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

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

Filed by the Registrant

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 §240.14a-12

Spyre Therapeutics, Inc.

(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 all boxes that apply):

No fee required.

Fee paid previously with preliminary materials.

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



221 Crescent Street, Building 23, Suite 105, Waltham, MA 02453

**NOTICE OF THE 2025 ANNUAL MEETING OF STOCKHOLDERS
TO BE HELD ON MAY 29, 2025**

To the Stockholders of Spyre Therapeutics:

Spyre Therapeutics, Inc. (the “Company”) will hold its 2025 Annual Meeting of Stockholders (the “Annual Meeting”) on Thursday, May 29, 2025, at 12:00 p.m. Eastern Time. The Annual Meeting will be a virtual meeting conducted exclusively online via live audio webcast at www.virtualshareholdermeeting.com/SYRE2025. The Annual Meeting will be held for the following purposes, as more fully described in the accompanying proxy statement (the “Proxy Statement”):

- (1) To elect the three Class III director nominees named in the Proxy Statement to serve until the 2028 Annual Meeting of Stockholders and until their successors are duly elected and qualified;
- (2) To approve, on a non-binding, advisory basis, the compensation of the Company’s named executive officers;
- (3) To ratify the appointment of KPMG LLP as the Company’s independent registered public accounting firm for the year ending December 31, 2025;
- (4) To transact any other matters that may properly come before the Annual Meeting or any adjournments or postponements thereof.

The Board of Directors has fixed April 4, 2025 as the Record Date. Only stockholders of record at the close of business on that date will be entitled to notice of, and to vote at, the Annual Meeting or any adjournment or postponement thereof.

Instructions for accessing the virtual Annual Meeting are provided in the Proxy Statement. Unless otherwise announced differently at the meeting or on the meeting website, in the event of a technical malfunction or other situation that the meeting chair determines may affect the ability of the Annual Meeting to satisfy the requirements for a meeting of stockholders to be held by means of remote communication under the Delaware General Corporation Law, or that otherwise makes it advisable to adjourn the Annual Meeting, the meeting chair or secretary will convene the meeting at 1:00 p.m. Eastern Time on the date specified above and at the Company’s address specified above solely for the purpose of adjourning the meeting to reconvene at a date, time and physical or virtual location announced by the meeting chair or secretary. Under either of the foregoing circumstances, we will post information regarding the announcement on the Investors & Media page of the Company’s website at <https://ir.spyre.com>.

By Order of the Board of Directors,

/s/ Cameron Turtle

Cameron Turtle, D.Phil.

Chief Executive Officer and Director

Waltham, Massachusetts

April 14, 2025

Whether or not you expect to participate in the virtual Annual Meeting, please vote as promptly as possible in order to ensure your representation at the Annual Meeting. You may vote online, by telephone or by using the proxy card or voting instruction form provided with the printed proxy materials.

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LEGAL MATTERS

Important Notice Regarding the Availability of Proxy Materials for the 2025 Annual Meeting of Stockholders to Be Held on May 29, 2025. The Proxy Statement and Annual Report for the year ended December 31, 2024 are available at www.proxyvote.com.

Forward-Looking Statements. The Proxy Statement contains “forward-looking statements” within the meaning of the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995, which statements are subject to substantial risks and uncertainties and are based on estimates and assumptions. All statements other than statements of historical fact included in the Proxy Statement, including statements about the Company’s Board of Directors, corporate governance practices and executive compensation program and equity compensation utilization, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “might,” “will,” “objective,” “intend,” “should,” “could,” “can,” “would,” “expect,” “believe,” “design,” “estimate,” “predict,” “potential,” “plan” or the negative of these terms, and similar expressions intended to identify forward-looking statements. These statements involve known and unknown risks, uncertainties and other factors that could cause our actual results to differ materially from the forward-looking statements expressed or implied in the Proxy Statement. Such risks, uncertainties and other factors include those risks described in “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in the Company’s most recent Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission (“SEC”) and other subsequent documents we file with the SEC. The Company expressly disclaims any obligation to update or alter any statements whether as a result of new information, future events or otherwise, except as required by law.

Website References. Website references throughout this document are inactive textual references and provided for convenience only, and the content on the referenced websites is not incorporated herein by reference and does not constitute a part of the Proxy Statement.

Use of Trademarks. Spyre Therapeutics is the trademark of Spyre Therapeutics, Inc. Other names and brands may be claimed as the property of others.



221 Crescent Street, Building 23, Suite 105, Waltham, MA 02453

**PROXY STATEMENT
FOR THE 2025 ANNUAL MEETING OF STOCKHOLDERS
QUESTIONS AND ANSWERS ABOUT THE PROXY MATERIALS AND VOTING**

What Is the Purpose of These Proxy Materials?

We are making these proxy materials available to you in connection with the solicitation of proxies by the Board of Directors (the “Board”) of Spyre Therapeutics, Inc. (“we,” “us,” “our” or the “Company”) for use at the 2025 Annual Meeting of Stockholders (the “Annual Meeting”) to be held virtually on May 29, 2025 at 12:00 p.m. Eastern Time, or at any other time following adjournment or postponement thereof. You are invited to participate in the Annual Meeting and to vote on the proposals described in this proxy statement (the “Proxy Statement”). The proxy materials are being made available to our stockholders beginning on or about April 14, 2025.

Why Did I Receive a Notice of Internet Availability?

Pursuant to SEC rules, we are furnishing the proxy materials to our stockholders primarily via the Internet instead of mailing printed copies. This process allows us to expedite our stockholders’ receipt of proxy materials, lower the costs of printing and mailing the proxy materials and reduce the environmental impact of our Annual Meeting. If you received a Notice of Internet Availability of Proxy Materials (the “Notice”), you will not receive a printed copy of the proxy materials unless you request one. The Notice provides instructions on how to access the proxy materials for the Annual Meeting via the Internet, how to request a printed set of proxy materials and how to vote your shares.

Why Are We Holding a Virtual Annual Meeting?

We have adopted a virtual meeting format for the Annual Meeting to provide a consistent experience to all stockholders regardless of geographic location. We believe this expands stockholder access, improves communications and lowers our costs while reducing the environmental impact of the meeting. In structuring our virtual Annual Meeting, our goal is to enhance rather than constrain stockholder participation in the meeting, and we have designed the meeting to provide stockholders with the same rights and opportunities to participate as they would have at an in-person meeting.

Who Can Vote?

Only stockholders of record at the close of business on April 4, 2025 (the “Record Date”) are entitled to notice of the Annual Meeting and to vote on the proposals described in this Proxy Statement. At the close of business on the Record Date, 60,275,561 shares of our common stock were issued and outstanding. Shares of our preferred stock generally do not have voting rights and holders of our preferred stock are therefore not entitled to vote at the Annual Meeting.

What Is the Difference between Holding Shares as a Registered Stockholder and as a Beneficial Owner?

Registered Stockholder: Shares Registered in Your Name

If your shares of common stock are registered directly in your name with our transfer agent, Equiniti Trust Company, LLC, you are considered to be, with respect to those shares of common stock, the registered stockholder, and these proxy materials are being sent directly to you by us.

Beneficial Owner: Shares Registered in the Name of a Broker, Fiduciary or Custodian

If your shares of common stock are held by a broker, fiduciary or custodian, you are considered the beneficial owner of shares of common stock held in “street name,” and these proxy materials are being forwarded to you from that broker, fiduciary or custodian.

How Can I Participate in the Virtual Annual Meeting?

Stockholders of record as of the close of business on the Record Date are entitled to participate in and vote at the Annual Meeting. To participate in the Annual Meeting, including to vote and ask questions, stockholders of record should go to the meeting website at www.virtualshareholdermeeting.com/SYRE2025, enter the 16-digit control number found on your proxy card or Notice, and follow the instructions on the website. If your shares are held in street name and your voting instruction form or Notice indicates that you may vote those shares through www.proxyvote.com, then you may access, participate in and vote at the Annual Meeting with the 16-digit access code indicated on that voting instruction form or Notice. Otherwise, stockholders who hold their shares in street name should contact their bank, broker or other nominee (preferably at least five days before the Annual Meeting) and obtain a “legal proxy” in order to be able to attend, participate in or vote at the Annual Meeting.

We will endeavor to answer as many stockholder-submitted questions as time permits that comply with the Annual Meeting rules of conduct. We reserve the right to edit profanity or other inappropriate language and to exclude questions regarding topics that are not pertinent to meeting matters or Company business. If we receive substantially similar questions, we may group such questions together and provide a single response to avoid repetition.

The meeting webcast will begin promptly at 12:00 p.m. Eastern Time. Online check-in will begin approximately 15 minutes before then, and we encourage you to allow ample time for check-in procedures. If you experience technical difficulties during the check-in process or during the meeting, please call the number listed on the meeting website for technical support. Additional information regarding the rules and procedures for participating in the Annual Meeting will be set forth in our meeting rules of conduct, which stockholders can view during the meeting at the meeting website.

What Am I Voting on?

The proposals to be voted on at the Annual Meeting are as follows:

- (1) Election of three Class III director nominees to serve until the 2028 Annual Meeting of Stockholders (“**Proposal 1**”);
- (2) Approval, on a non-binding, advisory basis, of the compensation of the Company’s named executive officers (“**Proposal 2**”); and
- (3) Ratification of the appointment of KPMG LLP as the Company’s independent auditor for 2025 (“**Proposal 3**”).

How Does the Board Recommend That I Vote?

The Board recommends that you vote your shares “**FOR**” each director nominee in Proposal 1 and “**FOR**” Proposals 2 and 3.

What If Another Matter Is Properly Brought before the Annual Meeting?

As of the date of filing this Proxy Statement, the Board knows of no other matters that will be presented for consideration at the Annual Meeting. If any other matters are properly brought before the Annual Meeting, it is the intention of the persons named as proxies in the proxy card to vote on such matters in accordance with their best judgment.

How Many Votes Do I Have?

Each share of common stock is entitled to one vote on each proposal to be voted on at the Annual Meeting.

What Does It Mean If I Receive More Than One Set of Proxy Materials?

If you receive more than one set of proxy materials, your shares may be registered in more than one name or held in different accounts. Please cast your vote with respect to each set of proxy materials that you receive to ensure that all of your shares are voted.

How Do I Vote?

Even if you plan to attend the Annual Meeting, we recommend that you also submit your vote as early as possible in advance so that your vote will be counted if you later decide not to, or are unable to, virtually attend the Annual Meeting.

Registered Stockholder: Shares Registered in Your Name

If you are the registered stockholder, you may vote your shares online during the virtual Annual Meeting (see “How Can I Participate in the Virtual Annual Meeting?” above) or by proxy in advance of the Annual Meeting by Internet (at www.proxyvote.com) or, if you requested paper copies of the proxy materials, by completing and mailing a proxy card or by telephone (at (800) 690-6903).

Beneficial Owner: Shares Registered in the Name of a Broker, Fiduciary or Custodian

If you are the beneficial owner, you may vote your shares online during the virtual Annual Meeting (see “How Can I Participate in the Virtual Annual Meeting?” above) or you may direct your broker, fiduciary or custodian how to vote in advance of the Annual Meeting by following the instructions they provide.

What Happens If I Do Not Vote?

Registered Stockholder: Shares Registered in Your Name

If you are the registered stockholder and do not vote in one of the ways described above, your shares will not be voted at the Annual Meeting and will not be counted toward the quorum requirement.

Beneficial Owner: Shares Registered in the Name of a Broker, Fiduciary or Custodian

If you are the beneficial owner and do not direct your broker, fiduciary or custodian how to vote your shares, your broker, fiduciary or custodian will only be able to vote your shares with respect to proposals considered to be “routine.” Your broker, fiduciary or custodian is not entitled to vote your shares with respect to “non-routine” proposals, which we refer to as a “broker non-vote.” Whether a proposal is considered routine or non-routine is subject to stock exchange rules and final determination by the stock exchange. Even with respect to routine matters, some brokers are choosing not to exercise discretionary voting authority. As a result, we urge you to direct your broker, fiduciary or custodian how to vote your shares on all proposals to ensure that your vote is counted.

What If I Sign and Return a Proxy Card or Otherwise Vote but Do Not Indicate Specific Choices?

Registered Stockholder: Shares Registered in Your Name

The shares represented by each signed and returned proxy will be voted at the Annual Meeting by the persons named as proxies in the proxy card in accordance with the instructions indicated on the proxy card. However, if you are the registered stockholder and sign and return your proxy card without giving specific instructions, the persons named as proxies in the proxy card will vote your shares in accordance with the recommendations of the Board. Your shares will be counted toward the quorum requirement.

Beneficial Owner: Shares Registered in the Name of a Broker, Fiduciary or Custodian

If you are the beneficial owner and do not direct your broker, fiduciary or custodian how to vote your shares, your broker, fiduciary or custodian will only be able to vote your shares with respect to proposals considered to be “routine.” Your broker, fiduciary or custodian is not entitled to vote your shares with respect to “non-routine” proposals, resulting in a broker non-vote with respect to such proposals.

Can I Change My Vote after I Submit My Proxy?

Registered Stockholder: Shares Registered in Your Name

If you are the registered stockholder, you may revoke your proxy at any time before the final vote at the Annual Meeting in any one of the following ways:

- (1) You may complete and submit a new proxy card, but it must bear a later date than the original proxy card;
- (2) You may submit new proxy instructions via telephone or the Internet;
- (3) You may send a timely written notice that you are revoking your proxy to our Corporate Secretary at the address set forth on the first page of this Proxy Statement; or
- (4) You may vote by attending the Annual Meeting virtually. However, your virtual attendance at the Annual Meeting will not, by itself, revoke your proxy.

Your last submitted vote is the one that will be counted.

Beneficial Owner: Shares Registered in the Name of a Broker, Fiduciary or Custodian

If you are the beneficial owner, you must follow the instructions you receive from your broker, fiduciary or custodian with respect to changing your vote.

What Is the Quorum Requirement?

The holders of a majority of the shares of common stock outstanding and entitled to vote at the Annual Meeting, either virtually or represented by proxy, must be present at the Annual Meeting to constitute a quorum. A quorum is required to transact business at the Annual Meeting.

Your shares will be counted toward the quorum only if you submit a valid proxy (or a valid proxy is submitted on your behalf by your broker, fiduciary or custodian) or if you attend the Annual Meeting virtually and vote. Abstentions and broker non-votes, if any, will be counted toward the quorum requirement. If there is no quorum, the chair of the Annual Meeting or the holders of a majority of shares of common stock present at the Annual Meeting, either virtually or represented by proxy, may adjourn the Annual Meeting to another time or date.

How Many Votes Are Required to Approve Each Proposal and How Are Votes Counted?

Votes will be counted by American Election Services, the Inspector of Elections appointed for the Annual Meeting.

Proposal 1: Election of Directors

A nominee will be elected as a director at the Annual Meeting if the nominee receives a plurality of the votes cast "FOR" his or her election. "Plurality" means that the individuals who receive the highest number of votes cast "FOR" are elected as directors. Broker non-votes, if any, and votes that are withheld will not be counted as votes cast on the matter and will have no effect on the outcome of the election. Stockholders do not have cumulative voting rights for the election of directors.

Proposal 2: Non-Binding Advisory Vote on Executive Compensation

The affirmative vote of the holders of at least a majority of shares of common stock present or represented at the Annual Meeting and entitled to vote on the matter is required to approve this proposal. Abstentions will have the same effect as a vote "AGAINST" the matter. Broker non-votes, if any, will have no effect on the outcome of the matter.

Proposal 3: Ratification of Independent Auditor Appointment

The affirmative vote of the holders of at least a majority of shares of common stock present or represented at the Annual Meeting and entitled to vote on the matter is required to approve this proposal. Abstentions will have the same effect as a vote "AGAINST" the matter. Broker non-votes, if any, will have no effect on the outcome of the matter.

Who Is Paying for This Proxy Solicitation?

We will pay the costs associated with the solicitation of proxies, including the preparation, assembly, printing and mailing of the proxy materials. We may also reimburse brokers, fiduciaries or custodians for the cost of forwarding proxy materials to beneficial owners of shares of common stock held in "street name."

Our employees, officers and directors may solicit proxies in person or via telephone or the Internet. We will not pay additional compensation for any of these services.

How Can I Find out the Voting Results?

We expect to announce preliminary voting results at the Annual Meeting. Final voting results will be published in a Current Report on Form 8-K to be filed with the SEC within four business days after the Annual Meeting.

PROPOSAL 1: ELECTION OF DIRECTORS

In accordance with our Certificate of Incorporation and Bylaws, the Board has fixed the number of directors constituting the Board at eight. At the Annual Meeting, the stockholders will vote to elect the three Class III director nominees named in this Proxy Statement to serve until the 2028 Annual Meeting of Stockholders and until their successors are duly elected and qualified or until their earlier resignation or removal. Our Board has nominated Peter Harwin, Michael Henderson and Sandra Milligan for election to our Board. Dr. Milligan was appointed to the Board in May 2024 and was initially identified for a position on our Board by a third-party search firm. Messrs. Harwin and Henderson were appointed to the Board in June 2023 in accordance with the Agreement and Plan of Merger, dated as of June 22, 2023, in connection with our acquisition of Spyre Therapeutics, Inc., ("Pre-Merger Spyre") that was completed in June 2023 (the "Asset Acquisition").

Our director nominees have indicated that they are willing and able to serve as directors. However, if any of them becomes unable or, for good cause, unwilling to serve, proxies may be voted for the election of such other person as shall be designated by our Board, or the Board may decrease the size of the Board.

Information Regarding Director Nominees and Continuing Directors

Our Board is divided into three classes, with members of each class holding office for staggered three-year terms. There are currently three Class I directors, whose terms expire at the 2026 Annual Meeting of Stockholders; two Class II directors, whose terms expire at the 2027 Annual Meeting of Stockholders; and three Class III directors, who are up for election at this meeting for a term expiring at the 2028 Annual Meeting of Stockholders.

Biographical and other information regarding our director nominees and directors continuing in office, including the primary skills and experiences considered by our Nominating and Corporate Governance Committee (the "Nominating Committee") in determining to recommend them as nominees, is set forth below.

Name	Class	Age (as of April 14)	Position
Mark McKenna	I	45	Director
Cameron Turtle	I	35	Chief Executive Officer and Director
Laurie Stelzer ⁽¹⁾⁽²⁾	I	57	Director
Jeffrey W. Albers ⁽²⁾⁽³⁾	II	53	Director
Tomas Kiselak ⁽³⁾	II	38	Director
Peter Harwin ⁽¹⁾	III	39	Director
Michael Henderson ⁽²⁾	III	35	Director
Sandra Milligan ⁽¹⁾⁽³⁾	III	61	Director

(1) Member of the Nominating Committee

(2) Member of the Audit Committee

(3) Member of the Compensation Committee

Class I Directors Continuing in Office

Mark McKenna. Mr. McKenna has served as a director since February 2024. Mr. McKenna is the founder of Mirador Therapeutics, Inc., a biotechnology company, and has served as its Chairman and Chief Executive Officer since March 2024. Mr. McKenna has also served as chairman of the board of directors of Apogee Therapeutics, Inc. (Nasdaq: APGE), a biotechnology company, since August 2023 and a director at New Amsterdam Pharma (Nasdaq: NAMS), a clinical biopharmaceutical company, since July 2024. In addition, Mr. McKenna has served as a venture partner at Arch Venture Partners, an investment firm, since February 2024 and Senior Advisor at Fairmount Funds Management LLC, a healthcare investment firm, since October 2023. Prior to Mirador, Mr. McKenna served as the President and Chief Executive Officer and a member of the board of directors of Prometheus Biosciences, Inc., a clinical stage biotechnology company, from September 2019 to June 2023, when Prometheus was acquired by Merck & Co, Inc. and as Chairman of the board of Prometheus from August 2021 to June 2023. Prior to Prometheus, Mr. McKenna was a corporate officer of Bausch Health Companies, Inc. and served as President of its subsidiary, Salix Pharmaceuticals, Inc., a pharmaceutical company, from March 2016 through August 2019. Prior to Salix Pharmaceuticals, Mr. McKenna spent more than a decade in various roles

with Bausch + Lomb, also a division of Bausch Health Companies, Inc., most recently as Senior Vice President and General Manager of its U.S. Vision Care business. Mr. McKenna holds a B.S. in marketing from Arizona State University and an M.B.A. from Azusa Pacific University. Mr. McKenna was Ernst & Young's Entrepreneur of the Year in 2023.

We believe Mr. McKenna is qualified to serve on our Board due to his extensive experience as an executive officer in the biopharmaceutical industry.

Cameron Turtle, Dphil. Dr. Turtle joined us as Chief Operating Officer in June 2023, and was appointed as our Chief Executive Officer and a director in November 2023. Prior to joining the Company, Dr. Turtle was an advisor to Pre-Merger Spyre from May 2023 to June 2023. Previously, he served as Venture Partner at Foresite Labs, a life sciences investment firm, from July 2022 to May 2023; Chief Strategy Officer of BridgeBio Pharma (Nasdaq: BBIO), a biopharmaceutical company, from January 2021 to April 2022; and Chief Business Officer of Eidos Therapeutics (Nasdaq: EIDX), a biopharmaceutical company, from November 2018 to January 2021, where he led business development, investor relations, and multiple operational functions as the company advanced an investigational medicine for a form of heart failure. Prior to joining BridgeBio and Eidos, he was a consultant at McKinsey & Company, where he worked with pharmaceutical and medical device companies on topics including M&A, growth strategy, clinical trial strategy, and sales force optimization. Dr. Turtle has served as a member of the board of directors of Oruka Therapeutics, Inc. (Nasdaq: ORKA) since August 2024. Dr. Turtle received his B.S. with honors in Bioengineering from the University of Washington and his D.Phil. in Cardiovascular Medicine from the University of Oxford, St. John's College. He is the recipient of several awards, including a Rhodes Scholarship, Goldwater Scholarship, Forbes 30 Under 30 and San Francisco Business Times 40 Under 40.

We believe Dr. Turtle is qualified to serve on our Board due to his experience as a leader in building, financing, and shaping biopharma organizations from preclinical development to late-stage clinical trials and commercialization.

Laurie Stelzer. Ms. Stelzer has served as a director since November 2023. Ms. Stelzer has served as Chief Financial Officer of Kailera Therapeutics, Inc., a biotechnology company focused on developing therapies for obesity, since January 2025. Prior to joining Kailera, Ms. Stelzer served as Chief Financial Officer of Orna Therapeutics, Inc., a biotechnology company focused on RNA therapeutics, from May 2024 to January 2025. Prior to joining Orna, Ms. Stelzer served as Chief Financial Officer of ReNAgade Therapeutics, Inc., a biotechnology company focused on RNA therapeutics, from September 2023 to May 2024. Prior to joining ReNAgade, Ms. Stelzer served as Chief Financial Officer of Mirati Therapeutics, Inc. (Nasdaq: MRTX), a commercial-stage targeted oncology company, from May 2022 to September 2023. Prior to joining Mirati Therapeutics, Ms. Stelzer served as Executive Vice President and Chief Financial Officer of Arena Pharmaceuticals, Inc. (acquired by Pfizer Inc.), a biopharmaceutical company, from March 2020 until the completion of Pfizer's acquisition in March 2022. Prior to joining Arena Pharmaceuticals, Ms. Stelzer served as Chief Financial Officer at Halozyne Therapeutics, Inc. (Nasdaq: HALO), a biopharma technology platform company, from June 2015 to March 2020, where she led the Finance, Information Technology, Business Development, Project Management and Site Operations organizations. Prior to joining Halozyne Therapeutics, Ms. Stelzer held senior management roles at Shire Plc (acquired by Takeda Pharmaceutical), including Senior Vice President of Finance, Division Chief Financial Officer for the Regenerative Medicine Division and Head of Investor Relations. Previously, she also worked at Amgen, Inc. (Nasdaq: AMGN), a global biopharmaceutical company, for 15 years, serving in positions of increasing responsibility in the areas of Finance, Treasury, Global Accounting and International/Emerging Markets. Ms. Stelzer has served as a member of the board of directors of Sionna Therapeutics (Nasdaq: SION), a clinical-stage cystic fibrosis company, since 2024, PMV Pharmaceuticals, Inc. (Nasdaq: PMVP), a precision oncology company, since 2020, Surface Oncology, Inc. (Nasdaq: SURF), a clinical-stage immunoncology company, from 2018 until its acquisition by Coherus in September 2023 and Longboard Pharmaceuticals, a clinical-stage neurology company from 2020 to 2021. Ms. Stelzer received her B.S. in Accounting from Arizona State University and her M.B.A. from University of California, Los Angeles, Anderson School of Management.

We believe Ms. Stelzer is qualified to serve on our Board because of her financial expertise and experience within the biopharmaceutical industry.

Class II Directors Continuing in Office

Jeffrey Albers. Mr. Albers has served as a director since November 2023. Mr. Albers has over 25 years of experience working in the biopharmaceutical industry and bringing important new medicines to patients with cancer and rare diseases. He has served as Chairman of Blueprint Medicines Corporation (Nasdaq: BPMC), a global precision therapy company,

since June 2021, and Venture Partner at Atlas Venture, a venture capital firm focused on investment in biotechnology companies, since January 2023. Mr. Albers served as Chief Executive Officer, President and Chairman of Blueprint Medicines from June 2021 to April 2022, Executive Chairman from April 2022 to December 2022 and as Chief Executive Officer, President and Director from July 2014 to June 2021. Prior to joining Blueprint Medicines in July 2014, Mr. Albers was President of Algeta ASA, a Norwegian biotechnology company from January 2012 to April 2014, where he oversaw the U.S. business. Prior to Algeta ASA, from July 2005 to November 2011, Mr. Albers was at Genzyme Corporation, a biotechnology company that is now a wholly owned subsidiary of Sanofi S.A., most recently as Vice President of the U.S. hematology and oncology business unit. In addition to Blueprint Medicines, Mr. Albers serves on the board of directors of Kymera Therapeutics, Inc. (Nasdaq: KYMR) and several private companies, and previously served on the board of directors of Magenta Therapeutics, Inc. (which later became Dianthus Therapeutics, Inc. (Nasdaq: DNTH)) from July 2017 to September 2023. Mr. Albers received a B.S. from Indiana University and an M.B.A. and a J.D. from Georgetown University.

We believe Mr. Albers is qualified to serve on our Board due to his extensive leadership experience in the biopharmaceutical industry.

Tomas Kiselak. Mr. Kiselak has served as a director since June 2023. Mr. Kiselak is a Managing Member at Fairmount Funds Management LLC, a healthcare investment firm he co-founded in April 2016. Prior to Fairmount, Mr. Kiselak was a managing director at RA Capital Management, LLC, a healthcare and life science investment firm. Mr. Kiselak serves as the chairman of the board of directors of Viridian Therapeutics, Inc. (Nasdaq: VRDN) and as a director for Apogee Therapeutics, Inc. (Nasdaq: APGE), Zenas BioPharma, Inc. (Nasdaq: ZBIO) as well as several private companies, and served as a director for Dianthus Therapeutics, Inc. (Nasdaq: DNTH) from September 2023 to March 2025. He received a B.S. in neuroscience and economics from Amherst College.

We believe Mr. Kiselak is qualified to serve on our Board because of his experience advising biotechnology companies and as a manager of funds specializing in the area of life sciences.

Class III Director Nominees

Peter Harwin. Mr. Harwin has served as a director since June 2023. Mr. Harwin is a Managing Member at Fairmount Funds Management LLC, a healthcare investment firm he co-founded in April 2016. Prior to Fairmount, Mr. Harwin was a member of the investment team at Boxer Capital, LLC, an investment fund that was part of the Tavistock Group, based in San Diego. Mr. Harwin also serves as chairman of the board of directors of Cogent Biosciences, Inc. (Nasdaq: COGT) and is a director of Apogee Therapeutics, Inc. (Nasdaq: APGE), Oruka Therapeutics, Inc. (Nasdaq: ORKA) and Paragon Therapeutics, Inc. (“Paragon”), and served as a director for Viridian Therapeutics, Inc. (Nasdaq VRDN) from October 2020 to March 2025. Mr. Harwin holds a B.B.A. from Emory University.

We believe Mr. Harwin is qualified to serve on our Board because of his experience serving as a director of biotechnology companies and as a manager of funds specializing in the area of life sciences.

Michael Henderson, M.D. Dr. Henderson has served as a director since June 2023. Dr. Henderson has served as Chief Executive Officer of Apogee Therapeutics, Inc. (Nasdaq: APGE), a biotechnology company, since September 2022 as well as a member of its board of directors since June 2023. Dr. Henderson is an experienced biotechnology executive with expertise in business leadership, drug development, and commercial strategy. He has overseen the creation of multiple companies, launched a significant number of drug development programs, and led teams to two FDA approvals, to date. Prior to joining Apogee, Dr. Henderson served as Chief Business Officer of BridgeBio Pharma, Inc. (Nasdaq: BBIO), a commercial-stage biopharmaceutical company, from January 2020 to September 2022, where he was responsible for furthering the overarching strategy of BridgeBio, identifying and investing in new technologies and running business development and operations. Prior to holding that position, he spent two years serving as BridgeBio’s Senior Vice President, Asset Acquisition, Strategy and Operations, where he was responsible for business development, strategy and operations. Dr. Henderson joined BridgeBio as Vice President of Asset Acquisition, Strategy and Operations in April 2016. Dr. Henderson also served as the Chief Executive Officer of a number of BridgeBio’s subsidiaries. Prior to BridgeBio, Dr. Henderson worked at McKinsey & Company, a global management consulting firm, from January 2015 to April 2016 and prior to that, he co-founded PellePharm, Inc., a biotechnology company, in August 2011. Dr. Henderson previously served on the board of directors of ARYA Sciences Acquisition Corp IV (Nasdaq: ARYD), a special purpose acquisition company focused on the healthcare industry, from February 2021 to August 2024. Dr. Henderson received his B.A. in global health from Harvard University and his M.D. from Stanford University.

We believe Dr. Henderson is qualified to serve on our Board because of his experience in business leadership, drug development and commercial strategy in the area of life sciences.

Sandra Milligan, M.D., J.D. Dr. Milligan has served as a director since May 2024. Dr. Milligan has served as SVP, Global Regulatory Affairs of Daiichi Sankyo, Inc. since February 2025. Prior to joining Daiichi, Dr. Milligan served as Interim CEO of Aspira Women's Health (Nasdaq: AWH), a biotechnology company focused on the development of gynecologic disease diagnostic tools, from December 2024 to January 2025, and as President from April 2024 to February 2025. Previously, from 2020 to 2024, Dr. Milligan served as the Head of Research and Development of Organon & Co. (NYSE: OGN), a global healthcare company, and, from 2015 to 2020, as Senior Vice President and Head of Global Regulatory Affairs and Clinical Safety of Merck & Co. (NYSE: MRK), a global healthcare company. Previously, from 2012 to 2015, she served as Vice President of Product Development Regulatory for Genentech, Inc., a biotechnology company, and, from 2002 to 2012, she was at Amgen Inc. (Nasdaq: AMGN), a biotechnology company, in positions of increasing responsibility across legal and regulatory affairs functions. Dr. Milligan served in the United States Army Medical Corps from 1987 to 1994. Dr. Milligan has served as a member of the board of directors of Gossamer Bio, Inc. (Nasdaq: GOSS), a biopharmaceutical company, since June 2021. Dr. Milligan was on the board of directors of the Drug Information Association, or DIA, from 2011 to 2017, including serving as chair, and is now a DIA fellow. Dr. Milligan received a B.S. in Biology and a B.A. in Psychology from the University of California, Irvine. Additionally, she is a graduate of George Washington University School of Medicine and received a J.D. from the Georgetown University Law Center.

We believe Dr. Milligan is qualified to serve on our Board because of her leadership experience in the biopharmaceutical industry and her expertise in clinical development and regulatory affairs, including within Inflammatory Bowel Disease.

Board Recommendation

The Board recommends a vote “**FOR**” the election of each of the Class III director nominees set forth above.

PROPOSAL 2: NON-BINDING ADVISORY VOTE ON EXECUTIVE COMPENSATION

In accordance with the rules of the SEC and pursuant to the Dodd-Frank Act, we are providing stockholders with an opportunity to make a non-binding, advisory vote on the compensation of our named executive officers. This non-binding advisory vote is commonly referred to as a “say-on-pay” vote.

The say-on-pay vote is a non-binding vote on the compensation of our “named executive officers,” as described in this Proxy Statement in the “Executive Compensation” section, the tabular disclosure regarding such compensation and the accompanying narrative disclosure. The say-on-pay vote is not a vote on our general compensation policies or compensation of our Board. Stockholders are urged to read the “Executive Compensation” section of the Proxy Statement, which discusses how our executive compensation policies and procedures implement our compensation philosophy. Our Compensation Committee and Board believe that these policies and procedures are effective in implementing our compensation philosophy and in achieving our goals.

As an advisory vote, this proposal is not binding. However, our Board and Compensation Committee, which is responsible for designing and administering our executive compensation program, value the opinions expressed by stockholders in their vote on this proposal and will consider the outcome of the vote when making future compensation decisions for our named executive officers.

We are required to hold a say-on-pay vote at least once every three years, and we have determined to hold a say-on-pay vote every year. Unless the Board modifies its policy on the frequency of holding say-on-pay advisory votes, the next say-on-pay vote is expected to occur in 2026.

Board Recommendation

The Board recommends a vote “**FOR**” this proposal.

PROPOSAL 3: RATIFICATION OF INDEPENDENT AUDITOR APPOINTMENT

Our Audit Committee has appointed KPMG LLP (“KPMG”) as the Company’s independent registered public accounting firm for the year ending December 31, 2025. In this Proposal 3, we are asking stockholders to vote to ratify this appointment. Representatives of KPMG are expected to be present at the Annual Meeting. They will have the opportunity to make a statement, if they desire to do so, and are expected to be available to respond to appropriate questions from stockholders. Representatives from PricewaterhouseCoopers LLP (“PwC”) are not expected to be present at the Annual Meeting.

Stockholder ratification of the appointment of KPMG as the Company’s independent auditor is not required by law or our Bylaws. However, we are seeking stockholder ratification as a matter of good corporate practice. If our stockholders fail to ratify the appointment, the committee will reconsider its appointment. Even if the appointment is ratified, the committee, in its discretion, may direct the appointment of a different independent auditor at any time during the year if it determines that such a change would be in the best interests of the Company and our stockholders.

Recent Change in Independent Auditor

Dismissal of Independent Registered Public Accounting Firm

As previously reported on the Company's Current Report on Form 8-K filed with the SEC on March 6, 2025, on February 28, 2025, the Audit Committee dismissed PwC as the Company’s independent registered public accounting firm, effective immediately. PwC served as the independent registered public accounting firm of the Company since 2014.

The reports of PwC on the consolidated financial statements of the Company for the fiscal years ended December 31, 2024 and 2023 did not contain an adverse opinion or disclaimer of opinion and were not qualified or modified as to uncertainty, audit scope or accounting principles.

During the Company's two most recent fiscal years ended December 31, 2024 and 2023 and the subsequent interim period from January 1, 2025 to February 28, 2025, there were (i) no disagreements (as defined in Item 304(a)(1)(iv) of Regulation S-K and the related instructions thereto) with PwC on any matter of accounting principles or practices, financial statement disclosure, or auditing scope or procedure, which disagreement, if not resolved to the satisfaction of PwC, would have caused it to make reference to the subject matter of the disagreement in connection with its report and (ii) no reportable events (as described in Item 304(a)(1)(v) of Regulation S-K), except for a material weakness identified as of December 31, 2024 related to the Company not designing and maintaining effective controls to evaluate the treatment of the Company’s Series A non-voting convertible preferred stock ("Series A Preferred Stock") and Series B non-voting convertible preferred stock ("Series B Preferred Stock") for the purpose of calculating earnings per share under the two-class method, which resulted in a restatement of the consolidated financial statements for the year ended December 31, 2023.

The Company provided PwC with a copy of the disclosures made in this section and requested PwC to furnish the Company with a letter addressed to the SEC stating whether it agrees with the statements made by the Company and, if not, stating the respects in which it does not agree. A copy of PwC’s letter to the SEC dated March 6, 2025 regarding these statements was filed as Exhibit 16.1 to the Company’s Current Report on Form 8-K filed with the SEC on March 6, 2025.

Appointment of New Independent Registered Public Accounting Firm

On February 28, 2025, the Audit Committee, after conducting a competitive process to determine the Company’s independent registered public accounting firm for the fiscal year ending December 31, 2025, appointed KPMG as the independent registered public accounting firm of the Company for the year ending December 31, 2025, effective immediately.

During the Company’s two most recent fiscal years ended December 31, 2024 and 2023 and the subsequent interim period from January 1, 2025 to February 28, 2025, neither the Company nor anyone on its behalf consulted KPMG regarding: (i) the application of accounting principles to a specified transaction, either completed or proposed, or the type of audit opinion that might be rendered on the Company’s financial statements, and neither a written report nor oral advice was provided to the Company that KPMG concluded was an important factor considered by the Company in reaching a decision as to any accounting, auditing or financial reporting issue; or (ii) any matter that was the subject of a disagreement

(as defined in Item 304(a)(1)(iv) of Regulation S-K and the related instructions thereto) or a reportable event (as described in Item 304(a)(1)(v) of Regulation S-K).

Fees for the fiscal years ended December 31, 2024 and 2023

The following table summarizes the audit fees billed and expected to be billed by PwC for the indicated fiscal years and the fees billed by PwC for all other services rendered during the indicated fiscal years. All services associated with such fees were pre-approved by our Audit Committee in accordance with the “Pre-Approval Policies and Procedures” described below.

Fee Category	Year Ended December 31,	
	2024	2023
Audit Fees ⁽¹⁾	\$ 1,574,031	\$ 1,513,184
Audit-Related Fees ⁽²⁾	—	—
Tax Fees ⁽³⁾	67,990	70,923
All Other Fees ⁽⁴⁾	2,125	2,125
Total Fees	<u>\$ 1,644,146</u>	<u>\$ 1,586,232</u>

- (1) Consists of fees for professional services rendered for the audit of our financial statements, review of our interim condensed financial statements, professional consultations with respect to accounting matters and assistance with registration statements filed with the SEC and services that are normally provided by PwC in connection with statutory and regulatory filings or engagements. Included in our 2024 and 2023 audit fees are fees of \$218,000 and \$40,000 respectively, related to comfort letter fees.
- (2) Consists of fees for assurance and related services reasonably related to the performance of the audit or review of our financial statements.
- (3) Consists of fees for professional services for tax compliance, tax advice and tax planning.
- (4) Consists of fees for all other services.

Pre-Approval Policies and Procedures

Our Audit Committee has adopted procedures requiring the pre-approval of all audit and non-audit services performed by our independent auditor in order to assure that these services do not impair the auditor’s independence. These procedures generally approve the performance of specific services subject to a cost limit for all such services. This general approval is reviewed, and if necessary modified, at least annually. Management must obtain the specific prior approval of the committee for each engagement of our auditor to perform other audit-related or non-audit services. The committee does not delegate its responsibility to pre-approve services performed by our auditor to any member of management. The committee has delegated authority to the committee chair to pre-approve audit and non-audit services to be provided to us by our auditor provided that the fees for such services do not exceed \$100,000. Any pre-approval of services by the committee chair pursuant to this delegated authority must be reported to the committee at its next regularly scheduled meeting.

Report of the Audit Committee

The Audit Committee has reviewed and discussed the audited financial statements for the year ended December 31, 2024 with the Company’s management and with PwC. The Audit Committee has discussed with PwC the matters required to be discussed by the applicable standards of the Public Company Accounting Oversight Board (“PCAOB”) and the SEC. The Audit Committee has also received the written disclosures and the letter from PwC pursuant to applicable PCAOB requirements regarding its communications with the Audit Committee concerning independence, and the Audit Committee has discussed with PwC its independence. Based on the foregoing, the Audit Committee recommended to the Board that the audited financial statements be included in the Company’s Annual Report on Form 10-K for the year ended December 31, 2024 for filing with the SEC.

This report is provided by the following directors, who serve on the Audit Committee:

Laurie Stelzer (Chair)
Jeffrey W. Albers
Michael Henderson

Board Recommendation

The Board recommends a vote “**FOR**” this proposal.

CORPORATE GOVERNANCE

Our business affairs are managed under the direction of our Board. Our Board has adopted a set of Corporate Governance Guidelines as a framework for the governance of the Company, which is posted on our website located at <https://ir.spyre.com/corporate-governance> under “Governance Documents.”

Our Governance Structure and Philosophy

Our governance practices reflect the environment in which we operate and are designed to support our mission to create next-generation inflammatory bowel disease (IBD) and other immune-mediated disease products by combining best-in-class antibody engineering, rational therapeutic combinations, and precision medicine approaches. Spyre is a recently public, pre-revenue clinical stage biotechnology company in an evolving industry, with a focus on developing our candidate pipeline through both business development and internal research efforts, and, like other companies in the biotechnology industry, faces extreme stock price and volume fluctuations that are often unrelated or disproportionate to our operating performance. With these business environment considerations in mind, the Board believes our current governance structure enables the management team to act with deliberation and to focus on delivering long-term value to stockholders and protect minority investors from the interests of potentially short-sighted investors who may seek to act opportunistically and not in the best interests of the Company or stockholders generally. This structure includes the following elements:

- **Classified board:** our directors serve three-year terms, with approximately 1/3 of the Board (instead of the entire Board) elected at each annual meeting. This helps to provide stability and continuity, permitting directors to develop and share institutional knowledge and focus on the long term, and encourages stockholders to engage directly with the Board and management team regarding significant corporation transactions.
- **Supermajority voting:** the voting standard for most items is a majority of shares present and entitled to vote on the proposal, but 2/3 of the outstanding shares are needed to amend certain provisions of our Certificate of Incorporation and Bylaws and remove directors. This helps protect against a small group of stockholders acting to amend our governing documents or to remove directors for reasons that may not be in the best interests of all stockholders.
- **Plurality voting for directors:** our directors are elected by a plurality of votes cast (instead of a majority of votes cast), meaning the nominees with the most votes are elected. This helps avoid potential disruption to the Board and management team as a result of a “failed election.”
- **Stockholders cannot call special meetings or act by written consent:** stockholders can propose business at each annual meeting (in accordance with our advance notice bylaws and Rule 14a-8) but cannot call a stockholder vote in between annual meetings or act by written consent. This helps avoid unnecessary diversion of Board and management time (potentially at the request of a limited number of stockholders acting to further short-term special interests) from executing on our long-term strategy.

Recognizing that the Company’s operating environment continues to evolve and that governance practices should not be static as a matter of course, the Board annually evaluates our governance structure to confirm it remains in the best interests of the Company and stockholders and values input from our stockholders on this topic.

Board Composition

Director Nomination Process

The Nominating Committee is responsible for, among other things, engaging in succession planning for directors and identifying qualified individuals to become members of the Board to oversee management’s execution of the Company’s strategy and safeguard the long-term interests of stockholders. In this regard, the committee is charged with developing and recommending Board membership criteria to the Board for approval, evaluating the composition of the Board annually to assess the skills and experience that are currently represented on the Board and to assess the criteria that may be needed in the future, and identifying, reviewing the qualifications of and recommending potential director candidates.

In identifying potential candidates for Board membership, the Nominating Committee considers recommendations from directors, stockholders, management and others, including, from time to time, third-party search firms to assist it in locating qualified candidates. Once potential director candidates are identified, the committee, with the assistance of management, undertakes a vetting process that considers each candidate's background, independence and fit with the Board's priorities. As part of this vetting process, the committee, as well as other members of the Board and the CEO, may conduct interviews with the candidates. If the committee determines that a potential candidate meets the needs of the Board and has the desired qualifications, it recommends the candidate to the full Board for appointment or nomination and to the stockholders for election at the annual meeting.

Criteria for Board Membership

In assessing potential candidates for Board membership and in assessing Board composition, the Nominating Committee considers a wide range of factors and generally seeks to balance the following skills, experiences and backgrounds on the Board:

- **Leadership:** experience serving in a leadership role of an organization, including driving strategy execution, organizational growth and managing human capital.
- **Finance & Accounting:** experience or expertise in finance, accounting, financial reporting processes and capital markets.
- **Biotechnology Industry:** experience and knowledge of the biotechnology industry, in particular regarding therapeutics for autoimmune and inflammatory diseases.
- **Clinical Development:** experience driving the development of therapeutics, including the design and management of clinical trials.
- **Drug Approval Planning/Commercialization:** experience driving the planning process for new drug approvals, including medical affairs, and managing commercialization operations for approved drug candidates, including product manufacturing, pricing, reimbursement, marketing and distribution.
- **Corporate Governance:** experience, whether currently or in the past, serving on other public company boards of directors.
- **Operations & Administration:** experience managing corporate operations, including in the areas of human resources, legal, regulatory, public relations and product quality.
- **Portfolio Management:** experience managing investments or driving business development, including collaborations, licensing transactions, M&A and joint ventures/partnerships.
- **Science & Research:** expertise or research experience in scientific disciplines related to biotechnology (e.g., biology, chemistry, medicine).

In addition to the above, the Nominating Committee generally believes it is important for all Board members to possess the highest personal and professional ethics, integrity and values, an inquisitive and objective perspective, a sense for priorities and balance, the ability and willingness to devote sufficient time and attention to Board matters, and a willingness to represent the long-term interests of all our stockholders.

Board Diversity

The Board and the Nominating Committee seek to achieve a diversity of occupational and personal backgrounds on the Board, including with respect to professional experience, vocation, education, nationality, geography, and other individual characteristics and demographics such as gender or age. As part of the search process for new directors, the Nominating Committee seeks to include women and minority candidates within its broader pool of candidates from which Board nominees ultimately are considered holistically and chosen through a merit-based process.

The Nominating Committee assesses its effectiveness in balancing these considerations in connection with its annual evaluation of the composition of the Board.

Director Time Commitments

While Board members benefit from service on the boards of other companies and such service is encouraged, under the Board's Corporate Governance Guidelines, directors are expected to limit the number of other boards on which they serve so as not to interfere with their service as a director of the Company. In this regard, the Company has adopted specific limits on the number of other public company boards upon which a director may sit. Ordinarily, directors may not serve on the boards of more than five public companies and the CEO and directors who are executive officers of public companies may not serve on the board of more than three public companies. At least once annually, the Nominating Committee considers directors' adherence to these expectations, and directors are expected to obtain the approval of the Nominating committee before accepting a seat on the board of another for-profit organization.

Stockholder Recommendations for Directors

It is the Nominating Committee's policy to consider written recommendations from stockholders for director candidates. The committee considers candidates recommended by our stockholders in the same manner as a candidate recommended by other sources. Any such recommendations should be submitted to the committee as described under "Stockholder Communications" and should include the same information required under our Bylaws for nominating a director, as described under "Stockholder Proposals and Director Nominations for Next Year's Annual Meeting."

Board Leadership Structure

Mr. Albers serves as our independent Chair of the Board ("Chair") while Dr. Turtle serves as our Chief Executive Officer. We do not have a policy regarding whether the roles of the Chair and the CEO should be separate or combined, and our Board believes that we should maintain our flexibility to select the Chair and CEO and determine the appropriate leadership structure, from time to time, based on criteria that are in our best interests and the best interests of our stockholders. Our Board periodically reviews its leadership structure to evaluate whether the structure remains appropriate for the Company. At any time when the Chair is not independent or there is not a Chair, the independent directors of the Board will designate an independent director to serve as lead independent director for a period of at least one year.

Currently, the roles of Chair and the CEO are separate, and the Chair is an independent director. The Board believes that this structure is appropriate for the Company as the independent Chair's leadership of the Board and oversight of corporate governance matters enables our CEO to focus on leading the Company's business and developing our drug candidate pipeline.

The independent directors have the opportunity to meet in executive sessions without management present at every regular Board meeting and at such other times as may be determined by the Chair. The purpose of these executive sessions is to encourage and enhance communication among the independent directors.

The Board believes that its programs for overseeing risk, as described under "Board Risk Oversight," would be effective under a variety of leadership frameworks. Accordingly, the Board's risk oversight function did not significantly impact its selection of the current leadership structure.

Director Independence

Our Board determines the independence of our directors by applying the applicable rules, regulations and listing standards of Nasdaq Stock Market ("Nasdaq"). These provide that a director is independent only if the Board affirmatively determines that the director does not have a relationship with us which, in the opinion of the Board, would interfere with the exercise of his or her independent judgment in carrying out the responsibilities of a director. Such relationships may include employment, commercial, accounting, family and other business, professional and personal relationships.

Applying these standards, our Board reviews the independence of our directors, taking into account all relevant facts and circumstances. Our Board has determined that the following members of our Board are currently independent under Nasdaq listing rules: Drs. Henderson and Milligan, Ms. Stelzer and Messrs. Albers, Harwin and Kiselak. Dr. Turtle is not independent as he is our CEO, and Mr. McKenna is not independent due to his consulting arrangement with the Company. In addition, former directors Russell J. Cox and Alison Lawton were independent during the period each served on the Board in 2024.

All members of our Audit Committee, Compensation Committee and Nominating Committee must be independent directors under the Nasdaq listing rules. Members of the Audit Committee and Compensation Committee also must satisfy the independence criteria set forth in Rule 10A-3 and Rule 10C, respectively, under the Securities Exchange Act of 1934, as amended (the “Exchange Act”). Our Board has determined that all members of our Audit Committee, Compensation Committee and Nominating Committee satisfy the relevant independence requirements for such committees.

Board Committees

Our Board has a separately designated Audit Committee, Compensation Committee and Nominating Committee, each of which has the composition and responsibilities described below. Members serve on these committees until their resignation or until otherwise determined by our Board. Each of these committees is empowered to retain outside advisors as it deems appropriate, regularly reports its activities to the full Board and has a written charter, which is posted on our website located at <https://ir.spyre.com/corporate-governance> under “Committee Charters.”

Name	Audit Committee	Compensation Committee	Nominating Committee
Jeffrey W. Albers	X	Chair	
Peter Harwin			X
Michael Henderson	X		
Tomas Kiselak		X	
Mark McKenna			
Sandra Milligan		X	Chair
Laurie Stelzer	Chair		X
Cameron Turtle			
# of Meetings in 2024	5	5	2

Audit Committee. The primary responsibilities of our Audit Committee are to oversee the accounting and financial reporting processes of the Company, including the audits of the Company’s financial statements, the integrity of the financial statements and the annual review of the performance, qualifications and independence of the outside auditor. This includes reviewing the financial information provided to stockholders and others and the adequacy and effectiveness of the Company’s internal controls. The committee also makes recommendations to the Board as to whether financial statements should be included in the Company’s Annual Report on Form 10-K.

Ms. Stelzer qualifies as an “audit committee financial expert,” as that term is defined in the rules and regulations established by the SEC, and all members of the Audit Committee are “financially literate” under Nasdaq listing rules.

Compensation Committee. The primary responsibilities of our Compensation Committee are to periodically review and approve the compensation and other benefits for our executive officers and directors. This includes reviewing and approving corporate goals and objectives relevant to the compensation of our CEO, evaluating the performance of our CEO in light of the goals and objectives and setting or recommending to the Board the CEO’s compensation based on the committee’s evaluation. The committee also oversees the evaluation of other executive officers and sets or recommends to the Board the compensation of such executive officers based upon the recommendation of the CEO, administers and makes recommendations to the Board regarding equity incentive plans that are subject to the Board’s approval and approves the grant of equity awards under the plans and oversees our strategies and policies related to human capital management, including with respect to matters such as diversity and inclusion, workplace environment and culture, and talent development and retention.

The Compensation Committee may delegate its duties and responsibilities to one or more subcommittees. The committee may also delegate authority to review and approve the compensation of our employees to certain of our executive officers. Even where the committee does not delegate authority, our executive officers will typically make recommendations to the committee regarding compensation to be paid to our employees and the size of equity awards under our equity incentive plans but will not be present during voting or deliberations on their own compensation. The committee has the authority to engage outside advisors, such as compensation consultants, to assist it in carrying out its responsibilities. The committee engaged Alpine Rewards, LLC in 2024 (“Alpine”) to provide advice regarding the amount

and form of executive and director compensation. The committee reviewed Alpine's independence in light of SEC rules and has affirmatively determined that the work performed by Alpine does not raise any conflict of interest.

Nominating Committee. The primary responsibilities of our Nominating Committee are to engage in succession planning for the Board, identify individuals qualified to become members of the Board, recommend director candidates to the Board, including for election or reelection to the Board at each annual stockholders' meeting, and perform a leadership role in shaping the Company's corporate governance. In addition, the committee is responsible for developing and recommending to the Board criteria for identifying and evaluating qualified director candidates and developing and recommending to the Board a set of corporate governance principles. The committee is also responsible for making recommendations to the Board concerning the size, structure, composition and functioning of the Board and its committees and oversees the management of the Company's strategy, initiatives, risks, opportunities and reporting on material environmental, social and governance ("ESG") matters.

Board Risk Oversight

We believe that risk management is an important part of establishing and executing on the Company's business strategy. Our Board, as a whole and at the committee level, focuses its oversight on the most significant risks facing the Company and on the Company's processes to identify, prioritize, assess, manage and mitigate those risks. The committees oversee specific risks within their purview, as follows:

- **The Audit Committee** has overall responsibility for overseeing the Company's practices with respect to risk assessment and management. Additionally, the committee is responsible for overseeing management of risks related to our financial statements and financial reporting process, compliance and information technology and cybersecurity.
- **The Compensation Committee** is responsible for overseeing management of risks related to our compensation policies and programs and human capital management practices.
- **The Nominating Committee** is responsible for overseeing management of risks related to director succession planning, corporate governance practices and ESG practices.

Our Board and its committees receive regular reports from members of the Company's senior management on areas of material risk to the Company, including strategic, operational, financial, legal and regulatory risks. While our Board has an oversight role, management is principally tasked with direct responsibility for assessing and managing risks, including implementing processes and controls to mitigate their effects on the Company.

Other Corporate Governance Practices and Policies

Director Attendance

The Board met seven (7) times during 2024. Each member of the Board attended at least 75% of the aggregate number of meetings of the Board and the committees on which he or she served during the period in which he or she was on the Board or committee.

Directors are encouraged to attend the annual meeting of stockholders. Seven (7) of our directors then serving on the Board attended our 2024 Annual Meeting of Stockholders.

Stockholder Communications

Stockholders and other interested parties may communicate with our Board or a particular director by sending a letter addressed to the Board or a particular director to our Corporate Secretary at the address set forth on the first page of this Proxy Statement. These communications will be compiled and reviewed by our Corporate Secretary, who will determine whether the communication is appropriate for presentation to the Board or the particular director. The purpose of this screening is to allow the Board to avoid having to consider irrelevant or inappropriate communications (such as advertisements, solicitations and hostile communications).

To enable the Company to speak with a single voice, as a general matter, senior management serves as the primary spokesperson for the Company and is responsible for communicating with various constituencies, including stockholders,

on behalf of the Company. Directors may participate in discussions with stockholders and other constituencies on issues where Board-level involvement is appropriate. In addition, the Board oversees the Company's stockholder engagement efforts.

In 2024, we reached out to our top 25 institutional investors to discuss our 2024 Say-on-Pay vote and engaged with all investors who expressed interest to connect. See "Executive Compensation - Investor Outreach and Response to 2024 Say-on-Pay Vote" for more information regarding our fiscal year 2024 stockholder engagement with respect to our advisory vote on executive compensation for fiscal year 2023. We believe our proactive engagement approach has resulted in constructive feedback and input from stockholders and we intend to continue these efforts.

Code of Business Conduct and Ethics

Our Board has adopted a Code of Business Conduct and Ethics that establishes the standards of ethical conduct applicable to all our directors, officers and employees, including our principal executive officer, principal financial officer and principal accounting officer, or persons performing similar functions. It addresses, among other matters, compliance with laws and policies, conflicts of interest, corporate opportunities, regulatory reporting, external communications, confidentiality requirements, insider trading, proper use of assets and how to report compliance concerns. A copy of the code is available on our website located at <https://ir.spyre.com/corporate-governance> under "Governance Documents." We intend to disclose any amendments to the code, or any waivers of its requirements, on our website to the extent required by applicable rules. Our Board is responsible for applying and interpreting the code in situations where questions are presented to it.

Clawback Policy and Restatement Analysis

We have a Compensation Recoupment (Clawback) Policy (the "Clawback Policy"), which is intended to comply with the requirements of Nasdaq Listing Standard 5608 implementing Rule 10D-1 under the Exchange Act. In the event the Company is required to prepare an accounting restatement of the Company's financial statements due to material non-compliance with any financial reporting requirement under the federal securities laws, the Company will recover, on a reasonably prompt basis, the excess incentive-based compensation received by any covered executive after October 2, 2023 and during the prior three fiscal years that exceeds the amount that the executive otherwise would have received had the incentive-based compensation been determined based on the restated financial statements.

During 2024, the Company was required to prepare an accounting restatement of the Company's consolidated financial statements as of and for the year ended December 31, 2023, as well as the quarterly condensed consolidated financial information for the 2024 interim periods ended March 31, 2024, June 30, 2024, and September 30, 2024, as described under Part II, Item 9A of our Annual Report on Form 10-K for the year ended December 31, 2024 in the section titled "Controls and Procedures." In accordance with the Clawback Policy, our Compensation Committee reviewed the restated financials and concluded that there was no recovery of erroneously awarded compensation required under the Clawback Policy because the restated financials did not impact any incentive-based compensation received on or after October 2, 2023.

Insider Trading Policy

We have adopted insider trading policies and procedures governing the purchase, sale and other transactions in Company securities by our directors, officers and employees, and other covered persons, as well as the Company itself, that we believe are reasonably designed to promote compliance with insider trading laws, rules and regulations, and Nasdaq listing rules, as applicable.

As part of these policies and procedures, we prohibit our directors, officers, employees and consultants from engaging in (a) short-term trading; (b) short sales; (c) transactions involving publicly traded options or other derivatives, such as trading in puts or calls with respect to Company securities; and (d) hedging transactions.

Equity Grant Timing Policy and Practices

In December 2024, our Compensation Committee adopted an Equity Grant Timing Policy (the "Equity Grant Policy"), which provides that it is the Company's policy to generally grant equity awards, including stock options, outside of blackout periods under our insider trading policy. With respect to grants of stock options to our named executive officers

and to the extent a grant during a close window is deemed necessary or appropriate by the Compensation Committee, awards typically may not occur during the period beginning four business days before and ending one business day after the filing of a Form 10-K or Form 10-Q or the filing or furnishing of a Form 8-K that contains material non-public information (“MNPI”). Under the Equity Grant Policy, annual equity grants to the Company’s employees are typically granted within one week following the first regularly scheduled Compensation Committee meeting each year (or, with respect to grants to the Chief Executive Officer, within one week following the first regularly scheduled Board meeting each year). Grants to new hires generally occur on the first business day of each month for new hires who commenced employment during the previous month. Employees, including the named executive officers, may enroll to purchase shares under the terms of our 2016 Employee Stock Purchase Plan, as amended (the “ESPP”), with purchase dates generally in February and August of each year using payroll deductions accumulated during the prior six-month period. During 2024, we did not time the disclosure of MNPI for the purpose of affecting the value of executive compensation.

The following table sets forth information regarding stock options issued to our named executive officers during 2024 during any period beginning four business days before and ending one business day after the filing of a Form 10-K or Form 10-Q or the filing or furnishing of a Form 8-K that contains MNPI. Dr. Sloan did not receive any stock options during any such period in 2024. The awards set forth in the following table were granted prior to the Company's adoption of the Equity Grant Policy.

Name	Grant Date	Number of Securities Underlying the Award	Exercise Price of the Award (\$/Sh)	Grant Date Fair Value of the Award	Percentage Change in the Closing Market Price of the Securities Underlying the Award Between the Trading Day Ending Immediately Prior to the Disclosure of MNPI and the Trading Day Beginning Immediately Following the Disclosure of MNPI ⁽¹⁾
Cameron Turtle	2/1/2024	277,750	\$ 25.86	\$ 5,914,353	(0.8)%
Scott Burrows	2/1/2024	70,000	\$ 25.86	\$ 1,490,566	(0.8)%

⁽¹⁾ Reflects the percentage change in the closing market price of our common stock between the trading day ending immediately prior to the disclosure of MNPI (\$25.74 on February 2, 2024) and the trading day beginning immediately following the disclosure of MNPI (\$25.53 on February 6, 2024).

Compensation Committee Interlocks

None of the members of our Compensation Committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past year has served, as a member of the board or compensation committee of any entity that has one or more executive officers serving on our Board or Compensation Committee.

Director Compensation

Each of our non-employee directors receives, compensation pursuant to the non-employee director cash and equity compensation program adopted by our Board pursuant to recommendations and peer group data from Alpine Rewards, the Company's independent compensation consultant. This program provides for the following annual cash retainers;

Annual Cash Retainer	\$	40,000
Annual Board Chair Retainer:	\$	35,000
Audit Committee Retainers		
Chair	\$	20,000
Non-Chair Member	\$	10,000
Compensation Committee Retainers:		
Chair	\$	15,000
Non-Chair Member	\$	7,500
Nominating and Corporate Governance Committee Retainers:		
Chair	\$	10,000
Non-Chair Member	\$	5,000

Each non-employee director who initially joins our Board receives an initial grant of stock options that vests in equal monthly installments over three years. Prior to May 9, 2024, new directors received stock options to purchase 40,000 shares, and following May 9, 2024, new directors received stock options with an aggregate grant date value approximating \$700,000. In accordance with this program, Mr. McKenna received a stock option to purchase 40,000 shares on February 1, 2024, and Dr. Milligan received a stock option to purchase 21,980 shares on May 14, 2024.

Each non-employee director who is serving as of the date of the Annual Meeting will receive a grant of stock options with an aggregate grant date value approximately \$350,000. Annual stock option grants vest in equal monthly installments over one year or, if earlier, upon the next Annual Meeting of Stockholders. For directors appointed on or after January 1, 2024, a director is only eligible to receive an annual stock option grant if the Annual Meeting of Stockholders is more than six months following the director's appointment to the Board. As such, each of Messrs. Albers, Harwin, and Kiselak, Dr. Henderson and Ms. Stelzer received a stock option to purchase 11,323 shares on May 14, 2024.

In addition, all non-employee directors are reimbursed their reasonable travel expenses incurred in attending board and committee meetings.

The following table provides information for the year ended December 31, 2024 regarding all compensation awarded to, earned by or paid to each person who served as a non-employee director for some portion of 2024. Employees who served on our Board during 2024 did not receive additional compensation for such service.

Name	Fees Earned or Paid in Cash (\$)	Option Awards (\$) ⁽¹⁾	Total (\$)
Jeffrey W. Albers	84,354	353,221	437,575
Russell J. Cox	35,962	—	35,962
Peter Harwin	47,888	353,221	401,109
Michael Henderson	50,000	353,221	403,221
Tomas Kiselak	47,500	353,221	400,721
Alison Lawton ⁽³⁾	4,396	N/A	4,396
Mark McKenna ⁽⁴⁾	36,593	838,124	874,717
Sandra Milligan, M.D., J.D. ⁽⁵⁾	33,445	703,512	736,957
Laurie Stelzer	65,000	353,221	418,221

(1) The amounts reported in this column represent the aggregate grant date fair value of the awards granted to our non-employee directors during the year ended December 31, 2024, as computed in accordance with Accounting Standards

Codification Topic 718 (“ASC 718”). The assumptions used in calculating the grant date fair value of the awards reported in the Option Awards column are set forth in Note 15 to our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2024. Note that the amounts reported in this column reflect the aggregate accounting cost for these awards, and do not necessarily correspond to the actual economic value that may be received by the non-employee directors from the awards. As of December 31, 2024, our non-employee directors held the following number of outstanding stock options: (i) Mr. Albers, 61,323; (ii) Mr. Cox, 86,228; (iii) Mr. Harwin, 89,323; (iv) Dr. Henderson, 89,323; (v) Mr. Kiselak, 89,323; (vi) Ms. Lawton, 3,488; (vii) Mr. McKenna, 517,000; (viii) Dr. Milligan, 21,980; and (ix) Ms. Stelzer, 61,323.

- (2) Mr. Cox did not stand for reelection at the 2024 Annual Meeting of Stockholders.
 - (3) Ms. Lawton resigned from the Board effective as of February 1, 2024.
 - (4) Mr. McKenna was appointed to the Board effective as of February 1, 2024.
 - (5) Dr. Milligan was appointed to the Board effective as of May 14, 2024.
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EXECUTIVE OFFICERS

Biographical and other information regarding our executive officers, who are appointed by the Board and serve at the Board’s discretion, is set forth below. There are no family relationships among any of our directors or executive officers.

Name	Age (as of April 14)	Position
Cameron Turtle ⁽¹⁾	35	Chief Executive Officer and Director
Scott Burrows	48	Chief Financial Officer
Heidy King-Jones	42	Chief Legal Officer and Corporate Secretary
Sheldon Sloan	67	Chief Medical Officer

(1) For Dr. Turtle’s biographical information, see “Information Regarding Director Nominees and Continuing Directors ” above.

Scott Burrows. Mr. Burrows joined as our Chief Financial Officer in September 2023. Prior to Spyre, Mr. Burrows most recently served as the Chief Financial Officer of Arcutis Biotherapeutics, Inc. (Nasdaq: ARQT), a biopharmaceutical company, from April 2021 to August 2023 and as Vice President of Finance from May 2019 to April 2021, where he helped lead Arcutis through a successful initial public offering, several further equity and debt financings, and the transition to a fully integrated commercial-stage company. Prior to Arcutis, Mr. Burrows was the head of international investor relations for Shire, plc, a biotechnology company that was acquired by Takeda Pharmaceutical Company Limited in 2019, from March 2018 to May 2019. Earlier in his career, he spent 15 years at Amgen, Inc. in roles of increasing responsibility across financial planning and analysis, treasury and investor relations. Mr. Burrows began his career at Arthur Andersen as a consultant. Mr. Burrows also serves as on the board of directors of Food Share of Ventura County, a non-profit organization. He earned his B.A. and M.B.A. from the University of California, Los Angeles, and is a licensed C.P.A. (inactive).

Heidy King-Jones. Ms. King-Jones joined as our Chief Legal Officer and Corporate Secretary in September 2023. Ms. King-Jones most recently served as the Chief Legal Officer and Corporate Secretary at Provention Bio, Inc., a biopharmaceutical company, from 2020 to 2023, including through various financings, the approval of Tzield®, the company’s successful transition from clinical-stage to commercial-stage as well as its acquisition by Sanofi in April 2023. Prior to her leadership role at Provention Bio, she was a Senior Vice President, General Counsel and Corporate Secretary at Axcella Health Inc., a biotechnology company, from 2019 to 2020 and as Vice President, Legal and Corporate Secretary from 2018 to 2019, where she was responsible for Axcella’s corporate legal function and strategy. From 2013 to 2018, she held positions of increasing responsibility in the legal department at Sarepta Therapeutics, Inc. (Nasdaq: SRPT), including overseeing all Corporate Law matters as Senior Director, Corporate Law. While at Sarepta, she served as a member of the company’s commercial readiness working group and was responsible for the development of the compliance program, contract and other legal work for the launch of its first product, Exondys 51®. Ms. King-Jones began her legal career in the Securities & Public Companies Practice Group at Ropes & Gray LLP, where she represented private and publicly traded companies in the pharmaceutical, utility and technology industries. She holds a J.D. and LL.M in International and Comparative Law from Cornell Law School, and a B.A. from Dartmouth College.

Sheldon Sloan, M.D., M.B.E. Dr. Sloan has served as our Chief Medical Officer since October 2024. Dr. Sloan most recently served as the Chief Medical Officer of Abivax S.A. (Nasdaq: ABVX), a biopharmaceutical company, from March 2023 to August 2024, where he was responsible for leading medical strategy to support the lead Phase 3 program, developing lifecycle strategy for lead and follow on compounds, investor interface, business development support, and building a Phase 3 medical infrastructure including Clinical Development, Pharmacovigilance, Bioinformatics, Medical Affairs and Clinical Pharmacology. From March 2022 to January 2023, Dr. Sloan was Vice President and Program Lead for etrasimod UC at Pfizer, Inc. (NYSE: PFE), a biopharmaceutical company, where he was responsible for leading the etrasimod UC cross functional team and overseeing NDA and MM submission. From November 2019 to March 2022, Dr. Sloan was Vice President and Program Lead for etrasimod GI at Arena Pharmaceuticals, Inc., a Nasdaq-listed biopharmaceutical company that was acquired by Pfizer in March 2022, where he was responsible for leading the cross functional etrasimod UC team for the Phase 3 program. Between September 1997 and October 2019, Dr. Sloan held different leadership positions at Johnson and Johnson (NYSE: JNJ), a pharmaceutical and medical technologies company, in Medical Affairs, Research and Development, and Science Policy, including Global Medical Affairs Leader for IBD, leading the global launch strategy and execution for CD and UC for Stelara. He holds a Doctor of Medicine from Rush

Medical College, Chicago, a Master of Bioethics from the University of Pennsylvania and a Bachelor of Science from University of Illinois Urbana-Champaign. Dr. Sloan currently serves on the Columbia University Masters of Bioethics Advisory Board, the Drexel University Dornsife School of Public Health Dean's Impact, Advancement and Learning Council, and the American Gastroenterological Association Ethics Committee.

EXECUTIVE COMPENSATION

Overview

This section provides an overview of the material components of our executive compensation program each for our Chief Executive Officer, other individuals who served as a principal executive officer during any part of 2024, and each of our two other most highly compensated executive officers (collectively, our “named executive officers” or “NEOs”) during 2024. The compensation provided to our named executive officers for 2024 is set forth in detail in the “Summary Compensation Table” and other tables that follow in this section, as well as the accompanying footnotes and narratives relating to those tables.

Our named executive officers for 2024 were:

Name	Title
Cameron Turtle	Chief Executive Officer
Sheldon Sloan	Chief Medical Officer ⁽¹⁾
Scott Burrows	Chief Financial Officer

(1) Dr. Sloan was appointed Chief Medical Officer of the Company effective October 1, 2024.

Investor Outreach and Response to 2024 Say-on-Pay Vote

Each year, we provide our stockholders the opportunity to cast a non-binding advisory vote on the compensation of our named executive officers (commonly known as a "Say-on-Pay" vote). Our Board and our Compensation Committee consider the results of the Say-on-Pay vote in determining the compensation of our executive officers, including our named executive officers. At our 2024 Annual Meeting of Stockholders, approximately 62% of the votes cast approved the compensation of our named executive officers. Since the vote, we reached out to our top 25 institutional investors and have spoken with the investment team or corporate governance contacts at several of our major stockholders (excluding Fairmount), including all of the stockholders that expressed interest in engaging with us, representing approximately 43% of our outstanding common stock based on public filings as of September 30, 2024. The primary stockholder concerns raised during our discussions included the lack of disclosure of clear performance goals and compensation rationale, lack of outreach due to prior year low Say-on-Pay vote and the magnitude of awards granted to executives.

We believe that proxy advisor voting recommendations and the voting results for our 2024 annual meeting reflect a general misunderstanding around legacy Aeglea pay decisions and the significance of our transformation in 2023. During 2023, the Company completed a reverse merger, which brought in an entirely new pipeline of product candidates targeting IBD, and refreshed the Board and executive team to lead development of this new pipeline and sunset legacy asset development. In 2024, annual equity grants to executives and the Company's other employees hired post-Merger were pro-rated based on each employee's start date in 2023, resulting in much smaller grants than each employee's 2023 new hire grant. The investment required to pivot the Company's business and strategy included situation-specific compensation arrangements necessary to recruit an executive team, which are not reflective of our go-forward compensation program. These investments drove significant value creation for stockholders in 2023, including going from a market capitalization of less than \$50 million prior to the closing of the reverse merger in June 2023 to a market capitalization well over \$1.0 billion by the end of 2023 and throughout 2024.

Our current Board, the Compensation Committee and our management team are committed to implementing a robust compensation program aligned with stockholder interests and supported by peer group and market data, which we believe is reflected in our 2024 compensation program described below. We value the opinion of our stockholders. Our Board and our Compensation Committee will continue to consider the result of the Say-on-Pay vote, as well as feedback received throughout the year, when making compensation decisions for our executive officers.

Summary Compensation Table

The following table provides information regarding all plan and non-plan compensation awarded to, earned by or paid to each of our named executive officers for the years ended December 31, 2024 and 2023.

Name and Principal Position	Year	Salary (\$)	Bonus (\$) ⁽¹⁾	Stock Awards (\$) ⁽²⁾	Option Awards (\$) ⁽³⁾	Non-Equity Incentive Plan Compensation (\$)	All Other Compensation (\$) ⁽⁴⁾	Total (\$)
Cameron Turtle	2024	625,000	—	—	5,914,353	412,500	8,333	6,960,186
Chief Executive Officer	2023	272,850	141,000	—	15,500,492	—	5,203	15,919,545
Sheldon Sloan	2024	124,000	120,000	—	9,075,480	59,500	9,760	9,388,740
Chief Medical Officer								
Scott Burrows	2024	475,000	—	—	1,490,566	228,000	13,800	2,207,366
Chief Financial Officer	2023	154,589	175,700	2,452,096	4,767,637	—	1,517	7,551,539

- (1) For 2024, the amount reported in this column reflects a sign-on bonus for Dr. Sloan in connection with the commencement of his employment with the Company during 2024, as described in more detail under “Narrative Disclosure to Summary Compensation Table—Offer Letters” below.
- (2) Amounts reported in this column for 2024 represent the aggregate grant date fair value of stock options granted to our NEOs, as computed in accordance with ASC 718. See Note 15 to our consolidated financial statements in our Annual Report on Form 10-K for the year ended December 31, 2024 for more information regarding the assumptions used in calculating the grant date fair value of stock options.
- (3) Amounts reported in this column for 2024 represent the annual bonuses earned under the 2024 annual bonus program, as described in more detail under “Narrative Disclosure to Summary Compensation Table—Elements of Compensation—Annual Bonus Program” below.
- (4) Amounts reported in this column for 2024 include matching contributions under our 401(k) plan made during 2024.

Narrative Disclosure to Summary Compensation Table

Under the Compensation Committee's compensation philosophy, compensation positioning is used to attract and retain key employees for the Company's continued success and growth. While market data is helpful to the Compensation Committee in setting compensation framework and guiding decisions, other factors such as general market practices, Company strategy, tenure, performance and criticality are also considered. The compensation philosophy serves as the foundation to reinforce the Company's business strategy and desired culture, while balancing internal and external alignment.

Peer Group

In October 2023, our Compensation Committee, in consultation with Alpine, its independent compensation consultant, established a peer group that focuses on U.S.-based, pre-clinical or early clinical biotechnology/pharmaceutical companies (with priority placed on companies with a similar therapeutic focus) with a market capitalization ranging from \$250 million

to \$2 billion and less than 100 employees. The peer group, which was approved by the Board and used in establishing executive compensation for 2024, includes the following companies:

ACELYRIN	Arcellx, Inc.	Kymera Therapeutics, Inc.
Aclaris Therapeutics, Inc.	Astria Therapeutics, Inc.	Morphic Holding, Inc.
Allakos Inc.	Cabaletta Bio, Inc.	Pliant Therapeutics, Inc.
Alpine Immune Sciences, Inc.	Celldex Therapeutics, Inc.	RAPT Therapeutics, Inc.
AnaptysBio, Inc.	IGM Biosciences, Inc.	Ventyx Biosciences, Inc.
Apogee Therapeutics, Inc.	Janux Therapeutics, Inc.	Vera Therapeutics, Inc.

In September 2024, our Compensation Committee, in consultation with Alpine, evaluated our peer group and approved updates to the peer group used in establishing executive compensation for 2025 based on market capitalization, pipeline stage, employee population and other relevant factors.

Elements of Compensation

Base Salary

Each NEO's base salary is a fixed annual amount that is intended to compensate the NEO for performing specific job responsibilities and is based on the NEO's level of experience and requisite skills. Our Compensation Committee annually evaluates and approves (or recommends to the Board for approval for our Chief Executive Officer) each NEO's base salary. As part of this annual evaluation in 2024, the Compensation Committee determined to increase the base salary for Mr. Burrows by \$20,000 in consideration of peer group data and recommendations from the Company's independent compensation consultant. In connection with his appointment, the Compensation Committee established Dr. Sloan's base salary of \$496,000 in consideration of peer group data and recommendations from the Company's independent compensation consultant. The table below sets forth the base salary as of December 31, 2024 for each NEO:

Named Executive Officer	Base Salary as of 12/31/2024	
Cameron Turtle	\$	625,000
Sheldon Sloan	\$	496,000
Scott Burrows	\$	475,000

Annual Bonus Program

We provide our executive officers, including our NEOs, with the opportunity to earn annual cash incentives to encourage the achievement of corporate objectives. We established our annual bonus program to motivate our executives to achieve short-term financial and business objectives, reflecting our "pay for performance" culture, resulting in a significant portion of NEO compensation tying directly to Company achievements.

For each NEO, the target annual bonus opportunity is determined as a percentage of his or her base salary (as indicated in the table below), which was established for 2024 by the Compensation Committee in consultation with Alpine, based on market data from companies in our peer group.

Named Executive Officer	2024 Annual Bonus Target
Cameron Turtle	55 %
Sheldon Sloan	40 %
Scott Burrows	40 %

The Board approved the objectives and key targeted results and stretch goals applicable to 2024 annual bonus program for our executives in December 2023. These milestones were intended to measure our performance in the following

categories: Portfolio, Platform, and Corporate, as further described below. The level of attainment of these performance milestones determines our NEOs' earned annual bonuses.

Objective	Weight	Summary of Key Result	Timing	Achieved
<u>Portfolio</u> : Advance Spyre Programs	60%	Prepare protocols and regulatory filings to enable SPY001 and SPY002 FIH initiations, SPY001 FIH data release in 2024, and Phase 2 UC initiation in 2025 Nominate SPY003 development candidate	Q2-Q4	100%
<u>Platform</u> : Advance Strategic Pillars	25%	Initiate preclinical studies to support advancement of combination drug candidates into clinical trials Assess precision medicine approaches in IBD clinical trials Develop and establish delivery device strategy and partners	Q2-Q4	100%
<u>Corporate</u> : Establish and Resource Spyre as an IBD Leader	15%	Continued development and execution of plans across Investor Relations, Finance, Human Resources, Compliance, Legal and Intellectual Property functions to support Spyre's growth and business plans	Q1-Q4	100%
<u>Portfolio</u> : Phase 2 readiness	Stretch 10%	Complete preclinical and regulatory activities, including early submission of SPY002 IND, to support FIH initiations and 2025 Phase 2 UC initiation	Q3-Q4	100%
<u>Corporate</u> : Additional support	Stretch 10%	Validating partnership, collaboration, or company investment	Q4	100%

At the end of 2024, the Board and the Compensation Committee reviewed the Company's performance against these performance measures and determined that performance was achieved at 120% of target, as each target result and all stretch goals were timely achieved.

As a result, each NEO received an annual bonus for 2024 equal to 120% of target; however, Dr. Sloan's annual bonus was pro-rated based on the date he commenced employment with the Company.

Named Executive Officer	2024 Annual Bonus
Cameron Turtle	\$ 412,500
Sheldon Sloan	\$ 59,500
Scott Burrows	\$ 228,000

Long-Term Incentive Compensation

For 2024, after taking into account the results of Alpine's market assessment, reviewing the practices of companies in our peer group and considering the important retentive value and performance alignment of our long-term incentive strategy, our Compensation Committee determined that it was appropriate to use stock options as 100% of the annual long-term incentive awards granted to our employees, including the NEOs. On February 1, 2024, Dr. Turtle and Mr. Burrows received annual grants of stock options to purchase 277,750 shares of our common stock and 70,000 shares of our common stock, respectively, which vest in equal monthly installments through the fourth anniversary of the grant date.

In connection with his appointment as Chief Medical Officer of the Company, Dr. Sloan received an initial grant of stock options to purchase 400,000 shares of our common stock, which vest as to 25% on October 1, 2025 (the first anniversary of the grant date) and in equal monthly installments thereafter through October 1, 2028.

Offer Letters

We have entered into offer letters with each of our NEOs in connection with their appointments (and, for Dr. Turtle, his promotion to Chief Executive Officer), which for Dr. Turtle was further amended in February 2024 (collectively, the "Offer Letters"). Each Offer Letter provides for an initial base salary, target bonus opportunity and stock option grant.

Under the Offer Letters, the NEOs are eligible for certain payments or benefits upon certain terminations of employment, as described under “Additional Narrative Disclosure-Potential Payments Upon Termination of Change in Control” below. Mr. Burrows’ Offer Letter also provided for a sign-on bonus of \$115,000, which was subject to repayment in the event of a termination for cause or resignation without good reason prior to September 1, 2024, and Dr. Sloan’s Offer Letter also provided for a sign-on bonus of \$120,000, which is subject to repayment in the event of a termination for cause or resignation without good reason prior to October 1, 2025.

Each of our NEOs is also party to our standard employee invention assignment, confidentiality and non-competition agreement, which, among other things, provides standard protections regarding our ownership of intellectual property, the confidentiality of our proprietary information, non-competition and non-solicitation.

Outstanding Equity Awards at December 31, 2024

The following table presents information regarding outstanding stock options, RSUs and restricted stock held by each named executive officers as of December 31, 2024.

Name	Grant Date	Option Awards				Stock Awards	
		Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested (\$) ⁽¹⁾
Cameron Turtle	6/22/2023	709,457	1,182,430 ⁽²⁾	\$7.50	6/22/2033	333,893 ⁽⁵⁾	7,773,029
	11/22/2023	101,291	272,709 ⁽³⁾	\$10.39	11/22/2033		
	2/1/2024 ⁽⁴⁾	57,864	219,886 ⁽²⁾	\$25.86	2/1/2034		
	10/1/2024	—		\$27.46	10/1/2034		
Sheldon Sloan			400,000 ⁽³⁾				
Scott Burrows	9/1/2023	126,517	287,340 ⁽³⁾	\$14.50	9/1/2033	101,214 ⁽⁶⁾	2,356,262
	2/1/2024	14,583	55,417 ⁽²⁾	\$25.86	2/1/2034		
	12/22/2023						

(1) The market value was determined by multiplying the number of shares by \$23.28, the closing price of our common stock as reported on the Nasdaq Global Select Market on December 31, 2024.

(2) These stock options vest in equal monthly installments through the fourth anniversary of the grant date, subject to the NEO’s continued service.

(3) These stock options vest as to 25% on the first anniversary of the grant date and in equal monthly installments thereafter through the fourth anniversary of the grant date, subject to the NEO’s continued service.

(4) In connection with the Asset Acquisition, outstanding shares of restricted common stock of Pre-Merger Spyre were assumed by the Company and converted into restricted common stock and restricted Series A Preferred Stock, which were subsequently converted to restricted and unrestricted common stock on November 24, 2023.

(5) These shares of restricted common stock vest in equal monthly installments through November 22, 2026, subject to the NEO’s continued service.

(6) These RSUs vest in equal annual installments through the fourth anniversary of the grant date, subject to the NEO’s continued service.

Additional Narrative Disclosure

Retirement Benefits

We maintain a tax-qualified 401(k) defined contribution plan that provides eligible U.S. employees, including our NEOs, with an opportunity to save for retirement on a tax-advantaged basis. Eligible employees may make voluntary contributions from their eligible pay, up to certain applicable annual limits set by the Internal Revenue Code of 1986, as

amended. We provide matching contributions equal to 100% of the first 3% of eligible compensation contributed by each employee, and 50% of the next 2% of eligible compensation contributed by each employee. All company matching contributions are immediately and fully vested. We do not maintain, and have not historically maintained, any non-qualified deferred compensation or defined benefit pension plan.

Potential Payments Upon Termination or Change in Control

Pursuant to the terms of the Offer Letters, in the event each NEO (other than Dr. Sloan) that is a current executive officer is terminated by the Company without “cause” or as a result of a resignation for “good reason” (collectively, an “Involuntary Termination”), such NEO will, subject to the execution of a release in favor of the Company, receive: (i) severance payments equal to 12 months of base salary and any earned but unpaid annual bonus for the preceding year; (ii) up to 12 months of partially subsidized COBRA coverage; and (iii) accelerated vesting of any time-based equity awards scheduled to vest in the 12 months following such termination. However, if the Involuntary Termination is within three months before or 12 months after a change in control of the Company, the NEO will instead receive: (A) severance payments equal to 18 months of base salary, any earned but unpaid annual bonus for the preceding year, and the target annual bonus for the year of termination (or, for Dr. Turtle, 1.5 times the target annual bonus for the year of termination); (B) up to 18 months of fully subsidized COBRA continuation coverage; and (C) full acceleration of all equity awards (with performance-based awards determined in accordance with the terms of the applicable award agreement or, if not specified in such award agreement, based on the greater of target or, if determinable, actual performance).

Pursuant to the terms of Dr. Sloan’s Offer Letter, in the event of his Involuntary Termination, Dr. Sloan will, subject to the execution of a release in favor of the Company, receive: (i) severance payments equal to nine months of base salary and (ii) up to nine months of partially subsidized COBRA coverage. However, if the Involuntary Termination is within three months before or 12 months after a change in control of the Company, the NEO will instead receive: (A) severance payments equal to 12 months of base salary and the target annual bonus for the year of termination; (B) up to 12 months of fully subsidized COBRA continuation coverage; and (C) full acceleration of all equity awards (with performance-based awards determined in accordance with the terms of the applicable award agreement or, if not specified in such award agreement, based on the greater of target or, if determinable, actual performance).

As used in the Offer Letters:

- “Cause” generally means (i) the NEO’s dishonest statements or acts with respect to the Company or any affiliate of the Company, or any current or prospective customers, suppliers, vendors or other third parties with which such entity does business that results in or is reasonably anticipated to result in material harm to the Company; (ii) the NEO’s conviction or plea of no contest to a felony or misdemeanor involving moral turpitude, deceit, dishonesty or fraud; (iii) the NEO’s failure to perform his or her duties or responsibilities, subject to a 30-day cure period; (iv) the NEO’s gross negligence, willful misconduct that results in or is reasonably anticipated to result in material harm to the Company; or (v) the NEO’s violation of any material provision of any agreement with the Company or any written Company policies.
- “Good Reason” generally means (i) a material diminution in the NEO’s base salary or target bonus (excluding across-the-board reductions of less than 10%); (ii) a material geographic relocation or requirement to change the NEO’s remote work location; (iii) a material reduction in the NEO’s duties, authority or responsibilities; (or, for Dr. Sloan, a requirement that he report to any person other than the Chief Executive Officer); (iv) the failure of the Company to obtain the assumption of the Offer Letter by a successor; or (v) the material breach of any agreement between the NEO and the Company, in each case, subject to standard notice and cure periods.

Pay Versus Performance

Our Compensation Committee approves and administers our executive compensation program to align executive compensation with stockholder interests by linking pay to performance. Our overall compensation program includes a mix of short-term and long-term components through our annual incentive plan and equity awards.

As required by Item 402(v) of Regulation S-K, we are providing the following information about the relationship between the compensation actually paid to our named executive officers and certain aspects of our financial performance.

During our fiscal year ended December 31, 2024, we were a smaller reporting company pursuant to Rule 405 of the Securities Act and, as such, are only required to include information for the past three fiscal years in the table below.

Pay-Versus-Performance Table

Year	Summary Compensation Table Total for Dr. Quinn (\$) ⁽¹⁾	Summary Compensation Table Total for Mr. Kastenmayer (\$) ⁽¹⁾	Summary Compensation Table Total for Mr. Goldberg (\$) ⁽¹⁾	Summary Compensation Table Total for Mr. Alspaugh (\$) ⁽¹⁾	Summary Compensation Table Total for Dr. Turtle (\$) ⁽¹⁾	Compensation Actually Paid to Dr. Quinn (\$)	Compensation Actually Paid to Mr. Kastenmayer (\$)	Compensation Actually Paid to Mr. Goldberg (\$)	Compensation Actually Paid to Mr. Alspaugh (\$)	Compensation Actually Paid to Dr. Turtle (\$) ⁽³⁾
2024	N/A	N/A	N/A	N/A	\$6,960,186	N/A	N/A	N/A	N/A	\$12,324,760
2023	N/A	N/A	\$830,207	\$8,360,029	\$15,919,545	N/A	N/A	\$122,206	\$13,594,354	\$35,296,939
2022	\$2,392,254	\$865,785	\$1,832,485	N/A ⁽⁶⁾	N/A	\$431,085	\$318,380	\$564,676	N/A ⁽⁶⁾	N/A

Year	Summary Compensation Table Total for Non-PEO NEOs (\$) ⁽²⁾	Average Compensation Actually Paid to Non-PEO NEOs (\$) ⁽³⁾	Total Stockholder Return Based on Initial Fixed \$100 Investment (\$) ⁽⁴⁾	Net Income (in thousands) (\$) ⁽⁵⁾
2024	\$ 5,798,053	\$ 5,566,084	\$ 20	\$ (208,018)
2023	\$ 7,069,877	\$ 9,563,596	\$ 18	\$ (338,790)
2022	\$ 1,049,862	\$ 202,299	\$ 9	\$ (83,815)

- (1) During years 2022, 2023 and 2024, the following individuals served as “principal executive officer” during the time periods set forth below:

Name	Dates as PEO During Years 2022 through 2024
Dr. Anthony Quinn	January 1, 2022 through August 23, 2022
Jim Kastenmayer	August 23, 2022 through November 29, 2022
Jeffrey M. Goldberg	November 29, 2022 through May 16, 2023
Jonathan Alspaugh	May 16, 2023 through August 31, 2023
Cameron Turtle	November 22, 2023 through December 31, 2024

The dollar amounts reported in these columns represent the amount of total compensation reported for each of Dr. Quinn and Messrs. Kastenmayer, Goldberg, Alspaugh and Turtle (collectively, our “PEOs”) for each covered fiscal year in the “Total” column of the Summary Compensation Table for each applicable year. Please refer to “Executive Compensation Summary Compensation Table” above.

- (2) The dollar amounts reported in this column represent the average amount of total compensation report for our NEOs as a group (excluding our PEOs) for each covered fiscal year in the “Total” column of the Summary Compensation Table for each applicable year. Please refer to “Executive Compensation Summary Compensation Table” above. The names of each NEO included for these purposes in each applicable year are as follows: (i) for 2024, Dr. Sheldon Sloan and Mr. Burrows; (ii) for 2023, Mr. Burrows and Ms. King-Jones, and (iii) for 2022, Mr. Alspaugh and Dr. Leslie Sloan.
- (3) The dollar amounts reported in these columns represent the amount of “compensation actually paid” to our PEOs or our NEOs as a group (excluding our PEOs), as computed in accordance with Item 402(v) of Regulation S-K, for each covered fiscal year. In accordance with these rules, these amounts reflect total compensation as set forth in the Summary Compensation Table, adjusted as shown below for 2024. Equity values are calculated in accordance with FASB ASC Topic 718, and the valuation assumptions used to calculate fair values did not materially differ from those disclosed at the time of grant. The dollar amounts do not reflect the actual amount of compensation earned or

received by or paid to the PEOs during the applicable fiscal year.

	Dr. Turtle	Average Non-PEO NEOs
Summary Compensation Table Total	\$ 6,960,186	\$ 5,798,053
Less, value of "Stock Awards" and "Option Awards" reported in Summary Compensation Table	\$ (5,914,353)	\$ (5,283,023)
Plus, year-end fair value of outstanding and unvested equity awards granted in the year	\$ 4,152,217	\$ 4,501,533
Plus, fair value as of vesting date of equity awards granted and vested in the year	\$ 2,129,038	\$ 40,957
Plus (less), year over year change in fair value of outstanding and unvested equity awards granted in prior years	\$ 1,381,127	\$ 174,038
Plus (less), change in fair value from last day of prior fiscal year to vesting date for equity awards granted in prior years that vested in the year	\$ 3,616,545	\$ 334,526
Compensation Actually Paid to PEOs	\$ 12,324,760	\$ 5,566,084

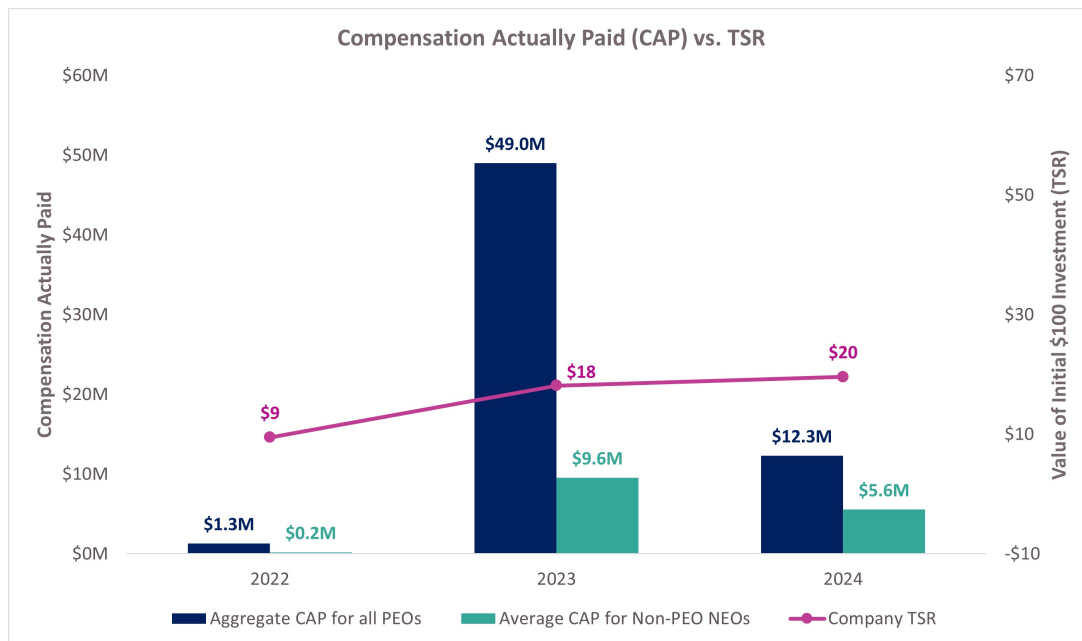
- (4) Cumulative total stockholder return ("TSR") is calculated by dividing (a) the sum of (i) the cumulative amount of dividends during the measurement period, assuming dividend reinvestment, and (ii) the difference between our stock price at the end of the applicable measurement period and the beginning of the measurement period by (b) our stock price at the beginning of the measurement period. The beginning of the measurement period for each year in the table is December 31, 2021.
- (5) The dollar amounts reported represent the amount of net income (loss) reflected in our audited financial statements for each covered fiscal year.
- (6) Mr. Alsbaugh only served as a PEO during fiscal year 2023; his compensation for fiscal year 2022 is included in the average for the Non-PEO NEOs.

Analysis of Information Presented in the Pay Versus Performance Table

In accordance with Item 402(v) of Regulation S-K, we are providing the following descriptions of the relationships between information presented in the Pay Versus Performance table above.

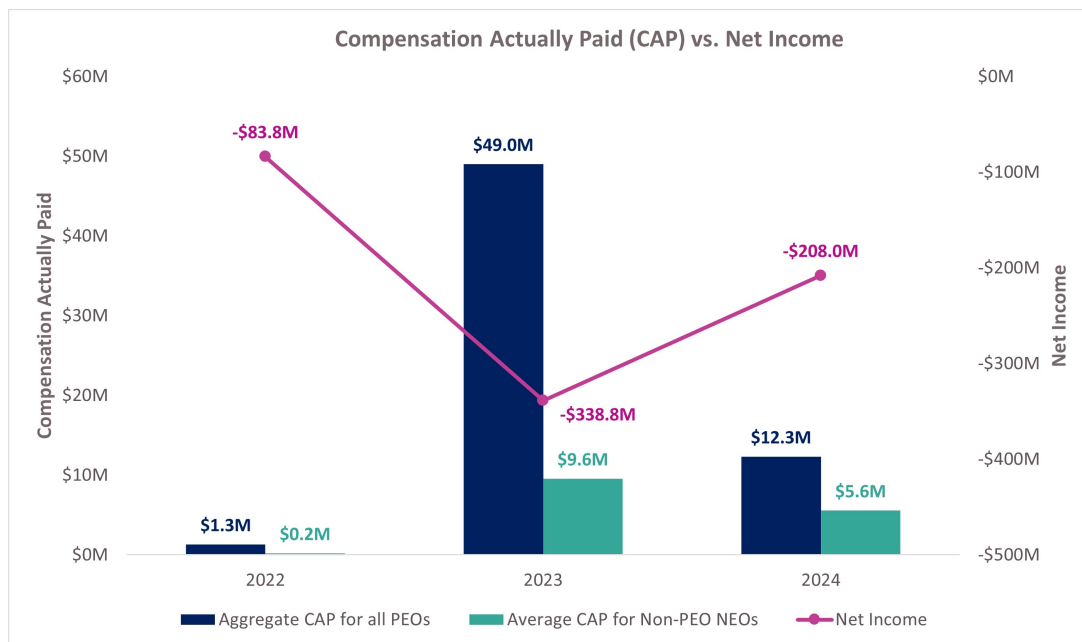
Compensation Actually Paid and Company TSR

The following graph displays the compensation actually paid to our NEOs compared to our TSR.



Compensation Actually Paid and Net Income

The following graph displays our compensation actually paid compared to our net income.



CERTAIN INFORMATION ABOUT OUR COMMON STOCK

Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

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 February 19, 2025 by:

- each of our directors and nominees;
- each of our NEOs;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to be a beneficial owner of greater than 5% of our common stock.

The column entitled “Shares Beneficially Owned” is based on a total of 60,275,561 shares of our common stock outstanding as of February 19, 2025.

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 the date of this table or subject to conversion of preferred stock up to applicable beneficial ownership limitations are considered outstanding and beneficially owned by the person holding the options or preferred stock, as applicable, 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. 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 Spyre Therapeutics, Inc., 221 Crescent Street, Building 23, Suite 105, Waltham, MA 02453.

Name of beneficial owner	Shares beneficially owned	
	Number	Percentage
5% Stockholders:		
FMR LLC ⁽¹⁾	7,623,881	12.65
Fairmount Healthcare Fund II L.P. ⁽²⁾	6,243,861	9.99
RTW Investments, LP ⁽³⁾	3,621,996	6.01
Peter Deutsch ⁽⁴⁾	3,550,276	5.89
Named Executive Officers and Directors:		
Scott Burrows ⁽⁵⁾	201,847	
Sheldon Sloan ⁽⁶⁾	5,968	
Cameron Turtle ⁽⁷⁾	1,804,041	2.94
Jeffrey W. Albers ⁽⁸⁾	59,961	
Peter Harwin ⁽²⁾⁽⁹⁾	6,738,278	10.77
Michael Henderson, M.D. ⁽¹⁰⁾	193,758	
Tomas Kiselak ⁽²⁾⁽¹¹⁾	6,738,278	10.77
Mark McKenna ⁽¹²⁾	174,555	
Sandra Milligan ⁽¹³⁾	6,716	
Laurie Stelzer ⁽¹⁴⁾	32,601	
All current executive officers and directors as a group (11 persons) ⁽¹⁵⁾	9,951,143	15.43

* Represents beneficial ownership of less than one percent.

(1) Based solely upon a Schedule 13G/A filed on November 12, 2024. The shares of common stock listed in the table above are held by funds and accounts managed by direct or indirect subsidiaries of FMR LLC. Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. The address of these funds and accounts is 245 Summer Street, Boston, MA 02210.

(2) Based solely upon a Schedule 13D/A filed on April 25, 2024 and the Company's records. Consists of (i) 4,018,101 shares of common stock and (ii) 2,225,760 shares of common stock issuable upon the conversion of 55,644 shares of Series A Preferred Stock held by Fairmount Healthcare Fund II LP ("Fund II"). Excludes shares of common stock issuable upon the conversion of shares of Series A Preferred Stock and Series B Preferred Stock held by Fund II in excess of the beneficial ownership limitation of 9.99%, which such limitation restricts Fairmount and its affiliates from converting those shares of preferred stock that would result in Fairmount and its affiliates owning, after conversion, a number of shares of common stock in excess of the applicable ownership limitation. Fairmount serves as investment manager for Fund II. Fund II has delegated to Fairmount Funds Management LLC ("Fairmount") the sole power to vote and the sole power to dispose of all securities held in Fund II's portfolio. Because Fund II has divested itself of voting and investment power over the securities it holds and may not revoke that delegation on less than 61 days' notice, Fund II disclaims beneficial ownership of the securities it holds. The general partner of Fairmount is Fairmount Funds Management GP LLC ("Fairmount GP"). As managing members of Fairmount GP, Peter Harwin and Tomas Kiselak may be deemed to have voting and investment power over the shares held by Fund II. Fairmount, Fairmount GP, Peter Harwin and Tomas Kiselak disclaim beneficial ownership of such shares, except to the extent of any pecuniary interest therein. The address of each of these persons and entities is 200 Barr Harbor Drive, Suite 400, West Conshohocken, PA.

(3) Based solely upon a Schedule 13G/A filed on February 14, 2025. RTW Investments, LP ("RTW"), in its capacity as the investment adviser to certain funds (the "RTW Funds"), has the power to vote and the power to direct the disposition of the shares held by the RTW Funds. Accordingly, RTW may be deemed to be the beneficial owner of such securities. Roderick Wong, M.D., as the Managing Partner of RTW, has the power to direct the vote and disposition of the securities held by RTW. Dr. Wong disclaims beneficial ownership of the shares held by the RTW Funds, except to the extent of his pecuniary interest therein. The address and principal office of RTW Investments, LP is 40 10th Avenue, Floor 7, New York, NY 10014, and the address of Dr. Wong and each of the RTW Funds is c/o RTW Investments, LP, 40 10th Avenue, Floor 7, New York, NY 10014.

(4) Based solely upon a Schedule 13G filed on October 23, 2024. The address of Peter E. Deutsch is 25 East Pointe Lane, Old Greenwich, CT 06870.

(5) Consists of (i) 15,208 shares of common stock held by Mr. Burrows and (ii) options exercisable for 186,639 shares of common stock within 60 days of the date of this table.

(6) Consists options exercisable for 5,968 shares of common stock within 60 days of the date of this table.

(7) Consists of (i) 747,540 shares of common stock held by Dr. Turtle and (ii) options exercisable for 1,056,501 shares of common stock within 60 days of the date of this table.

(8) Consists of (i) 27,360 shares of common stock held by Sessions LLC, which may be deemed to be indirectly beneficially owned by Mr. Albers, and (ii) options exercisable for 32,601 shares of common stock within 60 days of the date of this table.

(9) Includes (i) 406,038 shares of common stock held by Mr. Harwin; and (ii) options exercisable for 88,379 shares of common stock within 60 days of the date of this table.

(10) Consists of (i) 105,379 shares of common stock held by Dr. Henderson; and (ii) options exercisable for 88,379 shares of common stock within 60 days of the date of this table.

(11) Includes (i) 406,038 shares of common stock held by Mr. Kiselak; and (ii) options exercisable for 88,379 shares of common stock within 60 days of the date of this table.

(12) Consists of options exercisable for 174,555 shares of common stock within 60 days of the date of this table.

(13) Consists of options exercisable for 6,716 shares of common stock within 60 days of the date of this table.

(14) Consists of options exercisable for 32,601 shares of common stock within 60 days of the date of this table.

(15) Consists of (i) 5,726,648 shares of common stock; (ii) 2,225,760 shares of common stock issuable upon the exercise of Series A Preferred Stock; and (iii) options exercisable for 1,998,735 shares of common stock within 60 days of the date of this table.

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires our directors, officers and persons who beneficially own more than 10% of a registered class of our equity securities to file with the SEC initial reports of ownership and reports of changes in ownership of our common stock and other equity securities. To our knowledge, based solely on our review of Forms 3, 4 and 5 filed with the SEC or written representations that no Form 5 was required, during the year ended December 31, 2024, we believe that all of our directors, officers and persons who beneficially own more than 10% of a registered class of our equity securities timely filed all reports required under Section 16(a) of the Exchange Act.

Securities Authorized for Issuance Under Equity Compensation Plans

The following table presents information as of December 31, 2024 with respect to compensation plans under which shares of our common stock may be issued.

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights (#) ⁽¹⁾	Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights (\$) ⁽²⁾	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (a)) (#) ⁽³⁾
	(a)	(b)	(c)
Equity Compensation Plans Approved by Security Holders:			
2015 Equity Incentive Plan	952	\$ 320.25	— ⁽⁴⁾
2016 Equity Incentive Plan	3,145,248	\$ 16.72	4,047,971 ⁽⁵⁾
2023 Equity Incentive Plan	2,734	\$ 0.36	— ⁽⁶⁾
2016 Employee Stock Purchase Plan	—	N/A	416,592 ⁽⁷⁾
Equity Compensation Plans Not Approved by Security Holders:			
2018 Equity Inducement Plan	6,219,622	\$ 14.19	637,513
Total	9,368,556	\$ 15.08	5,102,076

(1) This column reflects outstanding stock options and RSUs under the listed equity compensation plan.

(2) This column reflects the weighted-average exercise price of stock options granted under the listed equity compensation plan that were outstanding as of December 31, 2024. RSUs reflected in column (a) are not reflected in this column as they do not have an exercise price.

- (3) This column reflects the total shares of our common stock remaining available for issuance under the listed equity compensation plan as of December 31, 2024.
 - (4) No further awards may be made under the 2015 Equity Incentive Plan (the “2015 Plan”); however, shares of common stock that are subject to outstanding awards under the 2015 Plan that expire or are forfeited for any reason without having been exercised in full will generally be available for future grant and issuance under the 2016 Plan.
 - (5) The 2016 Plan provides for an automatic increase in the number of shares reserved for issuance thereunder on January 1 of each year through January 1, 2028 equal to (a) 5% 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 the 2016 Plan increased by 3,814,905 shares on January 1, 2025.
 - (6) No further awards may be made under the 2023 Equity Incentive Plan, which was assumed in connection with the Asset Acquisition.
 - (7) The ESPP provides for an automatic annual increase in the number of shares reserved for issuance thereunder on January 1 of each year for through January 1, 2026 equal to (a) 1% of the number of issued and outstanding shares of common stock on December 31 of the immediately preceding year, or (2) a lesser amount as approved by the Board each year. Pursuant to this provision, the number of shares reserved for grant and issuance under the ESPP increased by 602,570 shares on January 1, 2025.
-

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Other than the executive officer and director compensation arrangements disclosed above under “Corporate Governance—Director Compensation” and “Executive Compensation,” below we describe the transactions to which we were a party since January 1, 2024, in which the amount involved exceeded \$120,000 and in which our directors, executive officers, holders of more than 5% of our common stock, or members of their immediate family had a direct or indirect material interest.

Related Party Transactions

Spyre's Relationships with Paragon, Parapyre and Fairmount

We are party to the Paragon Agreement (as defined below) with Paragon and Parapyre Holding LLC (“Parapyre”). Paragon and Parapyre each beneficially owns less than 5% of a class of our voting securities through their respective holdings of our common stock. Fairmount beneficially owns more than 5% of a class of our voting securities, has two seats on our Board (held by Peter Harwin and Tomas Kiselak) and beneficially owns more than 5% of Paragon. Fairmount appointed Paragon’s board of directors and has the contractual right to approve the appointment of any executive officers of Paragon. Parapyre is an entity formed by Paragon as a vehicle to hold equity in Spyre in order to share profits with certain employees of Paragon and will not perform any substantive role under the Paragon Agreement other than to receive warrants granted to Parapyre under the Paragon Agreement.

In connection with the Asset Acquisition, we assumed the rights and obligations of Pre-Merger Spyre under that certain antibody discovery and option agreement, dated May 25, 2023 and subsequently amended and restated on September 29, 2023 and May 14, 2024, by and among the Company, Paragon and Parapyre (the “Paragon Agreement”), pursuant to which we have exercised the option to acquire intellectual property license rights to or have the option to acquire intellectual property license rights with respect to certain research programs, including with respect to our product candidates. Under the Paragon 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 with mark-up costs pursuant to the terms of the Paragon Agreement. As of the date of the Asset Acquisition, Pre-Merger Spyre had incurred total expenses of \$19.0 million under the Paragon Agreement since inception, inclusive of a \$3.0 million research initiation fee that was due upon signing of the Paragon Agreement and \$16.0 million of reimbursable expenses under the Paragon Agreement for historical costs incurred by Paragon. As of the closing of the Asset Acquisition, \$19.0 million was unpaid and was assumed by us through the Asset Acquisition. As of the year ended December 31, 2024, approximately \$0.6 million was unpaid and owed to Paragon under the Paragon Agreement. Furthermore, following our amendment and restatement of the Paragon Agreement on September 29, 2023, we were obligated to provide certain equity grants to Parapyre upon the completion of each of the calendar years ending on December 31, 2023 and December 31, 2024 to purchase 1% of the then outstanding shares of our common stock, on a fully diluted basis, on the last business day of each applicable calendar year, at the fair market value determined by the Board (the “Parapyre Option Obligation”). We settled such 2023 and 2024 obligations by issuing Parapyre warrants to purchase 684,407 and 848,184 shares of common stock, respectively, less the \$21.52 and \$23.28 per share exercise price of each warrant, respectively. As of December 31, 2024, none of the warrants issued to Parapyre have been exercised.

In July 2023 and December 2023, we exercised our option available under the Paragon Agreement with respect to the SPY001 and SPY002 research programs, respectively, and, in May 2024, we entered into the SPY001 License Agreement and the SPY002 License Agreement. Under the terms of each of the SPY001 License Agreement and SPY002 License Agreement, we are obligated to pay Paragon up to \$22.0 million based on specific development, regulatory and clinical milestones for the first Company product to reach such milestones for each licensed research program, including a \$1.5 million fee for nomination of a development candidate, as applicable, and a further milestone payment of \$2.5 million upon the first dosing of a human patient in a Phase 1 trial. With respect to the SPY002 License Agreement only, on a product by product basis, we are obligated to pay sublicensing fees of up to approximately \$20.0 million upon the achievement of certain milestones.

In June 2024, we exercised our option available under the Paragon Agreement with respect to the SPY003 research program and in October 2024, we entered into the SPY003 License Agreement, which was subsequently amended and restated in February 2025. Under the terms of the SPY003 License Agreement, we are obligated to pay Paragon up to \$22.0 million based on specific development, regulatory and clinical milestones for the first Company product to reach such

milestones, including a \$1.5 million fee for nomination of a development candidate, as applicable, and 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 to acquire the intellectual property rights related to the SPY004 research program pursuant to the Paragon Agreement, we expect to be obligated to make similar payments upon and following the execution of a license agreement with respect to such research program. Our option available under the Paragon Agreement with respect to the SPY004 program remains unexercised.

Private Placement Transactions

On March 18, 2024, we entered into a definitive agreement for a private placement (“March 2024 SPA”) with existing and new investors (the “March 2024 Investors”) for gross proceeds of approximately \$180 million, pursuant to which the March 2024 Investors purchased an aggregate of 121,675 shares of Series B Preferred Stock at a price of \$1,480.00 per share. In connection with the March 2024 SPA, we issued (i) 6,755 shares of Series B Preferred Stock to Perceptive Life Sciences Master Fund, Ltd., (ii) 13,515 shares of Series B Preferred Stock to entities associated with RTW Investments, LP, and (iii) 1,350 shares of Series B Preferred Stock to Commodore Capital Master LP, at a price of \$1,480.00 per share of Series B Preferred Stock. On March 18, 2024, we also entered into a registration rights agreement with the March 2024 Investors, including the above-named investors, pursuant to which the March 2024 Investors are entitled to certain resale registration rights with respect to shares of our common stock held by such investors.

Consulting Agreement

In November 2023, we entered into a consulting agreement with Mr. McKenna, which was effective until he joined the Board in February 2024, pursuant to which Mr. McKenna agreed to provide consulting services to us as a senior advisor to the executive management team. As compensation for such consulting services, Mr. McKenna was granted non-qualified stock options to purchase up to 477,000 shares of our common stock under the 2016 Plan, vesting over four years with an exercise price of \$10.39 per share.

Exchange Agreement

In April 2024, we entered into an exchange agreement with Fund II, pursuant to which Fund II exchanged 90,992 shares of Series A Preferred Stock for 3,639,680 shares of our common stock for no consideration. Shares of our capital stock held by Fund II may be deemed to be beneficially owned by Messrs. Harwin and Kiselak.

Related Party Transaction Policy

Our Board has a written policy regarding the review and approval or ratification by our Audit Committee of related person transactions. For purposes of our policy only, a related person transaction is a transaction, arrangement or relationship or any series of similar transactions, arrangements or relationships between us or any of our subsidiaries and any related person in which the aggregate amount involved since the beginning of our last completed fiscal year exceeds or is expected to exceed \$120,000 and such related person has or will have a direct or indirect interest. A related person is defined to include any executive officers, directors or director nominees or beneficial owner of more than 5% of our common stock and any immediate family member of any of the foregoing persons. In determining to approve or ratify any such transaction, our Audit Committee is expected to take into account, among other factors it deems appropriate, whether the transaction is on terms no less favorable than terms generally available to an unaffiliated third-party under the same or similar circumstances and the extent of the related person’s interest in the transaction. Transactions involving compensation for services provided to us as an employee or director, among other limited exceptions, are deemed under the terms of the policy to have standing pre-approval by the Audit Committee but may be specifically reviewed if appropriate in light of the facts and circumstances. Any director who is a related person with respect to a transaction under review is not permitted to participate in the deliberations (other than to provide information concerning the transaction to the Audit Committee) or vote on approval of the transaction.

OTHER MATTERS

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

Pursuant to Rule 14a-8 of the Exchange Act, stockholders who wish to submit proposals for inclusion in the proxy statement for the 2026 Annual Meeting of Stockholders must send such proposals to our Corporate Secretary at the address set forth on the first page of this Proxy Statement. Such proposals must be received by us as of the close of business (6:00 p.m. Eastern Time) on December 15, 2025 and must comply with Rule 14a-8 of the Exchange Act. The submission of a stockholder proposal does not guarantee that it will be included in the proxy statement.

As set forth in our Bylaws, if a stockholder intends to make a nomination for director election or present a proposal for other business (other than pursuant to Rule 14a-8 of the Exchange Act) at the 2026 Annual Meeting of Stockholders, the stockholder's notice must be received by our Corporate Secretary at the address set forth on the first page of this Proxy Statement no earlier than the 120th day and no later than the close of business on the 90th day before the anniversary of the last annual meeting; provided, however, that if the date of the annual meeting is more than 30 days before or more than 60 days after such anniversary date, the stockholder's notice must be delivered not earlier than the close of business on the 120th day prior to such annual meeting and not later than the close of business on the later of the 90th day prior to such annual meeting or the 10th day following the date on which the first public announcement of the date of such annual meeting is made by the Company. Therefore, unless the 2026 Annual Meeting of Stockholders is more than 30 days before or more than 60 days after the anniversary of the Annual Meeting, notice of proposed nominations or proposals (other than pursuant to Rule 14a-8 of the Exchange Act) must be received by our Corporate Secretary no earlier than January 29, 2026 and no later than the close of business on February 28, 2026. Any such director nomination or stockholder proposal must be a proper matter for stockholder action and must comply with the terms and conditions set forth in our Bylaws (which includes the timing and information required under Rule 14a-19 of the Exchange Act). If a stockholder fails to meet these deadlines or fails to satisfy the requirements of Rule 14a-4 of the Exchange Act, we may exercise discretionary voting authority under proxies we solicit to vote on any such proposal as we determine appropriate. We reserve the right to reject, rule out of order or take other appropriate action with respect to any nomination or proposal that does not comply with these and other applicable requirements.

Delivery of Documents to Stockholders Sharing an Address

A number of brokerage firms have adopted a procedure approved by the SEC called "householding." Under this procedure, certain stockholders who have the same address and do not participate in electronic delivery of proxy materials will receive only one copy of the proxy materials, including this Proxy Statement, the Notice and our Annual Report on Form 10-K for the year ended December 31, 2024, until such time as one or more of these stockholders notifies us that they wish to receive individual copies. This procedure helps to reduce duplicate mailings and save printing costs and postage fees, as well as natural resources. If you received a "householding" mailing this year and would like to have additional copies of the proxy materials mailed to you, please send a written request to our Corporate Secretary at the address set forth on the first page of this Proxy Statement, or call (617) 651-5940, and we will promptly deliver the proxy materials to you. Please contact your broker if you received multiple copies of the proxy materials and would prefer to receive a single copy in the future, or if you would like to opt out of "householding" for future mailings.

Availability of Additional Information

We will provide, free of charge, a copy of our Annual Report on Form 10-K for the year ended December 31, 2024, including exhibits, on the written or oral request of any stockholder of the Company. Please send a written request to our Corporate Secretary at the address set forth on the first page of this Proxy Statement, or call the number above.



SPYRE THERAPEUTICS, INC.
221 CRESCENT STREET
BUILDING 23, SUITE 105
WALTHAM, MA 02453



SCAN TO
VIEW MATERIALS & VOTE



VOTE BY INTERNET

Before The Meeting - Go to www.proxyvote.com or scan the QR Barcode above

Use the Internet to transmit your voting instructions and for electronic delivery of information up until 11:59 p.m. Eastern Time on May 28, 2025. Have your proxy card in hand when you access the web site and follow the instructions to obtain your records and to create an electronic voting instruction form.

During The Meeting - Go to www.virtualshareholdermeeting.com/SYRE2025

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

VOTE BY PHONE - 1-800-690-6903

Use any touch-tone telephone to transmit your voting instructions up until 11:59 p.m. Eastern Time on May 28, 2025. Have your proxy card in hand when you call and then follow the instructions.

VOTE BY MAIL

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

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

V69715-P25602

KEEP THIS PORTION FOR YOUR RECORDS
DETACH AND RETURN THIS PORTION ONLY

THIS PROXY CARD IS VALID ONLY WHEN SIGNED AND DATED.

SPYRE THERAPEUTICS, INC.		For All	Withhold All	For All Except	To withhold authority to vote for any individual nominee(s), mark "For All Except" and write the number(s) of the nominee(s) on the line below.		
The Board of Directors recommends you vote FOR the following listed nominees:							
1. Election of Class III Directors for terms expiring in 2028.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				
Nominees:							
01) Peter Harwin							
02) Michael Henderson, M.D.							
03) Sandra Milligan, M.D., J.D.							
The Board of Directors recommends you vote FOR the following proposals:					For	Against	Abstain
2. To approve, on a non-binding, advisory basis, the compensation of the Company's named executive officers.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				
3. To ratify the appointment of KPMG LLP as the Company's independent registered public accounting firm for the year ending December 31, 2025.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>				
NOTE: Such other business as may properly come before the meeting or any adjournment or postponement thereof.							
Please sign exactly as your name(s) appear(s) hereon. When signing as attorney, executor, administrator, or other fiduciary, please give full title as such. Joint owners should each sign personally. All holders must sign. If a corporation or partnership, please sign in full corporate or partnership name by authorized officer.							
Signature [PLEASE SIGN WITHIN BOX]	Date	Signature (Joint Owners)			Date		

Important Notice Regarding the Availability of Proxy Materials for the Annual Meeting:

The Notice & Proxy Statement and Annual Report are available at www.proxyvote.com.

V69716-P25602

**SPYRE THERAPEUTICS, INC.
ANNUAL MEETING OF STOCKHOLDERS
MAY 29, 2025 12:00 PM EASTERN TIME**

THIS PROXY IS SOLICITED ON BEHALF OF THE BOARD OF DIRECTORS

The undersigned hereby appoints Cameron Turtle, Scott Burrows and Heidi King-Jones, or any of them, with power to act without the other and with power of substitution, as proxies and attorneys-in-fact and hereby authorizes them to represent and vote, as designated on the reverse side of this card, all the shares of common stock of Spyre Therapeutics, Inc. that the undersigned is entitled to vote at the Annual Meeting of Stockholders of Spyre Therapeutics, Inc. to be held at 12:00 p.m. Eastern Time on May 29, 2025, live via the Internet, at www.virtualshareholdermeeting.com/SYRE2025 or any adjournment or postponement thereof, with all powers which the undersigned would possess if present at the Annual Meeting.

THIS PROXY, WHEN PROPERLY EXECUTED, WILL BE VOTED IN THE MANNER DIRECTED HEREIN. IF NO SUCH DIRECTION IS MADE BUT THE CARD IS SIGNED, THIS PROXY WILL BE VOTED IN ACCORDANCE WITH THE BOARD OF DIRECTORS' RECOMMENDATIONS AND IN THE DISCRETION OF THE PROXIES WITH RESPECT TO SUCH OTHER BUSINESS AS MAY PROPERLY COME BEFORE THE MEETING OR ANY ADJOURNMENT OR POSTPONEMENT THEREOF. IN THE EVENT THAT ANY OF THE NOMINEES NAMED ON THE REVERSE SIDE OF THIS CARD ARE UNAVAILABLE FOR ELECTION OR UNABLE TO SERVE, THE SHARES REPRESENTED BY THE PROXY MAY BE VOTED FOR A SUBSTITUTE NOMINEE SELECTED BY THE BOARD OF DIRECTORS.

Continued and to be signed on reverse side