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

## SCHEDULE 14A
**(Rule 14a-101)**

**INFORMATION REQUIRED IN**
**PROXY STATEMENT**

**SCHEDULE 14A INFORMATION**

**Proxy Statement Pursuant to Section 14(a) of the**
**Securities Exchange Act of 1934**

Filed by the Registrant ☒ Filed by a Party other than the Registrant ☐

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 under to §240.14a-12

# AEGLEA BIOTHERAPEUTICS, INC.
**(Exact name of Registrant as Specified in its Charter)**
**(Name of Person(s) Filing Proxy Statement, if Other Than the Registrant)**

Payment of Filing Fee (Check the appropriate box):

☒ No fee required.

☐ Fee computed on table below per Exchange Act Rules 14a-6(i)(1) and 0-11.

(1) Title of each class of securities to which transaction applies:
(2) Aggregate number of securities to which transaction applies:
(3) Per unit price or other underlying value of transaction computed pursuant to Exchange Act Rule 0-11 (set forth the amount on which the filing fee is calculated and state how it was determined):
(4) Proposed maximum aggregate value of transaction:
(5) Total fee paid:

☐ Fee paid previously with preliminary materials.

☐ Check box if any part of the fee is offset as provided by Exchange Act Rule 0-11(a)(2) and identify the filing for which the offsetting fee was paid previously. Identify the previous filing by registration statement number, or the Form or Schedule and the date of its filing.

1. Amount Previously Paid
2. Form, Schedule or Registration Statement No.
3. Filing Party:
4. Date Filed:

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**PRELIMINARY PROXY STATEMENT DATED AUGUST 7, 2023 – SUBJECT TO COMPLETION**

**AEGLEA BIOTHERAPEUTICS, INC.**
**221 Crescent Street**
**Building 17, Suite 102B**
**Waltham, MA 02453**
**(617) 651-5940**

## NOTICE OF SPECIAL MEETING OF STOCKHOLDERS

**To be held , 2023**

Notice is hereby given that a special meeting of stockholders (the "Special Meeting") of Aeglea BioTherapeutics, Inc. (the "Company") will be held virtually, via live webcast at on , 2023 at a.m. Eastern Time. The purpose of the Special Meeting is the following:

1. To approve, in accordance with Nasdaq Listing Rule 5635(a), the issuance of the Company's common stock, par value $0.0001 per share ("Common Stock"), upon conversion of the Company's Series A Non-Voting Convertible Preferred Stock, par value $0.0001 per share ("Series A Preferred Stock") (the "Conversion Proposal" or "Proposal No. 1");
2. To approve an amendment and restatement of the Aeglea BioTherapeutics, Inc. 2016 Equity Incentive Plan (the "Equity Compensation Plan Proposal" or "Proposal No. 2");
3. To approve an amendment to our Certificate of Incorporation, as amended ("Certificate of Incorporation"), to increase the number of authorized shares of the Common Stock from 500,000,000 to (the "Authorized Shares Proposal" or "Proposal No. 3"); and
4. To approve the adjournment or postponement of the Special Meeting, if necessary, to continue to solicit votes for Proposals Nos. 1, 2 and/or 3 (the "Adjournment Proposal" or "Proposal No. 4").

Only Company stockholders of record at the close of business on , 2023 will be entitled to vote at the Special Meeting and any adjournment or postponement thereof.

Your vote is important. Whether or not you are able to attend the Special Meeting, it is important that your shares be represented. It is important that you retain a copy of the control number found on the proxy card, voting instruction form or Notice, as such number will be required in order for stockholders to gain access to the virtual meeting. To ensure that your vote is recorded promptly, please vote as soon as possible, even if you plan to virtually attend the Special Meeting, by submitting your proxy via the Internet at the address listed on the proxy card or by signing, dating and returning the proxy card.

For questions regarding your stock ownership, you may contact us through our website at http://ir.aeglea.com or, if you are a registered holder, our transfer agent, American Stock Transfer & Trust Company, by email through its website at www.astfinancial.com or by phone at (800) 937-5449. If you have any questions about submitting your proxy or require assistance, please contact our proxy solicitor, Innisfree M&A Incorporated ("*Innisfree*"):

Stockholders may call toll free: (877) 750-8310

Banks and Brokers may call collect: (212) 750-5833

Thank you for your ongoing support and continued interest in Aeglea BioTherapeutics, Inc.
By order of the Board of Directors,

Russell J. Cox
*Chair of the Board of Directors*

Waltham, Massachusetts
, 2023

**YOUR VOTE IS IMPORTANT**

**WE CURRENTLY PLAN TO HOLD THE SPECIAL MEETING VIA LIVE WEBCAST. WHETHER OR NOT YOU PLAN TO ATTEND THE SPECIAL MEETING, WE ENCOURAGE YOU TO VOTE AND SUBMIT YOUR PROXY BY INTERNET, TELEPHONE OR BY MAIL. FOR ADDITIONAL INSTRUCTIONS ON VOTING BY TELEPHONE OR THE INTERNET, PLEASE REFER TO YOUR PROXY CARD.**

**TO VOTE AND SUBMIT YOUR PROXY BY MAIL, PLEASE COMPLETE, SIGN AND DATE THE ENCLOSED PROXY CARD AND RETURN IT IN THE ENCLOSED ENVELOPE. IF YOU ATTEND THE SPECIAL MEETING, YOU MAY REVOKE YOUR PROXY AND VOTE IN PERSON. IF YOU HOLD YOUR SHARES THROUGH AN ACCOUNT WITH A BROKERAGE FIRM, BANK OR OTHER NOMINEE, PLEASE FOLLOW THE INSTRUCTIONS YOU RECEIVE FROM YOUR ACCOUNT MANAGER TO VOTE YOUR SHARES.**

**IT IS IMPORTANT THAT YOU RETAIN A COPY OF THE CONTROL NUMBER FOUND ON THE PROXY CARD, VOTING INSTRUCTION FORM OR NOTICE, AS SUCH NUMBER WILL BE REQUIRED IN ORDER FOR STOCKHOLDERS TO GAIN ACCESS TO THE VIRTUAL MEETING.**

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# Aeglea BioTherapeutics, Inc.

**AEGLEA BIOTHERAPEUTICS, INC.**
**221 Crescent Street**
**Building 17, Suite 102B**
**Waltham, MA 02453**
**(617) 651-5940**

**PROXY STATEMENT**

**SPECIAL MEETING OF STOCKHOLDERS**

**To Be Held on , 2023**

**INFORMATION CONCERNING SOLICITATION AND VOTING**

This proxy statement contains information about the Special Meeting of Stockholders of Aeglea BioTherapeutics, Inc. (the "Special Meeting"), which will be held virtually, via live webcast at on , 2023 at a.m. Eastern Time. The board of directors of Aeglea BioTherapeutics, Inc. (the "Board of Directors") is using this proxy statement to solicit proxies for use at the Special Meeting. In this proxy statement, the terms "Aeglea," "the Company," "we," "us," and "our" refer to Aeglea BioTherapeutics, Inc. The mailing address of our principal executive offices is Aeglea BioTherapeutics, Inc., 221 Crescent Street Building 17, Suite 102B Waltham, MA 02453.

All properly submitted proxies will be voted in accordance with the instructions contained in those proxies. If no instructions are specified, the proxies will be voted in accordance with the recommendation of our Board of Directors with respect to each of the matters set forth in the accompanying Notice of Meeting. You may revoke your proxy at any time before it is exercised at the meeting by giving our corporate secretary written notice to that effect.

At the Special Meeting:

1. Aeglea will ask its stockholders to approve, in accordance with Nasdaq Listing Rule 5635(a), the issuance of the Company's Common Stock, upon conversion of the Company's Series A Preferred Stock issued in June 2023;
2. Aeglea will ask its stockholders to approve the amendment and restatement of the Aeglea BioTherapeutics, Inc. 2016 Equity Incentive Plan;
3. Aeglea will ask its stockholders to approve an amendment to our Certificate of Incorporation to increase the number of authorized shares of the Common Stock from 500,000,000 to ; and
4. Aeglea will ask its stockholders to approve the adjournment or postponement of the Special Meeting, if necessary, to continue to solicit votes for Proposals Nos. 1, 2 and/or 3.

After careful consideration, the Board of Directors has approved the proposals referred to above, and has determined that they are advisable, fair and in the best interests of Aeglea's stockholders. Accordingly, the Board of Directors recommends that stockholders vote "FOR" each of the proposals set forth above.

Your vote is important. Whether or not you expect to virtually attend the Special Meeting, please vote by Internet or telephone following the instructions on the accompanying proxy card, or sign, date and promptly return the proxy card in the enclosed postage paid envelope to ensure that your shares will be represented and voted at the Special Meeting. If you hold your shares in "street name" through a broker, you should follow the procedures provided by your broker.

This proxy statement is dated , 2023 and is first being mailed to stockholders on or about , 2023.

## OVERVIEW

## QUESTIONS AND ANSWERS ABOUT THE SPECIAL MEETING

The following section provides answers to frequently asked questions about the Special Meeting. This section, however, only provides summary information. These questions and answers may not address all issues that may be important to you as a stockholder. You should carefully read this entire proxy statement, including each of the annexes.

**When are this proxy statement and the accompanying materials scheduled to be sent to stockholders?**

On or about , 2023, we will begin mailing our proxy materials, including the Notice of the Special Meeting, this proxy statement and the accompanying proxy card or, for shares held in street name (i.e., held for your account by a broker or other nominee), a voting instruction form.

**When and where will the Special Meeting take place?**

We will be hosting the Special Meeting via live webcast only. The Special Meeting will be held virtually, via live webcast at on , 2023 at a.m. Eastern Time. Regardless of whether you are the "record holder" of your shares or your shares are held in street name, if you held your shares as of the close of business on , 2023, you are welcome to attend the meeting. Stockholders may vote and submit questions while attending the Special Meeting online. The webcast will open 15 minutes before the start of the Special Meeting. In order to enter the Special Meeting, you will need the control number, which is included in the Notice or on your proxy card if you are a stockholder of record of shares of Common Stock, or included with your voting instruction card and voting instructions received from your broker, bank, or other agent if you hold shares of common stock in a "street name." Instructions on how to attend and participate online are also available at . Information on how to vote online at the virtual special meeting is discussed below.

**Who is soliciting my vote?**

Our Board of Directors is soliciting your vote for the Special Meeting.

**When is the record date for the Special Meeting?**

The record date for determination of stockholders entitled to vote at the Special Meeting is the close of business on , 2023 (the "record date").

**How many votes can be cast by all stockholders?**

There were shares of our Common Stock outstanding on the record date, all of which are entitled to vote with respect to all matters to be acted upon at the Special Meeting. Each outstanding share of our Common Stock is entitled to one vote on each matter considered at the Special Meeting. On the record date, there were 1,086,339 shares of Series A Preferred Stock issued and outstanding; the Series A Preferred Stock is not entitled to vote on the matters being considered at the Special Meeting.

Of the shares of our Common Stock issued and outstanding and entitled to vote, 12,945,385 shares of Common Stock were issued in the Asset Acquisition (as described in "*Proposal No. 1 – General – Spyre Acquisition Agreement*" below) and are not entitled to vote on Proposal No. 1 for purposes of the listing rules of the Nasdaq Stock Market. We anticipate that these 12,945,385 shares of Common Stock will be voted in favor of Proposal No. 1 for purposes of adopting the proposal under Delaware law. However, to comply with Nasdaq rules, we will instruct the inspector of elections to conduct a separate tabulation that subtracts 12,945,385 shares from the total number of shares voted in favor of Proposal No. 1 to determine whether that proposal has been adopted in accordance with applicable Nasdaq rules.

**How do I vote?**

If you are a "stockholder of record," meaning you have a stock certificate or hold your shares in an account with our transfer agent, American Stock Transfer & Trust Company, we are sending these proxy materials directly to you. As the stockholder of record, you have the right to direct the voting of your shares by voting over the Internet, by telephone, by returning your proxy or by voting during the Special Meeting.

Over the Internet: To vote over the Internet, please follow the instructions on the enclosed proxy card for submitting your proxy electronically. If you vote over the Internet, you do not need to vote your proxy by telephone or by mail. You must specify how you want your shares voted or your Internet vote cannot be completed, and you will receive an error message. You must submit your Internet proxy before the polls close on , 2023, for your proxy to be valid and your vote to count.

By Telephone: To vote by telephone, please follow the instructions provided on the proxy card. If you vote by telephone, you do not need to vote your proxy over the Internet or by mail. You must specify how you want your shares voted and confirm your vote at the end of the call or your telephone vote cannot be completed. You must submit your telephonic proxy before the polls close on , 2023, the date of the Special Meeting, for your proxy to be valid and your vote to count.

By Mail: To vote by mail, you must sign and date the proxy card and then mail the proxy card in accordance with the instructions on the proxy card. If you vote by mail, you do not need to vote your proxy over the Internet or by telephone. Your proxy card must be received not later than the time the polls close on , 2023 for your proxy to be valid and your vote to count. If you return your proxy card but do not specify how you want your shares voted on any particular matter, they will be voted in accordance with the recommendations of our board of directors.

At the Special Meeting: To vote during the Special Meeting, attend the Special Meeting by visiting , where stockholders may vote and submit questions during the Special Meeting. The meeting starts at a.m. Eastern Time. Please have your 16-Digit Control Number to join the Special Meeting. Instructions on how to attend and vote online during the Special Meeting, including how to demonstrate your stock ownership, are posted at .

*If your shares are held in "street name,"* meaning your shares are held in an account at a bank or at a brokerage firm or other nominee holder, these proxy materials are being forwarded to you by your bank, broker or other nominee who is considered the stockholder of record for purposes of voting at the Special Meeting. As the beneficial owner, you have the right to direct your bank, broker or other nominee on how to vote your shares and to participate in the Special Meeting. You should receive a proxy card and voting instructions with these proxy materials from that organization rather than from us. You will receive instructions from your bank, broker or other nominee explaining how you can vote your shares, whether they permit Internet or telephone voting, and what the deadlines for voting are. Follow the instructions from your bank, broker or other nominee included with these proxy materials, or contact your bank, broker or other nominee to request a proxy form. We encourage you to provide voting instructions to your bank, broker or other nominee by giving your proxy to them. This ensures that your shares will be voted at the Special Meeting according to your instructions.

**How do I change my vote?**

If you are a stockholder of record, you may revoke your proxy and change your vote at any time before the vote is taken at the Special Meeting. To do so, you must do one of the following:

1. Vote over the Internet or by telephone as instructed above. Only your latest Internet or telephone vote is counted.
2. Sign, date and return a new proxy card. Only your latest dated and timely received proxy card will be counted.

3. Attend the Special Meeting and vote as instructed above. Attending the Special Meeting will not alone revoke your Internet or telephone vote or proxy card submitted by mail, as the case may be.

If your shares are held in "street name," you may submit new voting instructions by contacting your broker or other nominee. If you hold your shares in street name and wish to vote at the meeting, you will need to obtain a "legal proxy" from your broker or other nominee in order to vote at the Special Meeting.

**How is a quorum reached?**

Our Amended and Restated By-laws (the "Bylaws") provide that a majority of the shares entitled to vote, present at the Special Meeting or represented by proxy, will constitute a quorum for the transaction of business at the Special Meeting.

Under the General Corporation Law of the State of Delaware ("DGCL"), shares that are voted "abstain" or "withheld" and "broker non-votes" (if any) are counted as present for purposes of determining whether a quorum is present at the Special Meeting. If a quorum is not present, the meeting may be adjourned until a quorum is obtained.

**What proposals will be voted on at the Special Meeting?**

There are four proposals scheduled to be voted on at the meeting:

- **Proposal No. 1** – Approval of the issuance of shares of Common Stock upon conversion of the Series A Preferred Stock.
- **Proposal No. 2** – Approval of an amendment and restatement of the Aeglea BioTherapeutics, Inc. 2016 Equity Incentive Plan.
- **Proposal No. 3** – Approval of an amendment to our Certificate of Incorporation to increase the number of authorized shares of the Common Stock from 500,000,000 to .
- **Proposal No. 4** – Approval, if necessary, of the adjournment or postponement of the Special Meeting, to continue to solicit votes for Proposals No. 1, No. 2 and/or No. 3.

**What vote is required to approve each item at the Special Meeting?**

You may vote "for," "against" or "abstain" on each of the proposals being placed before our stockholders. Under our Bylaws, any proposal other than an election of directors is decided by a majority of the votes properly cast for and against such proposal, except as otherwise provided by applicable law, the rules of any stock exchange upon which our securities are listed, or by our Certificate of Incorporation or Bylaws.

- **Proposal No. 1** – The affirmative vote of the holders of shares of Common Stock representing a majority of the votes cast on the matter is required for the approval of the Conversion Proposal, subject to the separate tabulation of votes described in "*How many votes can be cast by all stockholders?*" set forth above. Broker non-votes (if any) and abstentions will not be counted as votes cast on the matter and will have no effect on the outcome of this proposal.
- **Proposal No. 2** – The affirmative vote of the holders of shares of Common Stock representing a majority of the votes cast on the matter is required for the approval of an amendment and restatement of the Aeglea BioTherapeutics, Inc. 2016 Equity Incentive Plan (the "Equity Compensation Plan Proposal"). Broker non-votes (if any) and abstentions will not be counted as votes cast on the matter and will have no effect on the outcome of this proposal.
- **Proposal No. 3** – The affirmative vote of the holders of shares of Common Stock representing a majority of the votes cast on the matter is required for the approval of the Authorized Shares Proposal. Broker non-votes (if any) and abstentions will not be counted as votes cast on the matter and will have no effect on the outcome of this proposal.

- **Proposal No. 4** – If a quorum is present at the Special Meeting, the affirmative vote of the holders of shares of Common Stock representing a majority of the votes cast on the matter is required for the approval of the Adjournment Proposal. If a quorum is not present at the Special Meeting, the affirmative vote of the holders of a majority of the shares of Common Stock present at the Special Meeting or represented by proxy is required for the approval of the Adjournment Proposal.

**Do I Have Appraisal Rights?**

Our stockholders are not entitled to dissenters' or appraisal rights under the DGCL with respect to any of the proposals being voted on.

**How is the vote counted?**

If you are a stockholder of record, you have the right to direct the voting of your shares by voting over the Internet, by telephone, by returning your proxy or by voting during the Special Meeting. In contrast, if you are a beneficial owner and your shares are held in an account at a bank or at a brokerage firm or other nominee hold, you must tell your bank, broker or other nominee how you would like your shares to be voted, which you can do by following the instructions provided to you by the bank, broker or other nominee.

"Broker non-votes" occur when a beneficial owner of shares held in "street name" does not give instructions to the bank, broker or other nominee holding the shares as to how to vote. If your shares are held in "street name" and you do not give voting instructions to your broker, your broker or nominee may vote the shares with respect to matters that are considered to be "discretionary" (if any), but may not vote the shares with respect to "non-discretionary" matters. Where a broker does not have discretion to vote on a given proposal, the unvoted shares are considered "broker non-votes." For each of the proposals, broker non-votes will not be counted as votes cast on the matter and will have no effect on the outcome of the proposal. Similarly, abstentions will not be counted as votes cast on the matter and will have no effect on the outcome of the proposal.

**Who will count the vote?**

The votes will be counted, tabulated and certified by an Inspector of Elections appointed by the Board of Directors.

**How does the Board of Directors recommend that I vote on the proposals?**

Our Board of Directors recommends that you vote:

- **Proposal No. 1** – **FOR** the approval of the Conversion Proposal.
- **Proposal No. 2** – **FOR** the approval of the Equity Compensation Plan Proposal.
- **Proposal No. 3** – **FOR** the approval of the Authorized Shares Proposal.
- **Proposal No. 4** – **FOR** the approval of the Adjournment Proposal.

**Who pays the cost for soliciting proxies?**

We will pay the expenses of soliciting proxies. Following the original mailing of the soliciting materials, we and our agents, including directors, officers and other employees, without additional compensation, may solicit proxies by mail, electronic mail, telephone, facsimile, by other similar means, or in person. Following the original mailing of the soliciting materials, we will request brokers, custodians, nominees and other record holders to forward copies of the soliciting 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. In addition, we have retained Innisfree M&A Incorporated at a fee $15,000, plus certain out-of-pocket expenses, to act as our proxy solicitor in connection with the proposals to be acted upon at the Special Meeting. Pursuant to an agreement, Innisfree has agreed to solicit proxies from our stockholders on our behalf in connection with the Special Meeting. If you have any questions about submitting your proxy or require assistance, please contact Innisfree at:

Stockholders may call toll free: (877) 750-8310

Banks and Brokers may call collect: (212) 750-5833

**How can I know the voting results?**

We plan to announce preliminary voting results at the Special Meeting and will report the final results in a Current Report on Form 8-K to be filed with the Securities Exchange Commission (the "SEC") within four business days following the Special Meeting.

**Who can provide me with additional information and help answer my questions?**

If you would like additional copies, without charge, of this proxy statement or if you have questions about the proposals being considered at the Special Meeting, including the procedures for voting your shares, you should contact Innisfree, toll free at (877) 750-8310.

**Implications of Being a "Smaller Reporting Company"**

We are 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 our executive compensation arrangements.

## CAUTIONARY INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This proxy statement, and the documents incorporated by reference into this proxy statement, contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding stockholder approval of the conversion rights of the Series A Preferred Stock (as defined herein), any future payouts under the CVR (as defined herein), our ability to achieve the expected benefits or opportunities and related timing with respect to our acquisition of Spyre Therapeutics, Inc. ("Spyre") or to monetize any of our legacy assets, our future results of operations and financial position, business strategy, the length of time that we believe our existing cash resources will fund our operations, our market size, our potential growth opportunities, our preclinical and future clinical development activities, the efficacy and safety profile of our product candidates, the potential therapeutic benefits and economic value of our product candidates, the timing and results of preclinical studies and clinical trials, the expected impact of macroeconomic conditions, including inflation, increasing interest rates and volatile market conditions, current or potential bank failures, as well as global events, including the ongoing military conflict in Ukraine and geopolitical tensions in China on our operations, and the receipt and timing of potential regulatory designations, approvals and commercialization of product candidates. The use of words such as, but not limited to, "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "target," "will," or "would" and similar words expressions are intended to identify forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our clinical results and other future conditions. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements. We may not actually achieve the forecasts disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Such forward-looking statements are subject to a number of material risks and uncertainties including but not limited to those set forth under the caption "Risk Factors" in this proxy statement and in our most recent Quarterly Report on Form 10-Q filed with the SEC, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the SEC. Any forward-looking statement speaks only as of the date on which it was made. Neither we, nor our affiliates, advisors or representatives, undertake any obligation to publicly update or revise any forward-looking statement, whether as result of new information, future events or otherwise, except as required by law. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date hereof.

## RISK FACTOR SUMMARY

The following summarizes the principal factors that make an investment in the Company speculative or risky, all of which are more fully described in the Risk Factors section below. This summary should be read in conjunction with the Risk Factors section and should not be relied upon as an exhaustive summary of the material risks facing our business. The occurrence of any of these risks could harm our business, financial condition, results of operations and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. You should consider all of the risk factors described in our public filings when evaluating our business.

**Risks Related to Our Financial Condition and Capital Requirements**

- There is no guarantee that our acquisition of Spyre will increase stockholder value.
- We will not be able to continue as a going concern if we are unable to raise additional capital when needed.
- We have never generated any revenue from product sales and may never be profitable.
- We anticipate that we will continue to incur significant losses for the foreseeable future.
- Raising additional capital may cause dilution to our stockholders and restrict our operations.

**Risks Related to the Discovery, Development and Commercialization**

- We face competition that have developed or may develop competing programs.
- Our programs are in preclinical stages of development and may fail in development or suffer delays.
- We are substantially dependent on the success of our two most advanced programs, SPY001 and SPY002.
- We may fail to achieve our projected development goals in the time frames we announce and expect.
- We may not be successful in our efforts to build a pipeline of programs with commercial value.
- If our preclinical studies and clinical trials may not be sufficient to support regulatory approval of any of our programs, we may incur additional costs or experience delays in program development.
- We may encounter difficulties enrolling patients in our future clinical trials.
- Preliminary or “topline” data from our clinical trials may change as more data becomes available.
- Our and our future collaborators’ future clinical trials may reveal significant adverse events or side effects.
- We may fail to capitalize on more profitable or potentially successful programs than those we pursue.
- Any of our future approved products may not achieve adequate market acceptance for commercial success.
- Certain of our programs may compete with our other programs.
- The United States Food and Drug Administration (the “FDA”) may not accept data from clinical trials we conduct at sites outside the United States.

**Risks Related to Government Regulation**

- FDA and comparable foreign regulatory approval processes are lengthy and time-consuming and we may not be able to obtain or may be delayed in obtaining required regulatory approvals for our programs.
- We may not be able to meet requirements for the chemistry, manufacturing and control of our programs.
- Our programs for which we intend to seek approval as biologics may face competition sooner than anticipated.
- Even if we receive regulatory approval, we will be subject to extensive ongoing regulatory obligations.
- We may face difficulties from healthcare legislative reform measures.
- We may be unable to offer programs at competitive prices due to pricing regulations and/or coverage policies.
- We may face criminal liability and serious consequences for violations of U.S. and foreign trade regulations.
- Foreign governments may impose strict price controls, which may adversely affect our revenue.
- Any Fast Track Designation we may pursue may not hasten development or regulatory review.

**Risks Related to Our Intellectual Property**

- We may fail in obtaining or maintaining necessary rights to our programs through acquisitions and in-licenses.
- We may be subject to patent infringement claims or may need to file claims to protect our intellectual property.

- We may subject to claims of wrongful hiring of employees or wrongful use of confidential information.
- The value of patents and our ability to protect our products may be impaired by changes to patent laws.
- Our patent protection could be reduced or eliminated for non-compliance with regulatory requirements.
- We may fail to identify or interpret relevant third-party patents, diminishing our ability to market our products.
- We may become subject to claims challenging the inventorship or ownership of our intellectual property.
- Patent terms may be inadequate to protect our competitive position on our programs.
- Our technology licensed from various third parties may be subject to retained rights.

**Risks Related to Our Reliance on Third Parties**

- We may fail to maintain collaborations and licensing arrangements with third parties that we currently rely on.
- Third-parties we rely on for preclinical studies and clinical trials may fail to carry out their contractual duties.
- We may be unable to use third-party manufacturing suites or our third-party manufacturers may encounter difficulties in production.

**Risks Related to Employee Matters, Managing Growth and Other Risks Related to Our Business**

- We may experience difficulties in managing the growth of our organization.
- We may fail to attract and retain highly qualified personnel to allow us to successfully implement our strategy.
- Our future growth may be hindered if we fail to operate in foreign markets.
- Our third-party service providers may engage in misconduct or other improper activities.
- Our or our third-party service providers' internal computer systems may fail or suffer security breaches or other improper access to our data.
- Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.
- The actual or perceived failure to comply with privacy and data security obligations could lead to penalties.
- We may fail to comply with environmental, health and safety laws and regulations and be subject to penalties.
- We may be subject to adverse legislative or regulatory tax changes.
- We may fail to realize the benefits of our business or product acquisitions or our strategic alliances.

**Risks Related to Our Common Stock**

- We may fail to obtain stockholder approval of the conversion of our Series A Preferred Stock, as required by the Spyre Acquisition Agreement (as defined under the "*Description of the Transactions – Overview*" section), and be required to settle such shares of Series A Preferred Stock for cash.
- Our failure to meet the continued listing requirements of The Nasdaq Capital Market could result in a delisting of our Common Stock.
- Applicable anti-takeover provisions could make an acquisition of us more difficult and may prevent attempts by our stockholders to replace or remove our management.
- Our stockholders' ability to obtain a favorable judicial forum for disputes may be limited by the exclusive forum provisions in our restated certificate of incorporation and amended and restated bylaws.
- We do not anticipate paying any dividends and, thus, investment return may be limited to capital appreciation.
- Future sales of shares by existing stockholders could cause our stock price to decline.
- Future sales and issuances of equity and debt could result in additional dilution to our stockholders.
- Our principal stockholders will be able to exert significant control over matters subject to stockholder approval.

**General Risk Factors**

- The market price of our Common Stock has historically been volatile and may drop in the future.
- We incur significant expenses associated with public company reporting requirements.
- A lack of analyst coverage on our Common Stock may cause a decline in our stock price or trading volume.
- We may fail to maintain proper and effective internal controls, negatively affecting our financial reporting.

## DESCRIPTION OF THE TRANSACTIONS

### Overview

On June 22, 2023, we acquired Spyre (the "Asset Acquisition") pursuant to an Agreement and Plan of Merger (the "Spyre Acquisition Agreement"), by and among the Company, Aspen Merger Sub I, Inc., a Delaware corporation and a wholly owned subsidiary of the Company ("First Merger Sub"), Sequoia Merger Sub II, LLC, a Delaware limited liability company and wholly owned subsidiary of the Company ("Second Merger Sub"), and Spyre. Pursuant to the Spyre Acquisition Agreement, First Merger Sub merged with and into Spyre, pursuant to which Spyre was the surviving corporation and became a wholly owned subsidiary of the Company (the "First Merger"). Immediately following the First Merger, Spyre merged with and into Second Merger Sub, pursuant to which Second Merger Sub was the surviving entity and continued under the name "Spyre Therapeutics, LLC." References to our business in this proxy statement includes the business of Spyre prior to the Asset Acquisition.

Spyre was a pre-clinical stage biotechnology company that was incorporated on April 28, 2023 under the direction of Peter Harwin, a Managing Member of Fairmount Funds Management LLC ("Fairmount"), for the purpose of holding rights to certain intellectual property being developed by Paragon Therapeutics, Inc. ("Paragon"). Fairmount is a founder of Paragon. Prior to the Asset Acquisition, Spyre only held options (collectively, the "Option") to license intellectual property from Paragon with respect to four research programs but did not own any intellectual property itself. This remains unchanged following the closing of the Asset Acquisition except with respect to certain intellectual property rights related to SPY001, which Spyre is in the process of finalizing a license agreement based on the key terms described in the antibody discovery and option agreement, dated May 25, 2023 (the "Spyre Option Agreement"), by and among Spyre, Paragon and Parapyre Holding LLC ("Parapyre"), a related party of Paragon, pursuant to the exercise of its Option to acquire such rights under the Spyre Option Agreement. Prior to the Asset Acquisition, Spyre had no assembled workforce, strategic management processes, facilities or operations that could be used to form a process and applied to inputs in order to create an integrated set of activities and assets to produce outputs. Without creating these processes themselves, market participants would not be capable of acquiring Spyre and producing outputs. In addition, Spyre never had any revenues and only had one non-monetary asset, its Option to in-license intellectual property pursuant to the Spyre Option Agreement to identify, evaluate and develop one or more antibody candidates directed to certain mutually agreed therapeutic targets of interest to Spyre and pursuant to which Spyre would have the exclusive option to enter into separate license agreements with Paragon to develop, manufacture and commercialize the resulting antibodies with respect to a given target, subject to the conditions set forth in the Spyre Option Agreement.

Given Spyre's short operating history and highly limited research and development operations, we do not believe that the financial information set forth in Items 12 and 14 of Schedule 14A, with respect to Spyre, is material for our stockholders to exercise their prudent judgment with respect to the Conversion Proposal, the Equity Compensation Plan Proposal, the Authorized Shares Proposal or the Adjournment Proposal. This information is therefore not included in this proxy statement.

With respect to the Asset Acquisition, we determined that Aeglea was the acquiror for accounting purposes under ASC 805-10-25-4 and ASC 805-10-55-11. The primary factors considered were a) the relative voting rights in the combined entity not resulting in a change of control, b) legacy members of our Board of Directors maintained control of the Board of Directors, and c) the only change in the composition of senior management was the appointment of a new Chief Operating Officer. Next, we considered whether the Asset Acquisition should be defined as a business under ASC 805. ASC 805-10-55-5A through 55-5C describe a screen test to determine whether an acquired set of assets and activities is not a business. We determined that substantially all (greater than 90%) of the fair value of the assets acquired were concentrated in a single asset, Spyre's Option to license intellectual property rights related to SPY001, SPY002, SPY003 and SPY004 pursuant to the Spyre Option Agreement. Accordingly, we treated the Asset Acquisition as an asset acquisition for accounting purposes. Even if the transaction would have failed the screen test, Spyre lacked the financial resources to have inputs, processes, and outputs to constitute a business under ASC 805.

All references to "our product candidates," "our programs" and "our pipeline" in this proxy statement refer to the research programs with respect to which we have exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Spyre Option Agreement.

**Acquisition of Spyre**

The Asset Acquisition was structured as a stock-for-stock transaction pursuant to which all of Spyre's outstanding equity interests were exchanged based on a fixed exchange ratio for consideration as a combination of 12,945,385 shares of Common Stock and 364,887 shares of Series A Preferred Stock, which was a newly designated series of preferred stock ("Preferred Stock") that is intended to have economic rights equivalent to the Common Stock, but with only limited voting rights, (or 364,887,000 shares on an as-converted-to-common basis) in addition to the assumption of outstanding and unexercised stock options to purchase 68,365 shares of Common Stock from the Amended and Restated Spyre 2023 Equity Incentive Plan. The rights of the Series A Preferred Stock are set forth in a Certificate of Designation of Preferences, Rights and Limitations that we filed with the Secretary of State of the State of Delaware (the "Certificate of Designation"). Please see "*Description of the Series A Preferred Stock*" under Proposal No. 1 for a complete description of the Certificate of Designation and the rights of the Series A Preferred Stock. The Asset Acquisition was approved by our Board of Directors and the board of directors and stockholders of Spyre.

In connection with the execution of the Spyre Acquisition Agreement, the Company and Spyre entered into stockholder support agreements (the "Support Agreements") with certain of our officers and directors, which collectively own an aggregate of less than 1% of the outstanding shares of the Common Stock. The Support Agreements provide that, among other things, each of the parties thereto has agreed to vote or cause to be voted all of the shares of Common Stock owned by such stockholder in favor of the Conversion Proposal at our stockholders' meeting to be held in connection therewith.

Concurrently and in connection with the execution of the Spyre Acquisition Agreement, certain Spyre stockholders as of immediately prior to the Asset Acquisition, and certain of our directors and officers as of immediately prior to the Asset Acquisition entered into lock-up agreements with us and Spyre, pursuant to which each such stockholder will be subject to a 180-day lockup on the sale or transfer of shares of Common Stock held by each such stockholder at the closing of the Asset Acquisition, including those shares received by Spyre stockholders in the Asset Acquisition.

In connection with the Asset Acquisition, a non-transferrable contingent value right (a "CVR") was distributed to our stockholders of record as of the close of business on July 3, 2023, but was not distributed to holders of shares of Common Stock or Preferred Stock issued to Spyre or the Investors (as defined below) in the transaction. Holders of the CVR will be entitled to receive certain stock and/or cash payments from proceeds received by us, if any, related to the disposition or monetization of our legacy assets for a period of one year following the closing of the transaction.

On July 27, 2023, we announced that we entered into an agreement to sell the global rights to pegzilarginase, an investigational treatment for the rare metabolic disease Arginase 1 Deficiency, to Immedica Pharma AB ("Immedica") for $15.0 million in upfront cash proceeds and up to $100.0 million in contingent milestone payments (the "Immedica APA"). The sale of pegzilarginase to Immedica supersedes and terminates the license agreement between us and Immedica dated March 2021.

The milestone payments under the Immedica APA are contingent on formal reimbursement decisions by national authorities in key European markets and pegzilarginase approval by the FDA, among other events. The upfront payment and contingent milestone payments if paid, net of expenses and adjustments, will be distributed to holders of CVRs pursuant to the CVR Agreement that was entered into in connection with the Asset Acquisition.

**Concurrent Financing Transaction**

Concurrently with the acquisition of Spyre, we entered into a definitive agreement (the "Securities Purchase Agreement") for a PIPE investment with existing and new investors (the "Investors") to raise $210 million in which the investors were issued 721,452 shares of Series A Preferred Stock (or 721,452,000 shares on an as-converted-to-common basis) at a price of $291.08 per share of Series A Preferred Stock (or $0.29108 per share on an as-converted-to-common basis) (the "Financing" and, together with the Asset Acquisition, the "Transactions"). Subject to the approval of the Conversion Proposal, which will be voted on at the Special Meeting, each share of Series A Preferred Stock will automatically convert into 1,000 shares of Common Stock, subject to certain beneficial ownership limitations set by each holder. The closings of the Transactions were not subject to the approval of our stockholders. On an as-converted basis and after accounting for these Transactions, the total number of shares of our Common Stock was 1,193,629,561 (assuming the cashless exercise of all pre-funded warrants) immediately following the closing of such Transactions.

Concurrent with our entry into the Securities Purchase Agreement on June 22, 2023, we entered into a Registration Rights Agreement (the "New RRA") with the Investors. Pursuant to the New RRA, we are obligated to prepare and file a resale registration statement with the SEC within 45 calendar days following the closing of the Financing. The New RRA also contains customary terms, including an obligation to indemnify the Investors and certain affiliates from certain liabilities relating to any misstatements or omissions in the resale registration statement.

## BACKGROUND AND REASONS FOR THE TRANSACTIONS

In approving the Transactions, the Board of Directors considered the pros and cons of the Transactions versus other alternatives, including continuing to focus our resources on our legacy research and development pipeline, liquidation and discontinuation of the Company, other potential business development opportunities reviewed by the Board of Directors and the opportunities and risks presented with the Transactions. In particular, the Board of Directors took into account the following reasons, facts and circumstances in approving the Transactions:

- In April 2023, we announced interim results from our Phase 1/2 clinical trial of pegtarviliase for the treatment of classical homocystinuria and that, following a review of the interim results, we intended to explore strategic alternatives with the goal of maximizing stockholder value, including possible business combinations and/or a divestiture of our clinical programs. To assist with this process, the Board of Directors engaged an independent financial advisor.
- The Board of Directors believed that, as a result of arm's length negotiations with Spyre, we and our management team negotiated the most favorable implied value for our stockholders that Spyre was willing to agree to, and that the terms of the Spyre Acquisition Agreement include the most favorable terms to us in the aggregate to which Spyre was willing to agree. Moreover, we were able to successfully attract significant additional working capital in connection with the Asset Acquisition (as described below), such that we would have adequate resources to fund the near-term development of the research programs under the Spyre Option Agreement, subject to our exercise of the Option with respect to such research programs.
- The Board of Directors believed, after a thorough review of strategic alternatives and discussions with our senior management, our financial advisors and legal counsel, that the Asset Acquisition is more favorable to our stockholders than the potential value that might have resulted from other strategic options available to us, including a liquidation of Aeglea and the distribution of any available cash.
- The Board of Directors believed that the structure of the Asset Acquisition, the issuance of Common Stock and Series A Preferred Stock at a simultaneous sign and close of the Asset Acquisition ("Acquisition Structure") instead of structure where our stockholders could vote to approve or disapprove of the Asset Acquisition and the issuance of securities prior to the consummation of the Asset Acquisition ("Traditional Structure"), had benefits to our stockholders. First, a Traditional Structure typically takes approximately four months to consummate and we would have continued to burn cash to fund operations through that time, resulting in less net cash the upon closing of the Asset Acquisition and a less favorable implied value for our stockholders. Second, the ability to consummate the Acquisition Structure provided more cash at closing of the Asset Acquisition, which made us a more attractive merger candidate (and thus able to attract better terms for the Asset Acquisition).

As a result of the process to explore strategic options, our financial advisor contacted 197 companies regarding a potential transaction and sent 139 of such companies process letters. We entered into confidentiality agreements with 47 of the companies, one of which was Spyre on April 27, 2023. After reviewing the relative merits of each of these potential strategic alternatives, and discussions with several candidates, including material discussions with 6 other companies, the Board of Directors determined that Spyre offered the greatest opportunity. Following this determination by our Board of Directors, our senior management and our financial advisor engaged in expanded and more detailed discussions with Spyre.

The Board of Directors believes that, as a result of arm's length negotiations with Spyre, we and our management team negotiated the most favorable equity split for our stockholders that Spyre was willing to agree to, and that the terms of the Spyre Acquisition Agreement include the most favorable terms to us in the aggregate to which Spyre was willing to agree. Immediately prior to signing the Spyre Acquisition Agreement, our stock price was approximately $0.11 per share, as quoted on the Nasdaq Stock Market. Additionally, our right to sell certain legacy assets and for our stockholders through certain contractual value rights to receive certain cash payments from the net proceeds related to the disposition of such assets within one year following the closing of the Asset Acquisition was not initially offered by Spyre in our first proposal, but we successfully negotiated for these rights. We and Spyre initially agreed that Aeglea would have a valuation of $35 million, assuming $20 million of net cash, and Spyre would have a valuation of $110 million in the Asset Acquisition at the time of closing and the parties entered into a non-binding term sheet on June 1, 2023, which included binding exclusivity terms to negotiate the Asset Acquisition to each party through June 30, 2023. We and Spyre subsequently agreed, prior to the time of closing, that Aeglea would instead have a valuation of $27 million, assuming approximately $11 million of net cash after net cash adjustments. Based on these relative values, but before the Financing, our legacy stockholders retained approximately 20% of Aeglea on an as-converted-to-common basis. The Financing was completed at the implied per-share value of $0.29108 per share, which resulted in our legacy stockholders retaining approximately 8% of the combined company, while the Spyre stockholders received 32% of the combined company and the Investors received 60% of the combined company.

Following the Financing, we would have adequate resources to fund the near-term development of the research programs under the Spyre Option Agreement, subject to our exercise of the Option with respect to such research programs.

After giving consideration to these and other factors, the Board of Directors approved the Transactions, which the Board of Directors believes better position us for long-term success.

## RISK FACTORS

### Risks Related to Our Financial Condition and Capital Requirements

***There is no guarantee that our acquisition of Spyre will increase stockholder value.***

In June 2023, we acquired Spyre. We cannot guarantee that implementing the Asset Acquisition and related transactions will not impair stockholder value or otherwise adversely affect our business. The Asset Acquisition poses significant integration challenges between our businesses and management teams which could result in management and business disruptions, any of which could harm our results of operation, business prospects, and impair the value of the Asset Acquisition to our stockholders.

***We will need to raise additional capital, and if we are unable to do so when needed, we will not be able to continue as a going concern.***

Our most recent Quarterly Report filed on May 11, 2023 includes disclosures regarding our management's assessment of our ability to continue as a going concern. As of June 30, 2023, we had $235.4 million of cash and cash equivalents, and marketable securities. Our cash, cash equivalents and marketable securities balance as of June 30, 2023 is preliminary financial data. We have not completed our quarterly closing procedures and as a result this preliminary data is subject to change. The preliminary financial data included in this proxy statement has been prepared by, and is the responsibility of, our management. PricewaterhouseCoopers LLP has not audited, reviewed, examined, compiled, nor applied agreed upon procedures with respect to the preliminary financial data. Accordingly, PricewaterhouseCoopers LLP does not express an opinion or any other form of assurance with respect thereto. We expect that our current cash and cash equivalents, marketable securities, including approximately $210.0 million we received on June 26, 2023 from the sale of our Series A Preferred Stock in the PIPE transaction plus the cash held by Spyre at the time of the Asset Acquisition, will enable us to fund our operations into 2026. We will need to raise additional capital to continue to fund our operations and service our debt obligations in the future. If we are unable to raise additional capital when needed, we will not be able to continue as a going concern. If our stockholders do not timely approve the conversion of our Series A Preferred Stock, then the holders of our Series A Preferred Stock may be entitled to require us to settle their shares of Series A Preferred Stock for cash at a price per share equal to the fair value of the Series A Preferred Stock, as described in our Certificate of Designation relating to the Series A Preferred Stock. We do not expect we would not have sufficient liquidity to settle a significant amount of the Series A Preferred Stock, if required to do so. However, the cash redemption is not in our control and raises substantial doubt about our ability to continue as a going concern.

Developing our product candidates requires a substantial amount of capital. We expect our research and development expenses to increase in connection with our ongoing activities, particularly as we advance our product candidates through clinical trials. We will need to raise additional capital to fund our operations and such funding may not be available to us on acceptable terms, or at all, and such funding may become even more difficult to obtain due to rising interest rates and the current downturn in the U.S. capital markets and the biotechnology sector in general. Competition for additional capital among biotechnology companies may be particularly intense during this present economic downturn. We may be unable to raise capital through public offerings of our Common Stock and may need to turn to alternative financing arrangements. Such arrangements, if we pursue them, could involve issuances of one or more types of securities, including Common Stock, Preferred Stock, convertible debt, warrants to acquire Common Stock or other securities. These securities could be issued at or below the then prevailing market price for our Common Stock. In addition, if we issue debt securities, the holders of the debt would have a claim to our assets that would be superior to the rights of stockholders until the principal, accrued and unpaid interest and any premium or make-whole has been paid. Interest on any newly-issued debt securities and/or newly-incurred borrowings would increase our operating costs and reduce our net income (or increase our net loss), and these impacts may be material. If the issuance of new securities results in diminished rights to holders of our Common Stock, the market price of our Common Stock could be materially and adversely affected.

We do not currently have any products approved for sale and do not generate any revenue from product sales. Accordingly, we expect to rely primarily on equity and/or debt financings to fund our continued operations. Our ability to raise additional funds will depend, in part, on the success of our preclinical studies and clinical trials and other product development activities, regulatory events, our ability to identify and enter into licensing or

other strategic arrangements, and other events or conditions that may affect our value or prospects, as well as factors related to financial, economic and market conditions, many of which are beyond our control. There can be no assurances that sufficient funds will be available to us when required or on acceptable terms, if at all.

If we are unable to raise additional capital when required or on acceptable terms, we may be required to:

- significantly delay, scale back, or discontinue the development or commercialization of our product candidates;
- seek strategic partnerships, or amend existing partnerships, for research and development programs at an earlier stage than otherwise would be desirable or that we otherwise would have sought to develop independently, or on terms that are less favorable than might otherwise be available in the future;
- dispose of technology assets, or relinquish or license on unfavorable terms, our rights to technologies or any of our product candidates that we otherwise would seek to develop or commercialize ourselves;
- pursue the sale of our company to a third party at a price that may result in a loss on investment for our stockholders; or
- file for bankruptcy or cease operations altogether (and face any related legal proceedings).

Any of these events could have a material adverse effect on our business, operating results, and prospects.

Even if successful in raising new capital, we could be limited in the amount of capital we raise due to investor demand restrictions placed on the amount of capital we raise or other reasons. For example, as of the filing of this proxy statement, we are subject to the limitations set forth in Instruction I.B.6 of Form S-3.

Additionally, any capital raising efforts are subject to significant risks and contingencies, as described in more detail under the risk factor titled "*Raising additional capital may cause dilution to our stockholders, restrict our operations, or require us to relinquish rights.*"

***We have never generated any revenue from product sales and may never be profitable.***

We have no products approved for commercialization and have never generated any revenue from product sales. Our ability to generate revenue and achieve profitability depends on our ability, alone or with strategic collaborators, to successfully complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize one or more of our product candidates. We do not anticipate generating revenue from product sales for the foreseeable future. Our ability to generate future revenue from product sales depends heavily on our success in many areas, including but not limited to:

- completing research and development of our product candidates;
- obtaining regulatory and marketing approvals for our product candidates for which we complete clinical trials;
- manufacturing product candidates and establishing and maintaining supply and manufacturing relationships with third parties that are commercially feasible, meet regulatory requirements and our supply needs in sufficient quantities to meet market demand for our product candidates, if approved;
- qualify for adequate coverage and reimbursement by government and third-party payors for any product candidates for which we obtain regulatory and marketing approval;

- marketing, launching, and commercializing product candidates for which we obtain regulatory and marketing approval, either directly or with a collaborator or distributor;
- gaining market acceptance of our product candidates as treatment options;
- addressing any competing products and technological and market developments;
- implementing internal systems and infrastructure, as needed;
- protecting and enforcing our intellectual property rights, including patents, trade secrets, and know-how;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- obtaining coverage and adequate reimbursement from third-party payors and maintaining pricing for our product candidates that supports profitability; and
- attracting, hiring, and retaining qualified personnel.

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by regulatory authorities to perform clinical and other studies in addition to those that we anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. Portions of the research programs with respect to which we have exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Spyre Option Agreement may be in-licensed from third parties, which make the commercial sale of such in-licensed products potentially subject to additional royalty and milestone payments to such third parties. We will also have to develop or acquire manufacturing capabilities or continue to contract with contract manufacturers in order to continue development and potential commercialization of our product candidates. For instance, if the costs of manufacturing our drug product are not commercially feasible, we will need to develop or procure our drug product in a commercially feasible manner in order to successfully commercialize a future approved product, if any. Additionally, if we are not able to generate revenue from the sale of any approved products, we may never become profitable.

***We have historically incurred losses, have a limited operating history on which to assess our business, and anticipate that we will continue to incur significant losses for the foreseeable future.***

We are a biopharmaceutical company with a limited operating history. Since inception, we have incurred significant operating losses. We expect that our current cash and cash equivalents, including approximately $210.0 million we received on June 26, 2023 from the sale of our Series A Preferred Stock in the PIPE, will enable us to fund our operations into 2026. We will need to raise substantial additional capital to continue to fund our operations in the future.

Failure to raise capital as and when needed, on favorable terms or at all, would have a negative impact on our financial condition and our ability to develop our product candidates. Changing circumstances may cause us to consume capital significantly faster or slower than we currently anticipate. If we are unable to acquire additional capital or resources, we will be required to modify our operational plans to complete future milestones and we may be required to delay, limit, reduce or eliminate development or future commercialization efforts of product candidates and/or programs. We have based these estimates on assumptions that may prove to be wrong, and we could exhaust our available financial resources sooner than we currently anticipate. We may be forced to reduce our operating expenses and raise additional funds to meet our working capital needs, principally through the additional sales of our securities or debt financings or entering into strategic collaborations.

We have devoted substantially all of our financial resources to identify, acquire, and develop our product candidates, including conducting clinical trials and providing general and administrative support for our operations. Since our inception and through June 30, 2023, we have funded our operations primarily from the sale and issuance of convertible preferred and common equity securities, pre-funded warrants, the collection of grant proceeds, and the licensing of our product rights for commercialization of pegzilarginase in Europe and certain countries in the Middle East. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity or debt financings, strategic collaborations, or grants. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We expect our losses to increase as our product candidates enter more advanced clinical trials. It may be several years, if ever, before we complete pivotal clinical trials or have a product candidate approved for commercialization. We expect to invest significant funds into the research and development of our current product candidates to determine the potential to advance these product candidates to regulatory approval.

If we obtain regulatory approval to market a product candidate, our future revenue will depend upon the size of any markets in which our product candidates may receive approval, and our ability to achieve sufficient market acceptance, pricing, coverage and adequate reimbursement from third-party payors, and adequate market share for our product candidates in those markets. Even if we obtain adequate market share for our product candidates, because the potential markets in which our product candidates may ultimately receive regulatory approval could be very small, we may never become profitable despite obtaining such market share and acceptance of our products.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future and our expenses will increase substantially if and as we:

- continue the preclinical development and initiate the clinical development of our product candidates;
- continue efforts to discover and develop new product candidates;
- continue the manufacturing of our product candidates or increase volumes manufactured by third parties;
- advance our product candidates into larger, more expensive clinical trials;
- initiate additional preclinical studies or clinical trials for our product candidates;
- seek regulatory and marketing approvals and reimbursement for our product candidates;
- establish a sales, marketing, and distribution infrastructure to commercialize any products for which we may obtain marketing approval and market for ourselves;
- seek to identify, assess, acquire, and/or develop other product candidates;
- make milestone, royalty, or other payments under third-party license agreements;
- seek to maintain, protect, and expand our intellectual property portfolio;
- seek to attract and retain skilled personnel; and
- experience any delays or encounter issues with the development and potential for regulatory approval of our clinical and product candidates such as safety issues, manufacturing delays, clinical trial accrual delays, longer follow-up for planned studies or trials, additional major studies or trials, or supportive trials necessary to support marketing approval.

Further, the net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

***Raising additional capital may cause dilution to our stockholders, restrict our operations, or require us to relinquish rights.***

Until such time, if ever, as we can generate substantial revenue from the sale of our product candidates, we expect to finance our cash needs through a combination of equity offerings, debt financings and license and development agreements. To the extent that we raise additional capital through the sale of equity securities or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a holder of Common Stock. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements with third parties when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to third parties to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

To the extent that we raise additional capital through the sale of equity, including pursuant to any sales under convertible debt or other securities convertible into equity, the ownership interest of our stockholders will be diluted, and the terms of these new securities may include liquidation or other preferences that adversely affect the rights of our stockholders. For instance, in June 2023, we sold 721,452 shares of our Series A Preferred Stock in the Financing to the Investors for gross proceeds of approximately $210.0 million. Subject to receiving the requisite stockholder approval and certain beneficial ownership limitations set by each holder of Series A Preferred Stock, each share of Series A Preferred Stock will automatically convert into an aggregate of approximately 1,000 shares of our Common Stock. We are required to solicit the consent of our stockholders with regard to conversion of the shares of our Series A Preferred Stock, which will be voted on at the Special Meeting. If our stockholders fail to approve such matters, we may be subject to financial penalties that could materially harm our business, including the forced settlement of shares of Series A Preferred Stock for cash, as described in the Certificate of Designation.

Debt financing, if available, would likely involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, making additional product acquisitions, or declaring dividends. If we raise additional funds through strategic collaborations or licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates or future revenue streams or grant licenses on terms that are not favorable to us. We cannot be assured that we will be able to obtain additional funding if and when necessary to fund our entire portfolio of product candidates to meet our projected plans. If we are unable to obtain funding on a timely basis, we may be required to delay or discontinue one or more of our development programs or the commercialization of any product candidates or be unable to expand our operations or otherwise capitalize on potential business opportunities, which could materially harm our business, financial condition, and results of operations.

**Risks Related to Discovery, Development and Commercialization**

***We face competition from entities that have developed or may develop programs for the diseases addressed by our programs.***

The development and commercialization of drugs is highly competitive. Our programs, if approved, will face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration. We compete with a variety of multinational biopharmaceutical companies, specialized biotechnology companies and emerging biotechnology companies, as well as academic institutions, governmental agencies, and public and private research institutions, among others. Many of the companies with which we are currently competing or will complete against in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industry may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites, patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our competitors have developed, are developing or will develop programs and processes competitive with our programs and processes. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments. Our success will depend partially on our ability to develop and commercialize products that have a competitive safety, efficacy, dosing and/or presentation profile. Our commercial opportunity and success will be reduced or eliminated if competing products are safer, more effective, have a more attractive dosing profile or presentation or are less expensive than the products we develop, or if our competitors develop competing products or if biosimilars enter the market more quickly than we do and are able to gain market acceptance.

In addition, because of the competitive landscape for inflammatory and immunology ("I&I") indications, we may also face competition for clinical trial enrollment. Patient enrollment will depend on many factors, including if potential clinical trial patients choose to undergo treatment with approved products or enroll in competitors' ongoing clinical trials for programs that are under development for the same indications as our programs. An increase in the number of approved products for the indications we are targeting with our programs may further exacerbate this competition. Our inability to enroll a sufficient number of patients could, among others, delay our development timeline, which may further harm our competitive position.

***Our programs are in preclinical stages of development and may fail in development or suffer delays that materially and adversely affect their commercial viability. If we or our current or future collaborators are unable to complete development of, or commercialize our programs, or experience significant delays in doing so, our business will be materially harmed.***

We have no products on the market and all of our programs are in preclinical stages of development and have not been tested in humans. As a result, we expect it will be many years before we commercialize any program, if ever. Our ability to achieve and sustain profitability depends on obtaining regulatory approvals for, and successfully commercializing, our programs, either alone or with third parties, and we cannot guarantee you that we will ever obtain regulatory approval for any of our programs. We have not yet demonstrated our ability to initiate or complete any clinical trials, obtain regulatory approvals, manufacture a clinical development or commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Before obtaining regulatory approval for the commercial distribution of our programs, we or an existing or future collaborator must conduct extensive preclinical tests and clinical trials to demonstrate the safety and efficacy in humans of our programs and future product candidates.

We or our collaborators may experience delays in initiating or completing clinical trials. We or our collaborators also may experience numerous unforeseen events during, or as a result of, any current or future clinical trials that we could conduct that could delay or prevent our ability to receive marketing approval or commercialize our programs or any future programs, including:

- regulators or institutional review boards ("IRBs"), the FDA or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations ("CROs"), the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- clinical trials of any programs may fail to show safety or efficacy, produce negative or inconclusive results and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon product development programs;
- the number of subjects required for clinical trials of any programs may be larger than we anticipate, especially if regulatory bodies require completion of non-inferiority or superiority trials, enrollment in these clinical trials may be slower than we anticipate or subjects may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants in our trials are being exposed to unacceptable health risks;
- the cost of clinical trials of any of our programs may be greater than we anticipate;
- the quality of our programs or other materials necessary to conduct clinical trials of our programs may be inadequate to initiate or complete a given clinical trial;
- our inability to manufacture sufficient quantities of our programs for use in clinical trials;
- reports from clinical testing of other therapies may raise safety or efficacy concerns about our programs;
- our failure to establish an appropriate safety profile for a program based on clinical or preclinical data for such programs as well as data emerging from other therapies in the same class as our programs; and
- the FDA or other regulatory authorities may require us to submit additional data such as long-term toxicology studies, or impose other requirements before permitting us to initiate a clinical trial.

Commencing clinical trials in the United States is subject to acceptance by the FDA of an investigational new drug application ("IND"), biologics license application ("BLA") or similar application and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA requires us

to complete additional preclinical studies or we are required to satisfy other FDA requests prior to commencing clinical trials, the start of our first clinical trials may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials, delay the enrollment of our clinical trials or impose stricter approval conditions than we currently expect. There are equivalent processes and risks applicable to clinical trial applications in other countries, including countries in the European Union ("EU").

We may not have the financial resources to continue development of, or to modify existing or enter into new collaborations for, a program if we experience any issues that delay or prevent regulatory approval of, or our ability to commercialize, our programs. We or our current or future collaborators' inability to complete development of, or commercialize our programs, or significant delays in doing so, could have a material and adverse effect on our business, financial condition, results of operations and prospects.

***We are substantially dependent on the success of our two most advanced programs, SPY001 and SPY002, and our anticipated clinical trials of such programs may not be successful.***

Our future success is substantially dependent on our ability to timely obtain marketing approval for, and then successfully commercialize, our two most advanced programs, SPY001 and SPY002. We exercised our Option with respect to SPY001 on July 12, 2023 and we continue to hold the unexercised Option with respect to SPY002. We are investing a majority of our efforts and financial resources into the research and development of these programs. We anticipate initiating a Phase 1 clinical trial in healthy volunteers of SPY001 in the first half of 2024 and of SPY002 in the second half of 2024, each subject to the filing of an IND or foreign equivalent and regulatory approval. The success of our programs is dependent on observing a longer half-life of our programs in humans than other mAbs currently marketed and in development as we believe this longer half-life has the potential to result in a more favorable dosing schedule for our programs, assuming they successfully complete clinical development and obtain marketing approval. This is based in part on the assumption that the longer half-life we have observed in non-human primates ("NHPs") will translate into an extended half-life of our programs in humans. To the extent we do not observe this extended half-life when we dose humans with our programs, it would significantly and adversely affect the clinical and commercial potential of our programs.

Our programs will require additional clinical development, evaluation of clinical, preclinical and manufacturing activities, marketing approval in multiple jurisdictions, substantial investment and significant marketing efforts before we generate any revenues from product sales. We are not permitted to market or promote these programs, or any other programs, before we receive marketing approval from the FDA and comparable foreign regulatory authorities, and we may never receive such marketing approvals.

The success of our programs will depend on a variety of factors. We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any future collaborator. Accordingly, we cannot assure you that we will ever be able to generate revenue through the sale of these programs, even if approved. If we are not successful in commercializing SPY001 or SPY002, or are significantly delayed in doing so, our business will be materially harmed.

***If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our programs may be delayed and our expenses may increase and, as a result, our stock price may decline.***

From time to time, we estimate the timing of the anticipated accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials, such as the expected

timing for the anticipated commencement of our Phase 1 clinical trials in IBD, as well as the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are and will be based on numerous assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, or at all, the commercialization of our programs may be delayed or never achieved and, as a result, our stock price may decline. Additionally, delays relative to our projected timelines are likely to cause overall expenses to increase, which may require us to raise additional capital sooner than expected and prior to achieving targeted development milestones.

***Our approach to the discovery and development of our programs is unproven, and we may not be successful in our efforts to build a pipeline of programs with commercial value.***

Our approach to the discovery and development of the research programs with respect to which we have exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Spyre Option Agreement leverages clinically validated mechanisms of action and incorporates advanced antibody engineering to optimize half-life and other properties designed to overcome limitations of existing therapies. Our programs are purposefully designed to improve upon existing product candidates and products while maintaining the same, well-established mechanisms of action. However, the scientific research that forms the basis of our efforts to develop programs using half-life extension technologies, including YTE and LS amino acid substitutions, is ongoing and may not result in viable programs. We have limited clinical data on product candidates utilizing YTE and LS half-life extension technologies, especially in I&I indications, demonstrating whether they are safe or effective for long-term treatment in humans. The long-term safety and efficacy of these technologies and the extended half-life and exposure profile of our programs compared to currently approved products is unknown.

We may ultimately discover that utilizing half-life extension technologies for our specific targets and indications and any programs resulting therefrom do not possess certain properties required for therapeutic effectiveness. We currently have only preclinical data regarding the increased half-life properties of our programs and the same results may not be seen in humans. In addition, programs using half-life extension technologies may demonstrate different chemical and pharmacological properties in patients than they do in laboratory studies. This technology and any programs resulting therefrom may not demonstrate the same chemical and pharmacological properties in humans and may interact with human biological systems in unforeseen, ineffective or harmful ways.

In addition, we may in the future seek to discover and develop programs that are based on novel targets and technologies that are unproven. If our discovery activities fail to identify novel targets or technologies for drug discovery, or such targets prove to be unsuitable for treating human disease, we may not be able to develop viable additional programs. We and our existing or future collaborators may never receive approval to market and commercialize any program. Even if we or an existing or future collaborator obtains regulatory approval, the approval may be for targets, disease indications or patient populations that are not as broad as we intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. If the products resulting from the research programs with respect to which we have exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Spyre Option Agreement prove to be ineffective, unsafe or commercially unviable, such programs would have little, if any, value, which would have a material and adverse effect on our business, financial condition, results of operations and prospects.

***Preclinical and clinical development involves a lengthy and expensive process that is subject to delays and with uncertain outcomes, and results of earlier studies and trials may not be predictive of future clinical trial results. If our preclinical studies and clinical trials are not sufficient to support regulatory approval of any of our programs, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such program.***

Before obtaining marketing approval from regulatory authorities for the sale of any program, we must complete preclinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our program in humans. Our clinical trials may not be conducted as planned or completed on schedule, if at all, and failure can occur at any time during the preclinical study or clinical trial process. For example, we depend on the availability of NHPs to conduct certain preclinical studies that we are required to complete prior to submitting an IND and initiating clinical development. There is currently a global shortage of NHPs available for drug development. This could cause the cost of obtaining NHPs for our future preclinical studies to increase significantly and, if the shortage continues, could also result in delays to our development timelines. Furthermore, a failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their programs performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their programs. In addition, we expect to rely on patients to provide feedback on measures such as itch and quality of life, which are subjective and inherently difficult to evaluate. These measures can be influenced by factors outside of our control, and can vary widely from day to day for a particular patient, and from patient to patient and from site to site within a clinical trial.

We cannot be sure that the FDA will agree with our clinical development plan. We plan to use the data from our planned Phase 1 trials of SPY001 and SPY002 in healthy volunteers to support Phase 2 trials in IBD and other I&I indications. If the FDA requires us to conduct additional trials or enroll additional patients, our development timelines may be delayed. We cannot be sure that submission of an IND, BLA or similar application will result in the FDA or comparable foreign regulatory authorities, as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could cause regulatory authorities to suspend or terminate such clinical trials. Events that may prevent successful or timely initiation or completion of clinical trials include: inability to generate sufficient preclinical, toxicology or other *in vivo* or *in vitro* data to support the initiation or continuation of clinical trials; delays in reaching a consensus with regulatory authorities on study design or implementation of the clinical trials; delays or failure in obtaining regulatory authorization to commence a trial; delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites; delays in identifying, recruiting and training suitable clinical investigators; delays in obtaining required IRB approval at each clinical trial site; delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of our programs for use in clinical trials or the inability to do any of the foregoing; failure by our CROs, other third parties or us to adhere to clinical trial protocols; failure to perform in accordance with the FDA's or any other regulatory authority's good clinical practice requirements ("GCPs") or applicable regulatory guidelines in other countries; changes to the clinical trial protocols; clinical sites deviating from trial protocol or dropping out of a trial; changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data; transfer of manufacturing processes to larger-scale facilities operated by a contract manufacturing organization ("CMO") and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and third parties being unwilling or unable to satisfy their contractual obligations to us.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such clinical trials are being conducted, by the Data Safety Monitoring Board, if any, for such clinical trial or by the FDA or comparable foreign regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with

regulatory requirements or our clinical trial protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from the programs, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we are required to conduct additional clinical trials or other testing of our programs beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our programs, if the results of these trials are not positive or are only moderately positive or if there are safety concerns, our business and results of operations may be adversely affected and we may incur significant additional costs.

***If we encounter difficulties enrolling patients in our future clinical trials, our clinical development activities could be delayed or otherwise adversely affected.***

We may experience difficulties in patient enrollment in our future clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. The enrollment of patients in future trials for any of our programs will depend on many factors, including if patients choose to enroll in clinical trials, rather than using approved products, or if our competitors have ongoing clinical trials for programs that are under development for the same indications as our programs, and patients instead enroll in such clinical trials. Additionally, the number of patients required for clinical trials of our programs may be larger than we anticipate, especially if regulatory bodies require the completion of non-inferiority or superiority trials. Even if we are able to enroll a sufficient number of patients for our future clinical trials, we may have difficulty maintaining patients in our clinical trials. Our inability to enroll or maintain a sufficient number of patients would result in significant delays in completing clinical trials or receipt of marketing approvals and increased development costs or may require us to abandon one or more clinical trials altogether.

***Preliminary, "topline" or interim data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures.***

From time to time, we may publicly disclose preliminary or topline data from our preclinical studies and clinical trials, which are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data. We also make assumptions, estimations, calculations and conclusions as part of our analyses of these data without the opportunity to fully and carefully evaluate complete data. As a result, the preliminary or topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated or subsequently made subject to audit and verification procedures.

Any preliminary or topline data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular program and our company in general. In addition, the information we choose to publicly disclose regarding a particular preclinical study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the preliminary, topline or interim data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our programs may be harmed, which could harm our business, operating results, prospects or financial condition.

***Our future clinical trials or those of our future collaborators may reveal significant adverse events or undesirable side effects not seen in our preclinical studies and may result in a safety profile that could halt clinical development, inhibit regulatory approval or limit commercial potential or market acceptance of any of our programs.***

Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects, adverse events or unexpected characteristics. While our preclinical studies in NHPs have not shown any such characteristics to date, we have not yet initiated any clinical trials in humans. If significant adverse events or other side effects are observed in any of our future clinical trials, we may have difficulty recruiting patients to such trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of one or more programs altogether. We, the FDA or other applicable regulatory authorities, or an IRB, may suspend any clinical trials of any program at any time for various reasons, including a belief that subjects or patients in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential products developed in the biotechnology industry that initially showed therapeutic promise in early-stage studies and trials have later been found to cause side effects that prevented their further development. Other potential products have shown side effects in preclinical studies, which side effects do not present themselves in clinical trials in humans. Even if the side effects do not preclude the program from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance of the approved product due to its tolerability versus other therapies. In addition, an extended half-life could prolong the duration of undesirable side effects, which could also inhibit market acceptance. Treatment-emergent adverse events could also affect patient recruitment or the ability of enrolled subjects to complete our clinical trials or could result in potential product liability claims. Potential side effects associated with our programs may not be appropriately recognized or managed by the treating medical staff, as toxicities resulting from our programs may not be normally encountered in the general patient population and by medical personnel. Any of these occurrences could harm our business, financial condition, results of operations and prospects significantly.

In addition, even if we successfully advance our programs or any future program through clinical trials, such trials will only include a limited number of patients and limited duration of exposure to our programs. As a result, we cannot be assured that adverse effects of our programs will not be uncovered when a significantly larger number of patients are exposed to the program after approval. Further, any clinical trials may not be sufficient to determine the effect and safety consequences of using our programs over a multi-year period.

If any of the foregoing events occur or if one or more of the research programs with respect to which we have exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Spyre Option Agreement prove to be unsafe, our entire pipeline could be affected, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

***We may expend our limited resources to pursue a particular program and fail to capitalize on programs that may be more profitable or for which there is a greater likelihood of success.***

Because we have limited financial and managerial resources, we focus our research and development efforts on certain selected programs. For example, we are initially focused on our most advanced programs, SPY001 and SPY002. As a result, we may forgo or delay pursuit of opportunities with other programs that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for specific indications may not yield any commercially viable programs. If we do not accurately evaluate the commercial potential or target market for a particular program, we may relinquish valuable rights to that program through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such program.

***Any approved products resulting from our current programs or any future program may not achieve adequate market acceptance among clinicians, patients, healthcare third-party payors and others in the medical community necessary for commercial success and we may not generate any future revenue from the sale or licensing of such products.***

Even if regulatory approval is obtained for a product candidate resulting from one of our current or future programs, they may not gain market acceptance among physicians, patients, healthcare payors or the medical community. We may not generate or sustain revenue from sales of the product due to factors such as whether the product can be sold at a competitive cost and whether it will otherwise be accepted in the market. There are several approved products and product candidates in later stages of development for the treatment of IBD. However, our programs incorporate advanced antibody engineering to optimize the half-life and formulation of antibodies; to date, no such antibody has been approved by the FDA for the treatment of IBD. Market participants with significant influence over acceptance of new treatments, such as clinicians and third-party payors, may not adopt a biologic that incorporates half-life extension for our targeted indications, and we may not be able to convince the medical community and third-party payors to accept and use, or to provide favorable reimbursement for, any programs developed by us or our existing or future collaborators. An extended half-life may make it more difficult for patients to change treatments and there is a perception that half-life extension could exacerbate side effects, each of which may adversely affect our ability to gain market acceptance. Market acceptance of our programs will depend on many factors, including factors that are not within our control.

Sales of medical products also depend on the willingness of clinicians to prescribe the treatment. We cannot predict whether clinicians, clinicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our product is safe, therapeutically effective, cost effective or less burdensome as compared with competing treatments. If any current or future program is approved but does not achieve an adequate level of acceptance by such parties, we may not generate or derive sufficient revenue from that program and may not become or remain profitable.

***Certain of our programs may compete with our other programs, which could negatively impact our business and reduce our future revenue.***

We are developing product candidates for the same indication: IBD, and may in the future develop our programs for other I&I indications. Each such program targets a different mechanism of action. However, developing multiple programs for a single indication may negatively impact our business if the programs compete with each other. For example, if multiple programs are conducting clinical trials at the same time, they could compete for the enrollment of patients. In addition, if multiple programs are approved for the same indication, they may compete for market share, which could limit our future revenue.

***We plan to conduct clinical trials for programs at sites outside the United States, and the FDA may not accept data from trials conducted in such locations.***

We currently intend to conduct our Phase 1 clinical trial for SPY001 and for SPY002 in Australia and we may choose to conduct one or more of our future clinical trials outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with ethical principles. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U.S. laws and regulations. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and would delay or permanently halt our development of the applicable product candidates. Even if the FDA accepted such data, it could require us to modify our planned clinical trials to receive clearance to initiate such trials in the United States or to continue such trials once initiated.

Further, conducting international clinical trials presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs that could restrict or limit our ability to conduct our clinical trials, the administrative burdens of conducting clinical trials under multiple sets of foreign regulations, foreign exchange fluctuations, diminished protection of intellectual property in some countries, as well as political and economic risks relevant to foreign countries.

**Risks Related to Government Regulation**

***The regulatory approval processes of the FDA and other comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our programs, we will not be able to commercialize, or will be delayed in commercializing, our programs, and our ability to generate revenue will be materially impaired.***

The process of obtaining regulatory approvals, both in the United States and abroad, is unpredictable, expensive and typically takes many years following commencement of clinical trials, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the programs involved. We cannot commercialize programs in the United States without first obtaining regulatory approval from the FDA. Similarly, we cannot commercialize programs outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of our programs, including our most advanced programs, SPY001 and SPY002, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our programs are both safe and effective for each targeted indication. Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Further, our programs may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval. The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other data. Our programs could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including: the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials; we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a program is safe and effective for its proposed indication; the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval; serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our programs; we may be unable to demonstrate that a program's clinical and other benefits outweigh its safety risks; the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials; the data collected from clinical trials of our programs may not be acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere, and we may be required to conduct additional clinical trials; the FDA or the applicable foreign regulatory authority may disagree regarding the formulation, labeling and/or the specifications of our programs; the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our programs, which would significantly harm our business, results of operations and prospects.

If we were to obtain approval, regulatory authorities may approve any of our programs for fewer or more limited indications than we request, including failing to approve the most commercially promising indications, may grant

approval contingent on the performance of costly post-marketing clinical trials, or may approve a program with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that program. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our programs, we will not be able to commercialize, or will be delayed in commercializing, our programs and our ability to generate revenue will be materially impaired.

***We may not be able to meet requirements for the chemistry, manufacturing and control of our programs.***

In order to receive approval of our products by the FDA and comparable foreign regulatory authorities, we must show that we and our contract manufacturing partners are able to characterize, control and manufacture our drug products safely and in accordance with regulatory requirements. This includes synthesizing the active ingredient, developing an acceptable formulation, performing tests to adequately characterize the formulated product, documenting a repeatable manufacturing process, and demonstrating that our drug products meet stability requirements. Meeting these chemistry, manufacturing and control requirements is a complex task that requires specialized expertise. If we are not able to meet the chemistry, manufacturing and control requirements, we may not be successful in getting our products approved.

***Our programs for which we intend to seek approval as biologics may face competition sooner than anticipated.***

The Patient Protection and Affordable Care Act, as amended by the Healthcare and Education Reconciliation Act ("ACA"), includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a highly similar or "biosimilar" product may not be submitted to the FDA until four years following the date that the reference product was first approved by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first approved. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product.

We believe that any of our programs approved as biologics under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our programs to be reference products for competing products, potentially creating the opportunity for competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

***Even if we receive regulatory approval of our programs, we will be subject to extensive ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our programs.***

Any regulatory approvals that we may receive for our programs will require the submission of reports to regulatory authorities and surveillance to monitor the safety and efficacy of the program, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a risk evaluation and mitigation strategy ("REMS") in order to approve our programs, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In

addition, if the FDA or comparable foreign regulatory authorities approve our programs, our programs and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export will be subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable foreign regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as on-going compliance with current cGMPs and GCPs for any clinical trials that we conduct following approval. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMPs.

If we or a regulatory authority discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory authority may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials, restrictions on the manufacturing process, warning or untitled letters, civil and criminal penalties, injunctions, product seizures, detentions or import bans, voluntary or mandatory publicity requirements and imposition of restrictions on operations, including costly new manufacturing requirements. The occurrence of any event or penalty described above may inhibit our ability to commercialize our programs and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

***We may face difficulties from healthcare legislative reform measures.***

Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our programs. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

***Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.***

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our programs, if approved. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. If our operations are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly and time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

***Even if we are able to commercialize any programs, due to unfavorable pricing regulations and/or third-party coverage and reimbursement policies, we may not be able to offer such programs at competitive prices which would seriously harm our business.***

We intend to seek approval to market our programs in both the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our programs, we will be subject to rules and regulations in those jurisdictions. Our ability to successfully commercialize any programs that we may develop will depend in part on the extent to which reimbursement for these programs and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. These entities may create preferential access policies for a competitor's product, including a branded or generic/biosimilar product, over our products in an attempt to reduce their costs, which may reduce our commercial opportunity. Additionally, if any of our programs are approved and we are found to have improperly promoted off-label uses of those programs, we may become subject to significant liability, which would materially adversely affect our business and financial condition.

***We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. We can face criminal liability and other serious consequences for violations, which can harm our business.***

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to or from recipients in the public or private sector. We may engage third parties to sell our products outside the United States, to conduct clinical trials, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

***Governments outside the United States tend to impose strict price controls, which may adversely affect our revenue, if any.***

In some countries, particularly member states of the EU, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a therapeutic. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. To obtain coverage and reimbursement or pricing approvals in some countries, we or current or future collaborators may be required to conduct a clinical trial or other studies that

compare the cost-effectiveness of our programs to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any program approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be materially and adversely affected. Brexit could lead to legal uncertainty and potentially divergent national laws and regulations, including those related to the pricing of prescription pharmaceuticals, as the United Kingdom ("UK") determines which EU laws to replicate or replace. If the UK were to significantly alter its regulations affecting the pricing of prescription pharmaceuticals, we could face significant new costs.

***If we decide to pursue a Fast Track Designation by the FDA, it may not lead to a faster development or regulatory review or approval process.***

We may seek Fast Track Designation for one or more of our programs. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the product sponsor may apply for FDA Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular program is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program.

**Risks Related to Our Intellectual Property**

***Our ability to protect our patents and other proprietary rights is uncertain, exposing us to the possible loss of competitive advantage.***

We rely upon a combination of patents, trademarks, trade secret protection, confidentiality agreements and the Spyre Option Agreement to protect the intellectual property related to our programs and technologies and to prevent third parties from competing with us. Our success depends in large part on our ability to obtain and maintain patent protection for our platform technologies, programs and their uses, as well as our ability to operate without infringing on or violating the proprietary rights of others. However, we may not be able to protect our intellectual property rights throughout the world and the legal systems in certain countries may not favor enforcement or protection of patents, trade secrets and other intellectual property. Filing, prosecuting and defending patents on programs worldwide would be prohibitively expensive and our intellectual property rights in some foreign jurisdictions can be less extensive than those in the United States. As such, we may not have patents in all countries or all major markets and may not be able to obtain patents in all jurisdictions even if we apply for them. Our competitors may operate in countries where we do not have patent protection and can freely use our technologies and discoveries in such countries to the extent such technologies and discoveries are publicly known or disclosed in countries where we do have patent protection or pending patent applications.

Our intellectual property portfolio is at an early stage and we do not currently own or in-license any issued patents. Our pending and future patent applications may not result in patents being issued. Any issued patents may not afford sufficient protection of our programs or their intended uses against competitors, nor can there be any assurance that the patents issued will not be infringed, designed around, invalidated by third parties, or effectively prevent others from commercializing competitive technologies, products or programs. Even if these patents are granted, they may be difficult to enforce. Further, any issued patents that we may license or own covering our programs could be narrowed or found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad, including the United States Patent and Trademark Office ("USPTO"). Further, if we encounter delays in our clinical trials or delays in obtaining regulatory approval, the period of time during which we could market our programs under patent protection would be reduced. Thus, the patents that we may own and license may not afford us any meaningful competitive advantage.

In addition to seeking patents for some of our technology and programs, we may also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third-party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market. In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with our collaborators, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. We may need to share our proprietary information, including trade secrets, with future business partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors and those affiliated with or controlled by state actors. In addition, while the company undertakes efforts to protect its trade secrets and other confidential information from disclosure, others may independently discover trade secrets and proprietary information, and in such cases, we may not be able to assert any trade secret rights against such party. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

Lastly, if our trademarks and trade names are not registered or adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

***We may not be successful in obtaining or maintaining necessary rights to our programs through acquisitions and in-licenses.***

Because our development programs currently do and may in the future require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license, or use these third-party proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our programs. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

While we normally seek to obtain the right to control prosecution, maintenance and enforcement of the patents relating to our programs, there may be times when the filing and prosecution activities for patents and patent applications relating to our programs are controlled by our future licensors or collaboration partners. If any of our future licensors or collaboration partners fail to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patents covering our programs, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our ability to develop and commercialize those programs may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensees, our future licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

Our future licensors may rely on third-party consultants or collaborators or on funds from third parties such that our future licensors are not the sole and exclusive owners of the patents we in-license. If other third parties have ownership rights to our future in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

It is possible that we may be unable to obtain licenses at a reasonable cost or on reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to redesign our technology, programs, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected programs, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, manufacturing methods, programs, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

Disputes may arise between us and our future licensors regarding intellectual property subject to a license agreement, including: the scope of rights granted under the license agreement and other interpretation-related issues; whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; our right to sublicense patents and other rights to third parties; our right to transfer or assign the license; the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our future licensors and us and our partners; and the priority of invention of patented technology.

***We may be subject to patent infringement claims or may need to file claims to protect our intellectual property, which could result in substantial costs and liability and prevent us from commercializing our potential products.***

Because the intellectual property landscape in the biotechnology industry is rapidly evolving and interdisciplinary, it is difficult to conclusively assess our freedom to operate and guarantee that we can operate without infringing on or violating third party rights. If certain of our programs are ultimately granted regulatory approval, patent rights held by third parties, if found to be valid and enforceable, could be alleged to render one or more of our programs infringing. If a third party successfully brings a claim against us, we may be required to pay substantial damages, be forced to abandon any affected program and/or seek a license from the patent holder. In addition, any intellectual property claims (e.g. patent infringement or trade secret theft) brought against us, whether or not successful, may cause us to incur significant legal expenses and divert the attention of our management and key personnel from other business concerns. We cannot be certain that patents owned or licensed by us will not be challenged by others in the course of litigation. Some of our competitors may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise funds and on the market price of our Common Stock.

Competitors may infringe or otherwise violate our patents, trademarks, copyrights or other intellectual property. To counter infringement or other violations, we may be required to file claims, which can be expensive and time-consuming. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights. In addition, in a patent infringement proceeding, a court or administrative body may decide that one or more of the patents we assert is invalid or unenforceable, in whole or in part, construe the patent’s claims narrowly or refuse to prevent the other party from using the technology at issue on the grounds that our patents do not cover the technology. Similarly, if we assert

trademark infringement claims, a court or administrative body may determine that the marks we have asserted are invalid or unenforceable or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In such a case, we could ultimately be forced to cease use of such marks. In any intellectual property litigation, even if we are successful, any award of monetary damages or other remedy we receive may not be commercially valuable.

Further, we may be required to protect our patents through procedures created to attack the validity of a patent at the USPTO. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action.

In addition, if our programs are found to infringe the intellectual property rights of third parties, these third parties may assert infringement claims against our future licensees and other parties with whom we have business relationships and we may be required to indemnify those parties for any damages they suffer as a result of these claims, which may require us to initiate or defend protracted and costly litigation on behalf of licensees and other parties regardless of the merits of such claims. If any of these claims succeed, we may be forced to pay damages on behalf of those parties or may be required to obtain licenses for the products they use.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings.

***We may be subject to claims that we have wrongfully hired an employee from a competitor or that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.***

As is common in the biotechnology industry, in addition to our employees, we engage the services of consultants to assist us in the development of our programs. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology or pharmaceutical companies including our competitors or potential competitors. We could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other confidential information of former employers or competitors. Although we try to ensure that our employees and consultants do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may become subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor.

While we may litigate to defend ourselves against these claims, even if we are successful, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our programs, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

***Changes to patent laws in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.***

Changes in either the patent laws or interpretation of patent laws in the United States, including patent reform legislation such as the Leahy-Smith America Invents Act (the "Leahy-Smith Act") could increase the uncertainties and costs surrounding the prosecution of our owned and in-licensed patent applications and the maintenance, enforcement or defense of our owned and in-licensed issued patents. The Leahy-Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO-administered post-grant proceedings, including post-grant review, inter partes review and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first-to-file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. U.S. Supreme Court and U.S. Court of Appeals for the Federal Circuit rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations, including in the antibody arts. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future.

Geopolitical actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of patent applications and the maintenance, enforcement or defense of issued patents. For example, the United States and foreign government actions related to Russia's invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees that have citizenship or nationality in, are registered in, or have predominately primary place of business or profit-making activities in the United States and other countries that Russia has deemed unfriendly without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

In addition, a European Unified Patent Court ("UPC") entered into force on June 1, 2023. The UPC is a common patent court that hears patent infringement and revocation proceedings effective for member states of the EU. This could enable third parties to seek revocation of a European patent in a single proceeding at the UPC rather than through multiple proceedings in each of the jurisdictions in which the European patent is validated. Although we do not currently own any European patents or applications, if we obtain such patents and applications in the future, any such revocation and loss of patent protection could have a material adverse impact

on our business and our ability to commercialize or license our technology and products. Moreover, the controlling laws and regulations of the UPC will develop over time, and may adversely affect our ability to enforce or defend the validity of any European patents we may obtain. We may decide to opt out from the UPC any future European patent applications that we may file and any patents we may obtain. If certain formalities and requirements are not met, however, such European patents and patent applications could be challenged for non-compliance and brought under the jurisdiction of the UPC. We cannot be certain that future European patents and patent applications will avoid falling under the jurisdiction of the UPC, if we decide to opt out of the UPC.

***Obtaining and maintaining patent protection depends on compliance with various procedural, document submissions, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.***

Periodic maintenance fees, renewal fees, annuities fees and various other governmental fees on patents and/or patent applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent and/or patent application. The USPTO and various foreign governmental patent agencies also require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our programs, our competitive position would be adversely affected.

***We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might adversely affect our ability to develop and market our products.***

We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our programs in any jurisdiction. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect. For example, we may incorrectly determine that our products are not covered by a third-party patent or may incorrectly predict whether a third-party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our issued patents or our pending applications, or that we were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our patent applications or patents, which could require us to obtain rights to issued patents covering such technologies.

***We may become subject to claims challenging the inventorship or ownership of our patents and other intellectual property.***

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our programs or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Our future licensors may have relied on third-party consultants or collaborators or on funds from third parties, such as the U.S. government, such that our licensors are not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights or other rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

***Patent terms may be inadequate to protect our competitive position on our programs for an adequate amount of time.***

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest United States non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our programs are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of new programs, patents protecting such programs might expire before or shortly after such programs are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

***Our technology licensed from various third parties may be subject to retained rights.***

Our future licensors may retain certain rights under the relevant agreements with us, including the right to use the underlying technology for noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether our licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse.

**Risks Related to Our Reliance on Third Parties**

***We rely on collaborations and licensing arrangements with third parties, including our arrangement with Paragon Therapeutics, Inc. If we are unable to maintain these collaborations or licensing arrangements, or if these collaborations or licensing arrangements are not successful, our business could be negatively impacted.***

We currently rely on our collaborations and licensing arrangements with third parties, including Paragon Therapeutics, Inc., for a substantial portion of our discovery capabilities and in-licenses.

Collaborations or licensing arrangements that we enter into may not be successful, and any success will depend heavily on the efforts and activities of such collaborators or licensors. If any of our collaborators or licensors experiences delays in performance of, or fails to perform its obligations under their agreement with us, disagrees with our interpretation of the terms of such agreement or terminates their agreement with us, the research programs with respect to which we have exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Spyre Option Agreement and development timeline could be adversely affected. If we fail to comply with any of the obligations under our collaborations or license agreements, including payment terms and diligence terms, our collaborators or licensors may have the right to terminate such agreements, in which event we may lose intellectual property rights and may not be able to develop, manufacture, market or sell the products covered by our agreements or may face other penalties under our agreements. Our collaborators and licensors may also fail to properly maintain or defend the intellectual property we have licensed from them, if required by our agreement with them, or even infringe upon, our intellectual property rights, leading to the potential invalidation of our intellectual property or subjecting us to litigation or arbitration, any of which would be time-consuming and expensive and could harm our ability to commercialize our programs. In addition, collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our programs and products if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.

As part of our strategy, we plan to evaluate additional opportunities to enhance our capabilities and expand our development pipeline or provide development or commercialization capabilities that complement our own. We may not realize the benefits of such collaborations, alliances or licensing arrangements. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business.

We may face significant competition in attracting appropriate collaborators, and more established companies may also be pursuing strategies to license or acquire third-party intellectual property rights that we consider attractive. These companies may have a competitive advantage over us due to their size, financial resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Collaborations are complex and time-consuming to negotiate, document and execute. In addition, consolidation among large pharmaceutical and biotechnology companies has reduced the number of potential future collaborators. We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our programs or bring them to market.

***We currently rely, and plan to rely in the future, on third parties to conduct and support our preclinical studies and clinical trials. If these third parties do not properly and successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our programs.***

We have utilized and plan to continue to utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, contract testing labs and strategic partners, to conduct and support our preclinical studies and clinical trials under agreements with us. We will rely heavily on these third parties over the course of our preclinical studies and clinical trials, and we control only certain aspects of their activities. As a result, we will have less direct control over the conduct, timing and completion of these preclinical studies and clinical trials and the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and

our third-party contractors and CROs are required to comply with GCP regulations, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our programs in clinical development. If we or any of these third parties fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with products produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting our clinical trials will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot control whether they devote sufficient time and resources to our programs. These third parties may be involved in mergers, acquisitions or similar transactions and may have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could negatively affect their performance on our behalf and the timing thereof and could lead to products that compete directly or indirectly with our current or future programs. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our programs.

***We currently rely and expect to rely in the future on the use of manufacturing suites in third-party facilities or on third parties to manufacture our programs, and we may rely on third parties to produce and process our products, if approved. Our business could be adversely affected if we are unable to use third-party manufacturing suites or if the third-party manufacturers encounter difficulties in production.***

We do not currently own any facility that may be used as our clinical-scale manufacturing and processing facility and must currently rely on CMOs to manufacture our programs. We have not yet caused our programs to be manufactured on a commercial scale and may not be able to do so for any of our programs, if approved. We currently have a sole source relationship for our supply of SPY001. If there should be any disruption in such supply arrangement, including any adverse events affecting our sole supplier, it could have a negative effect on the clinical development of our programs and other operations while we work to identify and qualify an alternate supply source. We may not control the manufacturing process of, and may be completely dependent on, our contract manufacturing partners for compliance with cGMP requirements and any other regulatory requirements of the FDA or comparable foreign regulatory authorities for the manufacture of our programs. Beyond periodic audits, we have no control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our programs or if it withdraws any approval in the future, we may need to find alternative manufacturing facilities, which would require the incurrence of significant additional costs and materially adversely affect our ability to develop, obtain regulatory approval for or market our programs, if approved. Similarly, our failure, or the failure of our CMOs, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of programs or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our programs or drugs and harm our business and results of operations.

Moreover, our CMOs may experience manufacturing difficulties due to resource constraints, supply chain issues, or as a result of labor disputes or unstable political environments. If any CMOs on which we will rely fail to manufacture quantities of our programs at quality levels necessary to meet regulatory requirements and at a scale

sufficient to meet anticipated demand at a cost that allows us to achieve profitability, our business, financial condition and prospects could be materially and adversely affected. In addition, our CMOs are responsible for transporting temperature controlled materials that can be inadvertently degraded during transport due to several factors, rendering certain batches unsuitable for trial use for failure to meet, among others, our integrity and purity specifications. We and any of our CMOs may also face product seizure or detention or refusal to permit the import or export of products. Our business could be materially adversely affected by business disruptions to our third-party providers that could materially adversely affect our anticipated timelines, potential future revenue and financial condition and increase our costs and expenses. Each of these risks could delay or prevent the completion of our preclinical studies and clinical trials or the approval of any of our programs by the FDA, result in higher costs or adversely impact commercialization of our programs.

**Risks Related to Employee Matters, Managing Growth and Other Risks Related to Our Business**

***In order to successfully implement our plans and strategies, we will need to grow the size of our organization and we may experience difficulties in managing this growth.***

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of preclinical and clinical drug development, technical operations, clinical operations, regulatory affairs and, potentially, sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial personnel and systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team working together in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel.

***We are highly dependent on our key personnel and anticipate hiring new key personnel. If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.***

We are a preclinical stage biotechnology company with a limited operating history, and, as of June 30, 2023, we had 14 employees. We have been and will continue to be highly dependent on the research and development, clinical and business development expertise of our executive officers, as well as the other principal members of our management, scientific and clinical team. Any of our management team members may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees.

Attracting and retaining qualified personnel will also be critical to our success, including with respect to any strategic transaction that we may pursue. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, facilitate regulatory approval of and commercialize product candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

In addition, we rely on consultants and advisors, including scientific and clinical advisors such as our scientific advisory board, to assist us in formulating our discovery and nonclinical and clinical development and commercialization strategy. Our consultants and advisors, including members of our scientific advisory board, may be employed by employers other than us and may have commitments under consulting or advisory contracts

with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

***Our future growth may depend, in part, on our ability to operate in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.***

Our future growth may depend, in part, on our ability to develop and commercialize our programs in foreign markets for which we may rely on collaboration with third parties. We are not permitted to market or promote any of our programs before we receive regulatory approval from the applicable foreign regulatory authority, and may never receive such regulatory approval for any of our programs. To obtain separate regulatory approval in many other countries, we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our programs, and we cannot predict success in these jurisdictions. If we fail to comply with the regulatory requirements in international markets and receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our programs will be harmed and our business will be adversely affected. Moreover, even if we obtain approval of our programs and ultimately commercialize our programs in foreign markets, we would be subject to the risks and uncertainties, including the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements and reduced protection of intellectual property rights in some foreign countries.

***Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, CMOs, suppliers and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.***

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, CMOs, suppliers and vendors acting for or on our behalf may engage in misconduct or other improper activities. We will adopt a code of conduct, which will become effective as of the date of the effectiveness of the registration statement of which this prospectus forms a part, but it is not always possible to identify and deter misconduct by these parties and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations.

***Our internal computer systems, or those of any of our CROs, manufacturers, other contractors or consultants, third party service providers, or potential future collaborators, may fail or suffer security or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations.***

Despite the implementation of security measures in an effort to protect systems that store our information, given their size and complexity and the increasing amounts of information maintained on our internal information technology systems and those of our third-party CROs, other contractors (including sites performing our clinical trials), third party service providers and supply chain companies, and consultants, these systems are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners and/or other third parties, or from cyber-attacks by malicious third parties, which may compromise our system infrastructure or lead to the loss, destruction, alteration or dissemination of, or damage to, our data. To the extent that any disruption or security breach were to result in loss, destruction, unavailability, alteration or dissemination of, or damage to, our data or applications, or for it to be believed or reported that any of these occurred, we could incur liability and reputational damage and the development and commercialization of our programs could be delayed. Further, our insurance policies may not be adequate to compensate us for the potential losses arising from any

such disruption in, or failure or security breach of, our systems or third-party systems where information important to our business operations or commercial development is stored.

Our fully-remote workforce may create additional risks for our information technology systems and data because our employees work remotely and utilize network connections, computers, and devices working at home, while in transit and in public locations. Additionally, business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies.

While we have implemented security measures designed to protect against security incidents, there can be no assurance that these measures will be effective. We may be unable in the future to detect vulnerabilities in our information technology systems because such threats and techniques change frequently, are often sophisticated in nature, and may not be detected until after a security incident has occurred. Further, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities. Applicable data privacy and security obligations may require us to notify relevant stakeholders of security incidents. Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences.

We rely on third-party service providers and technologies to operate critical business systems to process sensitive information in a variety of contexts. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If our third-party service providers experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third-party partners' supply chains have not been compromised.

If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences, such as government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and/or oversight; restrictions on processing sensitive information (including personal data); litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations (including availability of data); financial loss; and other similar harms. Security incidents and attendant consequences may cause stakeholders (including investors and potential customers) to stop supporting our platform, deter new customers from products, and negatively impact our ability to grow and operate our business.

Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

***Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.***

Under Section 382 of the Internal Revenue Code of 1986, as amended (the "Code"), if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. It is possible that we may have triggered an "ownership change" limitation. We may also experience

ownership changes in the future as a result of subsequent shifts in our stock ownership (some of which are outside of our control). As a result, if we earn net taxable income, our ability to use our pre-change NOLs and other pre-change tax attributes to offset U.S. federal taxable income or taxes may be subject to limitations, which could potentially result in increased future tax liability to us. Our NOLs and other tax attributes arising before our conversion from a Delaware limited liability company to a Delaware corporation in 2015 also may be limited by the Separate Return Limitation Year rule, which could increase our U.S. federal tax liability. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

***We are subject to stringent and changing laws, regulations and standards, and contractual obligations relating to privacy, data protection and data security. The actual or perceived failure to comply with such obligations could lead to government enforcement actions (which could include civil or criminal penalties), fines and sanctions, private litigation and/or adverse publicity and could negatively affect our operating results and business.***

We, and third parties who we work with are or may become subject to numerous domestic and foreign laws, regulations, and standards relating to privacy, data protection and data security, the scope of which is changing, subject to differing applications and interpretations, and may be inconsistent among countries, or conflict with other rules. We are or may become subject to the terms of contractual obligations related to privacy, data protection and data security. Our obligations may also change or expand as our business grows. The actual or perceived failure by us or third parties related to us to comply with such laws, regulations and obligations could increase our compliance and operational costs, expose us to regulatory scrutiny, actions, fines and penalties, result in reputational harm, lead to a loss of customers, result in litigation and liability, and otherwise cause a material adverse effect on our business, financial condition, and results of operations.

***If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.***

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations may involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

***We may be subject to adverse legislative or regulatory tax changes that could negatively impact our financial condition.***

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our stockholders or us. We assess the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where we have operations to determine the potential effect on our business and any assumptions we have made about our future taxable income. We cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on our business if they were to be enacted. For example, the United States recently enacted the Inflation Reduction Act of 2022, which implements, among other changes, a 1% excise tax on certain stock buybacks. In addition, beginning in 2022, the Tax Cuts and Jobs Act eliminated the previously available option to deduct research and development expenditures and requires taxpayers to amortize them generally over five years for research activities conducted in the United States and over 15 years for research activities conducted outside the United States. The U.S. Congress is considering legislation that would restore the current deductibility of research and development

expenditures; however, we have no assurance that the provision will be repealed or otherwise modified. Such changes, among others, may adversely affect our effective tax rate, results of operation and general business condition.

***We may acquire businesses or products, or form strategic alliances, in the future, and may not realize the benefits of such acquisitions.***

We may acquire additional businesses or products, form strategic alliances, or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new programs or products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. There is no assurance that, following any such acquisition, we will achieve the synergies expected in order to justify the transaction, which could result in a material adverse effect on our business and prospects.

***We maintain our cash at financial institutions, often in balances that exceed federally-insured limits. The failure of financial institutions could adversely affect our ability to pay our operational expenses or make other payments***.

Our cash held in non-interest-bearing and interest-bearing accounts exceeds the Federal Deposit Insurance Corporation ("FDIC") insurance limits. If such banking institutions were to fail, we could lose all or a portion of those amounts held in excess of such insurance limitations. For example, the FDIC took control of Silicon Valley Bank on March 10, 2023. The Federal Reserve subsequently announced that account holders would be made whole. However, the FDIC may not make all account holders whole in the event of future bank failures. In addition, even if account holders are ultimately made whole with respect to a future bank failure, account holders' access to their accounts and assets held in their accounts may be substantially delayed. Any material loss that we may experience in the future or inability for a material time period to access our cash and cash equivalents could have an adverse effect on our ability to pay our operational expenses or make other payments, which could adversely affect our business.

**Risks Related to Our Common Stock**

***Pursuant to the terms of the Spyre Acquisition Agreement, we are required to recommend that our stockholders approve the conversion of all outstanding shares of our Series A Preferred Stock into shares of our Common Stock. We cannot guarantee that our stockholders will approve this matter, and if they fail to do so, we may be required to settle such shares in cash and our operations may be materially harmed.***

Under the terms of the Securities Purchase Agreement, we agreed to use reasonable best efforts to call and hold a meeting of our stockholders to obtain the requisite approval for the conversion of all outstanding shares of Series A Preferred Stock issued in the Transactions into shares of our Common Stock, as required by the Nasdaq listing rules, within 75 days from the closing of the Financing and, if such approval is not obtained at that meeting, to seek to obtain such approval at an annual or special stockholders meeting to be held at least every 90 days thereafter until such approval is obtained, which would be time consuming and costly. Additionally, if our stockholders do not timely approve the conversion of our Series A Preferred Stock, then the holders of our Series A Preferred Stock may be entitled to require us to settle their shares of Series A Preferred Stock for cash at a price per share equal to the fair value of the Series A Preferred Stock at such time, as described in our Certificate of Designation relating to the Series A Preferred Stock. If we are forced to settle a significant amount of the Series A Preferred Stock, it could materially affect our results of operations, including raising a substantial doubt about the entity's ability to continue as a going concern within one year from the date of this proxy statement.

***Our failure to meet the continued listing requirements of The Nasdaq Capital Market could result in a delisting of our Common Stock.***

Our Common Stock is currently listed on The Nasdaq Capital Market. To maintain the listing of our Common Stock on The Nasdaq Capital Market, we are required to meet certain listing requirements, including, among others, a minimum bid price of $1.00 per share (the "Minimum Bid Price Requirement").

If we fail to satisfy the continued listing requirements of The Nasdaq Capital Market, such as the corporate governance requirements or the Minimum Bid Price Requirement, The Nasdaq Capital Market may take steps to delist our Common Stock, which could have a materially adverse effect on our ability to raise additional funds as well as the price and liquidity of our Common Stock. Such a delisting would likely have a negative effect on the price of our Common Stock and would impair our stockholders' ability to sell or purchase our Common Stock when they wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our Common Stock to become listed again, stabilize the market price or improve the liquidity of our Common Stock, prevent our Common Stock from dropping below the Minimum Bid Price Requirement, or prevent future non-compliance with The Nasdaq Capital Market's listing requirements.

We are actively monitoring our stock price and will consider any and all options available to regain compliance. The alternatives to trading on the Nasdaq Stock Market or another national securities exchange are generally considered to be less efficient and less broad-based than the national securities exchanges and the liquidity of our Common Stock will likely be reduced if it fails to regain compliance with the Minimum Bid Price Requirement.

On July 13, 2023, we received approval (the "Approval") from Nasdaq to transfer the listing of our Common Stock from The Nasdaq Global Market to The Nasdaq Capital Market (the "Transfer"). The Nasdaq Capital Market operates in substantially the same manner as The Nasdaq Global Market, but with less stringent listing requirements, although listed companies must meet certain financial requirements and comply with Nasdaq's corporate governance requirements. In connection with the Approval, we have been granted an additional 180-calendar day grace period, or until January 8, 2024, to regain compliance with the Minimum Bid Price Requirement. To regain compliance with the Minimum Bid Price Requirement and qualify for continued listing on The Nasdaq Capital Market, the minimum bid price per share of our Common Stock must be at least $1.00 for at least ten consecutive business days during the additional 180-calendar day grace period. If we do not regain compliance during this additional grace period, our Common Stock would be subject to delisting by Nasdaq. As part of our Transfer application, we notified Nasdaq that in order to regain compliance with the Minimum Bid Price Requirement during the additional grace period, we intend to implement a reverse stock split at a ratio ranging from 1-for-10 shares up to a ratio of 1-for-25 shares, determined by our board of directors, which was approved by our stockholders on June 6, 2023. If our Common Stock becomes subject to delisting as a result of our failure to regain compliance with the Minimum Bid Price Requirement by January 8, 2024, we may appeal the decision to a Nasdaq Hearings Panel. In the event of an appeal, our Common Stock would remain listed on The Nasdaq Capital Market pending a written decision by the Nasdaq Hearings Panel following a hearing. In the event that the Nasdaq Hearings Panel determines not to continue our listing and our Common Stock is delisted from The Nasdaq Capital Market, our Common Stock may trade on the OTC Bulletin Board or other small trading markets, such as the pink sheets.

There can be no assurance that we will be successful in maintaining the listing of our Common Stock on The Nasdaq Capital Market. This could impair the liquidity and market price of our Common Stock. In addition, the delisting of our Common Stock from a national exchange could have a material adverse effect on our access to capital markets, and any limitation on market liquidity or reduction in the price of our Common Stock as a result of that delisting could adversely affect our ability to raise capital on terms acceptable to us, or at all.

***Anti-takeover provisions in our charter documents and under Delaware law and the terms of some of our contracts could make an acquisition of us more difficult and may prevent attempts by our stockholders to replace or remove our management.***

Provisions in our Certificate of Incorporation and Bylaws may delay or prevent an acquisition or a change in management. These provisions include a prohibition on actions by written consent of our stockholders and the ability of our Board of Directors to issue Preferred Stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the DGCL, which prohibits stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us. Although we believe these provisions collectively will provide for an opportunity to receive higher bids by requiring potential acquirers to negotiate with our Board of Directors, they would apply even if the offer may be considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove then current management by making it more difficult for stockholders to replace members of the Board of Directors, which is responsible for appointing the members of management.

In addition, the Certificate of Designation relating to our Series A Preferred Stock may delay or prevent a change in control of our company. At any time while at least 30% of the originally issued Series A Preferred Stock remains issued and outstanding, we may not consummate a Fundamental Transaction (as defined in the Certificate of Designation) or any merger or consolidation of the Company with or into another entity or any stock sale to, or other business combination in which our stockholders immediately before such transaction do not hold at least a majority of our capital stock immediately after such transaction, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series A Preferred Stock. This provision of the Certificate of Designation may make it more difficult for us to enter into any of the aforementioned transactions.

***Our Certificate of Incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum certain types of actions and proceedings that may be initiated by our stockholders, and our Bylaws designate the federal courts of the United States as the exclusive forum for actions arising under the Securities Act, each of which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or agents.***

Our Certificate of Incorporation provides that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or agents to us or our stockholders, any action asserting a claim arising pursuant to any provision of the DGCL, our Certificate of Incorporation or our Bylaws or any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein and the claim not being one which is vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery or for which the Court of Chancery does not have subject matter jurisdiction. Any person purchasing or otherwise acquiring any interest in any shares of our capital stock shall be deemed to have notice of and to have consented to this provision of our Certificate of Incorporation.

Our Bylaws provide that the federal district courts of the United States of America will, to the fullest extent permitted by law, be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (a "Federal Forum Provision"). Our decision to adopt a Federal Forum Provision followed a decision by the Supreme Court of the State of Delaware holding that such provisions are facially valid under Delaware law. While there can be no assurance that federal or state courts will follow the holding of the Delaware Supreme Court or determine that the Federal Forum Provision should be enforced in a particular case, application of the Federal Forum Provision means that suits brought by our stockholders to enforce any duty or liability created by the Securities Act must be brought in federal court and cannot be brought in state court.

These choice of forum provisions may limit our stockholders' ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, employees or agents, which may discourage such

lawsuits against us and our directors, officers, employees and agents even though an action, if successful, might benefit our stockholders. Stockholders who do bring a claim in the specified courts could face additional litigation costs in pursuing any such claim. The specified courts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders. Alternatively, if a court were to find these provisions of our governance documents inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could have a material adverse effect on our business, financial condition or results of operations.

***We do not anticipate that we will pay any cash dividends in the foreseeable future.***

The current expectation is that we will retain our future earnings, if any, to fund the development and growth of our business. As a result, capital appreciation, if any, of our Common Stock will be your sole source of gain, if any, for the foreseeable future.

***Future sales of shares by existing stockholders could cause our stock price to decline.***

Concurrently and in connection with the execution of the Spyre Acquisition Agreement, certain former Spyre securityholders as of immediately prior to the Asset Acquisition, and certain of our directors and officers as of immediately prior to the Asset Acquisition entered into the lock-up agreements with us, pursuant to which each such stockholder will be subject to a 180-day lockup on the sale or transfer of shares of our Common Stock held by each such stockholder at the closing of the Asset Acquisition, including those shares received by former Spyre securityholders in the Asset Acquisition. Upon expiration of this 180-day lockup period, these shares will become eligible for sale in the public market.

On June 22, 2023, we also entered into the New RRA with the Investors. Pursuant to the New RRA, we are obligated to prepare and file a resale registration statement with the SEC within 45 calendar days following the closing of the Financing (the “Filing Deadline”). We will use our reasonable best efforts to cause this registration statement to be declared effective by the SEC within 30 calendar days of the Filing Deadline (or within 60 calendar days if the SEC reviews the registration statement). Once this registration statement is declared effective, the shares subject to the registration statement will no longer constitute restricted securities and may be sold freely in the public markets, subject to lapse on any related contractual restrictions related thereto of any Investor.

If our stockholders sell, or indicate an intention to sell, substantial amounts of our Common Stock in the public market after legal restrictions on resale lapse, the trading price of our Common Stock could decline. In addition, shares of our Common Stock that are subject to our outstanding options will become eligible for sale in the public market to the extent permitted by the provisions of various vesting agreements and Rules 144 and 701 under the Securities Act.

***Future sales and issuances of equity and debt could result in additional dilution to our stockholders.***

We expect that we will need significant additional capital to fund our current and future operations, including to complete potential clinical trials for our product candidates. To raise capital, we may sell Common Stock, convertible securities, or other equity securities in one or more transactions at prices and in a manner we determine from time to time. As a result, our stockholders may experience additional dilution, which could cause our stock price to fall.

Pursuant to our equity incentive plans, we may grant equity awards and issue additional shares of our Common Stock to our employees, directors and consultants, and the number of shares of our Common Stock reserved for future issuance under certain of these plans will be subject to automatic annual increases in accordance with the

terms of the plans. To the extent that new options are granted and exercised, or we issue additional shares of Common Stock in the future, our stockholders may experience additional dilution, which could cause our stock price to fall.

***Our principal stockholders own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.***

Our directors, officers, 5% stockholders, and their affiliates currently beneficially own a substantial portion of our outstanding voting stock. Therefore, these stockholders have the ability and may continue to have the ability to influence us through this ownership position. These stockholders may be able to determine some or all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our Common Stock that you may believe are in your best interest as one of our stockholders.

**General Risk Factors**

***The market price of our Common Stock has historically been volatile, and the market price of our Common Stock may drop in the future.***

The market price of our Common Stock has been, and may continue to be, subject to significant fluctuations. Market prices for securities of early-stage pharmaceutical, biotechnology, and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of our Common Stock to fluctuate include:

- our ability to obtain regulatory approvals for our product candidates, and delays or failures to obtain such approvals;
- failure of any of our product candidates, if approved, to achieve commercial success;
- failure to maintain our existing third-party license and supply agreements;
- changes in laws or regulations applicable to our product candidates;
- any inability to obtain adequate supply of our product candidates or the inability to do so at acceptable prices;
- adverse regulatory authority decisions;
- introduction of new products, services, or technologies by our competitors;
- failure to meet or exceed financial and development projections we may provide to the public and the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators, and the investment community;
- announcements of significant acquisitions, strategic collaborations, joint ventures, or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;

- additions or departures of key personnel;
- significant lawsuits, including patent or stockholder litigation;
- if securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our business and stock;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions;
- sales of our Common Stock by us or our stockholders in the future;
- trading volume of our Common Stock;
- announcements by commercial partners or competitors of new commercial products, clinical progress or the lack thereof, significant contracts, commercial relationships, or capital commitments;
- the introduction of technological innovations or new therapies that compete with our potential products;
- changes in the structure of health care payment systems; and
- period-to-period fluctuations in our financial results.

Moreover, the capital markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of our Common Stock.

In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management attention and resources, which could significantly harm our profitability and reputation.

***We incur costs and demands upon management as a result of complying with the laws and regulations affecting public companies.***

We incur significant legal, accounting, and other expenses associated with public company reporting requirements. We also incur costs associated with corporate governance requirements, including requirements under the Sarbanes-Oxley Act, as well as rules implemented by the SEC and Nasdaq. These rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. These rules and regulations may also make it difficult and expensive for us to obtain directors' and officers' liability insurance. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our Board of Directors or as our executive officers, which may adversely affect investor confidence and could cause our business or stock price to suffer.

***If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business, or our market, our stock price and trading volume could decline.***

The trading market for our Common Stock is influenced by the research and reports that equity research analysts publish about us and our business. Equity research analysts may elect not to provide research coverage of our Common Stock and such lack of research coverage may adversely affect the market price of our Common Stock.

In the event we do have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our Common Stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of us or fails to publish reports on us regularly, demand for our Common Stock could decrease, which in turn could cause our stock price or trading volume to decline.

***If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our Common Stock may be negatively affected.***

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, and the rules and regulations of Nasdaq. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. We must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our annual report filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. This requires that we incur substantial professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. We may experience difficulty in meeting these reporting requirements in a timely manner for each period.

We may or any subsequent testing by our independent registered public accounting firm may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act, or if we are unable to maintain proper and effective internal controls, it could result in a material misstatement of our financial statements that would not be prevented or detected on a timely basis, which could require a restatement, cause us to be subject to sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities, cause investors to lose confidence in our financial information, or cause our stock price to decline.

As a public company, we incur significant legal, accounting, insurance, and other expenses, and our management and other personnel have and will need to continue to devote a substantial amount of time to compliance initiatives resulting from operating as a public company.

## DESCRIPTION OF BUSINESS

### Company Overview

On June 22, 2023, we completed the Asset Acquisition pursuant to Spyre Acquisition Agreement. Spyre was a pre-clinical stage biotechnology company that was incorporated on April 28, 2023 under the direction of Peter Harwin, a Managing Member of Fairmount, for the purpose of holding rights to certain intellectual property being developed by Paragon. Fairmount is a founder of Paragon.

Through the Asset Acquisition, we received the Option to acquire the intellectual property rights related to four research programs pursuant to the Spyre Option Agreement. On July 12, 2023, we exercised the Option with respect to one of these research programs to exclusively license intellectual property rights related to such research program directed to antibodies that selectively bind to α4b7 integrin and methods of using these antibodies, including methods of treating IBD using SPY001. If this research program is pursued non-provisionally and matures into issued patents, we would expect those patents to expire no earlier than 2044 subject to any disclaimers or extensions. The license agreement pertaining to such research program is currently being finalized. Furthermore, as of the date of this registration statement, the option remains unexercised with respect to the intellectual property rights related to the three remaining research programs under the Spyre Option Agreement. See "*Description of the Transactions – Overview*" for more information regarding Spyre prior to the Asset Acquisition.

On July 27, 2023, we announced that we entered into the Immedica APA to sell the global rights to pegzilarginase. The sale of pegzilarginase to Immedica supersedes and terminates the license agreement between us and Immedica dated March 2021. See "*Description of the Transactions – Acquisition of Spyre*" for more information regarding the Immedica APA.

Following the Asset Acquisition and the entry into the Immedica APA, we have significantly reshaped the business into a preclinical stage biotechnology company focused on developing next generation therapeutics for patients living with inflammatory bowel disease ("IBD"), including ulcerative colitis ("UC") and Crohn's disease ("CD"). Our portfolio of novel and proprietary monoclonal antibody product candidates has the potential to address unmet needs in IBD care by improving efficacy, safety, and/or dosing convenience relative to products currently available or product candidates in development. We have purposely engineered our product candidates to bind potently and selectively to target epitopes with extended half-lives. We plan to use combinations of our proprietary antibodies and patient enrichment strategies via companion diagnostics to enhance efficacy. We intend to deliver our product candidates through convenient, infrequently self-administered, subcutaneous ("SC") injection as a pre-filled pen.

### Our Strategy

Our goal is to develop next-generation therapeutics for the treatment of IBD, relying on three strategic pillars:

- Advancing novel, potentially best-in-class, long-acting antibodies against validated IBD targets;
- Evaluating rational therapeutic combinations of potentially best-in-class antibodies; and
- Developing genetic- or biomarker-based companion diagnostics to match treatment targets to IBD sub-populations.

### Inflammatory Bowel Disease

IBD is a chronic condition characterized by inflammation within the gastrointestinal tract. It encompasses two main disorders: UC and CD. UC primarily affects the colon and the rectum. Inflammation occurs in the innermost lining of the colon leading to ulcers. Symptoms include bloody diarrhea, abdominal pain, bowel urgency, and frequent bowel movements. CD can affect any part of the gastrointestinal tract, from the mouth to

the anus. It is characterized by inflammation that extends through multiple layers of the bowel wall. Symptoms include abdominal pain, diarrhea, weight loss, fatigue, and complications such as strictures or fistulas. Both conditions can significantly impact patients' quality of life in terms of physical health, emotional well-being, and the unpredictability of symptom onset.

IBD affects millions of individuals worldwide, with increasing prevalence and incidence in both developed and developing countries. In the United States, it is estimated that approximately 1.7 million individuals currently have IBD, with approximately 70,000 patients newly diagnosed every year. The prevalence of UC in the United States is approximately 900,000 individuals, and the prevalence of CD in the United States is approximately 800,000 individuals. Based on research from the Crohn's and Colitis Foundation of America, the market for IBD therapeutics is expected to experience steady growth, driven by rising disease prevalence, increasing diagnosis rates, and evolving treatment paradigms.

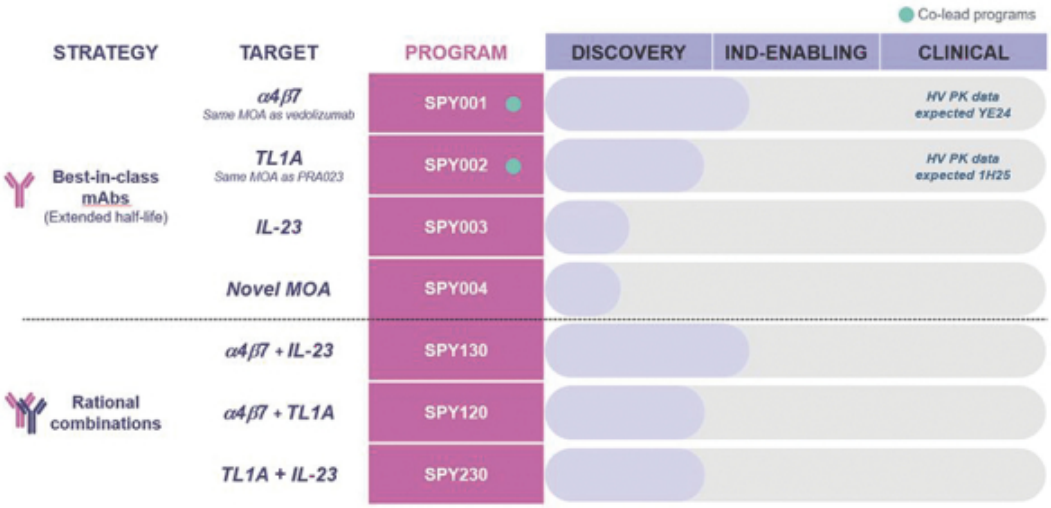
A range of pharmaceutical options exists, including anti-inflammatory drugs, immunosuppressants, and biologics. Treatment plans are often tailored to the individual patient's disease severity, location, and response to therapy. In some cases, surgical interventions such as bowel resection or ostomy formation may be necessary to manage complications or improve quality of life.

Despite available treatments, there remain substantial unmet needs in IBD management, including:

- Inadequate response or loss of response to existing therapies,
- Side effects and safety concerns associated with long-term medication use,
- Limited options for patients with refractory or severe disease, and
- Adherence to frequent and/or inconvenient dosing regimens.

**Our Portfolio**

We are advancing a broad pipeline of potentially best-in-class monoclonal antibodies ("mAbs") in connection with the research programs with respect to which we have exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Option Agreement and plan to develop a companion diagnostic for each program. See "*Risk Factors—Risks Related to the Discovery, Development and Commercialization*." The following table summarizes these programs*.




* We exercised an option to acquire intellectual property license rights related to SPY001 on July 12, 2023. Although we hold the option to acquire intellectual property license rights related to SPY002, SPY003 and

SPY004, such option remains unexercised as the date of this registration statement. See discussion under the heading "Spyre Option Agreement" in our next Quarterly Report on Form 10-Q, which will be incorporated by reference herein, for more information. For a discussion of intellectual property risks associated with the in-licensing of the rights required for our programs, see "*Risk Factors—Risks Related to our Intellectual Property—We may not be successful in obtaining or maintaining necessary rights to our programs through acquisitions and in-licenses*".

*SPY001 – anti-α4b7 mAb*

Our most advanced product candidate, SPY001, is a highly potent, highly selective and fully human monoclonal immunoglobulin G1 antibody designed to bind selectively to the α4b7 integrin. The α4b7 integrin is a protein found on the surface of immune cells known as lymphocytes. This integrin regulates the migration of lymphocytes to the gut where they contribute to the inflammatory process in IBD. By binding to the α4b7 integrin, SPY001 is designed to prevent the interaction of these lymphocytes with MAdCAM-1, a molecule expressed on endothelial cells lining the blood vessels in the gut. This interaction is responsible for guiding lymphocytes from the bloodstream into the gut tissue, where they cause inflammation. By blocking the interaction between α4b7 integrin and MAdCAM-1, SPY001 aims to reduce the recruitment of lymphocytes to the gut, leading to a decrease in inflammation. Since it specifically targets the gut immune system, SPY001 is designed to help minimize systemic immunosuppressive effects unrelated to IBD pathology.

Vedolizumab is an anti-α4b7 integrin mAb marketed by Takeda as Entyvio. It is available in the United States as an intravenously administered product with an every 8-week maintenance dosing regimen. A SC version with an every 2-week dosing regimen is under review by the FDA for use in the maintenance setting and is approved in Europe and Japan. Vedolizumab is one of the leading therapies for moderate-to-severe IBD given its exquisite safety profile as a gut selective mechanism and its high efficacy rates in UC (particularly in the maintenance setting where it has the highest remission rates among approved biologics). In the induction setting, exposure-response data suggests that higher exposures may increase the likelihood of early remission in UC. In 2022, Takeda reported $5.3 billion in sales for Entyvio and updated its peak annual sales guidance to $7.5-9.0 billion. We believe that there is a significant opportunity for a SC regimen with a more infrequent dosing schedule (every eight to twelve weeks) in the maintenance settings, and potential efficacy upside in induction.

Our preclinical development program has demonstrated that SPY001 binds to the same epitope as vedolizumab with similar potency and selectivity. Both SPY001 and vedolizumab potently block MAdCAM-1 adhesion and avoid interactions with α4b1 to prevent adhesion to VCAM-1, which can be associated with the risk of progressive multifocal leukoencephalopathy. Additionally, our preclinical studies have demonstrated that SPY001 binds to memory T-helper cells from human donors with a comparable potency as vedolizumab.
SPY001 is engineered with half-life extension technology. This approach relies on modifying the Fc domain to improve the pharmacokinetic ("PK") profile of the antibody and support infrequent dosing as a convenient SC injection. An evaluation of SPY001's PK in non-human primates suggests an increase in half-life of approximately 2-fold relative to vedolizumab, potentially supporting a SC dosing administration of every eight to twelve weeks in humans.

We aim to achieve the following target product profile for SPY001 in IBD:

- **Less frequent administration**: Lower the frequency of administration by incorporating half-life extension technology and deliver SPY001 through a single SC injection every eight to twelve weeks.
- **High concentration, citrate-free formulation**: Deliver at least 300 mg in a single 2 mL injection suitable for a pre-filled pen without the need for citrate to enhance patient comfort.
- **Potential for increased induction efficacy in UC**: Target greater exposure in the induction setting given exposure-response relationships observed with vedolizumab in UC.

SPY001 is currently progressing through IND-enabling studies and is expected to enter first-in-human ("FIH") studies in the first half of 2024. We believe SPY001 has the potential to meaningfully transform the standard of care in IBD as a potent, low-frequency and self-administered SC injection.

*SPY002 – anti-TL1A mAb*

Our co-lead product candidate, SPY002, is a highly potent, highly selective and fully human mAb designed to bind to tumor necrosis factor-like ligand 1A ("TL1A"). TL1A is a protein that plays a role in regulating the immune system and is found to be elevated in the gut tissue of individuals with IBD. TL1A interacts with its receptor, death receptor 3 ("DR3"), which is expressed in various immune cells, including T cells. This interaction triggers signaling pathways that contribute to inflammation and immune system activation, leading to IBD symptomology. SPY002 has been designed to block the interaction between TL1A and DR3 and thereby inhibit the downstream signaling events and dampen the inflammatory response. By neutralizing TL1A, SPY002 has the potential to modulate the immune response in IBD patients, potentially reducing disease activity and promoting mucosal healing.

TL1A is a clinically validated target that has been studied in multiple Phase 2 trials in UC and CD. Merck's anti-TL1A molecule (PRA023) was studied in a randomized controlled Phase 2 trial where it showed a 25% placebo-adjusted clinical remission rate at week 12 and a placebo-adjusted endoscopic improvement rate of 31% for patients with UC. PRA023 was additionally studied in a Phase 2a open label trial in CD where it showed a 49% clinical remission rate at week 12 compared to a prespecified 16% historical placebo rate and a 26% endoscopic response compared to a prespecified 12% historical placebo rate. Roivant is also advancing an anti-TL1A molecule (RVT-3101) that showed a 21% placebo-adjusted clinical remission rate and a 21% placebo-adjusted endoscopic response in a Phase 2b study in UC patients. In the maintenance setting at week 56, RVT-3101 showed a compelling clinical remission rate of 36% (absolute) at the expected Phase 3 dose. Both PRA023 and RVT-3101 lack any half-life extension technologies and are dosed every four weeks in the maintenance setting.

Like SPY001, SPY002 is engineered with half-life extension technology to support infrequent, self-administration as a convenient SC injection. It is expected that these modifications, along with a high concentration formulation, will enable dosing every eight weeks or less frequently in humans.

We aim to achieve the following target product profile for SPY002 in IBD and other inflammatory diseases:

- **Less frequent administration**: Lower the frequency of administration by incorporating half-life extension technology and deliver SPY002 through a single SC injection every eight weeks or less frequently.
- **High potency**: High affinity to TL1A trimers, enabling lower doses.
- **High concentration, citrate-free formulation**: Deliver at least 300 mg in a single 2 mL injection suitable for a pre-filled pen.

We expect to enter FIH studies in the second half of 2024. We believe SPY002 has the potential to be a best-in-class TL1A antibody compared to others in development as a highly potent, highly selective and infrequently self-administered SC injection.

*SPY003 – anti-IL-23 mAb*

Our third program, SPY003, is a discovery stage program designed to bind to Interleukin 23 ("IL-23"). IL-23 is a cytokine that is produced by immune cells and is involved in immune response regulation. IL-23 promotes the differentiation and activation of Th17 cells. Th17 cells produce other inflammatory cytokines, such as IL-17, which contribute to the inflammation seen in IBD. IL-23 also helps in the recruitment and activation of other immune cells, such as neutrophils, which further contribute to tissue damage in the gut.

Several IL-23 mAbs have been approved or are in late-stage development for IBD including Skyrizi (AbbVie), Tremfya (Johnson & Johnson), and mirikizumab (Lilly).

We aim to achieve the following target product profile for SPY003 in IBD:

- **Less frequent administration**: Lower the frequency of administration by incorporating half-life extension technology and deliver SPY003 through a single SC injection every eight weeks or less frequently.
- **High concentration, citrate-free formulation**: Deliver at least 300 mg in a single 2 mL injection suitable for a pre-filled pen.

*SPY004 – novel MOA mAb*

SPY004 is an undisclosed novel mechanism of action ("MOA") and incorporates half-life extension modifications.

*Our combination programs – SPY120, SPY130, and SPY230*

We aim to advance rational combinations of our therapeutic antibodies into clinical studies. SPY120 combines SPY001 (α4b7) and SPY002 (TL1A), SPY130 combines SPY001 (α4b7) and SPY003 (IL-23), and SPY230 combines SPY002 (TL1A) and SPY003 (IL23). We believe these combinations target orthogonal biology and could lead to greater remission rates in IBD.

Clinical proof-of-concept for the potential of combination therapy in IBD was demonstrated by Johnson & Johnson's VEGA study which evaluated their anti-TNFα antibody, Simponi, in combination with their anti-IL-23 antibody, Tremfya, in patients with UC. The combination resulted in an absolute clinical remission rate of 47% in the induction setting, which was nearly additive of the remission rates observed with either TNFα (25%) or IL-23 (24%) alone. We believe there is potential to build on this result by combining mechanisms that have shown greater efficacy rates in specific indications and settings and that exhibit a superior safety profile relative to the TNFα class.

*Our precision immunology approach*

We aim to develop genetic- or biomarker-based companion diagnostics across our portfolio of therapeutics to aid patients and physicians in selecting the optimal treatment regimen. Clinical proof-of-concept for the potential of companion diagnostic ("CDx") approaches in IBD was demonstrated by both Prometheus (now Merck) and Roivant for their anti-TL1A programs. In Phase 2 studies, UC patients that were CDx positive were more likely to respond to anti-TL1A therapy as evidenced by a 7-13% increase in clinical remission rate at week 12 compared to all-comers. We are in discussions with several potential partners with access to large scale IBD biobanks to support CDx development across our portfolio.

**Our Team and Investors**

Our portfolio of potentially best-in-class antibodies were discovered and developed by Paragon. Spyre is the second company that was founded upon technology spun out of Paragon, a group of leading entrepreneurial scientists and investors with extensive mAb experience. Its scientific founders' discoveries have also led to the successful creation of other biotechnology companies, including Cogent Biosciences, Inc., Viridian Therapeutics, Inc., Dianthus Therapeutics, Inc., and Apogee Therapeutics, Inc.

On June 22, 2023, we announced the completion of the Asset Acquisition with the sole focus on advancing a pipeline of next-generation antibodies for IBD with respect to which we have exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Spyre Option Agreement. Concurrent with the closing of the Asset Acquisition, we completed a $210 million private placement of our Series A Preferred Stock with a syndicate of healthcare investors led by Fairmount Funds Management LLC, with participation from Fidelity Management & Research Company, Venrock Healthcare Capital Partners, Commodore Capital, Deep Track Capital, Perceptive Advisors, RTW

Investments, Cormorant Asset Management, Driehaus Capital Management, Ecor1 Capital, RA Capital Management, Surveyor Capital (a Citadel company), and Wellington Management Company LLP, as well as additional institutional investors.

We have a strong management team and group of employees with diverse backgrounds and significant experience in developing novel treatments for patients at biopharmaceutical companies such as AbbVie, BridgeBio Pharma, Genentech, and Johnson & Johnson. Together, our team has a proven track record in the discovery, development, and commercialization of numerous approved therapeutics.

**Our Relationship with Paragon and Parapyre**

Paragon and Parapyre, a related party of Paragon, beneficially own more than 5% of our capital stock collectively through their holdings of our Common Stock and Series A Preferred Stock. Fairmount beneficially owns more than 5% of our capital stock, has two seats on our Board of Directors and beneficially owns more than 5% of Paragon, which is a joint venture between Fairmount and Fair Journey Biologics. Fairmount has appointed Paragon's board of directors and has the contractual right to approve the appointment of any executive officers.

In connection with the Asset Acquisition, we assumed the rights and obligations of Spyre under the Spyre Option Agreement. Under the Spyre Option Agreement, we are obligated to compensate Paragon on a quarterly basis for its services performed under each research program based on the actual costs incurred. As of the date of the Asset Acquisition, Spyre had incurred total expenses of $19.3 million under the Spyre Option Agreement since inception, inclusive of a $3.0 million research initiation fee that was due upon signing of the Spyre Option Agreement and $16.3 million of reimbursable expenses under the Spyre Option Agreement for historical costs incurred by Paragon. As of the acquisition date, $19.3 million was unpaid and was assumed by us through the Asset Acquisition.

In July 2023, we exercised our option for SPY001 with the remaining three options for SPY002, SPY003, SPY004 remaining outstanding.

In connection with the Asset Acquisition, the Company also assumed the Parapyre Option Obligation (as defined below) which provided for an annual equity grant of options to purchase 1% of the then outstanding shares of Spyre's common stock, on a fully diluted basis, on the last business day of each calendar year, at the fair market value determined by the board of directors of Spyre. As a result of the Asset Acquisition, the Parapyre Option Obligation shall continue and Parapyre shall be entitled to receive the equivalent shares of the Company with the same terms.

See the section titled "*Spyre Option Agreement*" below for more information on the Spyre Option Agreement.

**Spyre Option Agreement**

In May 2023, Spyre entered into the Spyre Option Agreement with Paragon and Parapyre. In consideration for the Option granted under the Spyre Option Agreement, Spyre was obligated to pay Paragon an upfront cash amount of $3.0 million in research initiation fees. In addition, Spyre was obligated to pay incurred reimbursable research costs of $16.3 million to Paragon as of the closing of the Asset Acquisition. Furthermore, the Spyre Option Agreement provided for an annual equity grant of options to purchase 1% of the then outstanding shares of Spyre's common stock, on a fully diluted basis, on the last business day of each calendar year, at the fair market value determined by the board of directors of Spyre (the "Parapyre Option Obligation"). As a result of the Asset Acquisition, we assumed the rights and obligations of Spyre under the Spyre Option Agreement, including the Parapyre Option Obligation. Pursuant to the Spyre Option Agreement, on a research program-by-research program basis following the finalization of the research plan for each respective research program, we are required to pay Paragon a nonrefundable fee in cash of $0.75 million. We are also obligated to compensate Paragon on a quarterly basis for its services performed under each research program based on the actual costs incurred. For the period from June 22, 2023 (Asset Acquisition date) to June 30, 2023, we did not make any payments to Paragon.

On July 12, 2023, we exercised our Option available under the Spyre Option Agreement with respect to the SPY001 research program and will enter into a SPY001 license agreement (the "SPY001 License Agreement"). Our Option available under the Spyre Option Agreement with respect to SPY002, SPY003 and SPY004 remains unexercised.

Following the execution of the SPY001 License Agreement, we will also be obligated to pay Paragon up to $22.0 million upon the achievement of specific development and clinical milestones for the first product under the SPY001 License Agreement that achieves such specified milestones. Upon execution of the SPY001 License Agreement, we will pay Paragon a $1.5 million fee for nomination of a development candidate, and we are obligated to make a further milestone payment of $2.5 million upon the first dosing of a human patient in a Phase 1 trial. Subject to the execution of the Option with respect to SPY002, SPY003 or SPY004, we expect to be obligated to make similar payments upon and following the execution of license agreements with respect to SPY002, SPY003 and SPY004, respectively. For additional detail regarding our arrangements with Paragon, see the section titled "*Our Relationship with Paragon and Parapyre*" above.

**Commercial**

Should any of our product candidates be approved for commercialization, we intend to develop a plan to commercialize them in the United States and other key markets, through internal infrastructure and/or external partnerships in a manner that will enable us to realize the full commercial value of our programs. Given our stage of development, we have not yet established a commercial organization or distribution capabilities.

**Manufacturing**

We do not currently own or operate facilities for product manufacturing, testing, storage, and distribution. We are currently in the process of novating certain agreements with third parties for the performance of future clinical manufacturing and toxicology activities from Paragon to us. The initial forms of these agreements are generally non-specific master services agreements that allow an entity to begin the process of future manufacturing or toxicology services, respectively. As clinical development activities are commenced by us, the agreements will be revised to provide for the specific deliverables and associated costs that are needed under our development plan.

**Competition**

We expect to face intense competition from other biopharmaceutical companies that are developing agents for the treatment of inflammatory diseases. If approved for the treatment of patients with moderate-to-severe IBD, our portfolio of products would compete with TNF antibodies including Humira (AbbVie), Remicade (Johnson & Johnson), and Simponi (Johnson & Johnson); IL-12/23 and IL-23 antibodies including Stelara (Johnson & Johnson) and Skyrizi (AbbVie); α4b7 antibody Entyvio (Takeda); JAK inhibitors including Xeljanz (Pfizer), Rinvoq (AbbVie); and S1P1 receptor modulating therapies including Zeposia (Bristol Myers Squibb).

We are aware of several companies with product candidates in development for the treatment of patients with IBD, including Merck's PRA023, Roivant's RVT-3101, and Teva's TEV-48574 TL1A antibodies; additional IL-23s including Tremfya (Johnson & Johnson) and mirikizumab (Lilly); additional S1P1 modulator etrasimod (Pfizer); and oral anti-integrin agents including Morphic Therapeutic's MORF-057 and Gilead's GS-1427, and a discovery program at Dice Therapeutics (Lilly).

**Government Regulation**

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval,

advertising, promotion, marketing, post-approval monitoring and post-approval reporting of biologics such as those we are developing. We, along with our third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or post-market may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

**United States Biologics Regulation**

In the United States, biological products are subject to regulation under the Federal Food, Drug, and Cosmetic Act ("FDCA") and the Public Health Service Act ("PHSA") and their implementing regulations, as well as other federal, state, local, and foreign statutes and regulations. The process required by the FDA before biologic product candidates may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with applicable regulations, including the FDA's current Good Laboratory Practices;
- submission to the FDA of an IND, which must become effective before clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an independent institutional review board ("IRB"), or ethics committee at each clinical site before the trial may be commenced;
- manufacture of the proposed biologic candidate in accordance with current Good Manufacturing Practices ("cGMPs");
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, current Good Clinical Practice ("cGCP") requirements and other clinical-trial related regulations to establish the safety, purity and potency of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of a BLA, after completion of all pivotal clinical trials;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMPs, and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and potential audit of selected clinical investigation sites to assess compliance with cGCPs;
- payment of user fees for FDA review of the BLA, unless a waiver is applicable; and
- FDA review and approval of a BLA to permit commercial marketing of the product for a particular indication(s) for use in the United States.

*Preclinical and Clinical Development*

Prior to beginning the first clinical trial with a product candidate, in the United States, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol or protocols for preclinical studies and clinical trials. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology and pharmacodynamic characteristics of the product, chemistry, manufacturing and controls information, and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on

clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial. Similar processes exist in countries outside the United States that we will be required to follow if we choose to execute trials in other countries.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with cGCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed.

Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may recommend halting the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing preclinical studies and clinical trials and clinical study results to public registries. Sponsors of clinical trials of FDA-regulated products, including biological products, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of a BLA. The FDA will accept a well-designed and well-conducted foreign clinical trial not conducted under an IND if the trial was conducted in accordance with cGCP requirements and the FDA is able to validate the data through an onsite inspection if deemed necessary.

For the purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

- Phase 1. The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, and the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2. The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3. The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a

condition to approval of the BLA. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data and clinical study investigators. Written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected suspected adverse events, any findings from other studies, tests in laboratory animals or in vitro testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information.

*BLA Submission and Review*

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. FDA approval of a BLA must be obtained before a biologic may be marketed in the United States. The BLA must include all relevant data available from pertinent preclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of the product, or from a number of alternative sources, including studies initiated and sponsored by investigators. The submission of a BLA requires payment of a substantial application user fee to the FDA, unless a waiver or exemption applies.

In addition, under the Pediatric Research Equity Act ("PREA"), a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The Food and Drug Administration Safety and Innovation Act requires that a sponsor who is planning to submit a marketing application for a biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial pediatric study plan ("PSP") within sixty days after an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 study as may be agreed between the sponsor and FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

Within 60 days following submission of the application, the FDA reviews the BLA to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems

incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with additional information. Once a BLA has been accepted for filing, the FDA's goal is to review standard applications within ten months after the filing date, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process may also be extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may convene an advisory committee to provide clinical insight on application review questions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCPs. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it typically will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response Letter will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response Letter without first conducting required inspections, testing submitted product lots and/or reviewing proposed labeling. In issuing the Complete Response Letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. If a Complete Response Letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application or request an opportunity for a hearing. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a REMs to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

*Expedited Development and Review Programs*

The FDA offers several expedited development and review programs for qualifying product candidates. The Fast Track program is intended to expedite or facilitate the process for reviewing new products that meet certain

criteria. Specifically, new products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a Fast Track product has opportunities for more frequent interactions with the review team during product development and, once a BLA is submitted, the product may be eligible for priority review. A Fast Track product may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.

A product intended to treat a serious or life-threatening disease or condition may also be eligible for Breakthrough Therapy designation to expedite its development and review. A product can receive Breakthrough Therapy designation if preliminary clinical evidence indicates that the product, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product, including involvement of senior managers.

Any marketing application for a biologic submitted to the FDA for approval, including a product with a Fast Track designation and/or Breakthrough Therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide a significant improvement in the treatment, diagnosis or prevention of a serious disease or condition. For original BLAs, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (as compared to ten months under standard review).

Additionally, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies with due diligence to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Under the Food and Drug Omnibus Reform Act of 2022 ("FDORA") the FDA may require, as appropriate, that such studies be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a product or indication approved under accelerated approval if the sponsor fails to conduct the required post-marketing studies or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Fast Track designation, Breakthrough Therapy designation and priority review do not change the standards for approval but may expedite the development or approval process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

*Post-Approval Requirements*

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping,

reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. After a BLA is approved for a biological product, the product also may be subject to official lot release. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA also may perform certain confirmatory tests on lots of some products before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency and effectiveness of biologics. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing user fee requirements, under which the FDA assesses an annual program fee for each product identified in an approved BLA. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMPs, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMPs and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMPs and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of a product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;
- product seizure or detention, or refusal of the FDA to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in

varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

*Biosimilars and Reference Product Exclusivity*

The ACA includes the BPCIA, which created an abbreviated approval pathway for biological products that are highly similar, or "biosimilar," to or interchangeable with an FDA-approved reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, is generally shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. A product shown to be biosimilar or interchangeable with an FDA-approved reference biological product may rely in part on the FDA's previous determination of safety and effectiveness for the reference product for approval, which can potentially reduce the cost and time required to obtain approval to market the product. Complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA. In September 2021, the FDA issued two guidance documents intended to inform prospective applicants and facilitate the development of proposed biosimilars and interchangeable biosimilars, as well as to describe the FDA's interpretation of certain statutory requirements added by the BPCIA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. FDA-approved interchangeable biosimilars may be substituted for the reference product without the intervention of the prescribing health care provider, subject to state laws, which differ by state.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In July 2018, the FDA announced an action plan to encourage the development and efficient review of biosimilars, including the establishment of a new office within the agency that will focus on therapeutic biologics and biosimilars. On December 20, 2020, Congress amended the PHSA as part of the COVID-19 relief bill to further simplify the biosimilar review process by making it optional to show that conditions of use proposed in labeling have been previously approved for the reference product, which used to be a requirement of the application. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and impact of the BPCIA is subject to significant uncertainty.

As discussed below, the Inflation Reduction Act of 2022 (“IRA”) is a significant new law that intends to foster generic and biosimilar competition and to lower drug and biologic costs.

*Other Healthcare Laws and Compliance Requirements*

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation: the federal Anti-Kickback Statute (“AKS”); the federal False Claims Act (“FCA”); the Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) and similar foreign, federal and state fraud, abuse and transparency laws.

The AKS prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, to induce, or in return for, either the referral of an individual, or the purchase, lease, order, arrangement, or recommendation of an item or service for which payment may be made under any federal healthcare program. The term remuneration has been interpreted broadly to include anything of value. The AKS has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand, and prescribers and purchasers on the other. The government often takes the position that to violate the AKS, only one purpose of the remuneration need be to induce referrals, even if there are other legitimate purposes for the remuneration. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from AKS prosecution, but they are drawn narrowly and practices that involve remuneration, such as consulting agreements, that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the AKS. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the FCA or federal civil monetary penalties.

Civil and criminal false claims laws, including the FCA, and civil monetary penalty laws, which impose criminal and civil penalties and can be enforced through civil whistleblower or qui tam actions, prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment of federal government funds, including in federal healthcare programs, that are false or fraudulent; knowingly making, using or causing to be made or used, a false statement of record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Pharmaceutical and other healthcare companies have been prosecuted under these laws for engaging in a variety of different types of conduct that “caused” the submission of false claims to federal healthcare programs. Under the AKS, for example, a claim resulting from a violation of the AKS is deemed to be a false or fraudulent claim for purposes of the FCA. The FCA also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery.

HIPAA created additional federal criminal statutes that prohibit, among other things, executing a scheme to defraud any healthcare benefit program, including private third-party payors, and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements or representations relating to healthcare matters.

The FDCA addresses, among other things, the design, production, labeling, promotion, manufacturing, and testing of drugs, biologics and medical devices, and prohibits such acts as the introduction into interstate commerce of adulterated or misbranded drugs or devices. The PHSA also prohibits the introduction into interstate commerce of unlicensed or mislabeled biological products.

The United States federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to annually report to the Centers for Medicaid & Medicare Services ("CMS") information related to payments or other transfers of value made to various healthcare professionals including physicians, certain other licensed health care practitioners, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Beginning on January 1, 2023, California Assembly Bill 1278 requires California physicians and surgeons to notify patients of the Open Payments database established under the federal Physician Payments Sunshine Act.

We are also subject to additional similar United States state and foreign law equivalents of each of the above federal laws, which, in some cases, differ from each other in significant ways, and may not have the same effect, thus complicating compliance efforts. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply, we may be subject to penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations.

*Data Privacy and Security*

Numerous state, federal, and foreign laws govern the collection, dissemination, use, access to, confidentiality, and security of personal information, including health-related information. In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations, govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. For example, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health, and their respective implementing regulations imposes privacy, security, and breach notification obligations on certain health care providers, health plans, and health care clearinghouses, known as covered entities, as well as their business associates and their covered subcontractors that perform certain services that involve using, disclosing, creating, receiving, maintaining, or transmitting individually identifiable health information for or on behalf of such covered entities. Entities that are found to be in violation of HIPAA may be subject to significant civil, criminal, and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with the U.S. Department of Health and Human Services ("HHS") to settle allegations of HIPAA non-compliance. Further, entities that knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA covered entity in a manner that is not authorized or permitted by HIPAA may be subject to criminal penalties.

Even when HIPAA does not apply, according to the FTC, violating consumers' privacy rights or failing to take appropriate steps to keep consumers' personal information secure may constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act.

In addition, state laws govern the privacy and security of personal information, including health-related information, in certain circumstances. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. For example, the California Consumer Privacy Act, which went into effect on January 1, 2020, has created new data privacy obligations for covered companies and provided new privacy rights to California residents.

*Coverage and Reimbursement*

In the United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental

healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels.

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical or biological product for which we obtain regulatory approval. Sales of any product, if approved, depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement, if any, for such product by third-party payors. Decisions regarding whether to cover any of our product candidates, if approved, the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. Further, no uniform policy for coverage and reimbursement exists in the United States, and coverage and reimbursement can differ significantly from payor to payor. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical or biological products, medical devices and medical services, in addition to questioning safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product that receives approval. Decreases in third-party reimbursement for any product or a decision by a third-party not to cover a product could reduce physician usage and patient demand for the product.

For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics.

In addition, net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the

government, such as average sales price, and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs.

Finally, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of its product candidates. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower.

*Healthcare reform*

The United States and some foreign jurisdictions are considering or have enacted a number of reform proposals to change the healthcare system. There is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by federal and state legislative initiatives, including those designed to limit the pricing, coverage, and reimbursement of pharmaceutical and biopharmaceutical products, especially under government-funded health care programs, and increased governmental control of drug pricing.

The ACA, which was enacted in 2010, substantially changed the way healthcare is financed by both governmental and private insurers in the United States, and significantly affected the pharmaceutical industry. The ACA contains a number of provisions of particular import to the pharmaceutical and biotechnology industries, including, but not limited to, those governing enrollment in federal healthcare programs. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future.

Other legislative changes have been proposed and adopted since the ACA was enacted. For example, the Budget Control Act of 2011 and subsequent legislation, among other things, created measures for spending reductions by Congress that include aggregate reductions of Medicare payments to providers of 2% per fiscal year, which remain in effect through 2032. Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025 absent further legislation. The United States American Taxpayer Relief Act of 2012 further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

In addition, the Bipartisan Budget Act of 2018, among other things, amended the Medicare Act (as amended by the ACA) to increase the point-of-sale discounts that manufacturers must agree to offer under the Medicare Part D coverage discount program to 70% off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs being covered under Medicare Part D.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state measures designed to, among other things, reduce the cost of prescription drugs, bring

more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, in May 2019, CMS adopted a final rule allowing Medicare Advantage Plans the option to use step therapy for Part B drugs, permitting Medicare Part D plans to apply certain utilization controls to new starts of five of the six protected class drugs, and requiring the Explanation of Benefits for Part D beneficiaries to disclose drug price increases and lower cost therapeutic alternatives.

In addition, the United States government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. The IRA includes several provisions that may impact our business to varying degrees, including provisions that reduce the out-of-pocket spending cap for Medicare Part D beneficiaries from $7,050 to $2,000 starting in 2025, thereby effectively eliminating the coverage gap; impose new manufacturer financial liability on certain drugs under Medicare Part D, allow the United States government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition; require companies to pay rebates to Medicare for certain drug prices that increase faster than inflation; and delay until January 1, 2032 the implementation of the HHS rebate rule that would have limited the fees that pharmacy benefit managers can charge. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one rare disease designation and for which the only approved indication is for that disease or condition. If a product receives multiple rare disease designations or has multiple approved indications, it may not qualify for the orphan drug exemption. These provisions will take effect progressively starting in fiscal year 2023, although the Medicare drug price negotiation program is currently subject to legal challenges. The effects of the IRA on its business and the healthcare industry in general is not yet known.

President Biden has also issued multiple executive orders that have sought to reduce prescription drug costs. In February 2023, HHS also issued a proposal in response to an October 2022 executive order from President Biden that includes a proposed prescription drug pricing model that will test whether targeted Medicare payment adjustments will sufficiently incentivize manufacturers to complete confirmatory trials for drugs approved through FDA's accelerated approval pathway. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

Notwithstanding the IRA and President Biden's executive orders, continued legislative and enforcement interest exists in the United States with respect to specialty drug pricing practices. Specifically, we expect regulators to continue pushing for transparency to drug pricing, reducing the cost of prescription drugs under Medicare, reviewing the relationship between pricing and manufacturer patient programs, and reforming government program reimbursement methodologies for drugs.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain drug access and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our drugs or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

*Other Government and Regulation Outside of the United States*

In addition to regulations in the United States, we are subject to a variety of regulations in other jurisdictions governing, among other things, research and development, clinical trials, testing, manufacturing, safety, efficacy, quality control, labeling, packaging, storage, record keeping, distribution, reporting, export and import, advertising, marketing and other promotional practices involving biological products as well as authorization, approval as well as post-approval monitoring and reporting of our products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like an IND prior to the commencement of human clinical trials.

The requirements and process governing the conduct of clinical trials, including requirements to conduct additional clinical trials, product licensing, safety reporting, post-authorization requirements, marketing and promotion, interactions with healthcare professionals, pricing and reimbursement may vary widely from country to country. No action can be taken to market any product in a country until an appropriate approval application has been approved by the regulatory authorities in that country. The current approval process varies from country to country, and the time spent in gaining approval varies from that required for FDA approval. In certain countries, the sales price of a product must also be approved. The pricing review period often begins after market approval is granted. Even if a product is approved by a regulatory authority, satisfactory prices may not be approved for such product, which would make launch of such products commercially unfeasible in such countries.

*Regulation in the European Union*

The collection and use of personal health data and other personal data regarding individuals in the European Economic Area (“EEA”) is governed by the provisions of the European General Data Protection Regulation (EU) 2016/679 (“EU GDPR”) and related data protection laws in individual EEA member states, including additional requirements relating to health, genetic and biometric data implemented through national legislation. Similar processing of personal health data and other personal data regarding individuals in the UK is governed by the UK General Data Protection Regulation (“UK GDPR”) and the UK Data Protection Act 2018. In this document, “GDPR” refers to both the EU GDPR and the UK GDPR, unless specified otherwise. The GDPR imposes a number of strict obligations and restrictions on the ability to process, including collecting, analyzing and transferring, personal data of individuals, in particular with respect to health data from clinical trials and adverse event reporting. The GDPR includes requirements relating to the legal basis of the processing (such as consent of the individuals to whom the personal data relates), the information provided to the individuals prior to processing their personal data, the notification obligations to the national data protection authorities, and the security and confidentiality of the personal data.

In addition, the GDPR imposes specific restrictions on the transfer of personal data to countries outside of the EEA/UK that are not considered by the European Commission (“EC”) and the UK government as providing an adequate level of data protection (third countries), including the United States. Appropriate safeguards are required to enable such transfers. Among the appropriate safeguards that can be used, the data exporter may use the EC approved standard contractual clauses (“SCCs”) and the UK International Data Transfer Agreement/Addendum (“UK IDTA”). Where relying on the SCCs or UK IDTA for data transfers, we may also be required to carry out transfer impact assessments to assess whether the recipient is subject to local laws which allow public authority access to personal data. The international transfer obligations under the EEA/UK data protection regimes will require effort and cost and may result in us needing to make strategic considerations around where EEA/UK personal data is located and which service providers we can utilize for the processing of EEA/UK personal data. Although the UK is regarded as a third country under the EU GDPR, the EC has issued a decision

recognizing the UK as providing adequate protection under the EU GDPR ("Adequacy Decision") and, therefore, transfers of personal data originating in the EEA to the UK remain unrestricted. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing. The UK government has also now introduced a Data Protection and Digital Information Bill ("UK Data Protection Bill") into the UK legislative process with the intention for this bill to reform the UK's data protection regime following Brexit. If passed, the final version of the UK Data Protection Bill may have the effect of further altering the similarities between the UK and EU data protection regime. This may lead to additional compliance costs and could increase our overall risk. The respective provisions and enforcement of the EU GDPR and UK GDPR may further diverge in the future and create additional regulatory challenges and uncertainties.

On March 25, 2022, the EC and the United States announced that they have agreed in principle on a new Trans-Atlantic Data Privacy Framework. Following this statement, on October 7, 2022, President Biden signed an Executive Order on 'Enhancing Safeguards for United States Signals Intelligence Activities', which implemented the agreement in principle. On that basis, the EC prepared a draft Adequacy Decision and launched its adoption procedure. While this new EU-United States privacy framework is expected to enter into force in 2023, there is still some uncertainty around the new framework.

Failure to comply with the requirements of the GDPR and the related national data protection laws of the EEA member states/UK may result in significant monetary fines for noncompliance of up to €20 million (£17.5 million for the UK) or 4% of the annual global revenues of the noncompliant company, whichever is greater, other administrative penalties and a number of criminal offenses (punishable by uncapped fines) for organizations and, in certain cases, their directors and officers, as well as civil liability claims from individuals whose personal data was processed. Data protection authorities from the different EEA member states/UK may still implement certain variations, enforce the GDPR and national data protection laws differently, and introduce additional national regulations and guidelines, which adds to the complexity of processing personal data subject to the EEA/UK data protection regimes. Guidance developed at both the EU level and at the national level in individual EU member states concerning implementation and compliance practices are often updated or otherwise revised.

Compliance with the GDPR is a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines, penalties and litigation in connection with European activities, which could in turn have a negative effect on our reputation and materially harm our business.

Furthermore, there is a growing trend towards the required public disclosure of clinical trial data in the EU, which adds to the complexity of obligations relating to processing health data from clinical trials. Such public disclosure obligations are provided in the new EU Clinical Trials Regulation (EU) No. 536/2014 (the "CTR"), European Medical Agency ("EMA") disclosure initiatives and voluntary commitments by industry. Failure to comply with these obligations could lead to government enforcement actions and significant penalties against us, harm to our reputation, and adversely impact our business and operating results. The uncertainty regarding the interplay between different regulatory frameworks, such as the CTR and the GDPR, further adds to the complexity that we face with regard to data protection regulation.

*Drug and Biologic Development Process*

Regardless of where they are conducted, all clinical trials included in applications for marketing authorization for human medicines in the EU must have been carried out in accordance with EU regulations. This means that clinical trials conducted in the EU have to comply with EU clinical trial legislation but also that clinical trials conducted outside the EU have to comply with ethical principles equivalent to those set out in the EU, including adhering to international good clinical practice and the Declaration of Helsinki. The conduct of clinical trials in the EU is governed by the CTR, which entered into force on January 31, 2022. The CTR replaced the Clinical Trials Directive 2001/20/EC, ("Clinical Trials Directive") and introduced a complete overhaul of the existing regulation of clinical trials for medicinal products in the EU.

Under the former regime, which will expire after a transition period of one or three years, respectively, as outlined below in more detail, before a clinical trial can be initiated it must be approved in each EU member state where there is a site at which the clinical trial is to be conducted. The approval must be obtained from two separate entities: the national competent authority in the applicable EU member state(s) and one or more ethics committees. The national competent authority of all EU member states in which the clinical trial will be conducted must authorize the conduct of the trial, and the independent ethics committee must grant a positive opinion in relation to the conduct of the clinical trial in the relevant EU member state before the commencement of the trial. Any substantial changes to the trial protocol or other information submitted with the clinical trial applications must be submitted to or approved by the relevant national competent authorities and ethics committees. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial must be reported to the national competent authority and to the ethics committees of the EU member state where they occur.

A more unified procedure applies under the CTR. A sponsor can submit a single application for approval of a clinical trial through a centralized EU clinical trials portal (the "CTIS"). One national competent authority (the reporting EU member state proposed by the applicant) will take the lead in validating and evaluating the application, and will consult and coordinate with the other concerned EU member states. If an application is rejected, it may be amended and resubmitted through the EU clinical trials portal. If an approval is issued, the sponsor may start the clinical trial in all concerned EU member states. However, a concerned EU member state may in limited circumstances declare an "opt-out" from an approval and prevent the clinical trial from being conducted in such member state. The CTR also aims to streamline and simplify the rules on safety reporting, and introduces enhanced transparency requirements such as mandatory submission of a summary of the clinical trial results to the EU database. The CTR foresees a three-year transition period. On January 31, 2023, submission of initial clinical trial applications via CTIS became mandatory, and by January 31, 2025, all ongoing trials approved under the former Clinical Trials Directive will need to comply with the CTR and have to be transitioned to CTIS.

Under both the former regime and the CTR, national laws, regulations, and the applicable Good Clinical Practice and Good Laboratory Practice standards must also be respected during the conduct of the trials, including the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use guidelines on Good Clinical Practice and the ethical principles that have their origin in the Declaration of Helsinki.

During the development of a medicinal product, the EMA and national regulators within the EU provide the opportunity for dialogue and guidance on the development program. At the EMA level, this is usually done in the form of scientific advice, which is given by the Committee for Medicinal Products for Human Use ("CHMP") on the recommendation of the Scientific Advice Working Party. A fee is incurred with each scientific advice procedure, but is significantly reduced for designated orphan medicines. Advice from the EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical studies, and pharmacovigilance plans and risk-management programs. Advice is not legally binding with regard to any future marketing authorization application ("MAA") for the product concerned.

*Drug Marketing Authorization*

In the EU, medicinal products are subject to extensive pre- and post-market regulation by regulatory authorities at both the EU and national levels. To obtain regulatory approval of a product under the EU regulatory systems, we must submit an MAA under either the EU centralized procedure, or one of the national procedures in the EU.

*Centralized Authorization Procedure*

The centralized procedure provides for the grant of a single marketing authorization ("MA") that is issued by the EC following the scientific assessment of the application by the EMA and that is valid for all EU member states

as well as in the three additional EEA member states (Norway, Iceland and Liechtenstein). The centralized procedure is compulsory for certain types of medicinal products, including for medicines developed by means of certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (gene therapy, somatic cell therapy or tissue-engineered medicines) and medicinal products with a new active substance indicated for the treatment of certain diseases (HIV/AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases). The centralized procedures is option for medicinal products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or for which the grant of an MA through the centralized procedure would be in the interest of public health at EU level.

Under the centralized procedure, the CHMP established at the EMA, is responsible for conducting the initial assessment of a drug. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure, the timeframe for the evaluation of an MAA by the EMA's CHMP is, in principle, 210 days from receipt of a valid MAA. However, this timeline excludes clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP, so the overall process typically takes a year or more, unless the application is eligible for an accelerated assessment. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. Upon request, the CHMP can reduce the time frame to 150 days if the applicant provides sufficient justification for an accelerated assessment. The CHMP will provide a positive opinion regarding the application only if it meets certain quality, safety and efficacy requirements. This opinion is then transmitted to the EC, which has the ultimate authority for granting the MA within 67 days after receipt of the CHMP opinion.

*Decentralized and Mutual Recognition Procedures*

Medicines that fall outside the mandatory scope of the centralized procedure can be authorized under a decentralized procedure where an applicant applies for simultaneous authorization in more than one EU member state, or they can be authorized in an EU member state in accordance with that state's national procedures and then be authorized in other EU countries by a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization (mutual recognition procedure).

The decentralized procedure permits companies to file identical MA applications for a medicinal product to the competent authorities in various EU member states simultaneously if such medicinal product has not received marketing approval in any EU member state before. The competent authority of a single EU member state, the reference member state, is appointed to review the application and provide an assessment report. The competent authorities of the other EU member states, the concerned member states, are subsequently required to grant a marketing authorization for their territories on the basis of this assessment. The only exception to this is where the competent authority of an EU member state considers that there are concerns of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the EC, whose decision is binding for all EU member states.

*Risk Management Plan*

All new MAAs must include a Risk Management Plan ("RMP") describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available. An updated RMP must be submitted: (i) at the request of EMA or a national competent authority, or (ii) whenever the risk-management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit-risk profile or as a result of an important pharmacovigilance or risk-minimization milestone being reached. The regulatory authorities may also impose specific obligations as a condition of the MA. RMPs and Periodic Safety Update Reports ("PSURs") are routinely available to third parties requesting access, subject to limited redactions.

*MA Validity Period*

In the EU, an MA has an initial duration of five years. After these five years, the authorization may subsequently be renewed on the basis of a reevaluation of the risk-benefit balance. Once renewed, the MA is valid for an unlimited period unless the EC or the national competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with only one additional five-year renewal. Applications for renewal must be made to the EMA at least nine months before the five-year period expires.

*Exceptional Circumstances/Conditional Approval*

Similar to accelerated approval regulations in the United States, conditional MAs can be granted in the EU for medicines intended for treating, preventing or diagnosing seriously debilitating or life-threatening diseases, or in a public health emergency. A conditional MA can be granted for medicinal products where, although comprehensive clinical data referring to the safety and efficacy of the medicinal product have not been supplied, the following criteria are fulfilled: (i) the benefit/risk balance of the product is positive, (ii) it is likely that the applicant will be in a position to provide the comprehensive clinical data post-authorization, (iii) unmet medical needs will be fulfilled by the grant of the MA and (iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. Once a conditional MA has been granted, the MA holder must fulfil specific obligations within defined timelines. A conditional MA must be renewed annually, but can be converted into a standard MA once the MA holder fulfils the obligations imposed and the complete data confirm that the medicine's benefits continue to outweigh its risks.

*Data and Market Exclusivity*

As in the United States, it may be possible to obtain a period of market and / or data exclusivity in the EU that would have the effect of postponing the entry into the marketplace of a competitor's generic, hybrid or biosimilar product (even if the pharmaceutical product has already received a MA) and prohibiting another applicant from relying on the MA holder's pharmacological, toxicological and clinical data in support of another MA for the purposes of submitting an application, obtaining an MA or placing the product on the market. Innovative medicinal products (sometimes referred to as new chemical entities ("NCEs")) approved in the EU generally qualify for eight years of data exclusivity and 10 years of marketing exclusivity.

If granted, the data exclusivity period begins on the date of the product's first MA in the EU and prevents generic or biosimilar applicants from referencing the innovator's preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU. After eight years, a generic product application may be submitted and generic companies may rely on the MA holder's data. However, a generic product cannot launch until two years later (or a total of 10 years after the first MA in the EU of the innovator product). An additional one-year period of marketing exclusivity is possible if, during the data exclusivity period (the first eight years of the 10-year marketing exclusivity period), the MA holder obtains an authorization for one or more new therapeutic indications that are deemed to bring a significant clinical benefit compared to existing therapies. Additionally, a standalone one-year period of data exclusivity can be granted where an application is made for a new indication for a well-established substance, provided that significant pre-clinical or clinical studies were carried out in relation to the new indication. Where a change of classification of a pharmaceutical product has been authorized on the basis of significant pre-trial tests or clinical trials, when examining an application by another applicant for or holder of an MA for a change of classification of the same substance the competent authority will not refer to the results of those tests or trials for one year after the initial change was authorized.

Products may not be granted data exclusivity since there is no guarantee that a product will be considered by the EU's regulatory authorities to include a NCE. Even if a compound is considered to be a NCE and the MA applicant is able to gain the prescribed period of data exclusivity, another company nevertheless could also

market another version of the medicinal product if such company can complete a full MAA with their own complete database of pharmaceutical tests, preclinical studies and clinical trials and obtain MA of its product.

*Pediatric Development*

In the EU, companies developing a new medicinal product are obligated to study their product in children and must therefore submit a PIP together with a request for agreement to the EMA, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The EMA issues a decision on the PIP based on an opinion of the EMA's Pediatric Committee. Companies must conduct pediatric clinical trials in accordance with the PIP approved by the EMA, unless a deferral (e.g. until enough information to demonstrate its effectiveness and safety in adults is available) or waiver (e.g. because the relevant disease or condition occurs only in adults) has been granted by the EMA. The MAA for the medicinal product must include the results of all pediatric clinical trials performed and details of all information collected in compliance with the approved PIP, unless such a waiver or a deferral has been granted. Medicinal products that are granted an MA on the basis of the pediatric clinical trials conducted in accordance with the approved PIP are eligible for a six month extension of the protection under a supplementary protection certificate ("SPC"), provided an application for such extension is made at the same time as filing the SPC application for the product, or at any point up to two years before the SPC expires, or, in the case of orphan medicinal products, a two year extension of the orphan market exclusivity. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the approved PIP are developed and submitted. An approved PIP is also required when an MA holder wants to add a new indication, medicinal form or route of administration for a medicine that is already authorized and covered by intellectual property rights.

*PRIME Designation*

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The Priority Medicines ("PRIME") scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies on the basis of compelling non-clinical data and tolerability data from initial clinical trials. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and potentially accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, once a candidate medicine has been selected for the PRIME scheme, a dedicated contact point and rapporteur from the CHMP or from the Committee for Advanced Therapeutics ("CAT") are appointed facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting with the CHMP/CAT rapporteur initiates these relationships and includes a team of multidisciplinary experts to provide guidance on the overall development plan and regulatory strategy. PRIME eligibility does not change the standards for product approval, and there is no assurance that any such designation or eligibility will result in expedited review or approval.

*Post-Approval Regulation*

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the EC and/or the competent regulatory authorities of the EU member states. This oversight applies both before and after grant of manufacturing licenses and marketing authorizations. It includes control of compliance with EU good manufacturing practices rules, manufacturing authorizations, pharmacovigilance rules and requirements governing advertising, promotion, sale, and distribution, recordkeeping, importing and exporting of medicinal products.

Failure by us or by any of our third-party partners, including suppliers, manufacturers and distributors to comply with EU laws and the related national laws of individual EU member states governing the conduct of clinical

trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of MA, statutory health insurance, bribery and anti-corruption or other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials or to grant an MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

The holder of an MA for a medicinal product must also comply with EU pharmacovigilance legislation and its related regulations and guidelines, which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products.

MA holders must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of PSURs in relation to medicinal products for which they hold MAs. The EMA reviews PSURs for medicinal products authorized through the centralized procedure. If the EMA has concerns that the risk benefit profile of a product has varied, it can adopt an opinion advising that the existing MA for the product be suspended, withdrawn or varied. The EMA can advise that the MA holder be obliged to conduct post-authorization Phase IV safety studies. If the EC agrees with the opinion, it can adopt a decision varying the existing MA. Failure by the MA holder to fulfill the obligations for which the EC's decision provides can undermine the ongoing validity of the MA.

More generally, non-compliance with pharmacovigilance obligations can lead to the variation, suspension or withdrawal of the MA for the product or imposition of financial penalties or other enforcement measures.
The manufacturing process for pharmaceutical products in the EU is highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice ("GMP"). These requirements include compliance with GMP standards when manufacturing pharmaceutical products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU. Similarly, the distribution of pharmaceutical products into and within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU member states. The manufacturer or importer must have a qualified person who is responsible for certifying that each batch of product has been manufactured in accordance with GMP, before releasing the product for commercial distribution in the EU or for use in a clinical trial. Manufacturing facilities are subject to periodic inspections by the competent authorities for compliance with GMP.

*Sales and Marketing Regulations*

The advertising and promotion of our products is also subject to EU laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other national legislation of individual EU member states may apply to the advertising and promotion of medicinal products and may differ from one country to another. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics ("SmPC") as approved by the national competent authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the marketing authorization granted for the medicinal product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion, which is prohibited in the EU. Direct-to-consumer advertising of prescription-only medicines is also prohibited in the EU.

Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment.

*Anti-Corruption Legislation*

In the EU, interactions between pharmaceutical companies and physicians are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct both at EU level and in the individual EU member states. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the EU. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of the EU member states. Violation of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain EU member states also must be publicly disclosed. Moreover, agreements with physicians must often be the subject of prior notification and approval by the physician's employer, his/her regulatory professional organization, and/or the competent authorities of the individual EU member states. These requirements are provided in the national laws, industry codes, or professional codes of conduct, applicable in the individual EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

*Other Markets*

The UK formally left the EU on January 31, 2020 and the transition period, during which EU laws continued to apply to the UK, expired on December 31, 2020. This means EU laws now only apply to the UK in respect of Northern Ireland as laid out in the Northern Ireland Protocol. Following the end of the transition period, the EU and the UK concluded a trade and cooperation agreement ("TCA"), which applied provisionally from January 1, 2021 and entered into force on May 1, 2021.

The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued but does not provide for wholesale mutual recognition of UK and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended). Except in respect of the new CTR, the regulatory regime in Great Britain therefore largely aligns with current EU medicines regulations, however it is possible that these regimes will diverge more significantly in future now that Great Britain's regulatory system is independent from the EU and the TCA does not provide for mutual recognition of UK and EU pharmaceutical legislation. However, notwithstanding that there is no wholesale recognition of EU pharmaceutical legislation under the TCA, under a new framework which will be put in place by the Medicines and Healthcare products Regulatory Agency ("MHRA"), from January 1, 2024, the MHRA has stated that it will take into account decisions on the approval of marketing authorizations from the EMA (and certain other regulators) when considering an application for a Great Britain marketing authorization.

On February 27, 2023, the UK government and the EC announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the "Windsor Framework". This new framework fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. In particular, the MHRA will be responsible for approving all medicinal products destined for the UK market (i.e., Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. A single UK-wide marketing authorization will be granted by the MHRA for all medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK. The Windsor Framework was approved by the EU-UK Joint Committee on March 24, 2023, so the UK government and the EU will enact legislative measures to bring it into law.

For other countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials must be conducted in accordance with cGCPs and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension of clinical trials, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

***Employees and Human Capital Resources***

As of June 30, 2023, we had 14 employees, all of whom were employed full time. None of our employees are represented by a labor union or covered under a collective bargaining agreement. We consider our relationship with our employees to be good.

**Recent Developments**

In the second quarter of 2023, we began exploring strategic alternatives with the goal of maximizing stockholder value. We engaged Wedbush Securities Inc. as an exclusive financial advisor to assist in the process of exploring strategic alternatives, including an acquisition, merger, reverse merger, other business combination, sales of assets or other strategic transactions. Additionally, we reduced our workforce and retained approximately 10 employees required to support the evaluation of strategic alternatives and ongoing business activities. We also announced the departures of Michael C. Hanley, MBA, chief business officer, Linda Neuman, MD, MBA, chief medical officer, Jeffrey Goldberg, the President and Chief Executive Officer, and Jim Kastenmayer, the General Counsel. In connection with Mr. Goldberg's departure, the Board of Directors appointed Mr. Jonathan Alspaugh, our Chief Financial Officer, as our President and principal executive officer. On June 22, 2023, we acquired Spyre, a privately held biotechnology company founded to transform the treatment of IBD by pursuing potentially best-in-class long-acting antibodies, rational therapeutics combinations, and precision immunology approaches. See "*Description of the Transactions*" for more information regarding the Asset Acquisition. The Board appointed Cameron Turtle, DPhil, as Chief Operating Officer, effective as of the closing of the Asset Acquisition on June 22, 2023. Including Dr. Turtle, we increased our workforce to a total of 14 employees, concurrently with the closing of the Asset Acquisition.

**Corporate Information**

We were formed as a limited liability company under the laws of the State of Delaware in December 2013 and converted to a Delaware corporation in March 2015. Our Common Stock began trading on The Nasdaq Global Market under the ticker symbol "AGLE" on April 7, 2016. On June 22, 2023, we completed the Asset Acquisition, pursuant to which all of Spyre's outstanding equity interests were exchanged based on a fixed exchange ratio of 13.73522 to 1 for consideration from Aeglea of 12,945,385 shares of Common Stock and 364,887 shares of Series A Preferred Stock in addition to the assumption of outstanding and unexercised stock options to purchase 68,365 shares of Common Stock from the Amended and Restated Spyre 2023 Equity Incentive Plan. Our principal executive offices are located at 221 Crescent Street, Building 17, Suite 102B, Waltham, MA 02453 and our telephone number is (512) 942-2935. Our website address is https://www.aeglea.com/. The information contained in, or accessible through, our website does not constitute part of this proxy statement. We have included our website address in this proxy statement solely as an inactive textual reference.

## PROPOSALS

### PROPOSAL NO. 1:
### APPROVAL OF CONVERSION PROPOSAL

***Overview***

As described above, we issued 364,887 shares of Series A Preferred Stock in the Asset Acquisition and 721,452 shares of Series A Preferred Stock in the Financing. The Series A Preferred Stock is intended to have rights that are generally equivalent to Common Stock, provided that the Series A Preferred Stock does not have the right to vote on most matters (including the election of directors). 1,086,339,000 shares of Common Stock are issuable upon conversion of the above-described Series A Preferred Stock, assuming the approval of the Proposal No. 1 and subject to certain beneficial ownership limitations.

Subject to stockholder approval and certain beneficial ownership limitations set by each holder of Series A Preferred Stock, each share of Series A Preferred Stock will automatically convert into approximately 1,000 shares of Common Stock. This Proposal No. 1 would provide the necessary approval to permit such conversion.

***Shares Issuable Upon Conversion***

Set forth below is a table summarizing the issued and outstanding Series A Preferred Stock and the number of shares of Common Stock that are potentially issuable upon conversion of the Series A Preferred Stock. The sale into the public market of the underlying Common Stock could materially and adversely affect the market price of our Common Stock. See "*Risk Factors – Risks Related to Our Common Stock—Pursuant to the terms of the Spyre Acquisition Agreement, we are required to recommend that our stockholders approve the conversion of all outstanding shares of our Series A Preferred Stock into shares of our Common Stock. We cannot guarantee that our stockholders will approve this matter, and if they fail to do so we may be required to settle such shares in cash and our operations may be materially harmed*."

| | Series A Preferred Stock Issued and Outstanding | Common Stock (as converted) |
|---|---|---|
| Asset Acquisition | 364,887 | 364,887,000 |
| Financing | 721,452 | 721,452,000 |
| Total | 1,086,339 | 1,086,339,000 |

***Description of Series A Preferred Stock***

***Conversion.*** Following stockholder approval of this Proposal No. 1, effective as of 5:00 p.m. (Eastern time) on the third business day after the date on which such stockholder approval is received, each share of Series A Preferred Stock will automatically convert into 1,000 shares of Common Stock, subject to certain beneficial ownership limitations, including that a holder of Series A Preferred Stock is prohibited from converting shares of Series A Preferred Stock into shares of Common Stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (initially set by the holder to a number up to 19.9% and thereafter adjusted) of the total number of shares of Common Stock issued and outstanding immediately after giving effect to such conversion.

***Voting Rights.*** Except as otherwise required by law (e.g. voting on a change to the authorized shares of Series A Non-Voting Preferred Stock or the rights of such shares as required by Delaware General Corporation Law) and the Certificate of Designation, the Series A Preferred Stock does not have voting rights. However, as long as any shares of Series A Preferred Stock are outstanding, we will not, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series A Preferred Stock, (a) alter or change adversely the powers,

preferences or rights given to the Series A Preferred Stock, or alter or amend the Certificate of Designation, amend or repeal any provision of, or add any provision to, the Certificate of Incorporation or our Bylaws, or file any articles of amendment, certificate of designations, preferences, limitations and relative rights of any series of our preferred stock, if such action would adversely alter or change the preferences, rights, privileges or powers of, or restrictions provided for the benefit of the Series A Preferred Stock, regardless of whether any of the foregoing actions shall be by means of amendment to the Certificate of Incorporation or by merger, consolidation, recapitalization, reclassification, conversion or otherwise, (b) issue further shares of Series A Preferred Stock or increase or decrease (other than by conversion) the number of authorized shares of Series A Preferred Stock, (c) prior to the stockholder approval of the Conversion Proposal or at any time while at least 30% of the originally issued Series A Preferred Stock remains issued and outstanding, consummate either (A) any Fundamental Transaction (as defined in the Certificate of Designation) or (B) any merger or consolidation of the Company or other business combination in which our stockholders immediately before such transaction do not hold at least a majority of our capital stock immediately after such transaction, or (d) enter into any agreement with respect to any of the foregoing.

***Dividends.*** Holders of Preferred Stock are entitled to receive dividends on shares of Series A Preferred Stock equal, on an as-if-converted-to-Common-Stock basis, and in the same form as dividends actually paid on shares of the Common Stock.

***Liquidation and Dissolution.*** The Series A Preferred Stock ranks on parity with Common Stock upon any liquidation, dissolution or winding-up of Aeglea.

***Reasons for Stockholder Approval.*** Our Common Stock is listed on The Nasdaq Capital Market, and, as such, we are subject to the applicable rules of the Nasdaq Stock Market LLC, including Nasdaq Listing Rule 5635(a), which requires stockholder approval in connection with the acquisition of another company if the Nasdaq-listed company will issue more than 20% of its common stock. For purposes of Nasdaq Listing Rule 5635(a), the issuance of any Common Stock in the Transactions would be aggregated together. Thus, in order to permit the issuance of Common Stock upon conversion of the Series A Preferred Stock, we must first obtain stockholder approval of this issuance.

***Beneficial Ownership Limitations.*** We are not seeking stockholder approval of a potential "change in control" under Nasdaq Listing Rule 5635(b), which generally prohibits Nasdaq-listed companies from issuing common stock to a stockholder in a transaction that would cause the holder to beneficially own more than 20% of the then-outstanding common stock (subject to certain exceptions). Assuming that Proposal No. 1 is approved, the Series A Preferred Stock will continue to have a beneficial ownership conversion limit that would prevent a stockholder from converting its shares if, as a result of such conversion, it would beneficially own a number of shares above its applicable conversion blocker (which cannot exceed 19.9% of the outstanding Common Stock).

***Interests of Certain Parties.*** Certain funds managed by Fairmount are a stockholder of us and were a stockholder of Spyre. As described in the Current Report on Form 8-K filed by us with the SEC on June 23, 2023, in connection with the Transactions, Peter Harwin and Tomas Kiselak were appointed as our directors. Messrs. Harwin and Kiselak are also managing members of Fairmount. In connection with the Transactions, these Fairmount-managed entities received the same consideration received by other holders of other Spyre securities.

**Vote Required; Recommendation of Board of Directors**

Stockholder approval of this Proposal No. 1 requires a "FOR" vote from the holders of a majority of votes properly cast at the Special Meeting (subject to the separate tabulation of votes described in "*How many votes can be cast by all stockholders?*" set forth above).

**THE BOARD OF DIRECTORS RECOMMENDS THAT OUR STOCKHOLDERS VOTE "FOR" THE APPROVAL OF, UNDER APPLICABLE NASDAQ LISTING RULES, THE ISSUANCE OF SHARES OF COMMON STOCK UPON CONVERSION OF THE SERIES A PREFERRED STOCK.**

## PROPOSAL NO. 2:
## APPROVAL OF AMENDMENT AND RESTATEMENT OF THE AEGLEA BIOTHERAPEUTICS, INC. 2016 EQUITY INCENTIVE PLAN

### Overview

The Aeglea BioTherapeutics, Inc. 2016 Equity Incentive Plan was originally adopted by the Board of Directors in December 2015 and subsequently approved by our stockholders in December 2015. The 2016 Equity Incentive Plan became effective in April 2016 as the successor to the Aeglea BioTherapeutics, Inc. 2015 Equity Incentive Plan (the "2015 Plan") in connection with our initial public offering. The material terms of the 2016 Equity Incentive Plan were reapproved by our stockholders on June 7, 2017. On October 8, 2018, our stockholders approved an amendment and restatement of the 2016 Equity Incentive Plan. We refer to the 2016 Equity Incentive Plan, as amended and restated on October 8, 2018, which is Aeglea's current equity incentive plan, as the "2016 Plan."

The 2016 Plan currently provides that the number of shares reserved for issuance thereunder automatically increases on each January 1 by 4% of the number of issued and outstanding shares of Common Stock on December 31 of the preceding calendar year, through 2028 (the "Evergreen Provision"), unless the Board of Directors determines to increase the share pool by a smaller number of shares.

The Board of Directors has determined that it is in the best interests of us and our stockholders to seek stockholder approval of an amendment and restatement our 2016 Plan (the "A&R 2016 Plan"). The following is a summary of the key changes to the 2016 Plan, as proposed to be amended and restated hereby. This summary, however, does not purport to be a complete description of all of the provisions of the A&R 2016 Plan and is qualified in its entirety by reference to the full text of the A&R 2016 Plan which is attached as Annex B to this proxy statement:

- ☐ Provide for an increase in the number of shares of Common Stock reserved for issuance thereunder by shares.
- ☐ Revise the annual limit on non-employee director compensation from 100,000 shares to (a) $750,000 in total value or (b) $1,000,000 in the year of the director's initial service as a non-employee director or in any year a director serves as chairman of the Board of Directors, in either case, applicable to fees paid in both cash and equity.
- ☐ Remove the fixed termination date of the 2016 Plan.
- ☐ Revise the Evergreen Provision from 4% to 5% of issued and outstanding shares of Common Stock on December 31 of the preceding calendar year and to include shares issuable upon exercise of pre-funded warrants in the calculation.

The Board of Directors adopted the A&R 2016 Plan, subject to approval by our stockholders. If the proposed A&R 2016 Plan is not approved, the 2016 Plan will remain as-is and the stock options contingent on the approval of the A&R 2016 Plan, as described below under "New Plan Benefits," will never become exercisable.

The closing price of our Common Stock, as reported on Nasdaq as of July 12, 2023, the latest practicable date prior to the filing of this proxy statement, was $0.55.

### Reasons for the Amendment and Restatement of the 2016 Plan

We are asking our stockholders to approve the A&R 2016 Plan because, among other things, we believe that the A&R 2016 Plan is in the best interests of us and our stockholders because of the continuing need to grant equity awards to attract and retain qualified personnel and to respond to relevant market changes in equity compensation practices. If our stockholders do not approve the A&R 2016 Plan, we will be limited in our ability to continue to issue awards under the 2016 Plan in numbers sufficient to attract and motivate the highly skilled employees we need to recruit and retain.

Equity compensation is a critical element of our compensation program. Offering a broad-based equity compensation program is vital to attracting and retaining highly skilled people in the highly competitive life sciences industry. We use equity awards to provide increased incentives to the eligible employees, non-employee directors and consultants who provide significant services to us and our affiliates. We believe that providing an equity stake in the future success of our business encourages our employees to be highly motivated to achieve our long-term business goals and to increase stockholder value. Their innovation and productivity are critical to our success. Accordingly, approving the A&R 2016 Plan is in the best interest of our stockholders because equity awards help us to:

- ☐ attract, motivate and retain talented employees, directors and consultants;
- ☐ align the interests of employees, non-employee directors and consultants with stockholder interests; and
- ☐ link employee compensation to Company performance.

We strongly believe that approval by stockholders of the A&R 2016 Plan will enable us to achieve our goals in attracting and retaining our most valuable asset: our employees.

Without stock options, restricted stock units ("RSUs") or other forms of equity incentives, we would be forced to consider cash replacement alternatives to provide a market-competitive total compensation package necessary to attract, retain and motivate the employee talent critical to our future successes. These cash replacement alternatives could, among other things, reduce the cash available for investment in growth and development and cause a loss of motivation by employees to achieve superior performance over a longer period of time. Equity-based awards also directly align a portion of the compensation of our employees, non-employee directors and consultants with the economic interests of our stockholders. If this Proposal No. 2 is not approved by our stockholders, we believe our ability to attract and retain the talent we need to compete in our industry would be adversely impacted, and this could affect our long-term success.

**Summary of the A&R 2016 Plan**

The following is a summary of the principal provisions of the A&R 2016 Plan. This summary, however, does not purport to be a complete description of all of the provisions of the A&R 2016 Plan and is qualified in its entirety by reference to the full text of the A&R 2016 Plan which is attached as Annex B to this proxy statement.

*Share Reserve.* As of July 12, 2023, the number of shares of Common Stock reserved for issuance under the 2016 Plan was 13,439,116 shares, of which 5,387,751 shares remained available for issuance. The Evergreen Provision currently provides that the number of shares reserved for issuance under the 2016 Plan automatically increases on each January 1 by 4% of the number of issued and outstanding shares of Common Stock on December 31 of the preceding calendar year, through 2028, unless our board of directors determines to increase the share pool by a smaller number of shares.

The following shares will be available for grant and issuance under the A&R 2016 Plan: the sum of (a) 5,387,751 shares, inclusive of shares initially reserved under the 2016 Plan in connection with our initial public offering, shares added to the 2016 Plan share reserve between the time of our initial public offering and the Special Meeting as a result of the 2018 amendment and restatement and the Evergreen Provision, (b) an additional shares to be added to the reserve on the date of the Special Meeting, provided stockholder approval of the A&R 2016 Plan is obtained, which includes 68,000,955 shares reserved for stock options issued contingent upon stockholder approval of the A&R 2016 Plan as described below under "New Plan Benefits," and (c) any shares subject to awards or issued under the 2015 Plan that return to the share reserve due to forfeitures, repurchases, or that are used or withheld to pay the exercise price of an option or to satisfy tax withholding obligations, less any shares that are issued under the 2016 Plan on or prior to, or subject to outstanding awards as of, the date of the Special Meeting.

The Evergreen Provision under the A&R 2016 Plan provides for an automatic increase in the number of shares reserved for issuance thereunder on January 1 of each year from 2024 through 2028 equal to (a) 5.0% of the aggregate number of issued and outstanding shares of Common Stock (inclusive of shares issuable upon exercise of any outstanding pre-funded warrants) on December 31 of the immediately preceding year, or (b) a lesser amount as approved by the Board of Directors each year.

In addition, the following shares are available for grant and issuance under the A&R 2016 Plan: (i) shares subject to options or stock appreciation rights ("SARs") granted under the A&R 2016 Plan that cease to be subject to the option or SAR for any reason other than exercise of the option or SAR; (ii) shares subject to awards granted under the A&R 2016 Plan that are subsequently forfeited or repurchased by us at the original issue price; (iii) shares subject to awards granted under the A&R 2016 Plan that otherwise terminate without shares being issued; (iv) shares surrendered pursuant to an exchange program as defined in the A&R 2016 Plan; and (v) shares subject to awards under the A&R 2016 Plan that are used to pay the exercise price of an option or withheld to satisfy the tax withholding obligations related to any award. Awards under the 2016 Plan settled in cash or other property rather than shares do not reduce the amount of shares available under the 2016 Plan.

*Plan Limits.* No more than shares will be issued pursuant to the exercise of incentive stock options ("ISOs"). Further, the aggregate value of all compensation (cash and equity-based) to be granted or paid in each fiscal year to each non-employee member of the Board of Directors for service as a non-employee director will not exceed (x) $750,000 in total value or (y) $1,000,000 in the fiscal year in which an individual first begins providing services as a non-employee director or in any fiscal year in which an individual is serving as chairman of the Board of Directors, calculating the value of any equity awards based on the grant date fair value of such awards for financial reporting purposes.

*Administration.* The A&R 2016 Plan is administered by the compensation committee of the Board of Directors, all of the members of which are non-employee directors, or by the Board of Directors acting in place of our compensation committee (as applicable, the "Plan Administrator"). The Plan Administrator has, among others, the authority to construe and interpret the A&R 2016 Plan, grant awards and make all other determinations necessary or advisable for the administration of the A&R 2016 Plan, and has full power to implement and carry out the A&R 2016 Plan, except that the Board of Directors will establish the terms of the grant of any awards to non-employee directors.

*Eligibility.* The A&R 2016 Plan provides for the grant of awards to eligible employees, directors, consultants, independent contractors and advisors, provided the consultants, independent contractors, directors and advisors render bona fide services not in connection with the offer and sale of securities in a capital-raising transaction. ISOs may be granted only to employees. As of July 12, 2023, approximately 14 employees, seven non-employee directors, and one consultant would be eligible to participate in the A&R 2016 Plan.

*Award Types.* The A&R 2016 Plan provides for the grant of awards in the form of stock options, restricted stock awards ("RSAs"), stock bonus awards ("Stock Bonus Awards"), SARs, RSUs and performance awards ("Performance Awards").

- *Stock Options.* A stock option is a right to purchase a share of Common Stock, subject to certain conditions, if applicable. The exercise price of stock options must be at least equal to the fair market value of the Common Stock on the date of grant. Stock options may vest based on time or achievement of performance conditions, or a combination of both. Stock options may be vested and exercisable within the times or upon the conditions as set forth in the award agreement and the Plan Administrator may provide for stock options to become exercisable at one time or from time to time, periodically or otherwise, in such number of shares or percentage of shares as it determines. The maximum term of options granted under the A&R 2016 Plan is ten years.

- *Restricted Stock Awards.* An RSA is a grant of Common Stock subject to restrictions, which may vest based on time or achievement of performance conditions. Unless otherwise determined by the Plan Administrator at the time of award, vesting will cease on the date the participant no longer provides services to us and unvested shares will be forfeited to or repurchased by us.

- *Stock Bonus Awards*. Stock bonuses may be granted as additional compensation for service or performance and, therefore, will not be issued in exchange for cash.

- *Stock Appreciation Rights.* SARs provide for a payment, or payments, in cash or shares of Common Stock, to the holder based upon the difference between the fair market value of the Common Stock on the date of exercise and the stated exercise price multiplied by the number of shares subject to the SAR. SARs may vest based on time or achievement of performance conditions.

- *Restricted Stock Units.* RSUs represent the right to receive shares of Common Stock (or cash equal to the fair market value thereof) at a specified date in the future, subject to forfeiture of that right because of failure to achieve vesting conditions. If an RSU has not been forfeited, then on the date specified in the RSU agreement, we will deliver to the holder of the RSU whole shares of Common Stock (which may be subject to additional restrictions), cash or a combination thereof.

- *Performance Awards.* A Performance Award is an award of a cash bonus or a number of shares of Common Stock that may be settled upon achievement of the pre-established performance goals in cash or by issuance of the underlying shares. The Plan Administrator may establish performance goals applicable to grants of Performance Awards but may also subject any other awards under the A&R 2016 Plan to the achievement of performance goals.

*Capitalization Adjustments.* If the number of outstanding shares of Common Stock is changed by a change in our capital structure without consideration, such as a stock split, proportionate adjustments will be made to the number of shares reserved under the A&R 2016 Plan, the exercise prices of and number of shares subject to outstanding stock options and SAR awards, the number of shares subject to other outstanding awards and the maximum number of shares that may be issued upon the exercise of ISOs, subject to any required action by the Board of Directors or our stockholders and in compliance with applicable securities laws.

*Transferability*. Awards granted under the A&R 2016 Plan may not be transferred in any manner other than by will or by the laws of descent and distribution or as determined by the Plan Administrator. Unless otherwise permitted by the Plan Administrator, stock options may be exercised during the lifetime of the optionee only by the optionee or the optionee's guardian or legal representative.

*Effect of Change in Control.* The A&R 2016 Plan provides that in the event of specified types of acquisitions, mergers or consolidations, a sale or other disposition of all or substantially all of our assets, a corporate transaction or a change in the effective control of the Company that occurs on the date that a majority of our directors are replaced during any 12-month period by directors whose appointment or election is not endorsed by a majority of the directors prior to the date of the appointment or election: (a) outstanding awards under the A&R 2016 Plan may be continued if the Company is the successor entity, (b) outstanding awards under the A&R 2016 Plan may be assumed by any surviving or acquiring corporation; (c) outstanding awards under the A&R 2016 Plan may be substituted by the surviving or acquiring corporation for similar awards; (d) the exercise or vesting of outstanding awards under the A&R 2016 Plan may fully or partially accelerate, expiration of such awards may accelerate and our right to repurchase or re-acquire shares acquired under an award may lapse and forfeiture rights with respect to such shares may lapse; (e) outstanding awards may be settled for the full value of such outstanding award (whether or not then vested or exercisable) in cash, cash equivalents, or securities of the successor entity with a fair market value equal to the required amount followed by the cancellation of such awards, provided that payment may be deferred until the date or dates the award would have become exercisable or vested; or (f) outstanding awards may be terminated for no consideration. The Board of Directors shall have full power to assign our right to repurchase or re-acquire or forfeiture rights to such successor or acquiring corporation. Awards need not be treated similarly in a corporate transaction.

The Plan Administrator has the discretion to provide that a stock award under the A&R 2016 Plan will immediately vest as to all or any portion of the shares subject to the stock award at the time of a corporate transaction or in the event a participant's service with us or a successor entity is terminated actually or constructively within a designated period following the occurrence of the transaction. Stock awards held by participants under the A&R 2016 Plan will generally not vest automatically on such an accelerated basis unless specifically provided in the participant's applicable award agreement. However, following a corporate transaction, 100% of the shares subject to an award held by an employee shall become vested if the holder is subject to an involuntary termination within 12 months after the corporate transaction, subject to certain release requirements. In addition, in the event of a corporate transaction, the vesting of all awards granted to non-employee directors shall accelerate and such awards shall become exercisable (as applicable) in full prior to the consummation of the corporate transaction at such times and on such conditions as the Plan Administrator determines.

*Amendment and Termination.* The Board of Directors may amend, suspend or terminate our 2016 Plan at any time, which must be subject to approval of our stockholders for any amendment that requires stockholder approval. No awards may be granted under the A&R 2016 Plan while the A&R 2016 Plan is suspended or after it is terminated. No ISOs may be granted after , 2033.

**Federal Income Tax Consequences**

The following is a brief summary of the federal income tax consequences applicable to awards granted under the A&R 2016 Plan based on federal income tax laws in effect on the date of this proxy statement. This summary is not intended to be exhaustive and does not address all matters that may be relevant to a particular participant. The summary does not discuss the tax laws of any state, municipality, or foreign jurisdiction, or the gift, estate, excise, payroll, or other tax laws other than federal income tax law. This summary does not discuss the impact of Section 280G of the Code governing parachute payments or Section 409A of the Code governing nonqualified deferred compensation plans. The following is not intended or written to be used, and cannot be used, for the purposes of avoiding taxpayer penalties. Because circumstances may vary, we advise all participants to consult their own tax advisors under all circumstances.

*Stock Options and Stock Appreciation Rights*. A recipient of a stock option or SAR will not recognize taxable income upon the grant of those awards. For NSOs and SARs, the participant will recognize ordinary income upon exercise in an amount equal to the difference between the fair market value of the shares and the exercise price on the date of exercise. Any gain or loss recognized upon any later disposition of the shares generally will be a capital gain or loss. The acquisition of shares upon exercise of an ISO will not result in any taxable income to the participant, except, possibly, for purposes of the alternative minimum tax. The gain or loss recognized by the participant on a later sale or other disposition of such shares will either be long-term capital gain or loss or ordinary income, depending upon whether the participant holds the shares for the legally required period (currently more than two years from the date of grant and more than one year from the date of exercise). If the shares are not held for the legally required period, the participant will recognize ordinary income equal to the lesser of (i) the difference between the fair market value of the shares on the date of exercise and the exercise price, or (ii) the difference between the sales price and the exercise price. Any additional gain recognized on the sale generally will be short-term or long-term capital gain. Different and complex rules may apply to incentive stock options that are early exercisable, and we encourage participants holding such any such awards to seek the advice of their own tax counsel.

*Restricted Stock Awards*. For RSAs, unless vested or the recipient elects under Section 83(b) of the Code to be taxed at the time of grant or purchase, the recipient will not have taxable income upon the grant, but will recognize ordinary income upon vesting equal to the fair market value of the shares at the time of vesting less the amount paid for such shares (if any). Any gain or loss recognized upon any later disposition of the shares generally will be a capital gain or loss.

*Restricted Stock Units*. A holder of an RSU does not recognize taxable income when the RSU is granted. When vested RSUs (and dividend equivalents, if any) are settled and distributed, the participant will recognize ordinary income equal to the amount of cash and/or the fair market value of shares received less the amount paid for such stock units (if any).

*Stock Bonus Awards*. The tax effects of stock bonus awards will vary depending on the type, terms and conditions of those awards.

*Performance Awards*. No income generally will be recognized upon the grant of a performance award. Upon payment in respect of a performance award, the recipient generally will be required to include as taxable ordinary income in the year of receipt an amount equal to the amount of cash received and the fair market value of any non-restricted shares of Common Stock or other property received.

*Impact of Section 162(m)*. Section 162(m) of the Code generally disallows public companies a tax deduction for federal income tax purposes of remuneration in excess of $1 million paid to certain executive officers. While our compensation committee may consider the deductibility of awards as one factor in determining executive compensation, our compensation committee also looks at other factors in making its decisions and retains the flexibility to award compensation that it determines to be consistent with the goals of our executive compensation program even if the awards are not deductible by us for tax purposes.

**New Plan Benefits**

In general, awards to executive officers, other employees and consultants are made at the discretion of the Plan Administrator. As a result, except as specifically described below, the benefits and amounts that will be received or allocated under the A&R 2016 Plan are not determinable at this time. The Board of Directors has approved certain awards under the 2016 Plan that are contingent on stockholder approval of this Proposal No. 2. These grants are set forth in the following table. If our stockholders do not approve this Proposal No. 2, these grants will not become exercisable.

| Name and Position | Number of Options |
|---|---|
| Jonathan Alspaugh, President and Chief Financial Officer | 19,787,969(1) |
| Jeffrey M. Goldberg, Former President and Chief Executive Officer | — |
| Jim Kastenmayer, Former General Counsel, Corporate Secretary and Former Interim Chief Executive Officer | — |
| Anthony G. Quinn, M.B Ch.B, Ph.D., Former President and Chief Executive Officer | — |
| Leslie Sloan, Ph.D., Former Chief Operating Officer | — |
| All current executive officers as a group (2 persons)(2) | 19,787,969(1) |
| All current non-employee directors as a group (7 persons)(2) | 13,650,000(1) |
| All current employees, including all current officers who are not executive officers, as a group(2) | 34,562,9861) |

(1) Mr. Alspaugh, each member of the Board of Directors and certain other employees of the Company received awards of stock options under the 2016 Plan that are contingent on stockholder approval of this Proposal No. 2. The contingent stock options have a per share exercise price of $0.30 and expire on June 22, 2033, the 10th anniversary of the date of grant. The contingent stock options granted to Mr. Alspaugh and certain other employees of the Company generally vest in equal monthly installments over four years, and the contingent stock options granted to the non-employee directors of the Company vest in equal monthly installments over 12 months.

(2) As of July 12, 2023.

**Aggregate Past Grants of Stock Options Under the 2016 Plan**

As of July 12, 2023, awards of stock options covering a total of 6,244,498 shares of Common Stock, excluding the contingent stock options described above, have been granted under the 2016 Plan since its effectiveness in April 2016. The following table shows information regarding the grant of such stock options (regardless of whether subsequently exercised or forfeited) to the persons and groups identified below.

| Name and Position | Number of Options |
|---|---|
| Jonathan Alspaugh, President and Chief Financial Officer | 860,000 |
| Jeffrey M. Goldberg, Former President and Chief Executive Officer | — |
| Jim Kastenmayer, Former General Counsel, Corporate Secretary and Interim Chief Executive Officer | 745,000 |
| Anthony G. Quinn, M.B Ch.B, Ph.D., Former President and Chief Executive Officer | 2,115,539 |
| Leslie Sloan, Ph.D., Former Chief Operating Officer | 833,000 |
| All current executive officers as a group (2 persons)(2) | 860,000 |
| All current non-employee directors as a group (7 persons)(2) | 599,209 |
| All current employees, including all current officers who are not executive officers, as a group(2) | 1,091,750 |

**Equity Compensation Plan Information**

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

| Plan Category | Number of securities to be issued upon exercise of outstanding options, warrants and rights (#) (a) | Weighted-average exercise price of outstanding options, warrants and rights ($) (b) | Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (#) (c) |
|---|---|---|---|
| Equity compensation plans approved by security holders | 7,931,209(1) | 5.22 | 3,019,736(2) |
| Equity compensation plans not approved by security holders | 2,195,838 | 2.12 | 789,000(3) |
| **Total** | **10,127,047** | **4.55** | **3,808,736** |

(1) Includes our 2015 Plan and 2016 Plan.

(2) Includes 1,216,647 shares that remain available for purchase under the 2016 Employee Stock Purchase Plan and 1,803,089 shares of Common Stock that remain available for grant under the 2016 Plan. There are no shares of Common Stock available for issuance under our 2015 Plan, but the plan continues to govern the terms of stock options granted thereunder. Any shares of Common Stock that are subject to outstanding awards under the 2015 Plan that are issuable upon the exercise of stock options that expire or become unexercisable for any reason without having been exercised in full will generally be available for future grant and issuance under our 2016 Plan. In addition, the 2016 Plan currently provides for an automatic increase in the number of shares reserved for issuance thereunder on January 1 of each year for the remaining term of the plan equal to (a) 4% of the number of issued and outstanding shares of Common Stock on December 31 of the immediately preceding year, or (b) a lesser amount as approved by the board each year. Pursuant to this provision, the number of shares reserved for grant and issuance under our 2016 Plan increased by 2,614,013 shares on January 1, 2023. Also, the 2016 Employee Stock Purchase Plan provides for an automatic annual increase in the number of shares reserved for issuance thereunder on January 1 of each year for the remaining term of the plan equal to (a) 1% of the number of issued and outstanding shares of Common Stock on December 31 of the immediately preceding year, or (b) a lesser amount as approved by the board each year. Pursuant to this provision, the number of shares reserved for grant and issuance under our 2016 Employee Stock Purchase Plan increased by 653,503 shares on January 1, 2023.

(3) Reflects shares of Common Stock that remain available for grant under the 2018 Equity Inducement Plan (the "2018 Plan"). On June 22, 2023, the shares authorized for grant under the 2018 Equity Inducement Plan was increased to 71,000,000 shares.

**Certain Interests of Directors**

In considering the recommendation of our board of directors with respect to the approval of the A&R 2016 Plan, stockholders should be aware that the members of the Board of Directors have certain interests that may present them with conflicts of interest in connection with such proposal. As discussed above, directors are eligible to receive awards under the A&R 2016 Plan. The Board of Directors recognizes that approval of this proposal may benefit our directors and their successors.

**THE BOARD OF DIRECTORS RECOMMENDS A VOTE "FOR" THE APPROVAL OF THE AMENDMENT AND RESTATEMENT OF THE AEGLEA BIOTHERAPEUTICS, INC. 2016 EQUITY INCENTIVE PLAN**

## PROPOSAL NO. 3:
## APPROVAL OF AMENDMENT OF CERTIFICATE OF INCORPORATION

***Overview***

Our Certificate of Incorporation currently authorizes the issuance of 500,000,000 shares of Common Stock and 10,000,000 shares of our Preferred Stock. On July 12, 2023, we had 97,457,166 shares of Common Stock and 1,086,339 shares of Preferred Stock issued and outstanding. In addition, we have reserved (A) (i) no shares of Common Stock for issuance under our 2013 Equity Incentive Plan, as amended (the "2013 Plan"), of which no shares have been reserved for issuance upon settlement of Company restricted stock units granted and outstanding under the 2013 Plan and no shares remain available for future issuance pursuant to the 2013 Plan, (ii) 492,447 shares of Common Stock for issuance under the 2015 Plan, of which 492,447 shares have been reserved for issuance upon exercise of Company options granted and outstanding under the 2015 Plan and no shares remain available for future issuance pursuant to the 2015 Plan, (iii) 13,439,116 shares of Common Stock for issuance under the 2016 Plan, of which 8,051,365 shares have been reserved for issuance upon exercise of stock options granted and outstanding under the 2016 Plan and 5,387,751 shares remain available for future issuance under the 2016 Plan, (iv) 71,100,000 shares of Common Stock for issuance under the 2018 Plan, of which 63,723,415 shares have been reserved for issuance upon exercise of stock options granted and outstanding under the 2018 Plan and 7,376,585 shares remain available for future issuance pursuant to the 2018 Plan, (v) 667,546 shares of Common Stock for issuance pursuant to our CEO Inducement Grant (the "2022 Inducement Grant"), of which 667,546 shares have been reserved for issuance upon exercise of stock options granted and outstanding pursuant to the 2022 Inducement Grant and no shares remain available for future issuance pursuant to the 2022 Inducement Grant, (B) 1,825,334 shares of Common Stock for future issuance pursuant to our 2016 Employee Stock Purchase Plan and (C) 9,870,386 shares of Common Stock for issuance upon the exercise of 9,870,386 pre-funded warrants to acquire shares of Common Stock, all of which remain subject to exercise in exchange for Common Stock, and (vi) 3,046,775 shares of Common Stock for issuance under the Spyre 2023 Equity Incentive Plan, as amended and assumed by us (the "Spyre Plan"), of which 68,365 shares have been reserved for issuance upon exercise of stock options previously granted and currently outstanding under the Spyre Plan, and 2,978,410 shares of Common Stock remaining available for future issuance of awards pursuant to the Spyre Plan. Subject to stockholder approval, each share of Preferred Stock is convertible into 1,000 shares of Common Stock. See "*Proposal No. 1 – Approval of Conversion Proposal.*"

The Board of Directors has unanimously approved, subject to stockholder approval, an amendment to our Certificate of Incorporation to effect an increase the number of authorized shares of Common Stock from 500,000,000 to (the "Authorized Share Increase"). The Board of Directors has not approved an increase in the shares of Preferred Stock. The additional shares of Common Stock authorized by the Authorized Share Increase, if and when issued, would have the same rights and privileges as the shares of Common Stock previously authorized. A copy of the certificate of amendment for the Authorized Share Increase (the "Certificate of Amendment") to the Certificate of Incorporation is attached hereto as Annex A.

The Board of Directors has recommended that the proposed Certificate of Amendment for the Authorized Share Increase be presented to our stockholders for approval.

***Reasons for Stockholder Approval***

On the record date, shares of our Common Stock were outstanding, out of the 500,000,000 authorized in our Certificate of Incorporation. The additional shares of Common Stock authorized by the Authorized Share Increase could be issued at the discretion of the Board of Directors from time to time for any proper corporate purpose, including, without limitation, the acquisition of other businesses, the raising of additional capital for use in our business, including in connection with the issuance and exercise of warrants, a split of or dividend on then outstanding shares or in connection with any employee stock plan or program. Except to the extent required by applicable law or regulation, any future issuances of authorized shares of Common Stock may be approved by

the Board of Directors without further action by the stockholders. The availability of additional shares of Common Stock would be particularly important in the event that the Board of Directors needs to undertake any of the foregoing actions on an expedited basis in order to avoid the time and expense of seeking stockholder approval in connection with the contemplated issuance of Common Stock, where such approval might not otherwise be required.

Although the Board of Directors will issue Common Stock only when required or when the Board of Directors considers such issuance to be in our best interests, the issuance of additional Common Stock may, among other things, have a dilutive effect on the earnings per share (if any) and on the equity and voting rights of our existing stockholders.

Additionally, the presence of such additional authorized but unissued shares of Common Stock could discourage unsolicited business combination transactions which might otherwise be desirable to stockholders. While it may be deemed to have potential anti-takeover effects, the proposed Authorized Share Increase is not prompted by any specific effort or takeover threat currently perceived by management. In addition, we do not have any plans to implement additional measures having anti-takeover effects. The Board of Directors believes that the benefits of providing it with the flexibility to issue shares without delay for any proper business purpose, including as an alternative to an unsolicited business combination opposed by the Board of Directors, outweigh the possible disadvantages of dilution and discouraging unsolicited business combination proposals and that it is prudent and in the best interests of stockholders to provide the advantage of greater flexibility which will result from the Authorized Share Increase.

***Anti-Takeover and Dilutive Effects***

The shares of Common Stock that are authorized but unissued provide the Board of Directors with flexibility to effect, among other transactions, public or private financings, including the issuance and exercise of warrants, acquisitions, stock dividends, stock splits and the granting of equity incentive awards. However, these authorized but unissued shares may also be used by the Board of Directors, consistent with and subject to its fiduciary duties, to deter future attempts to gain control of us or make such actions more expensive and less desirable. The Authorized Share Increase would continue to give our Board of Directors authority to issue additional shares from time to time without delay or further action by the stockholders except as may be required by applicable law or regulations. The Authorized Share Increase is not being recommended in response to any specific effort of which we are aware to obtain control of us, nor does our Board of Directors have any present intent to use the authorized but unissued Common Stock to impede a takeover attempt.

Except for our obligation to issue Common Stock upon the exercise or settlement of outstanding options (including stock options granted under the 2016 Plan contingent on approval of the Equity Compensation Plan Proposal), restricted stock units and warrants, the conversion of the Series A Preferred Stock and the Spyre Option Agreement, we have no specific plan, commitment, arrangement, understanding or agreement, either oral or written, regarding the issuance of Common Stock subsequent to the Authorized Share Increase at this time, and we have not allocated any specific portion of the authorized number of shares to any particular purpose.

***The Authorized Share Increase would Increase our Number of Authorized but Unissued Shares of Stock, which could Negatively Impact a Potential Investor if they Purchased our Common Stock.***

The Authorized Share Increase will increase the number of authorized shares of Common Stock and, as a result, the Board of Directors' ability to issue authorized and unissued shares without further stockholder action. The issuance of additional shares of Common Stock may have a dilutive effect on earnings per share and relative voting power and may cause a decline in the trading price of our Common Stock. We could use the shares that are available for future issuance in dilutive equity financing transactions, or to oppose a hostile takeover attempt or delay or prevent changes in control or changes in or removal of management, including transactions that are favored by a majority of the stockholders or in which the stockholders might otherwise receive a premium for

their shares over then-current market prices or benefit in some other manner. We may seek additional financing in the future. Other than the foregoing potential uses for our shares of Common Stock, we have no existing plans to issue any of the authorized, but unissued and unreserved shares, whether available as a result of the proposed Authorized Share Increase.

Except for our obligation to issue Common Stock upon the exercise or settlement of outstanding options (including stock options granted under the 2016 Plan contingent on approval of the Equity Compensation Plan Proposal), restricted stock units and warrants, the conversion of the Series A Preferred Stock and the Spyre Option Agreement, we have no specific plan, commitment, arrangement, understanding or agreement, either oral or written, regarding the issuance of Common Stock subsequent to the Authorized Share Increase at this time, and we have not allocated any specific portion of the authorized number of shares to any particular purpose.

**Procedure for Effecting the Authorized Share Increase**

When and if the Board of Directors decides to implement the Authorized Share Increase, we will promptly file the Certificate of Amendment with the Secretary of State of the State of Delaware to amend our existing Certificate of Incorporation. The Authorized Share Increase will become effective on the date of filing the Certificate of Amendment. The text of the Certificate of Amendment is set forth in Annex A to this proxy statement. The text of the Certificate of Amendment is subject to modification to include such changes as may be required by the office of the Secretary of State of the State of Delaware and as the Board of Directors deems necessary and advisable to effect the Authorized Share Increase.

The description of the Certificate of Amendment set forth above is qualified in its entirety by reference to the text of the Certificate of Amendment, which is attached as Annex A to this proxy statement.

**Vote Required and Board of Directors Recommendation**

The affirmative vote of a majority of the votes properly cast is required to approve this proposal.

**THE BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS THAT STOCKHOLDERS VOTE "FOR" THE APPROVAL OF THE AMENDMENT OF THE CERTIFICATE OF INCORPORATION.**

## PROPOSAL NO. 4:
## APPROVAL OF ADJOURNMENT OF THE SPECIAL MEETING

### General

If we fail to receive a sufficient number of votes to approve Proposals Nos. 1, 2 and/or 3, we may propose to adjourn or postpone the Special Meeting. We currently do not intend to propose adjournment or postponement at the Special Meeting if there are sufficient votes to approve Proposal No. 1, 2 and 3.

### Vote Required; Recommendation of Board of Directors

The affirmative vote of the holders of a majority of the votes properly cast at the Special Meeting is required for approval of Proposal No. 4 (for the purpose of soliciting additional proxies to approve Proposals No. 1, 2 and/or 3), if a quorum is present at the Special Meeting. If a quorum is not present at the Special Meeting, the affirmative vote of the stockholders holding a majority of the voting power present in person or by proxy at the Special Meeting is required for approval of Proposal No. 4.

**THE BOARD OF DIRECTORS RECOMMENDS THAT OUR STOCKHOLDERS VOTE "FOR" PROPOSAL NO. 4 TO ADJOURN THE SPECIAL MEETING, IF NECESSARY, TO SOLICIT ADDITIONAL PROXIES.**

## OTHER INFORMATION

## DESCRIPTION OF CAPITAL STOCK

### General

Our authorized capital stock consists of 500,000,000 shares of Common Stock, $0.0001 par value per share, and 10,000,000 shares of Preferred Stock, of which 1,086,341 shares have been designated as Series A Preferred Stock, $0.0001 par value per share. The following description summarizes the most important terms of our capital stock. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description, you should refer to our Certificate of Incorporation and Bylaws, which are included as exhibits to our most recent Annual Report on Form 10-K, and to the applicable provisions of Delaware law.

As of July 12, 2023, there were 97,457,166 shares of our Common Stock and 1,086,339 shares of Series A Preferred Stock outstanding.

### Common Stock

***Dividend rights***

Subject to preferences that may apply to any shares of Preferred Stock outstanding at the time, the holders of our Common Stock are entitled to receive dividends out of funds legally available if our Board of Directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our Board of Directors may determine.

***Voting rights***

Holders of our Common Stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders. We have not provided for cumulative voting for the election of directors in our Certificate of Incorporation. Accordingly, pursuant to our Certificate of Incorporation, holders of a majority of the shares of our Common Stock are able to elect all of our directors. Our Certificate of Incorporation establishes a classified board of directors, divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms.

***No preemptive or similar rights***

Our Common Stock is not entitled to preemptive rights, and is not subject to conversion, redemption or sinking fund provisions.

***Right to receive liquidation distributions***

Upon our liquidation, dissolution or winding-up, the assets legally available for distribution to our stockholders would be distributable ratably among the holders of our Common Stock and any participating Preferred Stock outstanding at that time, subject to prior satisfaction of all outstanding debt and liabilities and the preferential rights of and the payment of liquidation preferences, if any, on any outstanding shares of Preferred Stock.

### Preferred Stock

Our Board of Directors is authorized, subject to limitations prescribed by Delaware law, to issue Preferred Stock in one or more series, to establish from time to time the number of shares to be included in each series and to fix the designation, powers, preferences and rights of the shares of each series and any of their qualifications,

limitations or restrictions, in each case without further vote or action by our stockholders. Our Board of Directors can also increase or decrease the number of shares of any series of Preferred Stock, but not below the number of shares of that series then outstanding, without any further vote or action by our stockholders. Our Board of Directors may authorize the issuance of Preferred Stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our Common Stock. The issuance of Preferred Stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in control of our company and might adversely affect the market price of our Common Stock and the voting and other rights of the holders of our Common Stock. We have no current plan to issue any shares of Preferred Stock other than the shares of our Series A Preferred Stock that were issued in connection with the Transactions.

A description of the rights, preferences and privileges of the Series A Preferred Stock is set forth above under the caption, "*Description of Series A Preferred Stock*."

**Registration Rights**

Pursuant to the terms of our Registration Rights Agreement entered into on March 16, 2021 (the "Baker RRA") with Baker Brothers Life Sciences, L.P. and 667, L.P. (together, the "Baker Funds"), following a request by the Baker Funds, we are obligated to file a resale registration statement on Form S-3, or other appropriate form, covering the shares of our Common Stock held by the Baker Funds (the "Baker Registrable Securities"). Under the Baker RRA, the Baker Funds also have the right to up to two underwritten public offerings or block trades in any twelve month period, but not more than three underwritten public offerings and eight block trades in total, to effect the sale or distribution of the Baker Registrable Securities, subject to specified exceptions, conditions and limitations. The Baker RRA also includes customary indemnification obligations in connection with registrations conducted pursuant to the Baker RRA. The rights of the Baker Funds under the Baker RRA terminate automatically upon the earlier to occur of the following events: (i) all Baker Registrable Securities covered by the Baker RRA have been sold pursuant to an effective registration statement; (ii) all Baker Registrable Securities covered by the Baker RRA have been sold pursuant to Rule 144 under the Securities Act, or other similar rule ("Rule 144"); (iii) at any time after the Baker Funds are no longer our affiliate, all Baker Registrable Securities covered by the Baker RRA may be resold by the Baker Funds without limitations as to volume or manner of sale pursuant to Rule 144; or (iv) ten (10) years after the date of the Baker RRA.

Pursuant to the terms of our New RRA, certain of our stock holders are entitled to rights with respect to the registration of their shares (the "New Registrable Securities") under the Securities Act. Pursuant to the New RRA, we are obligated to prepare and file a resale registration statement covering the resale of all of the New Registrable Securities for an offering to be made on a continuous basis pursuant to Rule 415 under the Securities Act on Form S-3 (or, if we are ineligible to register for resale such shares on Form S-3, such other available form) with the SEC by the Filing Deadline. We shall use commercially reasonable efforts to cause this registration statement to be declared effective by the SEC as soon as practicable and no later than 30 calendar days of the Filing Deadline (or within 60 calendar days if the SEC reviews the registration statement) and use commercially reasonable efforts to keep the registration statement continuously effective under the Securities Act until the earlier of (i) such time as all of the registrable securities have been publicly sold by the holders; or (ii) the date that all registrable securities may be sold by non-affiliates without volume or manner-of-sale restrictions pursuant to Rule 144, without the requirement for us to be in compliance with the current public information requirement under Rule 144.

**Anti-Takeover Provisions**

The provisions of Delaware law, our Certificate of Incorporation and our Bylaws could have the effect of delaying, deferring or discouraging another person from acquiring control of our company. These provisions, which are summarized below, may have the effect of discouraging takeover bids. They are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our Board of Directors. We believe

that the benefits of increased protection of our potential ability to negotiate with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging a proposal to acquire us because negotiation of these proposals could result in an improvement of their terms.

***Delaware law***

We are subject to the provisions of Section 203 of the DGCL regulating corporate takeovers. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years following the date on which the person became an interested stockholder unless:

Prior to the date of the transaction, the Board of Directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

The interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, but not the outstanding voting stock owned by the interested stockholder, (1) shares owned by persons who are directors and also officers and (2) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

At or subsequent to the date of the transaction, the business combination is approved by the Board of Directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66.67% of the outstanding voting stock that is not owned by the interested stockholder.

**Certificate of Incorporation and Bylaw Provisions**

Our Certificate of Incorporation and our Bylaws include a number of provisions that could deter hostile takeovers or delay or prevent changes in control of our company, including the following:

***Board of Directors vacancies***. Our Certificate of Incorporation and Bylaws authorize our Board of Directors to fill vacant directorships, including newly created seats unless the Board of Directors determines that any such vacancies shall be filled by the stockholders. In addition, the number of directors constituting our Board of Directors is permitted to be set only by a resolution adopted by a majority vote of our entire Board of Directors. These provisions prevent a stockholder from increasing the size of our Board of Directors and then gaining control of our Board of Directors by filling the resulting vacancies with its own nominees. This makes it more difficult to change the composition of our Board of Directors but promotes continuity of management.

***Classified board***. Our Certificate of Incorporation and Bylaws provide that our Board of Directors is classified into three classes of directors, each with staggered three-year terms. A third party may be discouraged from making a tender offer or otherwise attempting to obtain control of us as it is more difficult and time consuming for stockholders to replace a majority of the directors on a classified board of directors.

***Stockholder action; special meetings of stockholders***. Our Certificate of Incorporation provides that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. As a result, a holder controlling a majority of our capital stock would not be able to amend our Bylaws or remove directors without holding a meeting of our stockholders called in accordance with our Bylaws. Further, our Bylaws provide that special meetings of our stockholders may be called only by a majority of our Board of Directors, the chairperson of our Board of Directors, our Chief Executive Officer or our President, thus

prohibiting a stockholder from calling a special meeting. These provisions might delay the ability of our stockholders to force consideration of a proposal or for stockholders controlling a majority of our capital stock to take any action, including the removal of directors.

***Advance notice requirements for stockholder proposals and director nominations***. Our Bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders or to nominate candidates for election as directors at our annual meeting of stockholders. Our Bylaws also specify certain requirements regarding the form and content of a stockholder's notice. These provisions might preclude our stockholders from bringing matters before our annual meeting of stockholders or from making nominations for directors at our annual meeting of stockholders if the proper procedures are not followed. We expect that these provisions might also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

***No cumulative voting***. The DGCL provides that stockholders are not entitled to the right to cumulate votes in the election of directors unless a corporation's certificate of incorporation provides otherwise. Our Certificate of Incorporation and Bylaws do not provide for cumulative voting.

***Directors removed only for cause***. Our Certificate of Incorporation provides that stockholders may remove directors only for cause.

***Amendment of charter provisions***. Any amendment of the above provisions in our Certificate of Incorporation requires approval by holders of at least two-thirds of our outstanding Common Stock, provided that if two-thirds of our Board of Directors approves such an amendment, then only the approval of a majority of holders is required.

***Issuance of Preferred Stock***. Our Board of Directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of Preferred Stock with rights and preferences, including voting rights, designated from time to time by our Board of Directors. The existence of authorized but unissued shares of Preferred Stock enables our Board of Directors to render more difficult or to discourage an attempt to obtain control of us by merger, tender offer, proxy contest or other means.

***Choice of forum***. Our Certificate of Incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the DGCL, our Certificate of Incorporation or our Bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. In addition, our Bylaws also provide that the federal district courts of the United States is the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act.

**Transfer Agent and Registrar**

The transfer agent and registrar for our Common Stock is American Stock Transfer and Trust Company, LLC. The transfer agent's address is 6201 15th Avenue, Brooklyn, New York 11219, and its telephone number is (800) 937-5449.

**Exchange Listing**

Our Common Stock is listed on The Nasdaq Capital Market under the symbol "AGLE."

## PRINCIPAL STOCKHOLDERS

The following table sets forth information, to the extent known by us or ascertainable from public filings, with respect to the beneficial ownership of our Common Stock as of July 12, 2023 by:

- each of our directors;
- each of our named executive officers;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially owner of greater than 5.0% of our Common Stock.

The column entitled "Shares Beneficially Owned" is based on a total of 97,457,166 shares of our Common Stock outstanding as of July 12, 2023.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our Common Stock. Shares of our Common Stock subject to options that are currently exercisable or exercisable within 60 days of July 12, 2023 are considered outstanding and beneficially owned by the person holding the options for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Due to the conversion limitations on the Series A Preferred Stock, shares of underlying Common Stock have been excluded from beneficial ownership set forth below. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our Common Stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise indicated in the table below, addresses of named beneficial owners are in care of Aeglea BioTherapeutics, Inc., 221 Crescent Street, Building 17, Suite 102B, Waltham, MA 02453.

| | Shares beneficially owned | |
|---|---|---|
| **Name and address of beneficial owner** | **Number** | **Percentage** |
| ***5% Stockholders:*** | | |
| Entities affiliated with Fairmount Funds Management LLC(1) | 9,460,540 | 9.7% |
| Entities affiliated with Venrock Healthcare Capital Partners III, LP(2) | 6,500,000 | 6.7% |
| Entities affiliated with Baker Bros. Advisors LP(3) | 6,384,013 | 6.6% |
| Entities affiliated with Suvretta Capital Management, LLC(4) | 6,376,373 | 6.5% |
| Logos Global Management LP(5) | 6,350,000 | 6.5% |
| BCLS II Equity Opportunities, LP(6) | 5,347,689 | 5.5% |
| Entities affiliated with EcoR1 Capital, LLC(7) | 5,000,000 | 5.1% |
| Entities affiliated with Affinity Healthcare Fund, LP(8) | 4,900,000 | 5.0% |
| ***Named Executive Officers and Directors:*** | | |
| Jonathan Alspaugh(9) | 404,288 | * |
| Jeffrey M. Goldberg(10) | 667,546 | * |
| Jim Kastenmayer(11) | 176,415 | * |
| Anthony G. Quinn, M.B Ch.B, Ph.D.(12) | 2,096,419 | 2.1% |
| Leslie Sloan, Ph.D. | - | * |
| Russell J. Cox(13) | 212,709 | * |
| Hunter C. Smith(14) | 76,333 | * |
| Ivana Magovčević-Liebisch, Ph.D.(15) | 160,300 | * |
| Alison Lawton (16) | 124,955 | * |
| Peter Harwin(17) | - | * |
| Tomas Kiselak(18) | - | * |
| Michael Henderson, M.D.(19) | - | * |
| All current executive officers and directors as a group(6 persons)(20) | 3,121,712 | 3.5% |

* Represents beneficial ownership of less than one percent.

(1) Based on our records and on a Schedule 13D filed by Fairmount Funds Management LLC ("Fairmount Funds Management") on June 30, 2023 with the SEC. Represents shares of Common Stock held by Fairmount Healthcare Fund LP ("Fairmount I") and Fairmount Healthcare Fund II LP (together with Fairmount I, the "Fairmount Funds"), which may be deemed to be indirectly beneficially owned by Fairmount. Fairmount Funds Management serves as investment manager for each of the Fairmount Funds and may be deemed a beneficial owner of any of our securities of held by each of the Fairmount Funds. The general partner of Fairmount Funds Management is Fairmount Funds Management GP LLC ("Fairmount GP"). As managing members of Fairmount GP, Peter Harwin and Tomas Kiselak may be deemed beneficial owners of any of our securities beneficially owned by Fairmount Funds Management. The address of Fairmount is 200 Barr Harbor Drive, Suite 400, West Conshohocken, PA 19428.

(2) Based on our records and on a Schedule 13G filed by Venrock Healthcare Capital Partners III, LP ("VHCP III") on July 10, 2023 with the SEC. Represents shares of Common Stock held by VHCP III, VHCP III Co-Investment Holdings III, LLC ("VHCP III Co") and Venrock Healthcare Capital Partners EG, L.P. ("VHCP EG"). VHCP Management III, LLC ("VHCPM") is the sole general partner of VHCP III and the sole manager of VHCP III Co. VHCP Management EG, LLC ("VHCPM EG") is the sole general partner of VHCP EG. Dr. Bong Koh and Nimish Shah are the voting members of VHCPM and VHCPM EG. The address of each of these persons and entities is 7 Bryant Park, 23rd Floor, New York, NY 10018.

(3) Based on our records and on a Schedule 13G filed by Baker Bros. Advisors LP (the "Baker") on February 14, 2023 with the SEC. Represents shares of Common Stock held by 667, L.P. ("667") and Baker Brothers Life Sciences, L.P. (together with 667, the "Baker Funds"), which may be deemed to be indirectly beneficially owned by Baker. Includes 3,620,386 shares of common stock issuable upon the exercise of pre-funded warrants. Baker Bros. Advisors (GP) LLC ("Baker GP"), Felix J. Baker and Julian C. Baker as managing members of Baker GP, may be deemed to indirectly beneficially own the shares held by Baker and may be deemed to have the sole power to vote or direct the vote of and the power to dispose or direct the disposition of such securities. The address of Baker is 860 Washington Street, 3rd Floor, New York, NY 10014.

(4) Based solely on a Schedule 13G/A filed by Suvretta Capital Management, LLC ("Suvretta") on February 13, 2023 with the SEC. Represents shares of Common Stock directly held by Averill Master Fund, Ltd., which may be deemed to be indirectly beneficially owned by Suvretta and Aaron Cowen, as well as shares of Common Stock issuable upon the exercise of pre-funded warrants. Aaron Cowen has beneficial ownership of such shares by virtue of his role as a control person of Suvretta. The mailing address of (i) Suvretta and Aaron Cowen is 540 Madison Avenue, 7th Floor, New York, NY 10022 and (ii) Averill Master Fund, Ltd. is c/o Maples Corporate Services Limited, P.O. Box 309, Ugland House, Grand Cayman KY1-1104, Cayman Islands.

(5) Based solely on a Schedule 13G filed by Logos Global Management LP ("Logos Global") on July 18, 2023 with the SEC. Represents shares of Common Stock beneficially owned by Logos Global Master Fund LP ("Global Fund"). Logos Global Management LP ("Logos Global") is the investment advisor to Global Fund. Logos Global Management GP LLC ("Logos Global GP") is the general partner of Logos Global. Mr. William is a control person of Logos Global and Logos Global GP. Mr. William disclaims beneficial ownership of these shares, except to the extent of his pecuniary interest in such shares, if any. The principal address of Global Fund is 1 Letterman Drive, Building C, Suite C3-350, San Francisco, CA 94129.

(6) Based solely on a Schedule 13G/A filed by BCLS II Equity Opportunities, LP ("BCLS") on February 14, 2023 with the SEC. Represents shares of Common Stock beneficially owned by BCLS. Bain Capital Life Sciences Investors, LLC, a Delaware limited liability company ("BCLSI"), is the manager of Bain Capital Life Sciences Investors II, LLC, a Cayman limited liability company, which is the general partner of Bain Capital Life Sciences Fund II, L.P., a Cayman exempted limited partnership, which is the manager of BCLS II Equity Opportunities GP, LLC, a Delaware limited liability company, which is the general partner of BCLS. BCLSI may be deemed to share voting and dispositive power with respect to such shares. The address of BCLS is 200 Clarendon Street, Boston, MA 02116.

(7) Based solely on a Schedule 13G filed by EcoR1 Capital, LLC ("EcoR1 Capital") on June 30, 2023 with the SEC. Represents shares of Common Stock held by EcoR1. Oleg Nodelman is the control person of EcoR1 Capital. Mr. Nodelman and EcoR1 Capital each disclaim beneficial ownership of the shares

except to the extent of their pecuniary interest therein. The address of each of EcoR1, EcoR1 Capital, Qualified and Oleg Nodelman is 357 Tehama Street #3, San Francisco, CA 94103.

(8) Based on our records and on a Schedule 13G filed by Affinity Healthcare Fund, LP ("Affinity Fund") on July 3, 2023 with the SEC. Affinity Asset Advisors, LLC (the "Affinity Advisor") is the investment manager of Affinity Fund and exercises investment discretion with regard to the shares of Common Stock owned by Affinity Fund. Affinity Fund and Affinity Advisor have the shared power to vote or to direct the vote and to dispose or direct the disposition of such shares of Common Stock owned by Affinity Fund. Affinity Advisor may be deemed to be the beneficial owner of such shares of Common Stock ownedby Affinity Fund by virtue of its position as investment manager of Affinity Fund. The address of each of these entities is 19 Barn Lane, Bridgehampton, NY 11932.

(9) Represents (i) 171,372 shares of Common Stock held by Mr. Alspaugh and (ii) options exercisable for 232,916 shares of Common Stock within 60 days of July 12, 2023. Does not include stock options issued contingent upon stockholder approval of the A&R 2016 Plan exercisable for an aggregate of 19,787,969 shares of Common Stock.

(10) Represents options exercisable for 667,546 shares of common stock within 60 days of July 12, 2023.

(11) Represents (i) 6,000 shares owned by Mr. Kastenmayer and (ii) options exercisable for 170,415 shares of Common Stock within 60 days of July 12, 2023.

(12) Represents (i) 821,922 shares of Common Stock held by Dr. Quinn and (ii) options exercisable for 1,274,497 shares of Common Stock within 60 days of July 12, 2023.

(13) Represents (i) 7,000 shares of Common Stock held by Mr. Cox and (ii) options exercisable for 205,709 shares of Common Stock within 60 days of July 12, 2023. Does not include stock options issued contingent upon stockholder approval of the A&R 2016 Plan exercisable for an aggregate of 1,950,000 shares of Common Stock.

(14) Represents options exercisable for 76,333 shares of Common Stock within 60 days of July 12, 2023. Does not include stock options issued contingent upon stockholder approval of the A&R 2016 Plan exercisable for an aggregate of 1,950,000 shares of Common Stock.

(15) Represents options exercisable for 160,300 shares of Common Stock within 60 days of July 12, 2023. Does not include stock options issued contingent upon stockholder approval of the A&R 2016 Plan exercisable for an aggregate of 1,950,000 shares of Common Stock.

(16) Represents options exercisable for 124,955 shares of Common Stock within 60 days of July 12, 2023. Does not include stock options issued contingent upon stockholder approval of the A&R 2016 Plan exercisable for an aggregate of 1,950,000 shares of Common Stock.

(17) Does not include stock options issued contingent upon stockholder approval of the A&R 2016 Plan exercisable for an aggregate of 1,950,000 shares of Common Stock.

(18) Does not include stock options issued contingent upon stockholder approval of the A&R 2016 Plan exercisable for an aggregate of 1,950,000 shares of Common Stock.

(19) Does not include stock options issued contingent upon stockholder approval of the A&R 2016 Plan exercisable for an aggregate of 1,950,000 shares of Common Stock.

(20) Represents (i) 755,071 shares of Common Stock and (ii) options exercisable for 2,942,301 shares of Common Stock within 60 days of July 12, 2023. Does not include stock options issued contingent upon stockholder approval of the A&R 2016 Plan exercisable for an aggregate of 68,000,955 shares of Common Stock.

## WHERE YOU CAN FIND ADDITIONAL INFORMATION

We file reports, proxy statements and other information with the SEC as required by the Exchange Act. You can review our electronically filed reports, proxy and information statements on the SEC's website at http://www.sec.gov or on our website at https://www.aeglea.com/. Information included on our web site is not a part of this proxy statement.

You should rely only on the information contained in this proxy statement or on information to which we have referred you. We have not authorized anyone else to provide you with any information. A representative of our independent registered public accounting firm, PricewaterhouseCoopers LLP, is not expected to be present at the

virtual Special Meeting, and will therefore not have an opportunity to make a statement if he or she desires to do so or to respond to appropriate questions from our stockholders.

If you have more questions about this proxy statement or how to submit your proxy, or if you need additional copies of this proxy statement or the enclosed proxy card or voting instructions, please contact our proxy solicitor at:

Stockholders may call toll free: (877) 750-8310

Banks and Brokers may call collect: (212) 750-5833

## HOUSEHOLDING

Some banks, brokers and other nominee record holders may be participating in the practice of "householding" proxy statements and annual reports. This means that only one copy of our proxy statement may have been sent to multiple stockholders in your household. We will promptly deliver a separate copy of the proxy statement to you upon written or oral request to Aeglea BioTherapeutics, Inc., 221 Crescent Street, Building 17, Suite 102B, Waltham, MA 02453, Attention: Secretary, telephone: (617) 651-5940. If you want to receive separate copies of the proxy statement or annual reports to stockholders in the future, or if you are receiving multiple copies and would like to receive only one copy per household, you should contact your bank, broker or other nominee record holder, or you may contact us at the above address and phone number.

## STOCKHOLDER PROPOSALS

### Stockholder Proposals and Director Nominations for Next Year's Annual Meeting

To be considered for inclusion in next year's proxy materials, your proposal must be submitted in writing by December 19, 2023, to our Secretary at 221 Crescent Street, Building 17, Suite 102B, Waltham, MA 02453. If you wish to submit a proposal (including a director nomination) at the meeting that is not to be included in next year's proxy materials, you must do so by no earlier than January 3, 2024, and no later than February 2, 2024. Any nominations for director or any proposal submission must comply with the requirements of our Bylaws. You are also advised to review our Bylaws, which contain additional requirements about advance notice of stockholder proposals and director nominations.

## INFORMATION INCORPORATED BY REFERENCE

Certain information has been "incorporated by reference" into this proxy statement, which means that we have disclosed important information to you by referring you to another document filed separately with the SEC. The documents incorporated by reference into this proxy statement contain important information that you should read about us.

The following documents are incorporated by reference into this proxy statement:

(a) our Annual Report on Form 10-K for the fiscal year ended December 31, 2022, filed with the SEC on March 2, 2023;

(b) our Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, filed with the SEC on May 11, 2023; and

(c) our Current Reports on Form 8-K filed on January 6, 2023, January 18, 2023, March 13, 2023, April 12, 2023, May 19, 2023, June 9, 2023, June 22, 2023, June 23, 2023 (excluding information in Item 7.01 and exhibit 99.1 furnished thereto), July 14, 2023 and July 27, 2023 (excluding information in Item 7.01 and exhibit 99.1 furnished thereto) (in each case, except for information contained therein which is furnished rather than filed).

We are delivering to our stockholders with this proxy statement the aforementioned annual report in accordance with Item 13(b)(2) of Schedule 14A. In addition, all reports and other documents that we subsequently file pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, after the date of this proxy statement and prior to the Special Meeting will be deemed to be incorporated by reference into this proxy statement and to be part of this proxy statement from the date of the filing of such reports and documents. Information in documents that is deemed, in accordance with SEC rules, to be furnished and not filed will not be deemed to be incorporated by reference in this proxy statement. Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes hereof to the extent that a statement contained herein modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this proxy statement.

Documents incorporated by reference are also available, without charge. You may obtain documents incorporated by reference in this proxy statement by requesting them in writing or by telephone at the following address:

Aeglea BioTherapeutics, Inc.
221 Crescent Street
Building 17, Suite 102B
Waltham, MA 02453
(512) 942-2935

THE PROXY STATEMENT DOES NOT CONSTITUTE AN OFFER TO SELL, OR A SOLICITATION OF AN OFFER TO BUY, ANY SECURITIES, OR THE SOLICITATION OF A PROXY, IN ANY JURISDICTION TO OR FROM ANY PERSON TO WHOM IT IS NOT LAWFUL TO MAKE ANY OFFER OR SOLICITATION IN THAT JURISDICTION. THE INFORMATION CONTAINED IN THIS PROXY STATEMENT SPEAKS ONLY AS OF THE DATE INDICATED ON THE COVER OF THIS PROXY STATEMENT UNLESS THE INFORMATION SPECIFICALLY INDICATES THAT ANOTHER DATE APPLIES.

WE HAVE NOT AUTHORIZED ANYONE TO GIVE YOU ANY INFORMATION OR TO MAKE ANY REPRESENTATION ABOUT THE PROPOSALS OR US THAT IS DIFFERENT FROM OR ADDS TO THE INFORMATION CONTAINED IN THIS PROXY STATEMENT OR IN THE DOCUMENTS WE HAVE PUBLICLY FILED WITH THE SEC. WE ARE NOT RESPONSIBLE FOR, AND CAN PROVIDE NO ASSURANCES AS TO THE RELIABILITY OF, ANY INFORMATION OTHER THAN THE INFORMATION CONTAINED OR INCORPORATED BY REFERENCE IN THIS PROXY STATEMENT.

## OTHER MATTERS

Our Board of Directors does not know of any other matters to be brought before the Special Meeting. If any other matters not mentioned in this proxy statement are properly brought before the Special Meeting, the individuals named in the enclosed proxy intend to use their discretionary voting authority under the proxy to vote the proxy in accordance with their best judgment on those matters.

**ANNEX A**

**CERTIFICATE OF AMENDMENT**

**OF**

**CERTIFICATE OF INCORPORATION**

**OF**

**AEGLEA BIOTHERAPEUTICS, INC.**

**AEGLEA BIOTHERAPEUTICS, INC.**, a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "DGCL"), does hereby certify:

**FIRST:** The name of the corporation is Aeglea BioTherapeutics, Inc. (the "Corporation").

**SECOND:** The Corporation was first formed on December 16, 2013 under the name Aeglea BioTherapeutics Holdings, LLC, a Delaware limited liability company. Aeglea BioTherapeutics Holdings, LLC converted into Aeglea BioTherapeutics, Inc. on March 10, 2015. The date of filing of the original Certificate of Incorporation of Aeglea BioTherapeutics, Inc. with the Secretary of State was March 10, 2015 under the name Aeglea BioTherapeutics, Inc.

**THIRD:** The Board of Directors (the "Board") of the Corporation, acting in accordance with the provisions of Sections 141 and 242 of the DGCL, adopted resolutions amending its Certificate of Incorporation as follows:

Section 1 of Article IV of the Certificate of Incorporation, as presently in effect, of the Corporation is hereby amended and restated in its entirety as follows:

"1. **Total Authorized**. The total number of shares of all classes of stock that the Corporation has authority to issue is [•] ([•]) shares, consisting of two classes: [•] ([•]) shares of Common Stock, $0.0001 par value per share ("Common Stock"), and Ten Million (10,000,000) shares of Preferred Stock, $0.0001 par value per share ("Preferred Stock")."

**FOURTH**: Thereafter, pursuant to a resolution by the Board, this Certificate of Amendment was submitted to the stockholders of the Corporation for their approval in accordance with the provisions of Section 211 and 242 of the DGCL. Accordingly, said proposed amendment has been adopted in accordance with Section 242 of the DGCL.

**In Witness Whereof, Aeglea BioTherapeutics, Inc.** has caused this Certificate of Amendment to be signed by its duly authorized officer this _____th day of _____, 202____.

**Aeglea BioTherapeutics, Inc.**

By: _____

Name:

Title:

**ANNEX B**

**AEGLEA BIOTHERAPEUTICS, INC.**
**2016 EQUITY INCENTIVE PLAN**

**AS AMENDED AND RESTATED EFFECTIVE _____, 2023**

**1. PURPOSE**. The purpose of this Plan is to provide incentives to attract, retain and motivate eligible persons whose present and potential contributions are important to the success of the Company, and any Parents, Subsidiaries and Affiliates that exist now or in the future, by offering them an opportunity to participate in the Company's future performance through the grant of Awards. The Plan was originally effective as of the Original Effective Date, was amended and restated as of October 8, 2018 (the "***2018 Amendment and Restatement***") and is hereby amended and restated effective as of the Stockholder Approval Date. Capitalized terms not defined elsewhere in the text are defined in Section 28.

**2. SHARES SUBJECT TO THE PLAN.**

**2.1.** Number of Shares Available. Subject to Sections 2.6 and 21 and any other applicable provisions hereof, the total number of Shares reserved and available for grant and issuance pursuant to this Plan (the "***Share Reserve***") is the sum of (a) 5,387,751 Shares, which is inclusive of Shares initially reserved under the Plan as of the Original Effective Date and Shares added to the Share Reserve between the Original Effective Date and the Stockholder Approval Date as a result of (i) the 2018 Amendment and Restatement and (ii) the "evergreen" provision in Section 2.4 of the Plan, (b) an additional Shares added to the Share Reserve as of the Stockholder Approval Date, and (c) the Prior Plan Returning Shares, less any Shares issued under the Plan on or prior to, or subject to outstanding Awards as of, the Stockholder Approval Date.

**2.2.** Lapsed, Returned Awards. Shares subject to Awards, and Shares issued under the Plan under any Award, will again be available for grant and issuance in connection with subsequent Awards under this Plan to the extent such Shares: (a) are subject to issuance upon exercise of an Option or SAR granted under this Plan but which cease to be subject to the Option or SAR for any reason other than exercise of the Option or SAR; (b) are subject to Awards granted under this Plan that are forfeited or are repurchased by the Company at the original issue price; (c) are subject to Awards granted under this Plan that otherwise terminate without such Shares being issued; or (d) are surrendered pursuant to an Exchange Program. To the extent an Award under the Plan is paid out in cash or other property rather than Shares, such cash payment will not result in reducing the number of Shares available for issuance under the Plan. Shares used to pay the exercise price of an Award or withheld to satisfy the tax withholding obligations related to an Award will become available for future grant or sale under the Plan. For the avoidance of doubt, Shares that otherwise become available for grant and issuance because of the provisions of this Section 2.2 shall not include Shares subject to Awards that initially became available because of the substitution clause in Section 21.2 hereof.

**2.3.** Minimum Share Reserve. At all times the Company shall reserve and keep available a sufficient number of Shares as shall be required to satisfy the requirements of all outstanding Awards granted under this Plan.

**2.4.** Automatic Share Reserve Increase. The number of Shares available for grant and issuance under the Plan shall be increased on January 1, of each of 2024 through 2028, by the lesser of (a) 5% of the number of Outstanding Shares on each December 31 immediately prior to the date of increase or (b) such number of Shares determined by the Board.

**2.5.** Limitations. No more than Shares shall be issued pursuant to the exercise of ISOs.

**2.6.** Adjustment of Shares. If the number of outstanding shares of Common Stock of the Company is changed by a stock dividend, recapitalization, stock split, reverse stock split, subdivision, combination,

reclassification or similar change in the capital structure of the Company, without consideration, then (a) the number of Shares reserved for issuance and future grant under the Plan set forth in Section 2.1, including Shares reserved under sub-clauses (a)-(c) of Section 2.1, (b) the Exercise Prices of and number of Shares subject to outstanding Options and SARs, (c) the number of Shares subject to other outstanding Awards, and (d) the maximum number of Shares that may be issued as ISOs set forth in Section 2.5 shall be proportionately adjusted, subject to any required action by the Board or the stockholders of the Company and in compliance with applicable securities laws; provided that fractions of a Share will not be issued.

**3. ELIGIBILITY**. ISOs may be granted only to Employees. All other Awards may be granted to Employees, Consultants, Directors and Non-Employee Directors; provided such Consultants, Directors and Non-Employee Directors render bona fide services not in connection with the offer and sale of securities in a capital-raising transaction.

**4. ADMINISTRATION.**

**4.1.** Committee Composition; Authority. This Plan will be administered by the Committee or by the Board acting as the Committee. Subject to the general purposes, terms and conditions of this Plan, and to the direction of the Board, the Committee will have full power to implement and carry out this Plan, except, however, the Board shall establish the terms for the grant of an Award to Non-Employee Directors. The Committee will have the authority to:

(a) construe and interpret this Plan, any Award Agreement and any other agreement or document executed pursuant to this Plan;

(b) prescribe, amend and rescind rules and regulations relating to this Plan or any Award;

(c) select persons to receive Awards;

(d) determine the form and terms and conditions, not inconsistent with the terms of the Plan, of any Award granted hereunder. Such terms and conditions include, but are not limited to, the exercise price, the time or times when Awards may vest and be exercised (which may be based on performance criteria) or settled, any vesting acceleration or waiver of forfeiture restrictions, the method to satisfy tax withholding obligations or any other tax liability legally due and any restriction or limitation regarding any Award or the Shares relating thereto, based in each case on such factors as the Committee will determine;

(e) determine the number of Shares or other consideration subject to Awards;

(f) determine the Fair Market Value in good faith and interpret the applicable provisions of this Plan and the definition of Fair Market Value in connection with circumstances that impact the Fair Market Value, if necessary;

(g) determine whether Awards will be granted singly, in combination with, in tandem with, in replacement of, or as alternatives to, other Awards under this Plan or any other incentive or compensation plan of the Company or any Parent, Subsidiary or Affiliate;

(h) grant waivers of Plan or Award conditions;

(i) determine the vesting, exercisability and payment of Awards;

(j) correct any defect, supply any omission or reconcile any inconsistency in this Plan, any Award or any Award Agreement;

(k) determine whether an Award has been earned;

(l) determine the terms and conditions of any, and to institute any Exchange Program;

(m) reduce or waive any criteria with respect to Performance Factors;

(n) adjust performance goals or Performance Factors as the Committee deems necessary or appropriate;

(o) adopt rules and/or procedures (including the adoption of any subplan under this Plan) relating to the operation and administration of the Plan to accommodate requirements of local law and procedures outside of the United States;

(p) make all other determinations necessary or advisable for the administration of this Plan;

(q) delegate any of the foregoing to a subcommittee consisting of one or more executive officers pursuant to a specific delegation as permitted by applicable law, including Sections 152 and 157 of the Delaware General Corporation Law, as provided in Section 4.3; and

(r) to exercise discretion with respect to Performance Awards, including, without limitation, increasing, reducing or eliminating the amount to be paid to Participants.

**4.2.** Committee Interpretation and Discretion. Any determination made by the Committee with respect to any Award shall be made in its sole discretion at the time of grant of the Award or, unless in contravention of any express term of the Plan or Award, at any later time, and such determination shall be final and binding on the Company and all persons having an interest in any Award under the Plan. Any dispute regarding the interpretation of the Plan or any Award Agreement shall be submitted by the Participant or Company to the Committee for review. The resolution of such a dispute by the Committee shall be final and binding on the Company and the Participant. The Committee may delegate to one or more executive officers the authority to review and resolve disputes with respect to Awards held by Participants who are not Insiders, and such resolution shall be final and binding on the Company and the Participant.

**4.3.** Delegation to Other Person or Body. The Board or any Committee may delegate to one or more persons or bodies the authority to do one or more of the following to the extent permitted by applicable law: (i) designate recipients, other than executive officers, of Awards, provided that no person or body may be delegated authority to grant an Award to themselves; (ii) determine the number of Shares subject to such Awards; and (iii) determine the terms of such Awards; provided, however, that the Board or Committee action regarding such delegation will fix the terms of such delegation in accordance with applicable law, including without limitation Sections 152 and 157 of the Delaware General Corporation Law. Unless provided otherwise in the Board or Committee action regarding such delegation, each Award granted pursuant to this section will be granted on the applicable form of Award Agreement most recently approved for use by the Board or the Committee, with any modifications necessary to incorporate or reflect the terms of such Award. Notwithstanding anything to the contrary herein, neither the Board nor any Committee may delegate to any person or body (who is not a Non-Employee Director or that is not comprised solely of Non-Employee Directors, respectively) the authority to determine the Fair Market Value of the Common Stock.

**4.4.** Rule 16b-3 Compliance. The Committee administering the Plan in accordance with the requirements of Rule 16b-3 shall consist of at least two individuals, each of whom qualifies as a Non- Employee Director under Rule 16b-3. Awards granted to Participants who are subject to Section 16 of the Exchange Act must be approved by two or more “non-employee directors” (as defined in the regulations promulgated under Section 16 of the Exchange Act).

**4.5.** Documentation. The Award Agreement for a given Award, the Plan and any other documents may be delivered to, and accepted by, a Participant or any other person in any manner (including electronic distribution or posting) that meets applicable legal requirements.

**4.6.** Foreign Award Recipients. Notwithstanding any provision of the Plan to the contrary, in order to comply with the laws in other countries in which the Company and its Subsidiaries and Affiliates operate or have employees or other individuals eligible for Awards, the Committee, in its sole discretion, shall have the power and authority to: (a) determine which Subsidiaries and Affiliates shall be covered by the Plan; (b) determine which individuals outside the United States are eligible to participate in the Plan; (c) modify the terms and conditions of any Award granted to individuals outside the United States to comply with applicable foreign laws; (d) establish subplans and modify exercise procedures and other terms and procedures, to the extent the Committee determines such actions to be necessary or advisable (and such subplans and/or modifications shall be attached to this Plan as appendices); provided, however, that no such subplans and/or modifications shall increase the share limitations contained in Section 2.1 hereof; and (e) take any action, before or after an Award is made, that the Committee determines to be necessary or advisable to obtain approval or comply with any local governmental regulatory exemptions or approvals. Notwithstanding the foregoing, the Committee may not take any actions hereunder, and no Awards shall be granted, that would violate the Exchange Act or any other applicable United States securities law, the Code, or any other applicable United States governing statute or law.

**5. OPTIONS**. An Option is the right but not the obligation to purchase a Share, subject to certain conditions, if applicable. The Committee may grant Options to eligible Employees, Consultants and Directors and will determine whether such Options will be Incentive Stock Options within the meaning of the Code ("***ISOs***") or Nonqualified Stock Options ("***NSOs***"), the number of Shares subject to the Option, the Exercise Price of the Option, the period during which the Option may vest and be exercised, and all other terms and conditions of the Option, subject to the following terms of this section.

**5.1.** Option Grant. Each Option granted under this Plan will identify the Option as an ISO or an NSO. An Option may be, but need not be, awarded upon satisfaction of such Performance Factors during any Performance Period as are set out in advance in the Participant's individual Award Agreement. If the Option is being earned upon the satisfaction of Performance Factors, then the Committee will: (a) determine the nature, length and starting date of any Performance Period for each Option; and (b) select from among the Performance Factors to be used to measure the performance, if any. Performance Periods may overlap and Participants may participate simultaneously with respect to Options that are subject to different performance goals and other criteria.

**5.2.** Date of Grant. The date of grant of an Option will be the date on which the Committee makes the determination to grant such Option, or a specified future date. The Award Agreement will be delivered to the Participant within a reasonable time after the granting of the Option.

**5.3.** Exercise Period. Options may be vested and exercisable within the times or upon the conditions as set forth in the Award Agreement governing such Option; provided, however, that no Option will be exercisable after the expiration of 10 years from the date the Option is granted; and provided further that no ISO granted to a person who, at the time the ISO is granted, directly or by attribution owns more than 10% of the total combined voting power of all classes of stock of the Company or of any Parent or Subsidiary ("***Ten Percent Stockholder***") will be exercisable after the expiration of five years from the date the ISO is granted. The Committee also may provide for Options to become exercisable at one time or from time to time, periodically or otherwise, in such number of Shares or percentage of Shares as the Committee determines.

**5.4.** Exercise Price. The Exercise Price of an Option will be determined by the Committee when the Option is granted; provided that: (a) the Exercise Price of an Option will be not less than 100% of the Fair Market Value of the Shares on the date of grant and (b) the Exercise Price of any ISO granted to a Ten Percent Stockholder will not be less than 110% of the Fair Market Value of the Shares on the date of grant. Payment for the Shares purchased may be made in accordance with Section 11 and the Award Agreement and in accordance with any procedures established by the Company.

**5.5.** Method of Exercise. Any Option granted hereunder will be vested and exercisable according to the terms of the Plan and at such times and under such conditions as determined by the Committee and set forth in the Award Agreement. An Option may not be exercised for a fraction of a Share. An Option will be deemed exercised when the Company receives: (a) notice of exercise (in such form as the Committee may specify from time to time) from the person entitled to exercise the Option, and (b) full payment for the Shares with respect to which the Option is exercised (together with applicable withholding taxes). Full payment may consist of any consideration and method of payment authorized by the Committee and permitted by the Award Agreement and the Plan. Shares issued upon exercise of an Option will be issued in the name of the Participant. Until the Shares are issued (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company), no right to vote or receive dividends or any other rights as a stockholder will exist with respect to the Shares, notwithstanding the exercise of the Option. The Company will issue (or cause to be issued) such Shares promptly after the Option is exercised. No adjustment will be made for a dividend or other right for which the record date is prior to the date the Shares are issued, except as provided in Section 2.6 of the Plan. Exercising an Option in any manner will decrease the number of Shares thereafter available, both for purposes of the Plan and for sale under the Option, by the number of Shares as to which the Option is exercised.

**5.6.** Termination of Service. If the Participant's Service terminates for any reason except for Cause or the Participant's death or Disability, then the Participant may exercise such Participant's Options only to the extent that such Options would have been exercisable by the Participant on the date Participant's Service terminates no later than three months after the date Participant's Service terminates (or such shorter or longer time period as may be determined by the Committee, with any exercise beyond three months after the date Participant's employment terminates deemed to be the exercise of an NSO), but in any event no later than the expiration date of the Options.

(a) Death. If the Participant's Service terminates because of the Participant's death (or the Participant dies within three months after Participant's Service terminates other than for Cause or because of the Participant's Disability), then the Participant's Options may be exercised only to the extent that such Options would have been exercisable by the Participant on the date Participant's Service terminates and must be exercised by the Participant's legal representative, or authorized assignee, no later than 12 months after the date Participant's Service terminates (or such shorter or longer time period as may be determined by the Committee), but in any event no later than the expiration date of the Options.

(b) Disability. If the Participant's Service terminates because of the Participant's Disability, then the Participant's Options may be exercised only to the extent that such Options would have been exercisable by the Participant on the date Participant's Service terminates and must be exercised by the Participant (or the Participant's legal representative or authorized assignee) no later than 12 months (or such shorter or longer time period as may be determined by the Committee) after the date Participant's Service terminates (with any exercise beyond (a) three months after the date Participant's employment terminates when the termination of Service is for a Disability that is not a "permanent and total disability" as defined in Section 22(e)(3) of the Code, or (b) 12 months after the date Participant's employment terminates when the termination of Service is for a Disability that is a "permanent and total disability" as defined in Section 22(e)(3) of the Code, deemed to be exercise of an NSO), but in any event no later than the expiration date of the Options.

(c) Cause. If the Participant is terminated for Cause, then Participant's Options shall expire on such Participant's date of termination of Service, or at such later time and on such conditions as are determined by the Committee, but in any no event later than the expiration date of the Options. Unless otherwise provided in the Award Agreement, Cause shall have the meaning set forth in the Plan.

**5.7.** Limitations on Exercise. The Committee may specify a minimum number of Shares that may be purchased on any exercise of an Option, provided that such minimum number will not prevent any Participant from exercising the Option for the full number of Shares for which it is then exercisable.

**5.8.** Limitations on ISOs. With respect to Awards granted as ISOs, to the extent that the aggregate Fair Market Value of the Shares with respect to which such ISOs are exercisable for the first time by the Participant during any calendar year (under all plans of the Company and any Parent or Subsidiary) exceeds one hundred thousand dollars ($100,000), such Options will be treated as NSOs. For purposes of this Section 5.8, ISOs will be taken into account in the order in which they were granted. The Fair Market Value of the Shares will be determined as of the time the Option with respect to such Shares is granted. In the event that the Code or the regulations promulgated thereunder are amended to provide for a different limit on the Fair Market Value of Shares permitted to be subject to ISOs, such different limit will be automatically incorporated herein and will apply to any Options granted after the effective date of such amendment.

**5.9.** Modification, Extension or Renewal. The Committee may modify, extend or renew outstanding Options and authorize the grant of new Options in substitution therefor, provided that any such action may not, without the written consent of a Participant, impair any of such Participant's rights under any Option previously granted. Any outstanding ISO that is modified, extended, renewed or otherwise altered will be treated in accordance with Section 424(h) of the Code. Subject to Section 18 of this Plan, by written notice to affected Participants, the Committee may reduce the Exercise Price of outstanding Options without the consent of such Participants; provided, however, that the Exercise Price may not be reduced below the Fair Market Value on the date the action is taken to reduce the Exercise Price.

**5.10.** No Disqualification. Notwithstanding any other provision in this Plan, no term of this Plan relating to ISOs will be interpreted, amended or altered, nor will any discretion or authority granted under this Plan be exercised, so as to disqualify this Plan under Section 422 of the Code or, without the consent of the Participant affected, to disqualify any ISO under Section 422 of the Code.

**6. RESTRICTED STOCK AWARDS**. A Restricted Stock Award is an offer by the Company to grant or sell to an eligible Employee, Consultant, or Director a number of Shares that are subject to restrictions ("***Restricted Stock***"). The Committee will determine to whom an offer will be made, the number of Shares the Participant may purchase, the Purchase Price (if any), the restrictions under which the Shares will be subject and all other terms and conditions of the Restricted Stock Award, subject to the Plan.

**6.1.** Restricted Stock Award Agreement. All purchases under a Restricted Stock Award will be evidenced by an Award Agreement. Except as may otherwise be provided in an Award Agreement, a Participant accepts a Restricted Stock Award by signing and delivering to the Company an Award Agreement with full payment of the Purchase Price (if any), within 30 days from the date the Award Agreement was delivered to the Participant. If the Participant does not accept such Award within 30 days, then the offer of such Restricted Stock Award will terminate, unless the Committee determines otherwise.

**6.2.** Purchase Price. The Purchase Price for a Restricted Stock Award will be determined by the Committee and the Committee may determine to grant Restricted Stock Awards with no Purchase Price. Payment of the Purchase Price must be made in accordance with Section 11 of the Plan, and the Award Agreement and in accordance with any procedures established by the Company.

**6.3.** Terms of Restricted Stock Awards. Restricted Stock Awards will be subject to such restrictions as the Committee may impose or are required by law. These restrictions may be based on completion of a specified number of years of service with the Company or upon completion of Performance Factors, if any, during any Performance Period as set out in advance in the Participant's Award Agreement. Prior to the grant of a Restricted Stock Award, the Committee shall: (a) determine the nature, length and starting date of any Performance Period or other vesting criteria for the Restricted Stock Award; (b) select from among the Performance Factors to be used to measure performance goals, if any; and (c) determine the number of Shares that may be awarded to the Participant. Performance Periods may overlap and a Participant may participate simultaneously with respect to Restricted Stock Awards that are subject to different Performance Periods and having different performance goals and other criteria.

**6.4.** Termination of Service. Except as may be set forth in the Participant's Award Agreement, vesting ceases on such date Participant's Service terminates (unless determined otherwise by the Committee).

**7. STOCK BONUS AWARDS**. A Stock Bonus Award is an award to an eligible Employee, Consultant, or Director of Shares (or cash based on the Fair Market Value of Shares) for Services to be rendered or for past Services already rendered to the Company or any Parent, Subsidiary or Affiliate. All Stock Bonus Awards shall be made pursuant to an Award Agreement. No payment from the Participant will be required for Shares awarded pursuant to a Stock Bonus Award.

**7.1.** Terms of Stock Bonus Awards. The Committee will determine the number of Shares to be awarded to the Participant under a Stock Bonus Award and any restrictions thereon. These restrictions may be based upon completion of a specified number of years of service with the Company or upon satisfaction of performance goals based on Performance Factors during any Performance Period as set out in advance in the Participant's Award Agreement. Prior to the grant of any Stock Bonus Award the Committee shall: (a) determine the nature, length and starting date of any Performance Period or other vesting criteria for the Stock Bonus Award; (b) select from among the Performance Factors to be used to measure performance goals; and (c) determine the number of Shares that may be awarded to the Participant. Performance Periods may overlap and a Participant may participate simultaneously with respect to Stock Bonus Awards that are subject to different Performance Periods and different performance goals and other criteria.

**7.2.** Form of Payment to Participant. Payment may be made in the form of cash, whole Shares, or a combination thereof, based on the Fair Market Value of the Shares earned under a Stock Bonus Award on the date of payment, as determined in the sole discretion of the Committee.

**7.3.** Termination of Service. Except as may be set forth in the Participant's Award Agreement, vesting ceases on such date Participant's Service terminates (unless determined otherwise by the Committee).

**8. STOCK APPRECIATION RIGHTS**. A Stock Appreciation Right ("***SAR***") is an award to an eligible Employee, Consultant, or Director that may be settled in cash or Shares (which may consist of Restricted Stock), having a value equal to (a) the difference between the Fair Market Value on the date of exercise over the Exercise Price multiplied by (b) the number of Shares with respect to which the SAR is being settled (subject to any maximum number of Shares that may be issuable as specified in an Award Agreement). All SARs shall be made pursuant to an Award Agreement.

**8.1.** Terms of SARs. The Committee will determine the terms of each SAR including, without limitation: (a) the number of Shares subject to the SAR; (b) the Exercise Price and the time or times during which the SAR may be settled; (c) the consideration to be distributed on settlement of the SAR; and (d) the effect of the Participant's termination of Service on each SAR. The Exercise Price of the SAR will be determined by the Committee when the SAR is granted, and may not be less than the Fair Market Value of a Share on the date of grant. A SAR may be awarded upon satisfaction of Performance Factors, if any, during any Performance Period as are set out in advance in the Participant's individual Award Agreement. If the SAR is being earned upon the satisfaction of Performance Factors, then the Committee will determine the nature, length and starting date of any Performance Period for each SAR and the Performance Factors to be used to measure the performance, if any. Performance Periods may overlap and Participants may participate simultaneously with respect to SARs that are subject to different Performance Factors and other criteria.

**8.2.** Exercise Period and Expiration Date. A SAR will be exercisable within the times or upon the occurrence of events determined by the Committee and set forth in the Award Agreement governing such SAR. The Award Agreement shall set forth the expiration date; provided that no SAR will be exercisable after the expiration of 10 years from the date the SAR is granted. The Committee may also provide for SARs to become exercisable at one time or from time to time, periodically or otherwise (including, without limitation, upon the attainment during a Performance Period of performance goals based on Performance Factors), in such number of Shares or percentage of the Shares subject to the SAR as the Committee determines.

**8.3.** Form of Settlement. Upon exercise of a SAR, a Participant will be entitled to receive payment from the Company in an amount determined by multiplying (a) the difference between the Fair Market Value of a Share on the date of exercise over the Exercise Price; times (b) the number of Shares with respect to which the SAR is exercised. At the discretion of the Committee, the payment from the Company for the SAR exercise may be in cash, in Shares of equivalent value, or in some combination thereof. The portion of a SAR being settled may be paid currently or on a deferred basis with such interest or dividend equivalent, if any, as the Committee determines, provided that the terms of the SAR and any deferral satisfy the requirements of Section 409A of the Code.

**8.4.** Termination of Service. Except as may be set forth in the Participant's Award Agreement or Section 5.6, vesting ceases on such date Participant's Service terminates (unless determined otherwise by the Committee).

**9. RESTRICTED STOCK UNITS**. A Restricted Stock Unit ("***RSU***") is an award to an eligible Employee, Consultant, or Director covering a number of Shares that may be settled in cash, or by issuance of those Shares (which may consist of Restricted Stock) based upon such conditions as determined by the Committee. All RSUs shall be made pursuant to an Award Agreement.

**9.1.** Terms of RSUs. The Committee will determine the terms of an RSU including, without limitation: (a) the number of Shares subject to the RSU; (b) the time or times during which the RSU may be settled; (c) the consideration to be distributed on settlement; and (d) the effect of the Participant's termination of Service on each RSU; provided that no RSU shall have a term longer than 10 years. An RSU may be awarded upon satisfaction of such performance goals based on Performance Factors during any Performance Period as are set out in advance in the Participant's Award Agreement. If the RSU is being earned upon satisfaction of Performance Factors, then the Committee will: (x) determine the nature, length and starting date of any Performance Period for the RSU; (y) select the Performance Factors to be used to measure the performance, if any; and (z) determine the number of Shares deemed subject to the RSU and any Performance Factor. Performance Periods may overlap and participants may participate simultaneously with respect to RSUs that are subject to different Performance Periods and different performance goals and other criteria.

**9.2.** Form and Timing of Settlement. Payment of earned RSUs shall be made as soon as practicable after the date(s) determined by the Committee and set forth in the Award Agreement. The Committee, in its sole discretion, may settle earned RSUs in cash, Shares, or a combination of both. The Committee may also permit a Participant to defer payment under a RSU to a date or dates after the RSU is earned provided that the terms of the RSU and any deferral satisfy the requirements of Section 409A of the Code.

**9.3.** Termination of Service. Except as may be set forth in the Participant's Award Agreement, vesting ceases on such date Participant's Service terminates (unless determined otherwise by the Committee).

**10. PERFORMANCE AWARDS**. A Performance Award is an award to an eligible Employee, Consultant, or Director of the Company or any Parent, Subsidiary or Affiliate of a cash bonus, an award of Performance Shares, or an award of Performance Units. Grants of Performance Awards shall be made pursuant to an Award Agreement.

**10.1.** Types of Performance Awards. Performance Awards shall include Performance Shares, Performance Units, and cash-based Awards as set forth in Sections 10.1(a), 10.1(b), and 10.1(c) below.

(a) Performance Shares. The Committee may grant Awards of Performance Shares, designate the Participants to whom Performance Shares are to be awarded and determine the number of Performance Shares and the terms and conditions of each such Award. Performance Shares shall consist of a unit valued by reference to a designated number of shares of Common Stock, the value of which may be paid to the Participant by delivery of shares of Common Stock or, if set forth in the instrument evidencing the Award, of such property as the Committee shall determine, including, without limitation, cash, shares of Common Stock, other property, or

any combination thereof, upon the attainment of performance goals, as established by the Committee, and other terms and conditions specified by the Committee. The amount to be paid under an Award of Performance Shares may be adjusted on the basis of such further consideration as the Committee shall determine in its sole discretion.

(b) Performance Units. The Committee may grant Awards of Performance Units, designate the Participants to whom Performance Units are to be awarded and determine the number of Performance Units and the terms and conditions of each such Award. Performance Units shall consist of a unit valued by reference to a designated amount of property other than shares of Common Stock, which value may be paid to the Participant by delivery of such property as the Committee shall determine, including, without limitation, cash, shares of Common Stock, other property, or any combination thereof, upon the attainment of performance goals, as established by the Committee, and other terms and conditions specified by the Committee.

(c) Cash-Settled Performance Awards. The Committee may also grant cash-settled Performance Awards to Participants under the terms of this Plan. Such awards will be based on the attainment of any Performance Factors that are established by the Committee for the relevant Performance Period.

**10.2.** Terms of Performance Awards. The Committee will determine, and each Award Agreement shall set forth, the terms of each Performance Award including, without limitation: (a) the amount of any cash bonus, (b) the number of Shares deemed subject to an award of Performance Shares; (c) the Performance Factors and Performance Period that shall determine the time and extent to which each award of Performance Award shall be settled; (d) the consideration to be distributed on settlement, and (e) the effect of the Participant's termination of Service on each Performance Award. In establishing Performance Factors and the Performance Period the Committee will: (x) determine the nature, length and starting date of any Performance Period; (y) select the Performance Factors to be used; and (z) determine the number of Shares deemed subject to the Performance Award, if any. Prior to settlement the Committee shall determine the extent to which Performance Awards have been earned. Performance Periods may overlap and Participants may participate simultaneously with respect to Performance Awards that are subject to different Performance Periods and different performance goals and other criteria.

**10.3.** Termination of Service. Except as may be set forth in the Participant's Award Agreement, vesting ceases on the date Participant's Service terminates (unless determined otherwise by the Committee).

**11. PAYMENT FOR SHARE PURCHASES**. Payment from a Participant for Shares purchased pursuant to this Plan may be made in cash or by check or, where approved for the Participant by the Committee and where permitted by law (and to the extent not otherwise set forth in the applicable Award Agreement):

(a) by cancellation of indebtedness of the Company to the Participant;

(b) by surrender of shares of Common Stock by the Participant that have a Fair Market Value on the date of surrender equal to the aggregate exercise price of the Shares as to which said Award will be exercised or settled;

(c) by waiver of compensation due or accrued to the Participant for services rendered or to be rendered to the Company or a Parent or Subsidiary of the Company;

(d) by consideration received by the Company pursuant to a broker-assisted or other form of cashless exercise program implemented by the Company in connection with the Plan;

(e) by any combination of the foregoing; or

(f) by any other method of payment as is permitted by the Committee and applicable law.

**12. GRANTS TO NON-EMPLOYEE DIRECTORS**. Non-Employee Directors are eligible to receive any type of Award offered under this Plan except ISOs. Awards pursuant to this Section 12 may be automatically made pursuant to policy adopted by the Board, or made from time to time as determined in the discretion of the Board. The aggregate value of all compensation granted or paid, as applicable, to any individual for service as a Non-Employee Director with respect to any fiscal year, including Awards granted and cash fees paid by the Company to such Non-Employee Director for his or her service as a Non-Employee Director, will not exceed (i) $750,000 in total value or (ii) in the event such Non-Employee Director is first appointed or elected to the Board during such fiscal year or in any fiscal year in which such Non-Employee Director serves as Chair of the Board, $1,000,000 in total value, in each case calculating the value of any equity awards based on the grant date fair value of such equity awards for financial reporting purposes.[1]

**12.1.** Eligibility. Awards pursuant to this Section 12 shall be granted only to Non-Employee Directors. A Non-Employee Director who is elected or re-elected as a member of the Board will be eligible to receive an Award under this Section 12.

**12.2.** Vesting, Exercisability and Settlement. Except as set forth in Section 21, Awards shall vest, become exercisable and be settled as determined by the Board. With respect to Options and SARs, the exercise price granted to Non-Employee Directors shall not be less than the Fair Market Value of the Shares at the time that such Option or SAR is granted.

**12.3.** Election to receive Awards in Lieu of Cash. A Non-Employee Director may elect to receive his or her annual retainer payments and/or meeting fees from the Company in the form of cash or Awards or a combination thereof, as determined by the Committee. Such Awards shall be issued under the Plan. An election under this Section 12.3 shall be filed with the Company on the form prescribed by the Company.

**13. WITHHOLDING TAXES.**

**13.1.** Withholding Generally. Whenever Shares are to be issued in satisfaction of Awards granted under this Plan or a tax event occurs, the Company may require the Participant to remit to the Company, or to the Parent, Subsidiary or applicable Affiliate employing the Participant, an amount sufficient to satisfy applicable U.S. federal, state, local and international withholding tax requirements or any other tax or social insurance liability legally due from the Participant prior to the delivery of Shares pursuant to exercise or settlement of any Award. Whenever payments in satisfaction of Awards granted under this Plan are to be made in cash, such payment will be net of an amount sufficient to satisfy applicable U.S. federal, state, local and international withholding tax or social insurance requirements or any other tax liability legally due from the Participant. The Fair Market Value of the Shares will be determined as of the date that the taxes are required to be withheld and such Shares shall be valued based on the value of the actual trade or, if there is none, the Fair Market Value of the Shares as of the previous trading day.

**13.2.** Stock Withholding. The Committee, or its delegate(s), as permitted by applicable law, in its sole discretion and pursuant to such procedures as it may specify from time to time and to limitations of local law, may require or permit a Participant to satisfy such tax withholding obligation or any other tax liability legally due from the Participant, in whole or in part by (without limitation) (a) paying cash, (b) electing to have the Company withhold otherwise deliverable cash or Shares, (c) delivering to the Company already-owned shares of Common Stock or (d) withholding from proceeds of the sale of otherwise deliverable Shares acquired pursuant to an Award either through a voluntary sale or through a mandatory sale arranged by the Company.

[1] Note to Draft: Company to confirm the dollar limits and to confirm whether to include the bracketed carveout on the Chair of the Board.

**14. TRANSFERABILITY.**

**14.1.** Transfer Generally. Unless determined otherwise by the Committee or pursuant to Section 14.2, an Award may not be sold, pledged, assigned, hypothecated, transferred, or disposed of in any manner other than by will or by the laws of descent or distribution. If the Committee makes an Award transferable, including, without limitation, by instrument to an inter vivos or testamentary trust in which the Awards are to be passed to beneficiaries upon the death of the trustor (settlor) or by gift or by domestic relations order to a Permitted Transferee, such Award will contain such additional terms and conditions as the Committee deems appropriate. All Awards shall be exercisable: (a) during the Participant's lifetime only by (i) the Participant, or (ii) the Participant's guardian or legal representative; (b) after the Participant's death, by the legal representative of the Participant's heirs or legatees; and (c) in the case of all awards except ISOs, by a Permitted Transferee.

**14.2.** Award Transfer Program. Notwithstanding any contrary provision of the Plan, the Committee shall have all discretion and authority to determine and implement the terms and conditions of any Award Transfer Program instituted pursuant to this Section 14.2 and shall have the authority to amend the terms of any Award participating, or otherwise eligible to participate in, the Award Transfer Program, including (but not limited to) the authority to (a) amend (including to extend) the expiration date, post-termination exercise period and/or forfeiture conditions of any such Award, (b) amend or remove any provisions of the Award relating to the Award holder's continued Service to the Company or its Parent, Subsidiary, or Affiliate, (c) amend the permissible payment methods with respect to the exercise or purchase of any such Award, (d) amend the adjustments to be implemented in the event of changes in the capitalization and other similar events with respect to such Award, and (e) make such other changes to the terms of such Award as the Committee deems necessary or appropriate in its sole discretion, to the extent permitted by applicable law. Notwithstanding anything to the contrary in the Plan, in no event will the Committee have the right to determine and implement the terms and conditions of any Award Transfer Program without stockholder approval.

**15. PRIVILEGES OF STOCK OWNERSHIP; RESTRICTIONS ON SHARES.**

**15.1.** Voting and Dividends. No Participant will have any of the rights of a stockholder with respect to any Shares until the Shares are issued to the Participant, except for any dividend equivalent rights permitted by an applicable Award Agreement ("***Dividend Equivalent Rights***"). After Shares are issued to the Participant, the Participant will be a stockholder and have all the rights of a stockholder with respect to such Shares, including the right to vote and receive all dividends or other distributions made or paid with respect to such Shares; provided, that if such Shares are Restricted Stock, then any new, additional or different securities the Participant may become entitled to receive with respect to such Shares by virtue of a stock dividend, stock split or any other change in the corporate or capital structure of the Company will be subject to the same restrictions as the Restricted Stock; provided, further, that the Participant will have no right to retain such stock dividends or stock distributions with respect to Shares that are repurchased at the Participant's Purchase Price or Exercise Price, as the case may be, pursuant to Section 15.2. However, the Committee, in its discretion, may provide in the Award Agreement evidencing any Award that the Participant shall be entitled to Dividend Equivalent Rights with respect to the payment of cash dividends on Shares underlying an Award during the period beginning on the date the Award is granted and ending, with respect to each Share subject to the Award, on the earlier of the date on which the Award is exercised or settled or the date on which it is forfeited. Such Dividend Equivalent Rights, if any, shall be credited to the Participant in the form of additional whole Shares (or cash as determined by the Committee) as of the date of payment of such cash dividends on Shares.

**15.2.** Restrictions on Shares. At the discretion of the Committee, the Company may reserve to itself and/or its assignee(s) a right to repurchase (a "***Right of Repurchase***") a portion of any or all Unvested Shares held by a Participant following such Participant's termination of Service at any time within 90 days (or such longer or shorter time determined by the Committee) after the later of the date Participant's Service terminates and the date the Participant purchases Shares under this Plan, for cash and/or cancellation of purchase money indebtedness, at the Participant's Purchase Price or Exercise Price, as the case may be.

**16. CERTIFICATES**. All Shares or other securities whether or not certificated, delivered under this Plan will be subject to such stock transfer orders, legends and other restrictions as the Committee may deem necessary or advisable, including restrictions under any applicable U.S. federal, state or foreign securities law, or any rules, regulations and other requirements of the SEC or any stock exchange or automated quotation system upon which the Shares may be listed or quoted and any non-U.S. exchange controls or securities law restrictions to which the Shares are subject.

**17. ESCROW; PLEDGE OF SHARES**. To enforce any restrictions on a Participant's Shares, the Committee may require the Participant to deposit all certificates representing Shares, together with stock powers or other instruments of transfer approved by the Committee, appropriately endorsed in blank, with the Company or an agent designated by the Company to hold in escrow until such restrictions have lapsed or terminated, and the Committee may cause a legend or legends referencing such restrictions to be placed on the certificates. Any Participant who is permitted to execute a promissory note as partial or full consideration for the purchase of Shares under this Plan will be required to pledge and deposit with the Company all or part of the Shares so purchased as collateral to secure the payment of the Participant's obligation to the Company under the promissory note; provided, however, that the Committee may require or accept other or additional forms of collateral to secure the payment of such obligation and, in any event, the Company will have full recourse against the Participant under the promissory note notwithstanding any pledge of the Participant's Shares or other collateral. In connection with any pledge of the Shares, the Participant will be required to execute and deliver a written pledge agreement in such form as the Committee will from time to time approve. The Shares purchased with the promissory note may be released from the pledge on a pro rata basis as the promissory note is paid.

**18. REPRICING; EXCHANGE AND BUYOUT OF AWARDS**. Without prior stockholder approval, the Committee may (a) reprice Options or SARs (and where such repricing is a reduction in the Exercise Price of outstanding Options or SARs, the consent of the affected Participants is not required provided written notice is provided to them, notwithstanding any adverse tax consequences to them arising from the repricing), and (b) with the consent of the respective Participants (unless not required pursuant to Section 5.9 of the Plan), pay cash or issue new Awards in exchange for the surrender and cancellation of any, or all, outstanding Awards.

**19. SECURITIES LAW AND OTHER REGULATORY COMPLIANCE**. An Award will not be effective unless such Award is in compliance with all applicable U.S. and foreign federal and state securities and exchange control laws, rules and regulations of any governmental body, and the requirements of any stock exchange or automated quotation system upon which the Shares may then be listed or quoted, as they are in effect on the date of grant of the Award and also on the date of exercise or other issuance. Notwithstanding any other provision in this Plan, the Company will have no obligation to issue or deliver certificates for Shares under this Plan prior to: (a) obtaining any approvals from governmental agencies that the Company determines are necessary or advisable; and/or (b) completion of any registration or other qualification of such Shares under any state or federal or foreign law or ruling of any governmental body that the Company determines to be necessary or advisable. The Company will be under no obligation to register the Shares with the SEC or to effect compliance with the registration, qualification or listing requirements of any foreign or state securities laws, exchange control laws, stock exchange or automated quotation system, and the Company will have no liability for any inability or failure to do so.

**20. MISCELLANEOUS**.

**20.1.** No Obligation to Employ. Nothing in this Plan or any Award granted under this Plan will confer or be deemed to confer on any Participant any right to continue in the employ of, or to continue any other relationship with, the Company or any Parent, Subsidiary or Affiliate or limit in any way the right of the Company or any Parent, Subsidiary or Affiliate to terminate Participant's employment or other relationship at any time.

**20.2.** Change in Time Commitment. In the event that a Participant's regular level of time commitment in the performance of his or her services for the Company or any Affiliate is reduced (for example, and without limitation, if the Participant is an Employee and has a change in status from a full-time Employee to a part-time Employee or takes an extended leave of absence) after the date of grant of any Award to Participant, the Committee has the right in its sole discretion to (i) make a corresponding reduction in the number of Shares or cash amount subject to any portion of such Award that is scheduled to vest or become payable after the date of such change in time commitment, and (ii) in lieu of or in combination with such a reduction, extend the vesting or payment schedule applicable to such Award. In the event of any such reduction, the Participant will have no right with respect to any portion of the Award that is so reduced or extended.

**21. CORPORATE TRANSACTIONS.**

**21.1.** Assumption or Replacement of Awards by Successor. In the event that the Company is subject to a Corporate Transaction, outstanding Awards acquired under the Plan shall be subject to the agreement evidencing the Corporate Transaction and subject to such other determinations made by the Committee, each of which need not treat all outstanding Awards in an identical manner. Such agreement or determination, without the Participant's consent, may provide for one or more of the following with respect to all outstanding Awards as of the effective date of such Corporate Transaction:

(a) The continuation of an outstanding Award by the Company (if the Company is the successor entity).

(b) The assumption of an outstanding Award by the successor or acquiring entity (if any) of such Corporate Transaction (or by its parents, if any), which assumption, will be binding on all selected Participants; provided that the exercise price and the number and nature of shares issuable upon exercise of any such Option or SAR, or any award that is subject to Section 409A of the Code, will be adjusted appropriately pursuant to Section 424(a) of the Code.

(c) The substitution by the successor or acquiring entity in such Corporate Transaction (or by its parents, if any) of equivalent awards with substantially the same terms for such outstanding Awards (except that the exercise price and the number and nature of shares issuable upon exercise of any such Option or SAR, or any award that is subject to Section 409A of the Code, will be adjusted appropriately pursuant to Section 424(a) of the Code).

(d) The full or partial acceleration of exercisability or vesting and accelerated expiration of an outstanding Award and lapse of the Company's right to repurchase or re-acquire Shares acquired under an Award or lapse of forfeiture rights with respect to Shares acquired under an Award.

(e) The settlement of the full value of such outstanding Award (whether or not then vested or exercisable) in cash, cash equivalents, or securities of the successor entity (or its parent, if any) with a Fair Market Value equal to the required amount, followed by the cancellation of such Awards; provided however, that such Award may be cancelled if such Award has no value, as determined by the Committee, in its discretion. Subject to Section 409A of the Code, such payment may be made in installments and may be deferred until the date or dates the Award would have become exercisable or vested. Such payment may be subject to vesting based on the Participant's continued service, provided that the vesting schedule shall not be less favorable to the Participant than the schedule under which the Award would have become vested or exercisable. For purposes of this Section 21.1(e), the Fair Market Value of any security shall be determined without regard to any vesting conditions that may apply to such security.

(f) The cancellation of outstanding Awards in exchange for no consideration.

The Board shall have full power and authority to assign the Company's right to repurchase or re- acquire or forfeiture rights to such successor or acquiring corporation. In addition, in the event such successor or acquiring corporation refuses to assume, convert, replace or substitute Awards, as provided above, pursuant to a Corporate Transaction, the Committee will notify the Participant in writing or electronically that such Award will be exercisable for a period of time determined by the Committee in its sole discretion, and such Award will terminate upon the expiration of such period. Awards need not be treated similarly in a Corporate Transaction. In addition, following a Corporate Transaction, 100% of the total number of Shares subject to each Award held by an Employee shall become vested if the holder is subject to an Involuntary Termination within 12 months after the Corporate Transaction; it being understood that the vesting acceleration set forth in the preceding clause is in addition to vesting of the Award or Shares that has occurred prior to the Involuntary Termination, subject to the Participant executing a general release (in a form prescribed by the Company) of all known and unknown claims that he or she may then have against the Company or persons affiliated with the Company and such release has become effective and agreeing not to prosecute any legal action or other proceeding based upon any of such claims except to the extent otherwise provided in an individual award agreement. The provisions of this Section 21.1 shall apply to Awards outstanding on the Original Effective Date under the Prior Plan; provided the vesting acceleration provisions set forth in any employment agreement or letter or similar agreement between the Company and an employee in effect on the Original Effective Date, to the extent more favorable to such employee, will continue to apply to the equity awards held by the employee on the Original Effective Date.

**21.2.** Assumption of Awards by the Company. The Company, from time to time, also may substitute or assume outstanding awards granted by another company, whether in connection with an acquisition of such other company or otherwise, by either; (a) granting an Award under this Plan in substitution of such other company's award; or (b) assuming such award as if it had been granted under this Plan if the terms of such assumed award could be applied to an Award granted under this Plan. Such substitution or assumption will be permissible if the holder of the substituted or assumed award would have been eligible to be granted an Award under this Plan if the other company had applied the rules of this Plan to such grant. In the event the Company assumes an award granted by another company, the terms and conditions of such award will remain unchanged (except that the Purchase Price or the Exercise Price, as the case may be, and the number and nature of Shares issuable upon exercise or settlement of any such Award will be adjusted appropriately pursuant to Section 424(a) of the Code). In the event the Company elects to grant a new Option in substitution rather than assuming an existing option, such new Option may be granted with a similarly adjusted Exercise Price. Substitute Awards shall not be credited toward the number of Shares authorized for grant under the Plan.

**21.3.** Non-Employee Directors' Awards. Notwithstanding any provision to the contrary herein, in the event of a Corporate Transaction, the vesting of all Awards granted to Non-Employee Directors shall accelerate and such Awards shall become exercisable (as applicable) in full prior to the consummation of such event at such times and on such conditions as the Committee determines.

**22. ADOPTION AND STOCKHOLDER APPROVAL**. This Plan shall be submitted for the approval of the Company's stockholders, consistent with applicable laws, within 12 months before or after the date this Plan is adopted by the Board.

**23. GOVERNING LAW**. This Plan and all Awards granted hereunder shall be governed by and construed in accordance with the laws of the State of Delaware (excluding its conflict of law rules).

**24. AMENDMENT OR TERMINATION OF PLAN.** The Board may at any time terminate or amend this Plan in any respect, including, without limitation, amendment of any form of Award Agreement or instrument to be executed pursuant to this Plan; provided, however, that the Board will not, without the approval of the stockholders of the Company, amend this Plan in any manner that requires such stockholder approval; provided further, that no amendment shall materially impair the rights of the holder of an Award without such holder's consent and a Participant's Award shall be governed by the version of this Plan then in effect at the time such Award was granted. No Awards may be granted under the Plan while the Plan is suspended or after it is

terminated. No ISOs may be granted after the tenth anniversary of the earlier of (i) the Adoption Date or (ii) the Stockholder Approval Date.

**25. NONEXCLUSIVITY OF THE PLAN**. Neither the adoption of this Plan by the Board, the submission of this Plan to the stockholders of the Company for approval, nor any provision of this Plan will be construed as creating any limitations on the power of the Board to adopt such additional compensation arrangements as it may deem desirable, including, without limitation, the granting of stock awards and bonuses otherwise than under this Plan, and such arrangements may be either generally applicable or applicable only in specific cases.

**26. INSIDER TRADING POLICY**. Each Participant who receives an Award shall comply with any policy adopted by the Company from time to time covering transactions in the Company's securities by Employees, officers and/or directors of the Company.

**27. ALL AWARDS SUBJECT TO COMPANY CLAWBACK OR RECOUPMENT POLICY**. All Awards shall be subject to clawback or recoupment pursuant to any compensation clawback or recoupment policy adopted by the Board or required by law during or after the term of Participant's employment or other service with the Company that is applicable to executive officers, employees, directors or other service providers of the Company. By accepting an Award, the Participant expressly agrees that, in addition to any other remedies available under such policy and applicable law, the Company may require the cancelation of outstanding Awards and the recoupment of any gains realized with respect to Awards pursuant to such policy.

**28. DEFINITIONS**. As used in this Plan, and except as elsewhere defined herein, the following terms will have the following meanings:

**28.1.** "***Adoption Date***" means _____, 2023, which is the date that this Plan, as amended and restated, was adopted by the Board.

**28.2.** "***Affiliate***" means any person or entity that directly or indirectly through one or more intermediaries controls, or is controlled by, or is under common control with, the Company, including any general partner, managing member, officer or director of the Company, in each case as of the date on which, or at any time during the period for which, the determination of affiliation is being made. For purposes of this definition, the term "control" (including the correlative meanings of the terms "controlled by" and "under common control with"), as used with respect to any person or entity, means the possession, directly or indirectly, of the power to direct or cause the direction of the management policies of such person or entity, whether through the ownership of voting securities or by contract or otherwise.

**28.3.** "***Award***" means any award under the Plan, including any Option, Restricted Stock, Stock Bonus, SAR, RSU, or Performance Award.

**28.4.** "***Award Agreement***" means, with respect to each Award, the written or electronic agreement between the Company and the Participant setting forth the terms and conditions of the Award, and any country-specific appendix thereto for grants to non-U.S. Participants, which shall be in substantially a form (which need not be the same for each Participant) that the Committee (or in the case of Award agreements that are not used for Insiders, the Committee's delegate(s)) has from time to time approved, and will comply with and be subject to the terms and conditions of this Plan.

**28.5.** "***Award Transfer Program***" means any program instituted by the Committee which would permit Participants the opportunity to transfer any outstanding Awards to a financial institution or other person or entity approved by the Committee.

**28.6.** "***Board***" means the Board of Directors of the Company.

**28.7.** "***Cause***" has the meaning set forth in the Award Agreement or the written employment, offer, services or severance agreement or letter between the Participant and the Company or an Affiliate, or if there is no such agreement or no such term is defined in such agreement, means (i) an unauthorized use or disclosure by Participant of the Company's confidential information or trade secrets, which use or disclosure causes material harm to the Company or is reasonably likely to cause material harm to the Company, (ii) a material breach of any agreement between Participant and the Company, (iii) a material failure to comply with the Company's written policies or rules that has caused or is reasonably likely to cause material injury to the Company, its successor, or its affiliates, or any of their business, (iv) conviction of, or plea of "guilty" or "no contest" to, a felony under the laws of the United States or any state thereof, (v) willful misconduct that has caused or is reasonably likely to cause material injury to the Company, its successor, or its affiliates, or any of their business, (vi) embezzlement, (vii) failure to cooperate with the Company in any investigation or formal proceeding if the Company has requested Participant's reasonable cooperation, (viii) violation of any applicable federal, state or foreign statutes or laws that govern or regulate employment, pharmaceutical drugs or securities, including but not limited to the laws enforced by the federal Equal Employment Opportunity Commission, Department of Labor, Food and Drug Administration, Securities and Exchange Commission and Department of Justice or (ix) a continued failure to perform assigned duties after receiving written notification of such failure from the Company's Chief Executive Officer (or with respect to the Company's Chief Executive Officer, the Board); *provided that* Participant must be provided with written notice of Participant's termination for "Cause" and Participant must be provided with a 30 day period following Participant's receipt of such notice to cure the event(s) that trigger "Cause," with the Company's Chief Executive Officer (or with respect to the Company's Chief Executive Officer, the Board) making the final determination whether Participant has cured any Cause. The determination as to whether a Participant is being terminated for Cause shall be made in good faith by the Company and shall be final and binding on the Participant. The foregoing definition does not in any way limit the Company's ability to terminate a Participant's employment or consulting relationship at any time as provided in Section 20 above, and the term "Company" will be interpreted to include any Parent, Subsidiary or Affiliate, as appropriate.

**28.8.** "***Code***" means the United States Internal Revenue Code of 1986, as amended, and the regulations promulgated thereunder.

**28.9.** "***Committee***" means the Compensation Committee of the Board or those persons to whom administration of the Plan, or part of the Plan, has been delegated as permitted by law.

**28.10.** "***Common Stock***" means the common stock of the Company.

**28.11.** "***Company***" means Aeglea BioTherapeutics, Inc., or any successor corporation.

**28.12.** "***Consultant***" means any person, including an advisor or independent contractor, engaged by the Company or a Parent, Subsidiary or Affiliate to render services to such entity.

**28.13.** "***Corporate Transaction***" means the occurrence of any of the following events: (a) any "Person" (as such term is used in Sections 13(d) and 14(d) of the Exchange Act) becomes the "beneficial owner" (as defined in Rule 13d-3 of the Exchange Act), directly or indirectly, of securities of the Company representing more than 50% of the total voting power represented by the Company's then-outstanding voting securities; provided, however, that for purposes of this subclause (a) the acquisition of additional securities by any one Person who is considered to own more than 50% of the total voting power of the securities of the Company will not be considered a Corporate Transaction; (b) the consummation of the sale or disposition by the Company of all or substantially all of the Company's assets; (c) the consummation of a merger or consolidation of the Company with any other corporation, other than a merger or consolidation which would result in the voting securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or its parent) at least 50% of the total voting power represented by the voting securities of the Company or such surviving entity or its parent outstanding immediately after such merger or consolidation; (d) any other transaction which qualifies as a

"corporate transaction" under Section 424 of the Code (and the Treasury Regulations promulgated thereunder) wherein the stockholders of the Company give up all of their equity interest in the Company (except for the acquisition, sale or transfer of all or substantially all of the outstanding shares of the Company) or (e) a change in the effective control of the Company that occurs on the date that a majority of members of the Board is replaced during any 12 month period by members of the Board whose appointment or election is not endorsed by a majority of the members of the Board prior to the date of the appointment or election. For purpose of this subclause (e), if any Person is considered to be in effective control of the Company, the acquisition of additional control of the Company by the same Person will not be considered a Corporate Transaction. For purposes of this definition, Persons will be considered to be acting as a group if they are owners of a corporation that enters into a merger, consolidation, purchase or acquisition of stock, or similar business transaction with the Company. Notwithstanding the foregoing, to the extent that any amount constituting deferred compensation (as defined in Section 409A of the Code) would become payable under this Plan by reason of a Corporate Transaction, such amount shall become payable only if the event constituting a Corporate Transaction would also qualify as a change in ownership or effective control of the Company or a change in the ownership of a substantial portion of the assets of the Company, each as defined within the meaning of Code Section 409A, as it has been and may be amended from time to time, and any proposed or final Treasury Regulations and IRS guidance that has been promulgated or may be promulgated thereunder from time to time.

**28.14.** "***Director***" means a member of the Board.

**28.15.** "***Disability***" means in the case of ISOs, permanent and total disability as defined in Section 22(e)(3) of the Code and in the case of other Awards, that the Participant is unable to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment that can be expected to result in death or can be expected to last for a continuous period of not less than 12 months.

**28.16.** "***Employee***" means any person, including officers and Directors, employed by the Company or any Parent, Subsidiary or Affiliate. Neither service as a Director nor payment of a director's fee by the Company will be sufficient to constitute "employment" by the Company.

**28.17.** "***Exchange Act***" means the United States Securities Exchange Act of 1934, as amended.

**28.18.** "***Exchange Program***" means a program pursuant to which (a) outstanding Awards are surrendered, cancelled or exchanged for cash, the same type of Award or a different Award (or combination thereof) or (b) the exercise price of an outstanding Award is increased or reduced.

**28.19.** "***Exercise Price***" means, with respect to an Option, the price at which a holder may purchase the Shares issuable upon exercise of an Option and with respect to a SAR, the price at which the SAR is granted to the holder thereof.

**28.20.** "***Fair Market Value***" means, as of any date, the value of a share of the Company's Common Stock determined as follows:

(a) if such Common Stock is publicly traded and is then listed on a national securities exchange, its closing price on the date of determination on the principal national securities exchange on which the Common Stock is listed or admitted to trading as reported in *The Wall Street Journal* or such other source as the Committee deems reliable;

(b) if such Common Stock is publicly traded but is neither listed nor admitted to trading on a national securities exchange, the average of the closing bid and asked prices on the date of determination as reported in *The Wall Street Journal* or such other source as the Committee deems reliable;

(c) in the case of an Option or SAR grant made on the Original Effective Date, the price per share at which shares of the Company's Common Stock were initially offered for sale to the public by the Company's underwriters in the initial public offering of the Company's Common Stock pursuant to a registration statement filed with the SEC under the Securities Act; or

(d) if none of the foregoing is applicable, by the Board or the Committee in good faith.

**28.21.** "***Good Reason***" has the meaning set forth in the Award Agreement or the written employment, offer, services or severance agreement or letter between the Participant and the Company or an Affiliate, or if there is no such agreement or no such term is defined in such agreement, means, without the Participant's consent, (i) a material reduction in the Participant's level of responsibility and/or scope of authority, (ii) a reduction by more than 10% in Participant's base salary (other than a reduction generally applicable to Participant officers of the Company and in generally the same proportion as for the Participant), or (iii) relocation of the Participant's principal workplace by more than 35 miles from Participant's then current place of employment. For the purpose of clause (i), a change in responsibility shall not be deemed to occur (A) solely because Participant is part of a larger organization or (B) solely because of a change in title. For the Participant to receive the benefits under this Agreement as a result of a voluntary resignation for Good Reason, all of the following requirements must be satisfied: (1) the Participant must provide notice to the Company of his or her intent to assert Good Reason within 60 days of the initial existence of one or more of the conditions set forth in subclauses (i) through (iii); (2) the Company will have 30 days (the "***Company Cure Period***") from the date of such notice to remedy the condition and, if it does so, the Participant may either withdraw his or her resignation or resign with no benefits; and (3) any termination of employment under this provision must occur within 10 days of the earlier of expiration of the Company Cure Period or written notice from the Company that it will not undertake to cure the condition set forth in subclauses (i) through (iii). Should the Company remedy the condition as set forth above and then one or more of the conditions arise again, the Participant may assert Good Reason again subject to all of the conditions set forth herein.

**28.22.** "***Insider***" means an officer or director of the Company or any other person whose transactions in the Company's Common Stock are subject to Section 16 of the Exchange Act.

**28.23.** "***Involuntary Termination***" means either (a) termination of Service without Cause or (b) resignation from Service for Good Reason.

**28.24.** "***IRS***" means the United States Internal Revenue Service.

**28.25.** "***Non-Employee Director***" means a Director who is not an Employee of the Company or any Parent, Subsidiary or Affiliate.

**28.26.** "***Option***" means an award of an option to purchase Shares pursuant to Section 5.

**28.27.** "***Original Effective Date***" means the day immediately prior to the date of the underwritten initial public offering of the Company's Common Stock pursuant to a registration statement that was declared effective by the SEC.

**28.28.** "***Outstanding Shares***" means, as of a specified date, the sum of (a) the then-issued and outstanding Shares and (ii) the number of Shares issuable pursuant to the exercise of any outstanding, pre-funded warrants to acquire Shares for a nominal exercise price.

**28.29.** "***Parent***" means any corporation (other than the Company) in an unbroken chain of corporations ending with the Company if each of such corporations other than the Company owns stock possessing 50% or more of the total combined voting power of all classes of stock in one of the other corporations in such chain.

**28.30.** "***Participant***" means a person who holds an Award under this Plan.

**28.31.** "***Performance Award***" means a cash or stock Award granted pursuant to Section 10 of the Plan.

**28.32.** "***Performance Factors***" means any of the factors selected by the Committee and specified in an Award Agreement, which, for the avoidance of doubt, may include any factors or measures that the Committee deems appropriate, either individually, alternatively or in any combination, applied to the Company as a whole or any business unit or Subsidiary, either individually, alternatively, or in any combination, on a GAAP or non-GAAP basis, and measured, to the extent applicable on an absolute basis or relative to a pre-established target, to determine whether the performance goals established by the Committee with respect to applicable Awards have been satisfied.

The Committee may, in recognition of unusual or non-recurring items such as acquisition-related activities or changes in applicable accounting rules, provide for one or more equitable adjustments (based on objective standards) to the Performance Factors to preserve the Committee's original intent regarding the Performance Factors at the time of the initial award grant. It is within the sole discretion of the Committee to make or not make any such equitable adjustments. The Committee is authorized to make adjustments as it deems appropriate in the method of calculating the attainment of Performance Factors.

**28.33.** "***Performance Period***" means one or more periods of time, which may be of varying and overlapping durations, as the Committee may select, over which the attainment of one or more Performance Factors will be measured for the purpose of determining a Participant's right to, and the payment of, a Performance Award.

**28.34.** "***Performance Share***" means an Award granted pursuant to Section 10 of the Plan, the payment of which is contingent upon achieving certain performance goals established by the Committee.

**28.35.** "***Performance Unit"*** means a right granted to a Participant pursuant to Section 10 to receive Shares or cash, the payment of which is contingent upon achieving certain performance goals established by the Committee.

**28.36.** "***Permitted Transferee***" means any child, stepchild, grandchild, parent, stepparent, grandparent, spouse, former spouse, sibling, niece, nephew, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law (including adoptive relationships) of the Employee, any person sharing the Employee's household (other than a tenant or employee), a trust in which these persons (or the Employee) have more than 50% of the beneficial interest, a foundation in which these persons (or the Employee) control the management of assets, and any other entity in which these persons (or the Employee) own more than 50% of the voting interests.

**28.37.** "***Plan***" means this Aeglea BioTherapeutics, Inc. 2016 Equity Incentive Plan, as amended from time to time.

**28.38.** "***Prior Plan Returning Shares***" means (a) shares that are subject to stock options or other awards granted under the Company's 2015 Equity Incentive Plan (the "***Prior Plan***") that cease to be subject to such stock options or other awards by forfeiture or otherwise after the Original Effective Date, (b) shares issued under the Prior Plan before or after the Original Effective Date pursuant to the exercise of stock options that are, after the Original Effective Date, forfeited, (c) shares issued under the Prior Plan that are repurchased by the Company at the original issue price and (d) shares that are subject to stock options or other awards under the Prior Plan that are used to pay the exercise price of an option or withheld to satisfy the tax withholding obligations related to any award.

**28.39.** "***Purchase Price***" means the price to be paid for Shares acquired under the Plan, other than Shares acquired upon exercise of an Option or SAR.

**28.40.** "***Restricted Stock Award***" means an award of Shares pursuant to Section 6 of the Plan, or issued pursuant to the early exercise of an Option.

**28.41.** "***Restricted Stock Unit***" means an Award granted pursuant to Section 9 of the Plan.

**28.42.** "***Rule 16b-3***" means Rule 16b-3 promulgated under the Exchange Act or any successor to Rule 16b-3, as in effect from time to time.

**28.43.** "***SEC***" means the United States Securities and Exchange Commission.

**28.44.** "***Securities Act***" means the United States Securities Act of 1933, as amended.

**28.45.** "***Service***" shall mean service as an Employee, Consultant, Director or Non-Employee Director, to the Company or a Parent, Subsidiary or Affiliate, subject to such further limitations as may be set forth in the Plan or the applicable Award Agreement. An Employee will not be deemed to have ceased to provide Service in the case of (a) sick leave, (b) military leave, or (c) any other leave of absence approved by the Company; provided, that such leave is for a period of not more than 90 days (x) unless reemployment upon the expiration of such leave is guaranteed by contract or statute, or (y) unless provided otherwise pursuant to formal policy adopted from time to time by the Company's Board and issued and promulgated to employees in writing. In the case of any Employee on an approved leave of absence or a reduction in hours worked (for illustrative purposes only, a change in schedule from that of full-time to part-time), the Committee may make such provisions respecting suspension of or modification to vesting of the Award while on leave from the employ of the Company or a Parent, Subsidiary or Affiliate or during such change in working hours as it may deem appropriate, except that in no event may an Award be exercised after the expiration of the term set forth in the applicable Award Agreement. In the event of military leave, if required by applicable laws, vesting shall continue for the longest period that vesting continues under any other statutory or Company approved leave of absence and, upon a Participant's returning from military leave (under conditions that would entitle him or her to protection upon such return under the Uniform Services Employment and Reemployment Rights Act), he or she shall be given vesting credit with respect to Awards to the same extent as would have applied had the Participant continued to provide Service to the Company throughout the leave on the same terms as he or she was providing Service immediately prior to such leave. An employee shall have terminated employment as of the date he or she ceases to provide Service (regardless of whether the termination is in breach of local employment laws or is later found to be invalid) and employment shall not be extended by any notice period or garden leave mandated by local law, *provided however*, that a change in status from an employee to a consultant or advisor shall not terminate the service provider's Service, unless determined by the Committee, in its discretion. The Committee will have sole discretion to determine whether a Participant has ceased to provide Service and the effective date on which the Participant ceased to provide Service.

**28.46.** "***Shares***" means shares of Common Stock and the common stock of any successor entity.

**28.47.** "***Stock Appreciation Right***" means an Award granted pursuant to Section 8 of the Plan.

**28.48.** "***Stock Bonus***" means an Award granted pursuant to Section 7 of the Plan.

**28.49.** "***Stockholder Approval Date***" means , 2023, the date of the Company's special meeting of the stockholders at which this amendment and restatement of the Plan was approved.

**28.50.** "***Subsidiary***" means any corporation (other than the Company) in an unbroken chain of corporations beginning with the Company if each of the corporations other than the last corporation in the

unbroken chain owns stock possessing 50% or more of the total combined voting power of all classes of stock in one of the other corporations in such chain.

**28.51.** "***Treasury Regulations***" means regulations promulgated by the United States Treasury Department.

**28.52.** "***Unvested Shares***" means Shares that have not yet vested or are subject to a right of repurchase in favor of the Company (or any successor thereto).