entities, and the Baker Funds, each a holder of more than 5% of our common stock and an affiliate of a member of our Board of Directors, each purchased, through their affiliated entities, 41,700 shares and 166,666 shares of our non-voting common stock, respectively, in our public offering at the public offering price in January 2021.

Equity Grants to Executive Officers and Directors

We have granted stock options to our executive officers and certain directors, as more fully described in the sections entitled "Executive Compensation" and "Proposal No. 1 Election of Class III Directors — Non-Employee Director Compensation," respectively.

Director and Executive Officer Compensation

Please see the sections entitled "Proposal No. 1 Election of Class III Directors — Non-Employee Director Compensation" and "Executive Compensation" for information regarding the compensation of our directors and executive officers.

Employment Agreements

We have entered into employment offer letters with our executive officers when their employment with the Company commenced. Each offer letter provides for "at will" employment. For more information regarding these agreements, see the section entitled "Executive Compensation — Employment Agreements."

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers. The indemnification agreements, our restated certificate of incorporation and our amended and restated bylaws will require us to indemnify our directors to the fullest extent not prohibited by Delaware law. Subject to certain limitations, our amended and restated bylaws also require us to advance expenses incurred by our directors and officers.

Policies and Procedures for Related-Party Transactions

Our Board of Directors has adopted a written related person transactions policy. Under this policy, our executive officers, directors, nominees for election as a director, beneficial owners of more than 5% of our common stock, and any members of the immediate family of and any entity affiliated with any of the foregoing persons, are not permitted to enter into a material related person transaction with us without the review and approval of our audit committee, or our nominating and corporate governance committee in the event it is inappropriate for our audit committee to review such transaction due to a conflict of interest. The policy provides that any request for us to enter into a transaction with an executive officer, director, nominee for election as a director, beneficial owner of more than 5% of our common stock or with any of their immediate family members or affiliates in which the amount involved exceeds \$120,000 will be presented to our audit committee for review, consideration and approval. In approving or rejecting any such proposal, our audit committee will consider the relevant facts and circumstances available and deemed relevant to the audit committee, including, but not limited to, the related party's relationship to the Company and interest in the transaction and the potential impact on a director's independence if the related party is a director.



ADDITIONAL INFORMATION

Stockholder Proposals to be Presented at Next Annual Meeting

<u>Requirements for Stockholder Proposals to be Brought Before an Annual Meeting</u>. Our amended and restated bylaws provide that for stockholder nominations to our Board of Directors or other proposals to be considered at an annual meeting of stockholders, the stockholder must give timely notice thereof in writing to the Corporate Secretary at Prelude Therapeutics Incorporated, 200 Powder Mill Road, Wilmington, Delaware 19803.

To be timely for our company's annual meeting of stockholders to be held in 2024 (2024 Annual Meeting), a stockholder's notice must be delivered to or mailed and received by our Corporate Secretary at our principal executive offices not earlier than the close of business on March 3, 2024 and not later than the close of business on April 2, 2024. A stockholder's notice to the Corporate Secretary must set forth as to each matter the stockholder proposes to bring before the 2024 Annual Meeting the information required by applicable law and our amended and restated bylaws. However, if the date of the 2024 Annual Meeting is more than 30 days before or more than 60 days after the one-year anniversary of the date of our 2023 Annual Meeting, for the stockholder notice to be timely, it must be delivered to the Corporate Secretary at our principal executive offices not earlier than the close of business on the 105th day prior to the currently proposed annual meeting and not later than the close of business on the later of (1) the 90th day prior to such annual meeting or (2) the close of business on the tenth day following the day on which public announcement of the date of such meeting is first made by us.

<u>Requirements for Stockholder Proposals to be Considered for Inclusion in our Proxy Materials</u>. Stockholder proposals submitted pursuant to Rule 14a-8 under the Exchange Act and intended to be presented at our 2024 Annual Meeting must be received by us not later than December 30, 2023 in order to be considered for inclusion in our proxy materials for that meeting. A stockholder's notice to the Corporate Secretary must set forth as to each matter the stockholder proposes to bring before the 2024 Annual Meeting the information required by applicable law and our amended and restated bylaws.

Available Information

The Form 10-K is also available at https://investors.preludetx.com/investor-relations.

"Householding" - Stockholders Sharing the Same Address

The SEC has adopted rules that permit companies and intermediaries (such as brokers) to implement a delivery procedure called "householding." Under this procedure, multiple stockholders who reside at the same address may receive a single copy of our Form 10-K and proxy materials, including the Notice of Internet Availability, unless the affected stockholder has provided other instructions. This procedure reduces printing costs and postage fees, and helps protect the environment as well.

We expect that a number of brokers with account holders who are our stockholders will be "householding" our Form 10-K and proxy materials, including the Notice of Internet Availability. A single Notice of Internet Availability and, if applicable, a single set of Form 10-K and other proxy materials will be delivered to multiple stockholders sharing an address unless contrary instructions have been received from one or more of the affected stockholders. Once you have received notice from your broker that it will be "householding" communications to your address, "householding" will continue until you are notified otherwise or until you revoke your consent. Stockholders may revoke their consent at any time by contacting their broker. Stockholders may revoke their consent at any time by contacting Computershare Trust Company, N.A., either by calling 1-800-736-3001, or by writing via regular mail to: Computershare Trust Company, PO Box 505000, Louisville, KY 40233-5000 UNITED STATES or by overnight delivery to: Computershare Trust Company, 462 South 4th Street, Suite 1600, Louisville, KY 40202 UNITED STATES.

Upon written or oral request, we will undertake to promptly deliver a separate copy of the Notice of Internet Availability and, if applicable, Form 10-K and other proxy materials to any stockholder at a shared address to which a single copy of any of those documents was delivered. To receive a separate copy of the Notice of Internet Availability and, if applicable, Form 10-K and other proxy materials, you may write our Investor Relations Department at Prelude Therapeutics Incorporated, 200 Powder Mill Road, Wilmington, Delaware 19803, Attn: Investor Relations, submit a request on our website at https://investors.preludetx.com/investor-relations or email Lindsey Trickett, Vice President of Investor Relations, at ltrickett@preludetx.com.

Any stockholders who share the same address and currently receive multiple copies of our Notice of Internet Availability or Form 10-K and other proxy materials who wish to receive only one copy in the future can contact their bank, broker or other holder of record to request information about "householding" or our Investor Relations Department at the address or telephone number listed above.

OTHER MATTERS

Our Board of Directors does not presently intend to bring any other business before the meeting and, so far as is known to the Board of Directors, no matters are to be brought before the meeting except as specified in the notice of the meeting. As to any business that may arise and properly come before the meeting, however, it is intended that proxies, in the form enclosed, will be voted in respect thereof in accordance with the judgment of the persons voting such proxies.

APPENDIX A

PRELUDE THERAPEUTICS INCORPORATED

AMENDED AND RESTATED CERTIFICATE OF INCORPORATION

Prelude Therapeutics Incorporated (the "*Corporation*"), a corporation organized and existing under and by virtue of the Delaware General Corporation Law, hereby certifies as follows:

- 1. The name of the Corporation is "Prelude Therapeutics Incorporated." The date of the filing of its original Certificate of Incorporation with the Secretary of State of the State of Delaware was February 5, 2016.
- 2. This Amended and Restated Certificate of Incorporation of the Corporation attached hereto as <u>Exhibit A</u>, which is incorporated herein by this reference, and which restates, integrates and further amends the provisions of the Restated Certificate of Incorporation of this Corporation, as previously amended and/or restated, has been duly adopted by this Corporation's Board of Directors and by the stockholders in accordance with Sections 242 and 245 of the General Corporation Law of the State of Delaware.

IN WITNESS WHEREOF, said Corporation has caused this Amended and Restated Certificate of Incorporation to be signed by its duly authorized officer under the seal of the Corporation this [] th day of [], 2023.

PRELUDE THERAPEUTICS INCORPORATED

By: _____ Name: Krishna Vaddi Title: Chief Executive Officer

EXHIBIT A

PRELUDE THERAPEUTICS INCORPORATED

AMENDED AND RESTATED CERTIFICATE OF INCORPORATION

ARTICLE I: NAME

The name of the corporation is Prelude Therapeutics Incorporated (the "Corporation").

ARTICLE II: AGENT FOR SERVICE OF PROCESS

The address of the registered office of this Company in the State of Delaware is 1201 North Market Street, 18th Floor, Post Office Box 1347, in the City of Wilmington, County of New Castle, Delaware 19801, and the name of the registered agent of this Corporation in the State of Delaware at such address is Delaware Corporation Organizers, Inc.

ARTICLE III: PURPOSE

The purpose of the Corporation is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law of the State of Delaware (the "*General Corporation Law*").

ARTICLE IV: AUTHORIZED STOCK

1. <u>Total Authorized</u>. The total number of shares of all classes of stock that the Corporation has authority to issue is 510,000,000 shares, consisting of two classes: 500,000,000 shares of Common Stock, \$0.0001 par value per share ("*Common Stock*"), and 10,000,000 shares of Preferred Stock, \$0.0001 par value per share ("*Preferred Stock*").

487,149,741 shares of the Common Stock are voting and are hereby designated as "*Voting Common Stock*" and 12,850,259 shares of the Common Stock are non-voting and are hereby designated as "*Non-Voting Common Stock*," each with the following rights, preferences, powers, privileges and restrictions, qualifications and limitations. For the avoidance of doubt, each reference to "Common Stock" in this Amended and Restated Certificate of Incorporation (as the same may be amended and/or restated from time to time, including pursuant to the terms of any Certificate of Designation designating a series of Preferred Stock, this "*Certificate of Incorporation*"), shall be deemed to include both Voting Common Stock and Non-Voting Common Stock.

2. Designation of Additional Series.

The Board of Directors of the Corporation (the "Board") is authorized, subject to any limitations prescribed by the law of the State of 2.1. Delaware, to provide for the issuance of the shares of Preferred Stock in one or more series, and, by filing a Certificate of Designation pursuant to the applicable law of the State of Delaware ("Certificate of Designation"), to establish from time to time the number of shares to be included in each such series, to fix the designation, vesting, powers (including voting powers), preferences and relative, participating, optional or other special rights, if any, of the shares of each such series and any qualifications, limitations or restrictions thereof, and, except where otherwise provided in the applicable Certificate of Designation, to thereafter increase (but not above the total number of authorized shares of the Preferred Stock) or decrease (but not below the number of shares of such series then outstanding) the number of shares of any such series. The number of authorized shares of Preferred Stock may also be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of two-thirds of the voting power of all then-outstanding shares of capital stock of the Corporation entitled to vote thereon, voting together as a single class, without a separate vote of the holders of the Preferred Stock, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law, unless a separate vote of the holders of one or more series is required pursuant to the terms of any Certificate of Designation; provided, however, that if two-thirds of the Whole Board (as defined below) has approved such increase or decrease of the number of authorized shares of Preferred Stock, then only the affirmative vote of the holders of a majority of the voting power of all then-outstanding shares of the capital stock of the Corporation entitled to vote thereon, voting together as a single class, without a separate vote of the holders of the Preferred Stock, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law, unless a separate vote of the holders of one or more series is required pursuant to the terms of any Certificate of Designation, shall be required to effect such increase or decrease. For purposes of this Certificate of Incorporation, the term "Whole Board" shall mean the total number of authorized directors whether or not there exist any vacancies in previously authorized directorships.

2.2 Except as otherwise expressly provided in any Certificate of Designation designating any series of Preferred Stock pursuant to the foregoing provisions of this Article IV, any new series of Preferred Stock may be designated, fixed and determined as provided herein by the Board without approval of the holders of Voting Common Stock or the holders of Preferred Stock, or any series thereof, and any such new series may have powers, preferences and rights, including, without limitation, voting powers, dividend rights, liquidation rights, redemption rights and conversion rights, senior to, junior to or pari passu with the rights of the Common Stock, any series of Preferred Stock or any future class or series of capital stock of the Corporation.

2.3 Each outstanding share of Voting Common Stock shall entitle the holder thereof to one vote on each matter properly submitted to the stockholders of the Corporation for their vote; *provided*, *that*, except as otherwise required by law, holders of Voting Common Stock shall not be entitled to vote on any amendment to this Certificate of Incorporation (including any Certificate of Designation relating to any series of Preferred Stock) that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together as a class with the holders of one or more other such series, to vote thereon pursuant to this Certificate of Incorporation (including any Certificate of Designation relating to any series of Preferred Stock).

2.4 Any holder of Non-Voting Common Stock may elect to convert each share of Non-Voting Common Stock into one fully paid and nonassessable share of Voting Common Stock at any time by providing written notice to the Corporation; provided, however, that such shares of Non-Voting Common Stock may only be converted by a holder of Non-Voting Common Stock into shares of Voting Common Stock during such time or times as immediately prior to or as a result of such conversion would not result in such holder (when aggregated with affiliates with whom such holder is required to aggregate beneficial ownership for purposes of Section 13(d) of the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder (collectively, the "*Exchange Act*")) being a beneficial owner (for purposes of Section 13(d) of the Exchange Act) (a "*Beneficial Owner*") in excess of the Beneficial Ownership Limitation (as defined in Section 6(b) below). Except for the fact that the Non-Voting Common Stock has no voting rights, the Non-Voting Common Stock is identical in all respects to the Voting Common Stock.

The "Beneficial Ownership Limitation" means initially 9.99% of any class of securities of the Corporation registered under the Exchange Act, which percentage may be increased (not to exceed 19.99%) or decreased to such other percentage as any holder may designate (solely with respect to such holder and not with respect to any other holder) in writing upon 61 days' notice to the Corporation, provided, however, that no holder may make such an election to change the percentage unless all holders managed by the same investment advisor as such electing holder make the same election.

ARTICLE V: AMENDMENT OF BYLAWS

The Board shall have the power to adopt, amend or repeal the Bylaws of the Corporation (as the same may be amended and/or restated from time to time, the "*Bylaws*"). Any adoption, amendment or repeal of the Bylaws by the Board shall require the approval of a majority of the Whole Board. The stockholders shall also have power to adopt, amend or repeal the Bylaws; *provided, that*, notwithstanding any other provision of this Certificate of Incorporation or any provision of law that might otherwise permit a lesser or no vote, but in addition to any vote of the holders of any class or series of stock of the Corporation required by applicable law or by this Certificate of Incorporation (including any Preferred Stock issued pursuant to a Certificate of Designation), the affirmative vote of the holders of at least two-thirds of the voting power of all then-outstanding shares of the capital stock of the Corporation of the Bylaws; *provided, further*, that, in the case of any proposed adoption, amendment or repeal of any provisions of the Bylaws that is approved by the Board and submitted to the stockholders for adoption thereby, if two-thirds of the Whole Board has approved such adoption, amendment or repeal of any provisions of the Bylaws, then only the affirmative vote of the holders of a majority of the voting power of all then-outstanding shares of the capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class, shall be required for any provisions of the Bylaws that is approved by the Board and submitted to the stockholders for adoption thereby, if two-thirds of the Whole Board has approved such adoption, amendment or repeal of any provisions of the Bylaws, then only the affirmative vote of the holders of a majority of the voting power of all then-outstanding shares of the capital stock of the Corporation nequired by applicable law or by this Certificate of Incorporation (including any Preferred Stock issued pursuant to a Certificate of Designation))

ARTICLE VI: MATTERS RELATING TO THE BOARD OF DIRECTORS

1. <u>Director Powers</u>. Except as otherwise provided by the General Corporation Law, the Bylaws of the Corporation or this Certificate of Incorporation, the business and affairs of the Corporation shall be managed by or under the direction of the Board.

2. <u>Number of Directors</u>. Subject to the special rights of the holders of any series of Preferred Stock to elect additional directors under specified circumstances, the total number of directors constituting the Whole Board shall be fixed from time to time exclusively by resolution adopted by a majority of the Whole Board.

3. <u>Classified Board</u>. Subject to the special rights of the holders of one or more series of Preferred Stock to elect additional directors under specified circumstances, the directors shall be divided, with respect to the time for which they severally hold office, into three classes designated as Class I, Class II and Class III, respectively (the "*Classified Board*"). The Board may assign members of the Board already in office to the Classified Board, which assignments shall become effective at the same time that the Classified Board becomes effective. Directors shall be assigned to each class in accordance with a resolution or resolutions adopted by the Board. The number of directors in each class shall be divided as nearly equal as is practicable. The initial term of office of the Class I directors shall expire at the Corporation's first annual meeting of stockholders following the closing of the Corporation's nitial public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, relating to the offer and sale of Voting Common Stock to the public (the "*Initial Public Offering*"), the initial term of office of the Class III directors shall expire at the Corporation's neeting of stockholders following the closing of the Initial Public Offering and the initial term of office of the Class III directors shall expire at the Corporation's third annual meeting of stockholders following the closing of the Initial Public Offering. At each annual meeting of stockholders following the closing of the succeed those directors of the class whose terms then expire shall be elected for a term of office expiring at the third succeeding annual meeting of stockholders after their election.

4. <u>Term and Removal</u>. Each director shall hold office until the annual meeting at which such director's term expires and until such director's successor is duly elected and qualified, or until such director's earlier death, resignation, disqualification or removal. Any director may resign at any time by delivering a resignation in writing or by electronic transmission to the Corporation at its principal office or to the Chairperson of the Board, the Chief Executive Officer, or the Secretary. Subject to the special rights of the holders of any series of Preferred Stock, no director may be removed from the Board except for cause and only by the affirmative vote of the holders of at least two-thirds of the voting power of the then-outstanding shares of capital stock of the Corporation entitled to vote thereon, voting together as a single class. In the event of any increase or decrease in the authorized number of directors, (a) each directorships resulting from such increase or decrease shall be apportioned by the Board among the classes of directors so as to make all classes as nearly equal in number as is practicable, provided that no decrease in the number of directors constituting the Board shall shorten the term of any director.

5. <u>Board Vacancies and Newly Created Directorships</u>. Subject to the special rights of the holders of any series of Preferred Stock, any vacancy occurring in the Board for any cause, and any newly created directorship resulting from any increase in the authorized number of directors, shall, unless (a) the Board determines by resolution that any such vacancies or newly created directorships shall be filled by the stockholders or (b) as otherwise provided by law, be filled only by the affirmative vote of a majority of the directors then in office, even if less than a quorum, or by a sole remaining director, and shall not be filled by the stockholders. Any director elected in accordance with the preceding sentence shall hold office for a term expiring at the annual meeting of stockholders at which the term of office of the class to which the director has been assigned expires and until such director's successor shall have been duly elected and qualified, or until such director's earlier death, resignation, disqualification or removal.

6. <u>Vote by Ballot</u>. Election of directors need not be by written ballot unless the Bylaws shall so provide.

ARTICLE VII: LIMITATION OF LIABILITY

1. <u>Limitation of Liability</u>. To the fullest extent permitted by law, neither a director of the Corporation nor an officer of the Corporation shall be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director or officer, as applicable. Without limiting the effect of the preceding sentence, if the General Corporation Law is hereafter amended to authorize the further elimination or limitation of the liability of a director or officer, then the liability of a director or officer of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law, as so amended.

2. <u>Change in Rights</u>. Neither any amendment nor repeal of this Article VII, nor the adoption of any provision of this Certificate of Incorporation inconsistent with this Article VII, shall eliminate, reduce or otherwise adversely affect any limitation on the personal liability of a director or officer of the Corporation existing at the time of such amendment, repeal or adoption of such an inconsistent provision.

ARTICLE VIII: MATTERS RELATING TO STOCKHOLDERS

1. <u>No Action by Written Consent of Stockholders</u>. Subject to the rights of any series of Preferred Stock then outstanding, no action shall be taken by the stockholders of the Corporation except at a duly called annual or special meeting of stockholders and no action shall be taken by the stockholders of the Corporation by written consent in lieu of a meeting.

2. <u>Special Meeting of Stockholders</u>. Special meetings of the stockholders of the Corporation may be called only by the Chairperson of the Board, the Chief Executive Officer, the Lead Independent Director (as defined in the Bylaws), the President, or the Board acting pursuant to a resolution adopted by a majority of the Whole Board and may not be called by the stockholders or any other person or persons.

3. <u>Advance Notice of Stockholder Nominations and Business Transacted at Special Meetings</u>. Advance notice of stockholder nominations for the election of directors of the Corporation and of business to be brought by stockholders before any meeting of stockholders of the Corporation shall be given in the manner provided in the Bylaws. Business transacted at special meetings of stockholders shall be limited to the purpose or purposes stated in the notice of meeting.

ARTICLE IX: CHOICE OF FORUM

Unless the Corporation consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall, to the fullest extent permitted by law, be the sole and exclusive forum for: (a) any derivative action or proceeding brought on behalf of the Corporation; (b) any action asserting a claim of breach of a fiduciary duty owed by, or other wrongdoing by, any director, officer, stockholder, employee or agent of the Corporation's stockholders; (c) any action asserting a claim against the Corporation or any director, officer, stockholder, employee or agent of the Corporation arising pursuant to any provision of the General Corporation Law, this Certificate of Incorporation or the Bylaws or as to which the General Corporation Law confers jurisdiction on the Court of Chancery of the State of Delaware; (d) any action to interpret, apply, enforce or determine the validity of this Certificate of Incorporation or the Bylaws; or (e) any action asserting a claim against the Corporation or any director, officer, stockholder, employee or agent of the Corporation governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring or holding any interest in shares of capital stock of the Corporation shall be deemed to have notice of and to have consented to the provisions of this Article IX.

ARTICLE X: AMENDMENT OF CERTIFICATE OF INCORPORATION

If any provision of this Certificate of Incorporation shall be held to be invalid, illegal, or unenforceable, then such provision shall nonetheless be enforced to the maximum extent possible consistent with such holding and the remaining provisions of this Certificate of Incorporation (including, without limitation, all portions of any section of this Certificate of Incorporation containing any such provision held to be invalid, illegal, or unenforceable, which is not invalid, illegal, or unenforceable) shall remain in full force and effect.

The Corporation reserves the right to amend or repeal any provision contained in this Certificate of Incorporation in the manner prescribed by the laws of the State of Delaware and all rights conferred upon stockholders are granted subject to this reservation; *provided*, *however*, that, notwithstanding any other provision of this Certificate of Incorporation or any provision of law that might otherwise permit a lesser vote or no vote (but subject to the rights of any series of Preferred Stock set forth in any Certificate of Designation), but in addition to any vote of the holders of any class or series of the stock of the Corporation required by law or by this Certificate of Incorporation, the affirmative vote of the holders of at least two-thirds of the voting power of all then-outstanding shares of the capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class, shall be required to amend or repeal of any provisions of this Certificate of Incorporation, then only the affirmative vote of the holders of a majority of the voting power of all then-outstanding shares of capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class (in addition to any other vote of the holders of any provisions of this Certificate of Incorporation, then only the affirmative vote of the holders of a majority of the voting power of all then-outstanding shares of capital stock of the Corporation entitled to vote generally in the election of directors, voting together as a single class (in addition to any other vote of the holders of any class or series of stock of the Corporation required by law of by this Certificate of Incorporation entitled to vote generally in the election of directors, voting together as a single class (in addition to any other vote of the holders of any class or series of stock of the Corporation required by law of by this Certificate of Incorporation, shall be required to amend or repe

* * * * * * * * * * * A -5 PRELUDE THERAPEUTICS INCORPORATED 200 POWDER MUL ROAD WILMINGTON, DE 19803



Use the Internet to transmit your voting instructions and for electronic delivery of information. Vote by 11:59 PM. Eastern Time on June 15, 2023. Have your proxy card in hand when you access the web site and follow the instructions to obtain your records and to create an electronic voting instruction form.

During The Meeting - Go to www.virtualshareholdermeeting.com/PRLD2023

You may attend the meeting via the Internet and vote during the meeting. Have the information that is printed in the box marked by the arrow available and follow the instructions.

VOTE BY PHONE - 1-800-690-6903 Use any touch-tone telephone to transmit your voting instructions. Vote by 11:59 PM. Eastern Time on June 15, 2023. Have your proxy card in hand when you call and then follow the instructions.

VOTE BY MAIL Mark, sign and date your proxy card and return it in the postage-paid envelope we have provided or return it to Vote Processing, c/o Broadnidge, 51 Mercedes Way, Edgewood, NY 11717.

TO VOTE, MARK BLOCKS BELOW IN BLUE OR BLACK INK AS FOLLOWS:

 V11518-P92815
 KEEP THIS PORTION FOR YOUR RECORDS

 THIS PROXY CARD IS VALID ONLY WHEN SIGNED AND DATED.
 DETACH AND RETURN THIS PORTION ONLY

| | E THERAPEUTICS INCORPORATED | For | Withhold | For All Except | To withhold authority to vote for any individual nominee(s), mark "For All Except" and write the | | | |
|------|--|---------------|--------------|-------------------|---|-----|---------|--------|
| | Board of Directors recommends you vote FOR following: | All | -411 | except | number(s) of the nominee(s) on the line below. | | _ | |
| 1. | Election of Class III Directors | 0 | 0 | 0 | | | | - 1 |
| | Nominees: | | | | | | | |
| | 01) Krishna Vaddi, Ph. D. 02) Mardi C. Dier | | | | | | | |
| The | Board of Directors recommends you vote FOR the foll | owing | proposal | | | For | Against | Abstai |
| 2. | Ratification of the appointment of Ernst & Young LLP as December 31, 2023. | the ind | ependent | registered | public accounting firm of the company for its fiscal year ending | 0 | 0 | 0 |
| The | Board of Directors recommends you vote FOR the foll | owing | proposal | : | | For | Against | Abstai |
| 3. | Approval of an amendment to our Restated Certificate of recent amendments to Delaware General Corporation Law | Incorpo v. | oration to I | imit the lia | bility of certain officers of the company as permitted pursuant to | 0 | 0 | 0 |
| NO | E: Such other business as may properly come before the m | eeting | or any adjo | ournment t | inereor. | | | |
| | | | | | | | | |
| | | | | | | | | |
| | | | | | | | | |
| adm | se sign exactly as your name(s) appear(s) hereon. When signistrator, or other fiduciary, please give full title as such. Jo onally. All holders must sign. If a corporation or partnership, artnership name by authorized officer. | int own | ners should | each sign | | | | |
| or p | | | | | | | | |
| or p | | | | | | | | |

Important Notice Regarding the Availability of Proxy Materials for the Annual Meeting: The Notice and Proxy Statement, Annual Report and Form 10-K are available at www.proxyvote.com.

| V11519-P92815 |
|--|
| PRELUDE THERAPEUTICS INCORPORATED ANNUAL MEETING OF STOCKHOLDERS JUNE 16, 2023, 1:00 P.M. EASTERN TIME THIS PROXY IS SOLICITED ON BEHALF OF THE BOARD OF DIRECTORS |
| The stockholder(s) hereby appoint(s) Krishna Vaddi and Laurent Chardonnet, or either of them, as proxies, each with the power to appoint his substitute, and hereby authorize(s) them to represent and to vote, as designated on the reverse side of this ballot, all of the shares of common stock of Prelude Therapeutics Incorporated that the stockholder(s) is/are entitled to vote at the Annual Meeting of Stockholders to be held virtually at www.virtualshareholdermeeting.com/PRLD2023 at 1:00 p.m. Eastern Time on Friday, June 16, 2023, and any adjournment or postponement thereof. |
| This proxy, when properly executed, will be voted in the manner directed herein. If no such direction is made, this proxy will be voted in accordance with the Board of Directors' recommendations. |
| PLEASE MARK, SIGN, DATE AND RETURN THIS PROXY CARD PROMPTLY USING THE ENCLOSED REPLY ENVELOPE |
| |
| |
| |
| CONTINUED AND TO BE SIGNED ON REVERSE SIDE |
| CONTINUED AND TO BE SIGNED ON REVERSE SIDE |