As filed with the Securities and Exchange Commission on April 18, 2024

Registration No. 333-

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

FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Spyre Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**46-4312787**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

221 Crescent Street
Building 23, Suite 105
Waltham, MA 02453
(617) 651-5940
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Heidy King-Jones
Chief Legal Officer and Corporate Secretary
Spyre Therapeutics, Inc.
221 Crescent Street
Building 23, Suite 105
Waltham, MA 02453
(617) 651-5940
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Ryan A. Murr
Branden C. Berns
Melanie E. Neary
Gibson, Dunn & Crutcher LLP
One Embarcadero Center, Suite 2600
San Francisco, CA 94111
(415) 393-8373

Approximate date of commencement of proposed sale to the public From time to time after the effective date of this Registration Statement.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☒

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. ☐

Pursuant to Rule 429 under the Securities Act of 1933, as amended, the prospectus included in this registration statement is a combined prospectus and also relates to the securities previously registered under the Registrant's Registration Statement on Form S-1 (File No. 333-273769) and Registration Statement on Form S-1 (File No. 333-276251). Accordingly, this registration statement, which is a new registration statement, also constitutes Post-Effective Amendment No. 4 to Registration Statement No. 333-273769 and Post-Effective Amendment No. 1 to Registration Statement No. 333-276251, which post-effective amendments shall hereafter become effective concurrently with the effectiveness of this registration statement in accordance with Section 8(c) of the Securities Act of 1933, as amended (the "Securities Act").

The Registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act, or until this registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

EXPLANATORY NOTE

Spyre Therapeutics, Inc., a Delaware corporation, initially filed with the Securities and Exchange Commission (the "SEC") a Registration Statement on Form S-1 (File No. 333-273769) on November 15, 2023, which was declared effective on November 20, 2023 (as subsequently

amended, the “November 2023 Prior Registration Statement”), and a Registration Statement on Form S-1 (File No. 333-276251) on March 26, 2024, which was declared effective on April 1, 2024 (the “April 2024 Prior Registration Statement” and together with the November 2023 Prior Registration Statement, the “Prior Registration Statements”). The Prior Registration Statements collectively registered the resale of up to (i) 24,809,064 shares of Common Stock (as defined below) and (ii) 6,000,000 shares of Common Stock issuable upon the conversion of 150,000 shares of Series B Preferred Stock (as defined below). A total of (i) 22,496,402 shares of Common Stock and (ii) 6,000,000 shares of Common Stock issuable upon the conversion of 150,000 shares of Series B Preferred Stock registered for resale under the Previous Registration Statements remain unsold.

Pursuant to Rule 429 under the Securities Act, the prospectus included in this registration statement is a combined prospectus and also relates to all the securities registered for resale and remaining unsold under the Prior Registration Statements. Accordingly, this registration statement, which is a new registration statement also constitutes Post-Effective Amendment No. 4 to the November 2023 Prior Registration Statement and Post-Effective Amendment No. 1 to the April 2024 Prior Registration Statement and is being filed to register the resale of up to an additional 4,865,000 shares of Common Stock issuable upon the conversion of 121,625 shares of Series B Preferred Stock that were purchased by certain Selling Stockholders in the March 2024 PIPE (as such terms are defined below). Such post-effective amendments shall hereafter become effective concurrently with the effectiveness of this registration statement in accordance with Section 8(c) of the Securities Act.

Accordingly, this registration statement (i) carries forward from the Prior Registration Statements all the securities registered in the Prior Registration Statements remaining unsold and (ii) registers the resale of up to an additional 4,865,000 shares of Common Stock issuable upon the conversion of 121,625 shares of Series B Preferred Stock.

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The information in this prospectus is not complete and may be changed. The selling stockholders named in this prospectus may not sell these securities until the registration statement filed with the Securities and Exchange Commission (the "SEC") is effective. This prospectus is not an offer to sell these securities, and it is not soliciting an offer to buy these securities, in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED APRIL 18, 2024

PRELIMINARY PROSPECTUS

Spyre Therapeutics, Inc.

33,361,402 Shares

Common Stock

Offered by the Selling Stockholders

This prospectus relates to the proposed resale or other disposition by the selling stockholders identified herein (the "Selling Stockholders") of up to (i) 8,864 shares (the "Merger Common Shares") of our Common Stock, (ii) 248,560 shares of Common Stock (the "Merger Conversion Shares") that were issued upon the conversion of 6,214 shares ("Merger Preferred Shares") of our Series A Preferred Stock, par value $0.0001 per share (the "Series A Preferred Stock"), (iii) 16,239,000 shares of Common Stock (the "June 2023 Private Placement Conversion Shares") that were issued upon the conversion of 405,975 shares (the "June 2023 Private Placement Preferred Shares") of Series A Preferred Stock, (iv) 5,999,978 shares (the "December 2023 Private Placement Common Shares") of our common stock, par value $0.0001 per share ("Common Stock"), (v) 6,000,000 shares of Common Stock (the "December 2023 Private Placement Conversion Shares") issuable upon the conversion of 150,000 shares (the "December 2023 Private Placement Preferred Shares") of Series B preferred stock, par value $0.0001 (the "Series B Preferred Stock"), and (vi) 4,865,000 shares (the "March 2024 Private Placement Conversion Shares") of Common Stock issuable upon the conversion of 121,625 shares (the "March 2024 Private Placement Preferred Shares") of Series B Preferred Stock. Subject to receiving the requisite stockholder approval and certain beneficial ownership limitations set by each preferred stockholder, each share of Series B Preferred Stock will automatically convert upon the requisite stockholder approval into an aggregate of 40 shares of Common Stock. The shares of Common Stock registered by this prospectus are referred to herein as the "Resale Shares."

The Merger Common Shares and Merger Preferred Shares were issued and sold to our former stockholders in connection with the Asset Acquisition (as defined below), which closed on June 22, 2023. The June 2023 Private Placement Preferred Shares were issued and sold to in a private placement (the "June 2023 PIPE" and, together with the Asset Acquisition, the "June 2023 Transactions"), which closed on June 26, 2023. The December 2023 Private Placement Preferred Shares and December 2023 Private Placement Common Shares were issued and sold to accredited investors in a private placement (the "December 2023 PIPE"), which closed on December 11, 2023. The March 2024 Private Placement Preferred Shares were issued and sold to accredited investors in a private placement (the "March 2024 PIPE"), which closed on March 20, 2024. We are not selling any Resale Shares under this prospectus and will not receive any of the proceeds from the sale or other disposition of Resale Shares by the Selling Stockholders.

The Selling Stockholders may sell the Resale Shares on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale, on the over-the-counter market, in one or more transactions otherwise than on these exchanges or systems, such as privately negotiated transactions, or using a combination of these methods, and at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at negotiated prices. See the disclosure under the heading "Plan of Distribution" elsewhere in this prospectus for more information about how the Selling Stockholders may sell or otherwise dispose of their Resale Shares hereunder.

The Selling Stockholders may sell any, all or none of the securities offered by this prospectus and we do not know when or in what amount the Selling Stockholders may sell their Resale Shares hereunder following the effective date of the registration statement of which this prospectus forms a part.

You should carefully read this prospectus and any applicable prospectus supplement before you invest in any of the securities being offered.

Our Common Stock is traded on The Nasdaq Global Select Market under the symbol "SYRE." On April 17, 2024, the last reported sale price for our Common Stock was $34.31 per share.

An investment in our securities involves a high degree of risk. You should carefully consider the information under the heading "Risk Factors" beginning on page 12 of this prospectus and any applicable prospectus supplement.

We are a "smaller reporting company" as defined by Rule 12b-2 of the Exchange Act and are subject to reduced public company reporting requirements.

Neither the SEC nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is , 2024

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the SEC using a “shelf” registration process. Under this shelf registration process, the Selling Stockholders may, from time to time, sell the securities described in this prospectus in one or more offerings.

This prospectus contains information that you should consider when making your investment decision. Neither we, nor the Selling Stockholders, have authorized anyone to give any information or to make any representation other than those contained in this prospectus. The Selling Stockholders are offering to sell, and seeking offers to buy, our securities only in jurisdictions where it is lawful to do so. We have not authorized anyone to provide you with different information. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in any accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

In this prospectus, unless the context otherwise requires, the terms “Spyre,” “Aeglea BioTherapeutics, Inc.,” the “Company,” “we,” “us,” and “our” refer to Spyre Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries.

This prospectus contains trade names, trademarks and service marks of others, which are the property of their respective owners. Solely for convenience, trademarks and trade names referred to in this prospectus may appear without the ® or TM symbols.

All references to “our product candidates,” “our programs” and “our pipeline” in this prospectus refer to the research programs with respect to which we have exercised the option to acquire intellectual property license rights to or have the option to acquire intellectual property license rights to pursuant to that certain antibody discovery and option agreement, dated May 25, 2023 and subsequently amended and restated on September 29, 2023, by and among Spyre Therapeutics, LLC, Paragon Therapeutics, Inc. (“Paragon”) and Parapyre Holding LLC (“Parapyre”) (the “Paragon Agreement”).

Please be advised that on September 8, 2023, we effected a reverse stock split of our Common Stock at a ratio of 1-for-25 (the “Reverse Split”). Except as indicated otherwise, all share numbers related to our Common Stock disclosed in this prospectus have been adjusted on a post-Reverse Split basis. In addition, on November 28, 2023, we changed our name from “Aeglea Biotherapeutics, Inc.” to “Spyre Therapeutics, Inc.”

CAUTIONARY STATEMENT CONCERNING FORWARD-LOOKING STATEMENTS

This prospectus contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended (the “Securities Act”), and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). These forward-looking statements involve a number of risks and uncertainties. We caution readers that any forward-looking statement is not a guarantee of future performance and that actual results could differ materially from those contained in the forward-looking statement. These statements are based on current expectations of future events.

All statements, other than statements of historical facts contained in this prospectus, including, without limitation, statements regarding: stockholder approval of the conversion rights of the Series B Preferred Stock; any future payouts under the CVR (as defined herein); our ability to achieve the expected benefits or opportunities with respect to our acquisition of Spyre Therapeutics, Inc. (“Pre-Merger Spyre”) or to monetize any of our legacy assets, our future results of operations and financial position, business strategy, the length of time that we believe our existing cash resources will fund our operations, our market size, our potential growth opportunities, our preclinical and future clinical development activities, the efficacy and safety profile of our product candidates, the potential therapeutic benefits and economic value of our product candidates, the timing and results of preclinical studies and clinical trials, the expected impact of macroeconomic conditions, including inflation, increasing interest rates and volatile market conditions, current or potential bank failures, as well as global events, including the ongoing military conflict in Ukraine, conflict in Israel and surrounding areas, and geopolitical tensions in China on our operations, and the receipt and timing of potential regulatory communications, designations, approvals and commercialization of product candidates. Forward-looking statements generally relate to future events or our future financial or operating performance. Forward-looking statements generally relate to future events or our future financial or operating performance. The words “believe,” “may,” “will,” “potentially,” “estimate,” “continue,” “anticipate,” “predict,” “target,” “intend,” “could,” “would,” “should,” “project,” “plan,” “expect,” and similar expressions that convey uncertainty of future events or outcomes are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. Factors that might cause such a difference are disclosed in the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” You should evaluate all forward-looking statements made in this prospectus in the context of these risks and uncertainties. We caution you that the risks, uncertainties and other factors referred to in this prospectus may not contain all of the risks, uncertainties and other factors that may affect our future results and operations.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based on information available to us as of the date of this prospectus. While we believe that such information provides a reasonable basis for these statements, such information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely on these statements.

All subsequent written or oral forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. We do not undertake any obligation to release publicly any revisions to these forward-looking statements to reflect events or circumstances after the date of this prospectus or to reflect the occurrence of unanticipated events,

except as may be required under applicable U.S. securities laws. If we do update one or more forward-looking statements, no inference should be drawn that we will make additional updates with respect to those or other forward-looking statements.

PROSPECTUS SUMMARY

This summary may not contain all the information that you should consider before investing in securities. You should read the entire prospectus carefully, including the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," and our consolidated financial statements and the related notes included elsewhere in this prospectus, before making an investment decision.

Company Overview

On June 22, 2023, we completed the acquisition of Pre-Merger Spyre (the "Asset Acquisition") pursuant to the Acquisition Agreement (as defined under the section titled "*Recent Developments*" below). Pre-Merger Spyre was a pre-clinical stage biotechnology company that was incorporated on April 28, 2023 under the direction of Peter Harwin, a Managing Member of Fairmount Funds Management LLC ("Fairmount"), for the purpose of holding rights to certain intellectual property being developed by Paragon. Fairmount is a founder of Paragon.

Through the Asset Acquisition, we received the option to license the intellectual property rights related to four research programs (collectively, the "Option") pursuant to the Paragon Agreement. On July 12, 2023, we exercised the Option with respect to one of these research programs to exclusively license intellectual property rights related to such research program directed to antibodies that selectively bind to α4ß7 integrin and methods of using these antibodies, including methods of treating inflammatory bowel disease ("IBD") using the SPY001 program. If this research program is pursued non-provisionally and matures into issued patents, we would expect those patents to expire no earlier than 2044, subject to any disclaimers or extensions. On December 14, 2023, we exercised the Option under the Paragon Agreement to be granted an exclusive license to all of Paragon's rights, title and interest in and to intellectual property rights, including inventions, patents, sequence information and results, under SPY002, Spyre's TL1A program, to develop and commercialize antibodies and products worldwide in all therapeutics disorders. If this research program is pursued non-provisionally and matures into issued patents, we would expect those patents to expire no earlier than 2044, subject to any disclaimers or extensions. The license agreements pertaining to such research programs are currently being finalized. Furthermore, as of the date of this registration statement, the Option remains unexercised with respect to the intellectual property rights related to the two remaining research programs under the Paragon Agreement. For more information on the Paragon Agreement, see discussion under the heading "*Paragon Agreement*" below.

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

Following the Asset Acquisition and the entry into the Immedica APA, we have significantly reshaped the business into a preclinical stage biotechnology company focused on developing next generation therapeutics for patients living with IBD, including ulcerative colitis ("UC") and Crohn's disease ("CD"). Through the Paragon Agreement, our portfolio of novel and proprietary monoclonal antibody product candidates has the potential to address unmet needs in IBD care by improving efficacy, safety, and/or dosing convenience relative to products currently available or product candidates in development. We have engineered our product candidates with the aim to bind potently and selectively to their target epitopes and to exhibit extended pharmacokinetic half-lives through modifications in the Fc domain, that increase affinity to human FcRn and increase antibody recycling. We anticipate that half-life extension will enable less frequent administration as compared to marketed or development-stage monoclonal antibodies ("mAbs") that do not incorporate half-life extension modifications. Nonetheless, the drug and/or device development process is inherently uncertain, our development approach is unproven, the preclinical evidence that supports our proposed development program is preliminary and limited,

and we have not yet tested any product candidate in humans. In addition to the development of our product candidates as potential monotherapies, we plan to investigate combinations of our proprietary antibodies in preclinical and clinical studies to evaluate whether combination therapy (co-administration or co-formulation of multiple monoclonal antibodies) can lead to greater efficacy, as compared to monotherapies in IBD. We also intend to examine patient selection strategies via complementary diagnostics utilized in our clinical studies to evaluate whether patients can be matched to the optimal therapy based on genetic background and/or other biomarker signatures. We intend to deliver our product candidates through convenient, infrequently dosed, self-administered, subcutaneous ("SC") injection, although the specific delivery mechanism or technology has not been selected given our early stage. Notwithstanding our efforts to develop safe and effective monotherapies and combination therapies, there can be no guarantee that we will be able to develop product candidates that will be found to be safe and effective so as to obtain the necessary regulatory approvals to market our product candidates.

Recent Developments

On September 8, 2023, we effected the Reverse Split, which resulted in the reverse split of our Common Stock at a ratio of 1-for-25. Readers should note that, except as indicated otherwise, all share numbers related to our Common Stock disclosed in this "Recent Developments" section have been adjusted on a post-Reverse Split basis.

On June 22, 2023, we acquired in accordance with the terms of the Agreement and Plan of Merger (the "Acquisition Agreement"), by and among us, Aspen Merger Sub I, Inc., a Delaware corporation and our wholly owned subsidiary, Sequoia Merger Sub II, LLC, a Delaware limited liability company and our wholly owned subsidiary, and Pre-Merger Spyre, the assets of Pre-Merger Spyre, a privately held biotechnology company advancing a pipeline of antibody therapeutics through the Paragon Agreement. Pre-Merger Spyre was incorporated on April 28, 2023, for the purpose of holding rights to certain intellectual property being developed by Paragon.

The Asset Acquisition was structured as a stock-for-stock transaction pursuant to which all of Pre-Merger Spyre's outstanding equity interests were exchanged based on a fixed exchange ratio of 0.5494488 to 1 for consideration from us of 517,809 shares of Common Stock and 364,887 shares of Series A Preferred Stock (convertible on a 40 to 1 basis) in addition to the assumption of outstanding and unexercised stock options to purchase 2,734 shares of Common Stock from the Amended and Restated Spyre 2023 Equity Incentive Plan. The Common Stock and the Series A Preferred Stock related to the Asset Acquisition were issued to Pre-Merger Spyre stockholders on July 7, 2023.

Concurrently with the Asset Acquisition, we entered into a definitive agreement (the "June 2023 SPA") for a PIPE investment with existing and new investors (the "June 2023 Investors") to raise approximately $210 million in which the June 2023 Investors were issued 721,452 shares of Series A Preferred Stock at a price of $291.08 per share. The Asset Acquisition was approved by our board of directors and the board of directors and stockholders of Pre-Merger Spyre. The closings of the June 2023 Transactions were not subject to the approval of our stockholders. Following receipt of stockholder approval of the conversion of Series A Preferred Stock in November 2023, each share of Series A Preferred Stock automatically converted into 40 shares of Common Stock, subject to certain beneficial ownership limitations set by each holder. Except as otherwise required by law (e.g. voting on a change to the authorized shares of Preferred Stock or the rights of such shares as required by Delaware General Corporation Law (the "DGCL")) and Spyre's Certificate of Designation of Series A Non-Voting Convertible Preferred Stock (the "Series A Certificate of Designation"), the Series A Preferred Stock does not have voting rights.

In connection with the execution of the Acquisition Agreement, Spyre and Pre-Merger Spyre entered into stockholder support agreements (the "Support Agreements") with certain of Spyre's officers and directors, which collectively own an aggregate of less than 1% of the outstanding shares of the Common Stock. The Support Agreements provide that, among other things, each of the parties thereto would vote or cause to be voted all of the shares of Common Stock owned by such stockholder in favor of the approval of the conversion of shares of the Series A Preferred Stock into shares of Common Stock in accordance with Nasdaq Stock Market Rules at Spyre's stockholders' meeting held in connection therewith.

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

In connection with the Asset Acquisition, a non-transferrable contingent value right (a "CVR") was distributed to Spyre stockholders of record as of the close of business on July 3, 2023, but was not distributed to holders of shares of Common Stock or Series A Preferred Stock issued to the June 2023 Investors or former stockholders of Pre- Merger Spyre in connection with the June 2023 Transactions. Holders of the CVRs will be entitled to receive cash payments from proceeds received by Spyre for a three-year period, if any, related to the disposition or monetization of certain legacy assets owned by us prior to the Asset Acquisition (the "Legacy Assets") for a period of one year following the closing of the Asset Acquisition.

On July 27, 2023, we announced that we entered the Immedica APA. The sale of pegzilarginase to Immedica supersedes and terminates the license agreement between us and Immedica dated March 2021.

The milestone payments under the Immedica APA are contingent on formal reimbursement decisions by national authorities in key European markets and pegzilarginase approval by the United States Food and Drug Administration (the "FDA"), among other events. The upfront payment has been paid and distributed and contingent milestone payments if paid, net of expenses and adjustments, will be distributed to holders of Spyre's CVR pursuant to the CVR Agreement that was entered into in connection with the Asset Acquisition.

On December 7, 2023, we entered into a definitive agreement (the "December 2023 SPA") for a PIPE investment with existing and new investors (the "December 2023 Investors") to raise $180 million, in which transaction the December 2023 Investors were issued an aggregate of 6,000,000 shares of Common Stock at a price of $15.00 per share and 150,000 shares of Series B Preferred Stock at a price of $600.00 per share. The closing of the December 2023 PIPE was not subject to Spyre stockholder approval. Subject to Spyre stockholder approval and certain beneficial ownership limitations set by each holder, each share of Series B Preferred Stock will automatically convert into 40 shares of Common Stock. We have filed a definitive proxy statement with the SEC to solicit such stockholder approval, among other matters, at the 2024 annual meeting of stockholders. Except as otherwise required by law (e.g. voting on a change to the authorized shares of Preferred Stock or the rights of such shares as required by DGCL) and as specified in our Certificate of Designation of Series B Non-Voting Convertible Preferred Stock ("Series B Certificate of Designation"), the Series B Preferred Stock does not have voting rights.

On March 18, 2024, we entered into a definitive agreement (the "March 2024 SPA") for a PIPE investment with existing and new investors (the "March 2024 Investors") to raise approximately $180 million, in which transaction the March 2024 Investors were issued an aggregate of 121,625 shares of Series B Preferred Stock at a price of $1,480.00 per share. The closing of the March 2024 PIPE was not subject to Spyre stockholder approval. Subject to Spyre stockholder approval and certain beneficial ownership limitations set by each holder, each share of Series B Preferred Stock will automatically convert into 40 shares of Common Stock. We have filed a

definitive proxy statement with the SEC to solicit such stockholder approval, among other matters, at the 2024 annual meeting of stockholders to be held on May 13, 2024. Except as otherwise required by law (e.g. voting on a change to the authorized shares of Preferred Stock or the rights of such shares as required by DGCL) and as specified in our Series B Certificate of Designation, the Series B Preferred Stock does not have voting rights.

Corporation Information

We were formed as a limited liability company under the laws of the State of Delaware in December 2013 and converted to a Delaware corporation in March 2015. On June 22, 2023, we completed the Asset Acquisition, pursuant to which all of Pre-Merger Spyre's outstanding equity interests were exchanged based on a fixed exchange ratio of 0.5494488 to 1 for consideration from Spyre of 517,809 shares of Common Stock and 364,887 shares of Series A Preferred Stock in addition to the assumption of outstanding and unexercised stock options to purchase 2,734 shares of Common Stock from the Amended and Restated Spyre 2023 Equity Incentive Plan. On November 28, 2023, we changed our name from "Aeglea Biotherapeutics, Inc." to "Spyre Therapeutics, Inc." and our Nasdaq ticker symbol from "AGLE" to "SYRE". Our principal executive offices are located at 221 Crescent Street, Building 23, Suite 105, Waltham, MA 02453, and our telephone number is (617) 651-5940.

On September 8, 2023, we effected a reverse stock split of our Common Stock at a ratio of 1-for-25. Except as indicated otherwise, all share numbers related to our Common Stock disclosed in this prospectus have been adjusted on a post-Reverse Split basis.

Implications of Being a Smaller Reporting Company

We are a "smaller reporting company," meaning that the market value of our Common Stock held by non-affiliates is less than $700.0 million and our annual revenue is less than $100.0 million during the most recently completed fiscal year. We may continue to be a smaller reporting company after this offering if either (i) the market value of our Common Stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our Common Stock held by non-affiliates is less than $700.0 million. As a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and smaller reporting companies have reduced disclosure obligations regarding executive compensation.

The Offering

Shares Offered by the Selling Securityholders	Up to (i) 22,496,402 shares of Common Stock and (ii) 10,865,000 shares of Common Stock issuable upon the conversion of 271,625 shares of Series B Preferred Stock.
Terms of the Offering	The selling securityholders will determine when and how they will dispose of the shares of Common Stock and shares of Common Stock issuable upon conversion of Series B Preferred Stock registered under this prospectus for resale.
Shares Outstanding	As of December 31, 2023, there were 36,057,109 shares of our Common Stock, 437,037 shares of our Series A Preferred Stock and 150,000 shares of our Series B Preferred Stock outstanding.
Use of Proceeds	We will not receive any proceeds from the sale of the Resale Shares offered by the Selling Stockholders under this prospectus. The net proceeds from the sale of the Resale Shares offered by this prospectus will be received by the Selling Stockholders. See the section titled “Use of Proceeds.”
Risk Factors	See the section titled “Risk Factors” and other information included in this prospectus for a discussion of factors that you should consider carefully before deciding to invest in our securities.
Trading Markets and Ticker Symbols	Our Common Stock is listed on The Nasdaq Global Select Market under the symbol “SYRE.”

Except as otherwise noted, the number of issued and outstanding shares of Common Stock does not include the following, as of December 31, 2023:

- 17,481,480 shares of Common Stock issuable upon the conversion of 437,037 shares of Series A Preferred Stock;
- 6,000,000 shares of Common Stock issuable upon the conversion of 150,000 shares of Series B Preferred Stock;
- 3,029 shares of Common Stock reserved for issuance under our 2015 Equity Incentive Plan;
- 4,931,476 shares of Common Stock reserved for issuance under our Amended and Restated 2016 Equity Incentive Plan (the “2016 Plan”);
- 6,044,000 shares of Common Stock reserved for issuance under our 2018 Equity Inducement Plan, as amended;
- 72,404 shares of Common Stock reserved for issuance pursuant to our 2016 Employee Stock Purchase Plan;
- 250,000 shares of Common Stock reserved for issuance upon the exercise of 250,000 pre-funded warrants to acquire shares of Common Stock;
- 684,407 shares of Common Stock reserved for issuance upon the exercise of 684,407 warrants to acquire shares of Common Stock;
- 121,871 shares of Common Stock reserved for issuance under the Spyre 2023 Equity Incentive Plan, as amended and assumed by us; and
- 4,865,000 shares of Common Stock issuable upon the conversion of 121,625 shares of Series B Preferred Stock issued subsequent to December 31, 2023 in the March 2024 PIPE.

Except as indicated otherwise, all share numbers related to our Common Stock disclosed in this prospectus have been adjusted on a post-Reverse Split basis.

For additional information concerning the offering, see the section titled " *Plan of Distribution*"

RISK FACTOR SUMMARY

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

Risks Related to Our Financial Condition and Capital Requirements

- We will not be able to continue as a going concern if we are unable to raise additional capital when needed.
- We have never generated any revenue from product sales and may never be profitable.
- We anticipate that we will continue to incur significant losses for the foreseeable future.
- We may not be able to raise the capital that we need to support our business plans and raising additional capital may cause dilution to our stockholders and restrict our operations.

Risks Related to the Discovery, Development and Commercialization

- We face competition from companies that have developed or may develop competing programs.
- Our programs are in preclinical stages of development and may fail in development or suffer delays.
- We are substantially dependent on the success of the SPY001 and SPY002 programs.
- We may fail to achieve our projected development goals in the time frames we announce and expect.
- Any drug delivery device used may have its own regulatory development, supply, and other risks.
- We may not be successful in building a pipeline of product candidates with commercial value.
- Our studies and trials may not be sufficient to support regulatory approval of any product candidates.
- If we are unable to successfully develop complementary diagnostics for our therapeutic product candidates, we may not realize their full commercial potential.
- We have limited experience in developing and commercializing diagnostics and have never applied for or obtained regulatory clearance or approval for any diagnostic tests.
- Additional time may be required to obtain regulatory approval for our product candidates and future product candidates because of their status as combination products.
- We may encounter difficulties enrolling participants in our future clinical trials.
- Preliminary or “topline” data from our clinical trials may change as more data becomes available.
- Our future clinical trials may reveal significant adverse events or side effects.
- We may fail to capitalize on more profitable or potentially successful product candidates.
- Our future products may not achieve regulatory approval or commercial success.
- Certain of our programs may compete with our other programs.
- The FDA may not accept data from clinical trials we conduct at sites outside the United States.

Risks Related to Government Regulation

- FDA and comparable foreign regulatory approval processes are lengthy and time-consuming and we may not be able to obtain or may be delayed in obtaining regulatory approvals for our product candidates.
- We may not be able to meet requirements for chemistry, manufacturing and control of our programs.
- Our product candidates may face competition sooner than anticipated based on rules and regulations that may apply or government decisions with respect to our intellectual property.
- Even if we receive regulatory approval, we will be subject to extensive ongoing regulatory obligations.
- We may face difficulties from healthcare legislative reform measures.
- Our operations and arrangements with third-parties are subject to healthcare regulatory laws.
- We may be unable to offer products at competitive prices due to unfavorable pricing regulations and/or third-party coverage and reimbursement policies.
- We may face criminal liability or other consequences for violations of U.S. and foreign trade regulations.

- Foreign governments may impose strict price controls, which may adversely affect our revenue.
- Any accelerated review designations (e.g. fast track designation) we may pursue may not hasten development or regulatory review.

Risks Related to Our Intellectual Property

- Our ability to obtain and protect our patents and other proprietary rights is uncertain.
- We may fail in obtaining or maintaining necessary rights to our programs.
- We may be subject to patent infringement claims or may need to file such claims.
- We may subject to claims of wrongful hiring of employees or wrongful use of confidential information.
- Our patents and our ability to protect our products may be impaired by changes to patent laws.
- Our patent protection could be reduced or eliminated for non-compliance with regulatory requirements.
- We may fail to identify or interpret relevant third-party patents.
- We may become subject to claims challenging the inventorship or ownership of our intellectual property.
- Patent terms may be inadequate to protect our competitive position of our programs.
- Our technology licensed from various third parties may be subject to retained rights.

Risks Related to Our Reliance on Third Parties

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

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

- We may experience difficulties in managing the growth of our organization.
- We may fail to attract or retain highly qualified personnel.
- Our ability to operate in foreign markets is subject to regulatory burdens, risks and uncertainties.
- Our estimates of market opportunity and forecasts of market growth may be inaccurate and our business may not grow at similar rates, or at all.
- Our employees or third-parties may engage in misconduct or other improper activities.
- We may be impacted by security or data breaches or other improper access to our data.
- Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.
- We may fail to comply with privacy and data security regulations.
- We may fail to comply with environmental, health and safety laws and regulations.
- We may be subject to adverse legislative or regulatory tax changes.
- We may fail to realize the benefits of our business or product acquisitions or our strategic alliances.
- We may be impacted by the failure of financial institutions.

Risks Related to Our Common Stock

- We may fail to obtain stockholder approval of the conversion of our Series B Preferred Stock.
- Our certificate of incorporation, Delaware law and certain contracts include anti-takeover provisions.
- Our certificate of incorporation and bylaws contain exclusive forum provisions.
- We do not anticipate paying any dividends in the foreseeable future.
- Future sales of shares by existing stockholders could cause our stock price to decline.
- Future sales and issuances of equity and debt could result in additional dilution to our stockholders.
- Our principal stockholders own a significant percentage of our stock.

General Risk Factors

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

RISK FACTORS

Risks Related to Our Financial Condition and Capital Requirements

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

As of December 31, 2023, we had $339.6 million of cash, cash equivalents, marketable securities, and restricted cash. We will need to raise additional capital to continue to fund our operations and service our debt obligations in the future. If we are unable to raise additional capital when needed, we will not be able to continue as a going concern.

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

We do not currently have any products approved for sale and do not generate any revenue from product sales. Accordingly, we expect to rely primarily on equity and/or debt financings to fund our continued operations. Our ability to raise additional funds will depend, in part, on the success of our preclinical studies and clinical trials and other product development activities, regulatory events, our ability to identify and enter into licensing or other strategic arrangements, and other events or conditions that may affect our value or prospects, as well as factors related to financial, economic and market conditions, many of which are beyond our control. There can be no assurances that sufficient funds will be available to us when required or on acceptable terms, if at all.

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

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

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

Even if successful in raising new capital, we could be limited in the amount of capital we raise due to investor demand restrictions placed on the amount of capital we raise or other reasons.

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

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

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

- completing research and development of our product candidates;
- obtaining regulatory and marketing approvals for our product candidates for which we complete clinical trials;
- manufacturing product candidates and establishing and maintaining supply and manufacturing relationships with third parties that are commercially feasible, meet regulatory requirements and our supply needs in sufficient quantities to meet market demand for our product candidates, if approved;
- qualify for adequate coverage and reimbursement by government and third-party payors for any product candidates for which we obtain regulatory and marketing approval;
- marketing, launching, and commercializing product candidates for which we obtain regulatory and marketing approval, either directly or with a collaborator or distributor;
- gaining market acceptance of our product candidates as treatment options;
- addressing any competing products and technological and market developments;
- implementing internal systems and infrastructure, as needed;
- protecting and enforcing our intellectual property rights, including patents, trade secrets, and know-how;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- obtaining coverage and adequate reimbursement from third-party payors and maintaining pricing for our product candidates that supports profitability; and
- attracting, hiring, and retaining qualified personnel.

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

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

We are a biopharmaceutical company with a limited operating history. Since inception, we have incurred significant operating losses. For the years ended December 31, 2023, 2022 and 2021, we reported a net loss of $338.8 million, $83.8 million and $65.8 million, respectively. As of December 31, 2023, we had an accumulated deficit of $764.4 million. We will need to raise substantial additional capital to continue to fund our operations in the future. If our stockholders do not timely approve the conversion of our Series B Preferred Stock, then the holders of our Series B Preferred Stock may be entitled to require us to settle their shares of Series B Preferred Stock for cash at a price per underlying share of Common Stock equal to the last reported closing sale price of Common Stock on the principal trading market on which the Common Stock is listed as of the trading day immediately prior to the date on which a request to convert shares of Series B Preferred Stock into shares of Common Stock is delivered to us by a holder in accordance with the terms of the Series B Certificate of Designation and we fail to deliver such shares of Common Stock, as described in our Series B Certificate of Designation relating to the Series B Preferred Stock. Because the specific timing of the exercise of the cash redemption is not under our control and is dependent the closing sale price of our Common stock at the time of such conversion, we cannot quantify the aggregate amount of the potential cash settlement; however, for illustrative purposes only, if all of our holders of Series B Preferred Stock had delivered requests to convert their shares of Series B Preferred Stock on April 12, 2024 and assuming we were obligated to settle such conversions in cash pursuant to the terms of the Series B Certificate of Designation, a total of $418,302,500 would have been payable to such holders as a result of the cash settlement of all 10,865,000 shares of Common Stock issuable upon the conversion of 271,625 shares of Series B Preferred Stock, at a price of $38.50 per share of Common Stock, which was the closing sale price of our Common Stock on the Nasdaq Global Select Market on April 11, 2024.

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

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

If we obtain regulatory approval to market a product candidate, our future revenue will depend upon the size of any markets in which our product candidates may receive approval, and our ability to achieve sufficient market

acceptance, pricing, coverage and adequate reimbursement from third-party payors, and adequate market share for our product candidates in those markets. Even if we obtain adequate market share for our product candidates, because the potential markets in which our product candidates may ultimately receive regulatory approval could be very small, we may never become profitable despite obtaining such market share and acceptance of our products.

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

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

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

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

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

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our research programs or

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

To the extent that we raise additional capital through the sale of equity, including pursuant to any sales under convertible debt or other securities convertible into equity, the ownership interest of our stockholders will be diluted, and the terms of these new securities may include liquidation or other preferences that adversely affect the rights of our stockholders. For instance, in December 2023, we sold an aggregate of 6,000,000 shares of Common Stock and 150,000 shares of our Series B Preferred Stock in the December 2023 PIPE to the December 2023 Investors for gross proceeds of $180.0 million and, in March 2024, we sold an aggregate of 121,625 shares of our Series B Preferred Stock in the March 2024 PIPE to the March 2024 Investors for gross proceeds of approximately $180.0 million. Subject to receiving the requisite stockholder approval and certain beneficial ownership limitations set by each holder of Series B Preferred Stock, each share of Series B Preferred Stock will automatically convert into an aggregate of 40 shares of our Common Stock. We are required to solicit the consent of our stockholders with regard to conversion of the shares of our Series B Preferred Stock, which will be voted on at our 2024 annual meeting of stockholders. If our stockholders fail to approve such matters, we may be subject to financial penalties that could materially harm our business, including the forced settlement of shares of Series B Preferred Stock for cash, as described herein and in our Series B Certificate of Designation.

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

Risks Related to Discovery, Development and Commercialization

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

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

Our competitors have developed, are developing or will develop programs and processes competitive with our programs and processes. Competitive therapeutic treatments include those that have already been approved and

accepted by the medical community and any new treatments. Our success will depend partially on our ability to develop and commercialize products that have a competitive safety, efficacy, dosing and/or presentation profile. Our commercial opportunity and success will be reduced or eliminated if competing products are safer, more effective, have a more attractive dosing profile or presentation or are less expensive than the products we develop, or if our competitors develop competing products or if biosimilars enter the market more quickly than we do and are able to gain market acceptance. See the section titled "Business – Competition" for more discussion about our competitors.

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

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

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

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

- regulators or institutional review boards ("IRBs"), the FDA or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations ("CROs"), the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- clinical trials of any product candidates may fail to show safety or efficacy, produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon product development programs;
- the number of subjects required for clinical trials of any product candidates may be larger than we anticipate, especially if regulatory bodies require completion of non-inferiority or superiority trials, enrollment in these clinical trials may be slower than we anticipate or subjects may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;

- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants in our trials are being exposed to unacceptable health risks;
- the cost of clinical trials of any of our programs may be greater than we anticipate;
- the quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be inadequate to initiate or complete a given clinical trial;
- our inability to manufacture sufficient quantities of our product candidates for use in clinical trials;
- reports from clinical testing of other therapies may raise safety or efficacy concerns about our programs;
- our failure to establish an appropriate safety profile for a product candidate based on clinical or preclinical data for such product candidates as well as data emerging from other therapies in the same class as our product candidates; and
- the FDA or other regulatory authorities may require us to submit additional data such as long-term toxicology studies, or impose other requirements before permitting us to initiate a clinical trial.

Commencing clinical trials in the United States is subject to acceptance by the FDA of an investigational new drug application ("IND"), biologics license application ("BLA") or similar application and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA requires us to complete additional preclinical studies or we are required to satisfy other FDA requests prior to commencing clinical trials, the start of our first clinical trials may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials, delay the enrollment of our clinical trials or impose stricter approval conditions than we currently expect. There are equivalent processes and risks applicable to clinical trial applications in other countries, including countries in the European Union ("EU").

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

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

Our future success is substantially dependent on our ability to timely obtain marketing approval for, and then successfully commercialize, our two most advanced programs, SPY001 and SPY002. We exercised our Option with respect to the SPY001 and SPY002 programs on July 12, 2023 and December 14, 2023, respectively. We are investing a majority of our efforts and financial resources into the research and development of these programs. We anticipate initiating a Phase 1 clinical trial in healthy volunteers of SPY001 in the first half of 2024 and of SPY002 in the second half of 2024, each subject to the filing of an IND or foreign equivalent and regulatory approval. The success of our programs is dependent on observing a longer half-life of our product candidates in humans than other mAbs currently marketed and in development as we believe this longer half-life

has the potential to result in a more favorable dosing schedule for our product candidates, assuming they successfully complete clinical development and obtain marketing approval. This is based in part on the assumption that the longer half-life we have observed in non-human primates ("NHPs") will translate into an extended half-life of our product candidates in humans. To the extent we do not observe this extended half-life when we dose humans with our product candidates, it would significantly and adversely affect the clinical and commercial potential of our product candidates.

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

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

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

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

Any drug delivery device that we potentially use to deliver our product candidates may have its own regulatory, development, supply and other risks.

We expect to deliver our product candidates via a drug delivery device, such as an injector or other delivery system. There may be unforeseen technical complications related to the development activities required to bring such a product to market, including primary container compatibility and/or dose volume requirements. Our product candidates may not be approved or may be substantially delayed in receiving approval if the devices that we choose to develop do not gain and/or maintain their own regulatory approvals or clearances. Where approval of the drug product and device is sought under a single application, the increased complexity of the review process may delay approval. In addition, some drug delivery devices are provided by single-source unaffiliated third-party companies. We may be dependent on the sustained cooperation and effort of those third-party companies both to supply the devices and, in some cases, to conduct the studies required for approval or other regulatory clearance of the devices. Even if approval is obtained, we may also be dependent on those third-party companies continuing to maintain such approvals or clearances once they have been received. Failure of third-party companies to supply the devices, to successfully complete studies on the devices in a timely manner, or to

obtain or maintain required approvals or clearances of the devices could result in increased development costs, delays in or failure to obtain regulatory approval and delays in product candidates reaching the market or in gaining approval or clearance for expanded labels for new indications.

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

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

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

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

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

Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidate in humans. Our clinical trials may not be conducted as planned or completed on schedule, if at all, and failure can occur at any time during the preclinical study or clinical trial process. For example, we depend on the availability of NHPs to conduct certain preclinical studies that we are required to complete prior to

submitting an IND and initiating clinical development. There is currently a global shortage of NHPs available for drug development. This could cause the cost of obtaining NHPs for our future preclinical studies to increase significantly and, if the shortage continues, could also result in delays to our development timelines.

Furthermore, a failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates. In addition, we expect to rely on participants to provide feedback on measures such as measures of quality of life, which are subjective and inherently difficult to evaluate. These measures can be influenced by factors outside of our control, and can vary widely from day to day for a particular participant, and from participant to participant and from site to site within a clinical trial.

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

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such clinical trials are being conducted, by the Data Safety Monitoring Board, if any, for such clinical trial or by the FDA or comparable foreign regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical trial protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from the programs, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates, if the results of these trials are not positive or are only moderately positive or if there are safety concerns, our business and results of operations may be adversely affected and we may incur significant additional costs.

We are researching the potential use of complementary diagnostics in connection with the development of our product candidates, and although we do not currently anticipate such diagnostics would be required for the regulatory approval of any of our product candidates, they may be helpful to maximize the clinical and commercial success of our product candidates and if we fail to develop such complementary diagnostics or obtain regulatory approvals that may be required if they will be used commercially alongside any of our product candidates, our products may not be as competitive or commercially successful as they could be.

A complementary diagnostic is a medical device, often an in vitro device, which provides information that is valuable for the safe and effective use of a corresponding therapeutic drug or biologic product. A complementary diagnostic can be used to identify patients or subsets of patients who are most likely to benefit from the therapeutic product.

A complementary diagnostic is generally developed in conjunction with the clinical program for an associated therapeutic product. The development path of a complementary diagnostic may include additional meetings with regulatory authorities, such as a pre-submission meeting and the requirement to submit an investigational device exemption application. In the case of a complementary diagnostic that is designated as “significant risk device,” approval of an investigational device exemption by the FDA and IRB is required before such diagnostic is used in conjunction with the clinical trials for a corresponding product candidate.

To be successful in developing, validating, obtaining approval of and commercializing a complementary diagnostic, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. We have no prior experience with medical device or diagnostic test development. If we choose to develop and seek FDA approval for complementary diagnostic tests on our own, we may require additional personnel. We may rely on third parties for the design, development, testing, validation and manufacture of complementary diagnostic tests for our therapeutic product candidates that may benefit from such tests, the application for and receipt of any required regulatory approvals, and the commercial supply of these complementary diagnostics.

Although we currently plan to focus our complementary diagnostic development program on diagnostics that may help to identity high/better responding patients for our product candidates, we do not believe such complementary diagnostics will be required by regulatory authorities in connection with granting regulatory approval for our product candidates but may aid in clinical trial recruitment, post-approval treatment decisions and maximizing the commercial success of our product candidates. If we or third parties we engage are unable to successfully develop complementary diagnostics for our product candidates, or experience delays in doing so:

- we may be unable to maximize our potential to identify appropriate patients for enrollment in our clinical trials, which may adversely affect the development of our therapeutic product candidates;
- if the FDA or other regulators determine that the safe and effective use of our therapeutic product candidates, if any, depends on the complementary diagnostics we develop then we would have to expend time and resources to obtain regulatory approval of such complementary diagnostics which could cause delays in the commercial launch or success of our product candidates; and
- we may not realize the full commercial potential of any therapeutics that receive marketing approval.

As a result of any of these events, our business, financial condition, results of operations and prospects could be materially and adversely affected.

We have limited experience in developing and commercializing diagnostics and have never applied for or obtained regulatory clearance or approval for any diagnostic tests.

To be successful in developing and commercializing therapeutic product candidates in combination with diagnostic candidates, we will need to address a number of scientific, technical, regulatory and logistical challenges. We currently anticipate that we or a collaborator may need to obtain marketing authorization from

the FDA in order to legally market such diagnostics in the United States. As a company, we have little experience in the development of diagnostic tests and may not be successful in developing appropriate diagnostics to pair with any of our therapeutic product candidates that receive marketing approval, and have never applied for or obtained regulatory clearance or approval of any such diagnostic tests. Given our limited experience in developing diagnostic tests, we may rely in part or in whole on third parties for their design, development and manufacture of such tests.

Before a new medical device, or a new intended use of, claim for, or significant modification to an existing device, can be marketed in the United States, a company must first submit an application for and receive 510(k) clearance pursuant to a premarket notification submitted under Section 510(k) of the Federal Food, Drug, and Cosmetic Act ("FDCA"), de-novo classification, or PMA approval from FDA, unless an exemption applies. The PMA approval pathway, which we expect to pursue for our complementary diagnostic product candidates, requires an applicant to demonstrate the safety and effectiveness of the product based, in part, on valid scientific evidence, including, but not limited to, technical, preclinical, and clinical data. The 510(k) pathway requires a FDA finding that the test is substantially equivalent to a legally marketed predicate device. If no legally marketed predicate can be identified to enable use of the 510(k) pathway, the device is automatically classified under the FDCA into Class III, which generally requires PMA approval. However, for low- to moderate-risk novel devices, FDA allows for the possibility of marketing authorization through the "*de novo* classification" process rather than requiring the device to be subject to PMA approval. Products that are approved through a PMA application generally need prior FDA approval before modifications can be made that affect safety or effectiveness, and certain modifications to a 510(k)-cleared device may also require FDA premarket review before the modified product can be marketed. If we are unable to successfully develop, obtain regulatory clearance for and commercialize diagnostics to pair with our therapeutic product candidates, it could adversely impact our ability to develop and generate revenue from our product candidates.

Additional time may be required to obtain regulatory approval for our product candidates and future product candidates because of their status as combination products.

We may pursue development of combination products that require coordination within the FDA and comparable foreign regulatory authorities for review of its device and biologic components. Although the FDA and comparable foreign regulatory authorities have systems in place for the review and approval of combination products such as ours, we may experience delays in the development and commercialization of our product candidates due to regulatory timing constraints and uncertainties in the product development and approval process. Of note, prior clearance or approval of one component of a combination product does not increase the likelihood that FDA will approve a later product combining the previously cleared product or approved active ingredient with a novel active ingredient.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Government Regulation

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

The process of obtaining regulatory approvals, both in the United States and abroad, is unpredictable, expensive and typically takes many years following commencement of clinical trials, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. We cannot commercialize product candidates in the United States without first obtaining regulatory approval from the FDA. Similarly, we cannot commercialize product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of our product candidates, including our most advanced product candidates, SPY001 and SPY002, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for each targeted indication. Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Further, our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or

unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval. The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other data. Our product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including: the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials; we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication; the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval; serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates; we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks; the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials; the data collected from clinical trials of our product candidates may not be acceptable or sufficient to support the submission of a BLA or other submission or to obtain regulatory approval in the United States or elsewhere, and we may be required to conduct additional clinical trials; the FDA or the applicable foreign regulatory authority may disagree regarding the formulation, labeling and/or the specifications of our product candidates; the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

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

If we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, including failing to approve the most commercially promising indications, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our product candidates, we will not be able to commercialize, or will be delayed in commercializing, our product candidates and our ability to generate revenue will be materially impaired.

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

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

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

The Patient Protection and Affordable Act, as amended by the Healthcare and Education Reconciliation Act (the "ACA"), includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable

with an FDA-licensed reference biological product. Under the BPCIA, an application for a highly similar or "biosimilar" product may not be submitted to the FDA until four years following the date that the reference product was first approved by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first approved. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product.

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

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

Any regulatory approvals that we may receive for our product candidates will require the submission of reports to regulatory authorities and surveillance to monitor the safety and efficacy of the product candidate, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a risk evaluation and mitigation strategy ("REMS") in order to approve our product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or comparable foreign regulatory authorities approve our product candidates, our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export will be subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable foreign regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as on-going compliance with current cGMPs and GCPs for any clinical trials that we conduct following approval. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMPs.

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

We may face difficulties from healthcare legislative reform measures.

Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability. See the section titled "Business – Government Regulation – Healthcare Reform" for a more detailed description of healthcare reform measures that may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates.

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

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. See the section titled "Business – Government Regulation – Other Healthcare Laws and Compliance Requirements" for a more detailed description of the laws that may affect our ability to operate.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. If our operations are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly and time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

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

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

Reimbursement" and "Business – Other Government Regulation Outside of the United States – Regulation in the European Union" for a more detailed description of the government regulations and third party payor practices that may affect our ability to commercialize our product candidates.

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

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

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

In some countries, particularly member states of the EU, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a therapeutic. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. To obtain coverage and reimbursement or pricing approvals in some countries, we or current or future collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any product candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be materially and adversely affected. Brexit could lead to legal uncertainty and potentially divergent national laws and regulations, including those related to the pricing of prescription pharmaceuticals, as the United Kingdom ("UK") determines which EU laws to replicate or replace. If the UK were to significantly alter its regulations affecting the pricing of prescription pharmaceuticals, we could face significant new costs.

A breakthrough therapy, fast track, or other expedited designation for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that those product candidates will receive marketing approval.

We may seek a breakthrough therapy, fast track, or other designation for appropriate product candidates. Designations such as these are within the discretion of the FDA, or other comparable regulatory authorities. The

receipt of a designation for a product candidate may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify under one of FDA's designation programs, the FDA may later decide that the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. See the section titled "Business – Government Regulation – Expedited Development and Review Programs" for a more detailed description of the process for seeking expedited designations such as fast track or breakthrough therapy designations.

Risks Related to Our Intellectual Property

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

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

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

In addition to seeking patents for some of our technology and programs, we may also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third-party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market. In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with our collaborators, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate

remedy in the event of unauthorized disclosure of confidential information. We may need to share our proprietary information, including trade secrets, with future business partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or state actors and those affiliated with or controlled by state actors. In addition, while we undertake efforts to protect our trade secrets and other confidential information from disclosure, others may independently discover trade secrets and proprietary information, and in such cases, we may not be able to assert any trade secret rights against such party. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

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

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

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

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

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

It is possible that we may be unable to obtain licenses at a reasonable cost or on reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same

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

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

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

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

Competitors may infringe or otherwise violate our patents, trademarks, copyrights or other intellectual property. To counter infringement or other violations, we may be required to file claims, which can be expensive and time-consuming. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights. In addition, in a patent infringement proceeding, a court or administrative body may decide that one or more of the patents we assert is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to prevent the other party from using the technology at issue on the grounds that our patents do not cover the technology. Similarly, if we assert trademark infringement claims, a court or administrative body may determine that the marks we have asserted are invalid or unenforceable or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In such a case, we could ultimately be forced to cease use of such marks. In any intellectual property litigation, even if we are successful, any award of monetary damages or other remedy we receive may not be commercially valuable.

Further, we may be required to protect our patents through procedures created to attack the validity of a patent at the USPTO. An adverse determination in any such submission or proceeding could reduce the scope or

enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action.

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

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

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

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

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

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

Changes in either the patent laws or interpretation of patent laws in the United States, including patent reform legislation such as the Leahy-Smith America Invents Act (the “Leahy-Smith Act”) could increase the uncertainties and costs surrounding the prosecution of our owned and in-licensed patent applications and the maintenance, enforcement or defense of our owned and in-licensed issued patents. The Leahy-Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for

competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO-administered post-grant proceedings, including post-grant review, inter partes review and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first-to-file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. U.S. Supreme Court and U.S. Court of Appeals for the Federal Circuit rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations, including in the antibody arts. For example, the United States Supreme Court in *Amgen, Inc. v. Sanofi* (*Amgen*) recently held that Amgen's patent claims to a class of antibodies functionally defined by their ability to bind a particular antigen were invalid for lack of enablement where the patent specification provided twenty-six exemplary antibodies, but the claimed class of antibodies covered a "vast number" of additional antibodies not disclosed in the specification. The Court stated that if patent claims are directed to an entire class of compositions of matter, then the patent specification must enable a person skilled in the art to make and use the entire class of compositions. This decision makes it unlikely that we will be granted U.S. patents with composition of matter claims directed to antibodies functionally defined by their ability to bind a particular antigen. Even if we are granted claims directed to functionally defined antibodies, it is possible that a third party may challenge our patents, when issued, relying on the reasoning in *Amgen* or other recent precedential court decisions. Additionally, there have been proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to enforce our proprietary technology. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future.

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

In addition, a European Unified Patent Court ("UPC") entered into force on June 1, 2023. The UPC is a common patent court that hears patent infringement and revocation proceedings effective for member states of the EU. This could enable third parties to seek revocation of a European patent in a single proceeding at the UPC rather than through multiple proceedings in each of the jurisdictions in which the European patent is validated.

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

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

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

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

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

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

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

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

Our current and future licensors may have relied on third-party consultants or collaborators or on funds from third parties, such as the U.S. government, such that our licensors are not the sole and exclusive owners of the patents we in-licensed. For example, certain intellectual property we license from the University of Texas at Austin includes inventions that were made with U.S. government support. The U.S. government therefore has certain rights in such inventions under the applicable funding agreements and under applicable law. If other third parties have ownership rights or other rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Patent terms may be inadequate to protect the competitive position of our product candidates for an adequate amount of time.

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

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

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

Risks Related to Our Reliance on Third Parties

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

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

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

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

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

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

We have utilized and plan to continue to utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, contract testing labs and strategic partners, to conduct and support our preclinical studies and clinical trials under agreements with us. We will rely heavily on these third parties over the course of our preclinical studies and clinical trials, and we control only certain aspects of their activities. As a result, we will have less direct control over the conduct, timing and completion of these preclinical studies and clinical trials and the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third-party contractors and CROs are required to comply with GCP regulations, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our programs in clinical development. If we or any of these third parties fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with products produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

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

In addition, we currently rely on foreign CROs and CMOs, including WuXi Biologics, and will likely continue to rely on foreign CROs and CMOs in the future. We or the foreign CROs or CMOs we work with may be subject to U.S. legislation, including the proposed BIOSECURE bill, trade restrictions and other foreign regulatory requirements which could increase the cost or reduce the supply of material available to us, delay the procurement or supply of such material or have an adverse effect on our ability to secure significant commitments from governments to purchase our potential therapies or disrupt our supply chain. If we are not able to secure supply of our product candidates as a result of the BIOSECURE bill or other applicable legislation, this could result in a material adverse effect on our Company.

For example, the biopharmaceutical industry in China is strictly regulated by the Chinese government. Changes to Chinese regulations or government policies affecting biopharmaceutical companies are unpredictable and may have a material adverse effect on our collaborators in China which could have an adverse effect on our business, financial condition, results of operations and prospects. Evolving changes in China’s public health, economic, political, and social conditions and the uncertainty around China’s relationship with other governments, such as

the United States and the UK, could also negatively impact our ability to manufacture our product candidates for our planned clinical trials or have an adverse effect on our ability to secure government funding, which could adversely affect our financial condition and cause us to delay our clinical development programs.

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

We do not currently own any facility that may be used as our clinical or commercial manufacturing and processing facility and must currently rely on CMOs to manufacture our product candidates. We have not yet caused our product candidates to be manufactured on a commercial scale and may not be able to do so for any of our programs, if approved. We currently have a sole source relationship for our supply of the SPY001 program. If there should be any disruption in such supply arrangement, including any adverse events affecting our sole supplier, it could have a negative effect on the clinical development of our programs and other operations while we work to identify and qualify an alternate supply source. We may not control the manufacturing process of, and may be completely dependent on, our contract manufacturing partners for compliance with cGMP requirements and any other regulatory requirements of the FDA or comparable foreign regulatory authorities for the manufacture of our product candidates. Beyond periodic audits, we have limited control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any approval in the future, we may need to find alternative manufacturing facilities, which would require the incurrence of significant additional costs, delays, and materially adversely affect our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Similarly, our failure, or the failure of our CMOs, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations.

Moreover, our CMOs may experience manufacturing difficulties due to resource constraints, supply chain issues, or as a result of labor disputes or unstable political environments. If any CMOs on which we will rely fail to manufacture quantities of our product candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a cost that allows us to achieve profitability, our business, financial condition and prospects could be materially and adversely affected. In addition, our CMOs are responsible for transporting temperature-controlled materials that can be inadvertently degraded during transport due to several factors, rendering certain batches unsuitable for trial use for failure to meet, among others, our integrity and purity specifications. We and any of our CMOs may also face product seizure or detention or refusal to permit the import or export of products. Our business could be materially adversely affected by business disruptions to our third-party providers that could materially adversely affect our anticipated timelines, potential future revenue and financial condition and increase our costs and expenses. Each of these risks could delay or prevent the completion of our preclinical studies and clinical trials or the approval of any of our product candidates by the FDA, result in higher costs or adversely impact commercialization of our product candidates. See the section titled “Business – Manufacturing” for a more detailed description of our manufacturing plans and assumptions and the factors that may affect the success of our programs.

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

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

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of preclinical and clinical drug development, technical operations, clinical operations,

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

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

We are a preclinical stage biotechnology company with a limited operating history, and, as of December 31, 2023, we had 30 employees. We have been and will continue to be highly dependent on the research and development, clinical and business development expertise of our executive officers, as well as the other principal members of our management, scientific and clinical team. Any of our management team members may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees.

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

In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our discovery and nonclinical and clinical development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

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

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

complex and changing foreign regulatory, tax, accounting and legal requirements and reduced protection of intellectual property rights in some foreign countries.

Our estimates of market opportunity and forecasts of market growth may prove to be inaccurate, and even if the markets in which we compete achieve the forecasted growth, our business may not grow at similar rates, or at all.

Our market opportunity estimates and growth forecasts are subject to significant uncertainty and are based on assumptions and estimates which may not prove to be accurate. Our estimates and forecasts relating to size and expected growth of our target market may prove to be inaccurate. Even if the markets in which we compete meet our size estimates and growth forecasts, our business may not grow at similar rates, or at all. Our growth is subject to many factors, including our success in implementing our business strategy, which is subject to many risks and uncertainties.

Our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to obtain coverage and reimbursement and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect or the treatment population is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved.

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

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

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

In the ordinary course of our business, we and the third parties upon which we rely collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, process) proprietary, confidential, and sensitive data, including personal data, intellectual property, trade secrets, and other sensitive data (collectively, sensitive information).

Despite the implementation of security measures in an effort to protect systems that store our information, given their size and complexity and the increasing amounts of information maintained on our internal information technology systems and those of our third-party CROs, other contractors (including sites performing our clinical trials), third party service providers and supply chain companies, and consultants, these systems are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners and/or other third parties, or from cyber-attacks by malicious third parties, which may compromise our system infrastructure or lead to the loss, destruction, alteration or dissemination of, or damage to, our data.

Some actors now engage and are expected to continue to engage in cyber-attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we, and the third parties upon which we rely, may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our goods and services. In particular, severe ransomware attacks are becoming increasingly prevalent and can lead to significant interruptions in our operations, ability to provide our products or services, loss of sensitive data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments.

To the extent that any disruption or security breach were to result in loss, destruction, unavailability, alteration or dissemination of, or damage to, our data or applications, or for it to be believed or reported that any of these occurred, we could incur liability and reputational damage and the development and commercialization of our product candidates could be delayed. Further, our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption in, or failure or security breach of, our systems or third-party systems where information important to our business operations or commercial development is stored.

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

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

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

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

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

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

Under Section 382 of the Internal Revenue Code of 1986, as amended (the "Code"), if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. Upon certain events since our conversion from a Delaware limited liability company to a Delaware corporation in 2015, it is possible that we may have triggered an "ownership change" limitation. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership (some of which are outside of our control). As a result, if we earn net taxable income, our ability to use our pre-change NOLs and other pre-change tax attributes to offset U.S. federal taxable income or taxes may be subject to limitations, which could potentially result in increased future tax liability to us. Our NOLs and other tax attributes arising before our conversion from a Delaware limited liability company to a Delaware corporation in 2015 also may be limited by the Separate Return Limitation Year rule, which could increase our U.S. federal tax liability. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

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

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

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

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

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

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our stockholders or us. We assess the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where we have operations to determine the potential effect on our business and any assumptions we have made about our future taxable income. We cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on our business if they were to be enacted. For example, the United States recently enacted the Inflation Reduction Act of 2022, which implements, among other changes, a 1% excise tax on certain stock buybacks. In addition, beginning in 2022, the Tax Cuts and Jobs Act eliminated the previously available option to deduct research and development expenditures and requires taxpayers to amortize them generally over five years for research activities conducted in the United States and over 15 years for research activities conducted outside the United States. The U.S. Congress is considering legislation that would restore the current deductibility of research and development expenditures; however, we have no assurance that the provision will be repealed or otherwise modified. Such changes, among others, may adversely affect our effective tax rate, results of operation and general business condition.

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

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

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

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

Risks Related to Our Common Stock

Pursuant to the terms of the December 2023 SPA and the March 2024 SPA, we are required to recommend that our stockholders approve the conversion of all outstanding shares of our Series B Preferred Stock into shares of our Common Stock. We cannot guarantee that our stockholders will approve this matter, and if they fail to do so, we may be required to settle such shares in cash and our operations may be materially harmed.

Under the terms of the December 2023 SPA and the March 2024 SPA, we agreed to use best efforts to obtain the requisite approval for the conversion of all outstanding shares of Series B Preferred Stock issued in the December 2023 PIPE and the March 2024 PIPE, respectively, into shares of our Common Stock, as required by the Nasdaq listing rules, at our 2024 annual meeting of stockholders and, if such approval is not obtained at that meeting, to seek to obtain such approval at a stockholders meeting to be held at least every 90 days thereafter until such approval is obtained, which would be time consuming and costly. Additionally, if our stockholders do not timely approve the conversion of our Series B Preferred Stock, then the holders of our Series B Preferred Stock may be entitled to require us to settle their shares of Series B Preferred Stock for cash at a price per share equal to the fair value of the Series B Preferred Stock at such time, as described in our Series B Certificate of Designation relating to the Series B Preferred Stock. If we are forced to settle a significant amount of the Series B Preferred Stock, it could materially affect our results of operations.

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

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

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

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

Our Certificate of Incorporation and Bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or agents to us or our stockholders, any action asserting a claim arising pursuant to

any provision of the DGCL, our Certificate of Incorporation or our Bylaws or any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein and the claim not being one which is vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery or for which the Court of Chancery does not have subject matter jurisdiction. Any person purchasing or otherwise acquiring any interest in any shares of our capital stock shall be deemed to have notice of and to have consented to this provision of our Certificate of Incorporation and Bylaws.

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

These choice of forum provisions will not apply to claims brought to enforce a duty or liability created by the Exchange Act. These choice of forum provisions may limit our stockholders' ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, employees or agents, which may discourage such lawsuits against us and our directors, officers, employees and agents even though an action, if successful, might benefit our stockholders. Stockholders who do bring a claim in the specified courts could face additional litigation costs in pursuing any such claim. The specified courts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders. Alternatively, if a court were to find these provisions of our governance documents inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could have a material adverse effect on our business, financial condition or results of operations.

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

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

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

We are party to a number of registration rights agreements with certain groups of investors, including a registration rights agreement (the "March 2024 RRA") with the March 2024 Investors. Pursuant to each of these registration rights agreements, we agreed to file a resale registration statement to register the Registrable Securities (as defined in the respective registration rights agreement). This registration statement is being filed in order to satisfy our obligations under the March 2024 RRA. We have agreed to use our commercially reasonable efforts to cause this registration statement to be declared effective by the SEC as soon as practicable. If, following receipt of stockholder approval of the Series B Conversion Proposal (as defined in the section titled "*Description Of Capital Stock – Preferred Stock – Series B Preferred Stock*" below), this registration statement is not declared effective prior to, subject to certain limited exceptions pursuant to the March 2024 RRA, the 90th calendar day following the closing date of the March 2024 PIPE (or, in the event the SEC reviews and has written comments to this registration statement, the 120th calendar day following such closing date), among other events (each event, a "Registration Failure"), then we will be required to make pro rata payments to each March 2024 Investor of the then outstanding Registrable Securities in an amount equal to one percent of the aggregate

amount invested by such March 2024 Investor for the Registrable Securities then held by such March 2024 Investor for the initial day of a Registration Failure and for each 30 day period thereafter until the Registration Failure is cured. If this Registration Statement is declared effective, the shares subject to this Registration Statement will no longer constitute restricted securities and may be sold freely in the public markets, subject to lapse on any related contractual restrictions related thereto of any March 2024 Investor and, for shares of Common Stock issuable upon the conversion of Series B Preferred Stock, the approval of our stockholders of such conversion.

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

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

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

Pursuant to our equity incentive plans, we may grant equity awards and issue additional shares of our Common Stock to our employees, directors and consultants, and the number of shares of our Common Stock reserved for future issuance under certain of these plans will be subject to automatic annual increases in accordance with the terms of the plans. To the extent that new options are granted and exercised, or we issue additional shares of Common Stock in the future, our stockholders may experience additional dilution, which could cause our stock price to fall.

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

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

General Risk Factors

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

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

- our ability to obtain regulatory approvals for our product candidates, and delays or failures to obtain such approvals;
- failure of any of our product candidates, if approved, to achieve commercial success;

- failure to maintain our existing third-party license and supply agreements;
- changes in laws or regulations applicable to our product candidates;
- any inability to obtain adequate supply of our product candidates or the inability to do so at acceptable prices;
- adverse regulatory authority decisions;
- introduction of new products, services, or technologies by our competitors;
- failure to meet or exceed financial and development projections we may provide to the public and the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators, and the investment community;
- announcements of significant acquisitions, strategic collaborations, joint ventures, or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- additions or departures of key personnel;
- significant lawsuits, including patent or stockholder litigation;
- if securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our business and stock;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions, including global inflationary pressures, rising interest rates, general economic slowdown or a recession, changes in monetary policy, instability in financial institutions and the prospect of a shutdown of the U.S. federal government;
- geopolitical instability, including the ongoing military conflict in Ukraine, conflict in Israel and surrounding areas, and geopolitical tensions in China;
- sales of our Common Stock by us or our stockholders in the future;
- trading volume of our Common Stock;
- announcements by commercial partners or competitors of new commercial products, clinical progress or the lack thereof, significant contracts, commercial relationships, or capital commitments;
- the introduction of technological innovations or new therapies that compete with our potential products;
- changes in the structure of health care payment systems; and
- period-to-period fluctuations in our financial results.

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

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

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

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

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

The trading market for our Common Stock is influenced by the research and reports that equity research analysts publish about us and our business. Equity research analysts may elect not to provide research coverage of our Common Stock and such lack of research coverage may adversely affect the market price of our Common Stock. In the event we do have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our Common Stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of us or fails to publish reports on us regularly, demand for our Common Stock could decrease, which in turn could cause our stock price or trading volume to decline.

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

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

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

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

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

USE OF PROCEEDS

We are not selling any securities under this prospectus and we will not receive any proceeds from the sale of the Resale Shares covered hereby. The net proceeds from the sale of the Resale Shares offered by this prospectus will be received by the Selling Stockholders.

Subject to limited exceptions, the Selling Stockholders will pay any underwriting discounts and commissions and expenses incurred by the Selling Stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the Selling Stockholders in disposing of any of the Resale Shares. We will bear the costs, fees and expenses incurred in effecting the registration of the Resale Shares covered by this prospectus, including all registration and filing fees, Nasdaq listing fees and fees and expenses of our counsel and our independent registered public accounting firm.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion of our financial condition and results of operations in conjunction with the consolidated financial statements and the related notes thereto and other financial information included elsewhere in this prospectus. This discussion contains forward-looking statements based upon current beliefs, plans and expectations related to future events and our future financial performance that involve risks, uncertainties and assumptions. Our actual results could differ materially from those discussed in these forward-looking statements as a result of various factors. Factors that could cause or contribute to these differences include, but are not limited to, those discussed below and elsewhere in this prospectus, particularly in the section titled "Risk Factors." Please also see the section titled "Special Note Regarding Forward-Looking Statements." As used in this prospectus, unless the context suggests otherwise, "we", "us", "our", "the Company". "Aeglea BioTherapeutics, Inc." or "Spyre" refers to Spyre Therapeutics, Inc. and its subsidiaries, including Spyre Therapeutics, LLC.

Acquisition of Pre-Merger Spyre

On June 22, 2023, we acquired Pre-Merger Spyre pursuant to the Acquisition Agreement, by and among us, Aspen Merger Sub I, Inc., a Delaware corporation and a wholly owned subsidiary of the Company ("First Merger Sub"), Sequoia Merger Sub II, LLC, a Delaware limited liability company and our wholly owned subsidiary ("Second Merger Sub"), and Pre-Merger Spyre. Pursuant to the Acquisition Agreement, First Merger Sub merged with and into Pre-Merger Spyre, pursuant to which Pre-Merger Spyre was the surviving corporation and became our wholly owned subsidiary (the "First Merger"). Immediately following the First Merger, Pre-Merger Spyre merged with and into Second Merger Sub, pursuant to which Second Merger Sub became the surviving entity. Pre-Merger Spyre was a pre-clinical stage biotechnology company that was incorporated on April 28, 2023 under the direction of Peter Harwin, a Managing Member of Fairmount, for the purpose of holding rights to certain intellectual property being developed by Paragon. Fairmount is a founder of Paragon.

Through the Asset Acquisition, we received the Option to license the in-process and research development ("IPR&D") rights related to four research programs. On July 12, 2023 we exercised the Option with respect to one of these research programs to exclusively license intellectual property rights related to such research program directed to antibodies that selectively bind to α4ß7 integrin and methods of using these antibodies, including methods of treating inflammatory bowel disease ("IBD") using SPY001. If this research program is pursued non-provisionally and matures into issued patents, we would expect those patents to expire no earlier than 2044, subject to any disclaimers or extensions. On December 14, 2023, we exercised the Option under the Paragon Agreement to be granted an exclusive license to all of Paragon's rights, title and interest in and to intellectual property rights, including inventions, patents, sequence information and results, under SPY002, our TL1A program, to develop and commercialize antibodies and products worldwide in all therapeutics disorders. If this research program is pursued non-provisionally and matures into issued patents, we would expect those patents to expire no earlier than 2044, subject to any disclaimers or extensions. The license agreements pertaining to such research programs are currently being finalized on previously agreed terms. Furthermore, as of the date of the filing of this prospectus, the Option remains unexercised with respect to the IPR&D related to the two remaining research programs under the Paragon Agreement.

Overview

Following the Asset Acquisition and the entry into the Immedica APA, we have significantly reshaped the business into a preclinical stage biotechnology company focused on developing next generation therapeutics for patients living with IBD, including UC and CD. Through the Paragon Agreement, our portfolio of novel and proprietary monoclonal antibody product candidates has the potential to address unmet needs in IBD care by improving efficacy, safety, and/or dosing convenience relative to products currently available or product candidates in development. We have engineered our product candidates with the aim to bind potently and selectively to their target epitopes and to exhibit extended pharmacokinetic half-lives through modifications in

the Fc domain, which modifications are designed to increase affinity to human FcRn and increase antibody recycling. We anticipate that half-life extension will enable less frequent administration as compared to marketed or development-stage mAbs that do not incorporate half-life extension modifications. Nonetheless, the drug and/or device development process is inherently uncertain, our development approach is unproven, the preclinical evidence that supports our proposed development program is preliminary and limited, and we have not yet tested any product candidate in humans. In addition to the development of our product candidates as potential monotherapies, we plan to investigate combinations of our proprietary antibodies in preclinical and clinical studies in order to evaluate whether combination therapy (co-administration or co-formulation of multiple monoclonal antibodies) can lead to greater efficacy, as compared to monotherapies in IBD. We also intend to examine patient selection strategies via complementary diagnostics utilized in our clinical studies to evaluate whether patients may be matched to the optimal therapy based on genetic background and/or other biomarker signatures. We intend to deliver our product candidates through convenient, infrequently dosed, self-administered, SC injection, although the specific delivery mechanism or technology has not been selected given our early stage. Notwithstanding our efforts to develop safe and effective monotherapies and combination therapies, there can be no guarantee that we will be able to develop product candidates that will be found to be safe and effective so as to obtain the necessary regulatory approvals to market our product candidates.

Our Relationship with Paragon and Parapyre

Paragon and Parapyre each beneficially owns less than 5% of our capital stock through their respective holdings of our Common Stock. Fairmount beneficially owns more than 5% of our capital stock on an as-converted basis, has two seats on our board of directors and beneficially owns more than 5% of Paragon, which is a joint venture between Fairmount and Fair Journey Biologics. Fairmount appointed Paragon's board of directors and has the contractual right to approve the appointment of any executive officers. Parapyre is an entity formed by Paragon as a vehicle to hold equity in Pre-Merger Spyre in order to share profits with certain employees of Paragon.

In connection with the Asset Acquisition, we assumed the rights and obligations of Pre-Merger Spyre under the Paragon Agreement. Under the Paragon Agreement, we are obligated to compensate Paragon 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 owed to Paragon. As of the acquisition date, $19.0 million was unpaid and was assumed by us through the Asset Acquisition.

For the year ended December 31, 2023, we recognized $48.5 million in research and development expenses that are due to Paragon under the Paragon Agreement. As of December 31, 2023, $16.6 million was unpaid and owed to Paragon under the Paragon Agreement.

In July 2023 and December 2023, we exercised our Option for the SPY001 and SPY002 programs, respectively, and the remaining two options for the SPY003 and SPY004 programs remain outstanding.

In connection with the Asset Acquisition, we assumed the Parapyre Option Obligation which provides for an annual equity grant of warrants 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 our board of directors. Under the terms of the Paragon Agreement, an annual equity grant of options will not be made for any calendar year ending after December 31, 2024 regardless of whether the term of the Paragon Agreement has continued beyond such date. On September 29, 2023, the Company amended the Paragon Agreement to amend and restate certain terms of the option grant pertaining to the Parapyre Option Obligation, including but not limited to (i) defining that the annual equity grant of options is based on the outstanding shares of our Common Stock, (ii) establishing the grant date as the last business day of each applicable calendar year, and (iii) defining the term of the options granted as ten years. The pro-rated fair value

of the Parapyre Option Obligation will be recorded as a liability at each interim reporting period and reclassified as permanent equity when settled through the issuance of the related warrants. If the term of the Paragon Agreement ends prior to the end of an applicable calendar year, the equity grant for such calendar year will be pro-rated for such calendar year and effected within five business days of the end of the term. The term of the Paragon Agreement ends upon the earlier of (i) the effective date of the license agreement for the last research program with respect to which we have exercised our Option, unless an extension is mutually agreed between the parties, or (ii) 120 days following our receipt of deliverables for the last research program with respect to which we have not exercised our Option or such longer period as agreed upon by the parties. As of December 31, 2023, the grant-date fair value of the equity granted to Parapyre on December 29, 2023 was approximately $11.5 million, of which $0.1 million was recognized as part of the liabilities assumed with the Asset Acquisition. For the year ended December 31, 2023, $11.4 million was recognized as stock compensation expense related to the Parapyre Option Obligation. The Company's obligation for the year ended December 31, 2023 under the Parapyre Option Obligation was settled through the issuance of 684,407 warrants to purchase the Company's Common Stock at an exercise price of $21.52 per warrant.

Corporate Developments

In July 2023, we announced that we had entered into an agreement to sell the global rights to pegzilarginase, an investigational treatment for the rare metabolic disease Arginase 1 Deficiency, to Immedica for $15 million in upfront cash proceeds and up to $100 million in contingent milestone payments. The sale of pegzilarginase to Immedica superseded and terminated the previous license agreement between us and Immedica.

On August 30, 2023, our board of directors appointed Scott Burrows to succeed Jonathan Alspaugh as our Chief Financial Officer effective September 1, 2023. Mr. Burrows also succeeded Mr. Alspaugh as our principal financial officer and principal accounting officer on the effective date.

On September 1, 2023, Heidy Abreu King-Jones was appointed as Chief Legal Officer and Corporate Secretary.

On October 6, 2023, our board of directors appointed Dr. Cameron Turtle, our then-current Chief Operating Officer, as our principal executive officer effective the same day.

On November 22, 2023, Dr. Turtle was promoted from Chief Operating Officer to Chief Executive Officer and was appointed to our board of directors. In addition, Jeffrey W. Albers and Laurie Stelzer were appointed to our board of directors to fill the vacancies resulting from the resignations of Hunter Smith and Ivana Magovčević-Liebisch, each of which was effective that same day.

On November 28, 2023, we changed our name from "Aeglea Biotherapeutics, Inc." to "Spyre Therapeutics, Inc." and our Nasdaq ticker symbol from "AGLE" to "SYRE".

On December 11, 2023, we closed the December 2023 PIPE and sold an aggregate of 6,000,000 shares of Common Stock and 150,000 shares of Series B Preferred Stock for gross proceeds of $180 million. If our stockholders do not timely approve the conversion of our Series B Preferred Stock, then the holders of our Series B Preferred Stock may be entitled to require us to settle their shares of Series B Preferred Stock for cash at a price per underlying share of Common Stock equal to the last reported closing sale price of Common Stock on the principal trading market on which the Common Stock is listed as of the trading day immediately prior to the date on which a request to convert shares of Series B Preferred Stock into shares of Common Stock is delivered to us by a holder in accordance with the terms of the Series B Certificate of Designation and we fail to deliver such shares of Common Stock, as described in our Series B Certificate of Designation relating to the Series B Preferred Stock.

On January 19, 2024, our listing of Common Stock was upgraded from The Nasdaq Capital Market to the Nasdaq Global Select Market.

On February 1, 2024, Mark McKenna was appointed to our board of directors to fill the vacancy resulting from the resignation of Alison Lawton, which was effective that same day.

On March 20, 2024, we closed the March 2024 PIPE and sold an aggregate of 121,625 shares of Series B Preferred Stock for gross proceeds of approximately $180 million. If our stockholders do not timely approve the conversion of our Series B Preferred Stock, then the holders of our Series B Preferred Stock may be entitled to require us to settle their shares of Series B Preferred Stock for cash at a price per underlying share of Common Stock equal to the last reported closing sale price of Common Stock on the principal trading market on which the Common Stock is listed as of the trading day immediately prior to the date on which a request to convert shares of Series B Preferred Stock into shares of Common Stock is delivered to us by a holder in accordance with the terms of the Series B Certificate of Designation and we fail to deliver such shares of Common Stock, as described in our Series B Certificate of Designation relating to the Series B Preferred Stock.

Restructuring

During the second quarter of 2023, we implemented a restructuring plan based on the review of the inconclusive interim results from our Phase 1/2 clinical trial of pegtarviliase for the treatment of classical homocystinuria and other business considerations, as well as our plan to explore strategic alternatives. Under the restructuring plan, our workforce was reduced by 83%, various lab equipment, consumables, and furniture and fixtures were sold, and our corporate headquarters lease in Austin, TX was abandoned. All charges related to the restructuring activities was recognized during the second quarter of 2023. No further restructuring charges will be incurred under the restructuring plan.

Critical Accounting Policies and Estimates

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States (“U.S. GAAP”). The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue, costs and expenses, and related disclosures. These estimates form the basis for judgments we make about the carrying values of our assets, liabilities and equity and the amount of revenues and expenses, which are not readily apparent from other sources. We base our estimates on historical experience and on various other assumptions that we believe are reasonable under the circumstances. On an ongoing basis, we evaluate our estimates and assumptions. Our actual results may differ materially from these estimates under different assumptions or conditions.

Our critical accounting policies are those policies which require the most significant judgments and estimates in the preparation of our consolidated financial statements. The most significant estimates and assumptions that management considers in the preparation of our financial statements relate to accrued research and development costs; the valuation of consideration transferred in acquiring IPR&D; the discount rate, probabilities of success, and timing of estimated cash flows in the valuation of the CVR liability; inputs used in the Black-Scholes model for stock-based compensation expense; estimated future cash flows used in calculating the impairment of right-of-use lease assets; and estimated cost to complete performance obligations related to revenue recognition. The consideration transferred in acquiring IPR&D in connection with the acquisition of Pre-Merger Spyre was comprised of our Common Stock and shares of Series A Preferred Stock. To determine the fair value of the equity transferred, we considered the per share value of the June 2023 PIPE, which was a financing involving a group of accredited investors.

We define our critical accounting policies as those accounting principles generally accepted in the United States that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations, as well as the specific manner in which we apply those principles. Our significant accounting policies are more fully described in Note 2 to our consolidated financial statements as of December 31, 2023 and 2022 and for each of the three years in the period ended December 31, 2023 (the “2023 Annual Financials”) appearing elsewhere in this prospectus.

Revenue recognition

We enter into license agreements related to our technologies that we have determined are within the scope of Accounting Standards Codification 606. Based on the terms and conditions of our agreements, we identify the goods and services that we promise to transfer to the customer, which may consist of the licensing of technologies, the performance of research and development activities, and/or the supply of products related to our technologies. Based on the nature of the goods and services provided and the customer's intended benefit of the arrangement, we evaluate which of the promised goods and services are distinct and, therefore, represent a performance obligation, which may require us to combine certain promised goods and services that are determined to not be distinct from one another. We also evaluate whether an agreement provides the customer an option to purchase future goods or services at a discounted price, or a material right, which would also represent a performance obligation.

In exchange for the performance obligations, we estimate the amount of consideration promised by the customer, or transaction price, which may include both fixed and variable consideration. Variable consideration, which may consist of various milestone payments based upon the achievement of certain events or conditions, sales-based royalties, or payments contingent on the performance of research and development services, are included in the transaction price only if we expect to receive such consideration and determine it is likely that the inclusion of the variable consideration will not result in a significant reversal in the cumulative amount of revenue recognized under the arrangement. Sales-based royalty and milestone payments that we determine are predominantly related to the license of our intellectual property are excluded from the transaction price we expect to receive until the underlying sales occur.

We allocate the estimated transaction price to the identified performance obligations based on the relative estimated stand-alone selling price ("SSP"), of each performance. SSP is based on the observable price of our goods and services, or when SSP is not directly observable, we estimate SSP based on factors such as forecasted revenues or costs, development timelines, discount rates, probabilities of technical and regulatory success, and considerations such as market conditions and entity-specific factors. We recognize revenue allocated to each performance obligation either at a point-in-time or over time in a manner that depicts the transfer of control of the promised goods and services to the customer. For performance obligations that are recognized over time, we estimate the measure of progress associated with the satisfaction of the performance obligation based on an input or output method, which may be based on factors such as costs incurred, labor hours expended, time elapsed, among other measures based on the nature of the performance obligation. The estimates made on an input or output method are subject to change and may result in material changes to revenue that could materially affect our results of operations. Please refer to Note 12, Strategic License Agreements, to our 2023 Annual Financials included elsewhere in this prospectus.

Accrued research and development costs

We record the costs associated with research nonclinical studies, clinical trials, and manufacturing as incurred. These costs are a significant component of our research and development expenses, with a substantial portion of our on-going research and development activities conducted by third-party service providers, including CROs, CMOs and our related-party Paragon.

We accrue for expenses resulting from obligations under the Paragon Agreement and agreements with CROs, CMOs, and other outside service providers for which payment flows do not match the periods over which materials or services are provided to us. We record accruals based on estimates of services received and efforts expended pursuant to agreements established with Paragon, CROs, CMOs, and other outside service providers. These estimates are typically based on contracted amounts applied to the proportion of work performed and determined through analysis with internal personnel and external service providers as to the progress or stage of completion of the services. We make significant judgments and estimates in determining the accrual balance in each reporting period. In the event advance payments are made to Paragon, a CRO, a CMO, or an outside service

provider, the payments will be recorded as a prepaid asset which will be amortized as the contracted services are performed. As actual costs become known, we adjust our accruals. Inputs, such as the services performed, the number of patients enrolled, or the study duration, may vary from our estimates, resulting in adjustments to research and development expense in future periods. Changes in these estimates that result in material changes to our accruals could materially affect our results of operations. However, there have been no material changes in estimates for the periods presented.

Impairment of ROU Assets and Leasehold Improvements

We are required to test for impairment of our long-lived assets when events arise that would call into question the recoverability of an asset group. We determined that the abandonment of our leased office space in Austin, Texas would meet this criteria. Accordingly, we tested for impairment using a discounted future cash flow model using estimated cash flows that could be obtained through a hypothetical sub-letting of the leased space.

Convertible Preferred Stock Issued through PIPE

We record shares of convertible preferred stock at their respective fair values on the dates of issuance, net of issuance costs. We classified the Series B Preferred Stock outside of stockholders' equity because, if conversion to common stock is approved by the stockholders, the Series B Preferred Stock will be redeemable at the option of the holders for cash equal to the closing price of the common stock on the last trading day prior to the holder's redemption request. We determined that the conversion and redemption are outside of our control. Additionally, we determined the Series B Preferred Stock did not contain any embedded derivatives and therefore the conversion and redemption features did not require bifurcation.

Contingent Value Rights Liability

On July 3, 2023, we issued a CVR to certain of our securityholders of record as of the close of business on that date (the "Legacy Stockholders"), but these were not issued to holders of shares of common stock or preferred stock issued to former stockholders of Pre-Merger Spyre or the June 2023 Investors in the June 2023 PIPE. Each CVR entitles the holder thereof to receive cash payments in the future calculated on the monetization or disposal of Legacy Assets within the CVR period. Certain contingent payments under the CVR Agreement qualify as derivatives under ASC 815, Derivatives and Hedging, and are recorded as a liability on the balance sheet as of December 31, 2023. The CVR liability is considered a Level 3 instrument that is initially measured at its estimated fair value on the transaction date and subsequently remeasured at each reporting date with changes recorded in the consolidated statement of operations. The determination of the initial and subsequent fair value of the CVR liability requires significant judgment by management. Changes in any of the inputs not related to facts and circumstances existing as of the transaction date may result in a significant fair value adjustment, which can impact the results of operations in the period in which the adjustment is made.

Results of Operations

Comparison of the Years Ended December 31, 2023 and 2022

The following table summarizes our results of operations for the years ended December 31, 2023 and 2022, together with the changes in those items in dollars and as a percentage:

	Year Ended December 31,		Dollar	%
	2023	2022	Change	Change
	(in thousands)			
Revenue:				
Development fee and royalty	886	2,329	(1,443)	(62%)
Total revenue	886	2,329	(1,443)	
Operating expenses:				
Research and development	89,504	58,579	30,925	53%
General and administrative	39,946	28,531	11,415	40%
Acquired in-process research and development	130,188	—	130,188	*
Gain on sale of in-process research and development asset	(16,449)	—	(16,449)	*
Total operating expenses	243,189	87,110	156,079	*
Loss from operations	(242,303)	(84,781)	(157,522)	*
Other (expense) income:				
Interest income	6,147	837	5,310	*
Change in fair value of forward contract liability	(83,530)	—	(83,530)	*
Other expense, net	(19,130)	(7)	(19,123)	*
Total other (expense) income	(96,513)	830	(97,343)	*
Loss before income tax expense	(338,816)	(83,951)	(254,865)	*
Income tax benefit	26	136	(110)	*
Net loss	$(338,790)	$(83,815)	$(254,975)	

* Percentage not meaningful

Development Fee and Royalty Revenue . For the year ended December 31, 2023, we recognized $0.9 million of revenue in connection with the Immedica Agreement. The revenue generated was attributable to the PEACE Phase 3 trial and drug supply and royalties from an early access program in France. For the year ended December 31, 2022, we recognized $2.3 million of development fee revenue in connection with the Immedica Agreement, which was attributable to the PEACE Phase 3 trial and BLA package.

Research and Development Expenses . Our research and development expenses incurred during the year ended December 31, 2023 were primarily related to clinical trial costs associated with our Legacy Assets, costs associated with the wind down of those Legacy Assets, and costs associated with furthering our IBD pipeline candidates. Wind down costs included final patient visits, collection and analysis of final patient data, the creation and submission of final research reports, site and pharmacy closeouts, and formally closing the trials with regulatory agencies. Research and development expenses increased by $30.9 million, or 53%, to $89.5 million for the year ended December 31, 2023, from $58.6 million for the year ended December 31, 2022. The increase in research and development expenses was primarily due to:

- a $39.3 million increase in preclinical development and manufacturing expenses for our IBD pipeline candidates;
- a $11.4 million increase in stock compensation expense related to the Parapyre Option Obligation; partially offset by

- a $19.9 million decrease in activities and staff costs associated with the legacy rare disease pipeline we had been advancing prior to the Asset Acquisition.

External research and development expenses include costs associated with third parties contracted to conduct research and development activities on behalf of the Company, including through Paragon, CROs, CMOs, and third-party laboratories. For the year ended December 31, 2023 and 2022, external research and development costs accounted for $72.7 million and $36.4 million, respectively. The increase in external research and development expenses is primarily due to increases in costs associated with our IBD pipeline candidates and stock compensation expense related to the Parapyre Option Obligation, partially offset by a decrease in activities associated with the Legacy Assets.

Internal research and development expenses include compensation and related costs associated our research and development employees, as well as costs associated with the Company's on-premises research laboratory. For the year ended December 31, 2023 and 2022, internal research and development costs accounted for $16.8 million and $22.1 million. The decrease in internal research and development expenses is primarily due to a decrease in costs associated with our on-premises research laboratory that was decommissioned, including the elimination of related internal roles, in the first half of 2023.

General and Administrative Expenses. General and administrative expenses increased by $11.4 million, or 40%, to $39.9 million for the year ended December 31, 2023, from $28.5 million for the year ended December 31, 2022. The increase in general and administrative expenses was primarily due to a $9.0 million increase in stock compensation expense, $2.6 million increase in restructuring costs, net of restructuring savings, and an increase in legal and professional service fees of $3.4 million, partially offset by a $2.1 million decrease in legacy commercial readiness activities.

Gain on Sale of In-Process Research and Development Asset . Gain on sale of in-process research and development asset during the year ended December 31, 2023 was due to the gain recognized on the sale of pegzilarginase to Immedica. There was no similar gain or loss during the year ended December 31, 2022.

Acquired In-process Research and Development Expenses . Acquired IPR&D expenses were $130.2 million for the year ended December 31, 2023, as the acquisition of Pre-Merger Spyre was determined by management to be an asset acquisition, in accordance with U.S. GAAP as the product candidates were determined to have no alternative future use. There was no similar expense during the year ended December 31, 2022.

Change in Fair Value of Forward Contract Liability. Non-cash expenses associated with the change in fair value of the forward contract liability were $83.5 million for the year ended December 31, 2023. This expense was due to the change in fair value of the underlying Series A Preferred Stock between June 22, 2023 and the forward contract's settlement on July 7, 2023. There was no similar expense during the year ended December 31, 2022.

Other expense, net. Our Other expense, net incurred during the year ended December 31, 2023 were primarily related to a $19.0 million increase in the fair value of our CVR liability since its issuance. The increase was driven by changes in the expected timing of achievement of certain milestones and changes in the likelihood of certain milestones related to the approval received from the European Medicines Agency by Immedica, partially offset by a change in the likelihood of a successful disposition of pegtarviliase and updates to expenses and deductions. There were no such expenses during the year ended December 31, 2022.

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021, together with the changes in those items in dollars and as a percentage:

	Year Ended December 31, 2022	2021	Dollar Change	% Change
		(in thousands)		
Revenue:				
License	$ —	$ 12,000	$(12,000)	*
Development fee	2,329	6,739	(4,410)	-65%
Total revenue	2,329	18,739	(16,410)	-88%
Operating expenses:				
Research and development	58,579	57,069	1,510	3%
General and administrative	28,531	27,319	1,212	4%
Total operating expenses	87,110	84,388	2,722	3%
Loss from operations	(84,781)	(65,649)	(19,132)	29%
Interest income	837	111	726	*
Other expense, net	(7)	(122)	115	-94%
Loss before income tax expense	(83,951)	(65,660)	(18,291)	28%
Income tax benefit (expense)	136	(141)	277	-196%
Net loss	$ (83,815)	$ (65,801)	$(18,014)	27%

* Percentage not meaningful

License and Development Fee Revenue. For the year ended December 31, 2022, we recognized $2.3 million of development fee revenue allocated to the PEACE Phase 3 trial and BLA package of the Immedica Agreement. For the year ended December 31, 2021, we recognized $18.7 million of license and development fee revenue in connection with the Immedica Agreement. The total revenue generated was attributable to $12.0 million allocated to the license and $6.7 million allocated to the PEACE Phase 3 trial and BLA package. Please refer to Note 12, Strategic License Agreements, to the 2023 Annual Financials included elsewhere in this prospectus for additional disclosures around revenue recognition.

Research and Development Expenses . Research and development expenses increased $1.5 million, or 3%, to $58.6 million for the year ended December 31, 2022 from $57.1 million for the year ended December 31, 2021. The change in research and development expenses was due to:

- a $1.1 million increase in expenses associated with pegzilarginase primarily due to a $1.4 million increase related to activities involved in closing the PEACE trial and ramping up the new open-label extension trial for the treatment of patients with Arginase 1 Deficiency, partially offset by a $0.3 million decrease in professional services to support the pegzilarginase program;
- a $2.8 million increase in expense associated with IND-enabling activities of AGLE-325 for the treatment of patients with Cystinuria;
- a $0.6 million increase in personnel-related expenses, primarily driven by an increase of headcount expenses;
- a $1.5 million decrease in expenses primarily associated with the completion of non-clinical toxicology studies in the prior year for pegtarviliase for the treatment of patients with Homocystinuria;
- a $0.6 million decrease due to reduction in preclinical lab work; and
- a $0.9 million decrease in other research and development expenses, primarily related to a reduction of consulting and recruiting activities.

External research and development expenses include costs associated with third parties contracted to conduct research and development activities on behalf of the Company, including clinical research organizations, clinical manufacturing organizations, and third-party laboratories. For the twelve months ended December 31, 2022 and 2021, external research costs accounted for $36.4 million and $35.0 million, respectively. The increase in external research and development costs is primarily driven by an increase in costs associated with two candidates in the Legacy Pipeline, partially offset by a decrease in costs associated with a third candidate in the Legacy Pipeline as described above.

Internal research and development expenses include compensation and related costs associated with the Company's research and development employees, as well as costs associated with the Company's on-premises research laboratory. For the twelve months ended December 31, 2022 and 2021, internal research and development costs accounted for $22.2 million and $22.1 million, respectively. Internal research and development expenses remained flat for the periods presented.

General and Administrative Expenses. General and administrative expenses increased by $1.2 million, or 4%, to $28.5 million for the year ended December 31, 2022 from $27.3 million for the year ended December 31, 2021. The increase in general and administrative expenses was primarily due to a $0.8 million increase in expense related to our commercial capabilities and infrastructure and $0.4 million increase in expenses related to financing activities.

Liquidity and Capital Resources

We are a preclinical stage biotechnology company with a limited operating history, and due to our significant research and development expenditures, we have generated operating losses since our inception and have not generated any revenue from the sale of any products. There can be no assurance that profitable operations will ever be achieved, and, if achieved, whether profitability can be sustained on a continuing basis.

Since our inception and through December 31, 2023, we have funded our operations by raising an aggregate of approximately $896.2 million of gross proceeds from the sale and issuance of convertible preferred stock and common stock, pre-funded warrants, the collection of grant proceeds, and the licensing of our product rights for commercialization of pegzilarginase in Europe and certain countries in the Middle East. As of December 31, 2023, we had an accumulated deficit of $764.4 million.

Our primary use of cash is to fund the development of our product candidates, and advance our pipeline. This includes both the research and development costs and the general and administrative expenses required to support those operations. Since we are a preclinical stage biotechnology company, we have incurred significant operating losses since our inception and we anticipate such losses, in absolute dollar terms, to increase as we pursue clinical development of our product candidates, prepare for the potential commercialization of our product candidates, and expand our development efforts in our pipeline of nonclinical candidates. Based on current operating plans, we have sufficient resources to fund operations for at least one year from the issuance date of the financial statements included in the 2023 Annual Financials with existing cash, cash equivalents, and marketable securities. We will need to secure additional financing in the future to fund additional research and development, and before a commercial drug can be produced, marketed and sold. If we are unable to obtain additional financing or generate license or product revenue, the lack of liquidity could have a material adverse effect on the Company.

Recent Sources of Liquidity

In March 2021, we entered into the Immedica Agreement, pursuant to which Immedica licensed the product rights for commercialization of pegzilarginase in the European Economic Area, United Kingdom, Switzerland, Andorra, Monaco, San Marino, Vatican City, Turkey, Saudi Arabia, United Arab Emirates, Qatar, Kuwait, Bahrain, and Oman. In April 2021, we received an upfront payment of $21.5 million from Immedica. In July

2021, the Immedica Agreement was modified to include additional development services, up to $3.0 million, to support the PEACE Phase 3 trial and BLA package performance obligation. In July 2023, the Immedica Agreement was terminated through the sale of pegzilarginase to Immedica for $15.0 million in upfront cash proceeds and up to $100.0 million in contingent milestone payments.

During the year ended December 31, 2020, we raised $163.3 million of gross proceeds through an underwritten public offering and an at-the-market offering program. We sold 617,692 shares of Common Stock and pre-funded warrants to purchase up to 544,413 shares of Common Stock in an underwritten public offering for gross proceeds of $138.0 million, resulting in net proceeds of $129.0 million after deducting underwriting discounts, commissions, and offering costs. Additionally, we sold an aggregate of 129,803 shares of Common Stock under an at-the-market offering program for gross proceeds of $25.3 million, resulting in net proceeds of $24.6 million, after deducting underwriting discounts, commissions, and offering costs.

In May 2022, we sold 430,107 shares of Common Stock and pre-funded warrants to purchase up to 694,892 shares of Common Stock in a registered direct offering for gross proceeds of $45.0 million, resulting in net proceeds of $42.9 million after deducting placement agent fees and offering costs.

In June 2023, we sold 721,452 shares of convertible Series A Preferred Stock in a private placement offering for gross proceeds of $210.0 million before deducting approximately $12.7 million of placement agent and other offering expenses.

In December 2023, we sold 6,000,000 shares of Common Stock and 150,000 shares of convertible Series B Preferred Stock for gross proceeds of $180.0 million before deducting approximately $10.9 million of placement agent and other offering expenses.

Recent Developments

On November 21, 2023, our stockholders approved the issuance of shares of our Common Stock upon conversion of Series A Preferred Stock, eliminating the potential requirement to settle shares of Series A Preferred Stock in cash.

On December 7, 2023, we entered into the December 2023 SPA for a PIPE investment with the December 2023 Investors to raise $180 million in which the December 2023 Investors were issued an aggregate of 6,000,000 shares of Common Stock at a price of $15.00 per share and 150,000 shares of Series B Preferred Stock at a price of $600.00 per share. See section titled "*Liquidity – Recent Sources of Liquidity*" above.

Cash Flows for the Years Ended December 31, 2023 and 2022

The following table summarizes our cash flows for the periods indicated (in thousands):

	Year Ended December 31,	
	2023	2022
Net cash and cash equivalents (used in) provided by:		
Operating activities	$ (99,910)	$(80,144)
Investing activities	(108,393)	57,008
Financing activities	361,077	42,678
Effect of exchange rate on cash, cash equivalents, and restricted cash	25	(106)
Net increase (decrease) in cash and cash equivalents	$ 152,799	$ 19,436

Cash Used in Operating Activities

Cash used in operating activities for the year ended December 31, 2023 was $99.9 million and reflected a net loss of $338.8 million. Our net loss was offset in part by non-cash expenses of $130.2 million for acquired IPR&D, $83.5 million change in fair value of forward contract liability, $25.7 million in stock-based compensation, $19.0 million change in fair value of CVR liability, $2.6 million impairment loss on lease abandonment, $0.9 million loss on disposal of long-lived assets, and $0.7 million in depreciation and amortization. The net change in operating assets and liabilities of $5.2 million was primarily due to a $4.9 million decrease in accrued and other liabilities, a $3.2 million decrease in prepaid expenses and other assets, a $2.4 million decrease in related party payable, a $2.3 million decrease in operating lease liabilities primarily due to the termination of the Las Cimas lease, and a $0.4 million decrease in development receivables, partially offset by a $0.6 million increase in deferred revenue and a $0.2 million increase in accounts payable.

Cash used in operating activities for the year ended December 31, 2022 was $80.1 million and reflected a net loss of $83.8 million. Our net loss was offset in part by non-cash expense of $7.1 million for stock-based compensation and $1.6 million for depreciation and amortization. The net change in operating assets and liabilities of $5.5 million was primarily related to a $2.6 million decrease in accounts payable, a $1.1 million increase in prepaid expenses and other assets, a $0.9 million decrease in deferred revenue due to receiving payments under the Immedica Agreement offset by the recognition of revenue allocated to the license, PEACE Phase 3 trial and BLA filing, a $0.9 million decrease in accrued expenses and other liabilities, and a $0.4 million decrease in operating lease liabilities due to lease payments made during the year, partially offset by a $0.4 million increase in accounts receivable for incremental services provided to Immedica and not yet paid.

Cash (Used in) Provided by Investing Activities

Cash used in investing activities for the year ended December 31, 2023 was $108.4 million and primarily consisted of $166.8 million in purchases of marketable securities, partially offset by $39.9 million in maturities and sales of marketable securities, $15.0 million in proceeds from the sale of IPR&D assets, and $3.0 million cash assumed from the Asset Acquisition.

Cash provided by investing activities for the year ended December 31, 2022 was $57.0 million and consisted of $96.5 million in maturities and sales of marketable securities, partially offset by $39.5 million in purchases of marketable securities.

Cash Provided by Financing Activities

Cash provided by financing activities for the year ended December 31, 2023 was $361.1 million, which primarily consisted of the net proceeds from the issuance of the shares of Series A Preferred Stock in the June 2023 PIPE and the issuance of the shares of common stock and Series B Preferred Stock in the December 2023 PIPE.

Cash provided by financing activities for the year ended December 31, 2022 was $42.7 million, which primarily consisted of $42.9 million from the registered direct offering of our common stock and pre-funded warrants in May 2022, net of placement agent fees and offering costs, and $0.2 million from the sale of common stock under our 2016 Employee Stock Purchase Plan, partially offset by $0.4 million in principal payments made on our finance lease obligations.

Cash flows for the Years Ended December 31, 2022 and 2021

The following table summarizes our cash flows for the periods indicated (in thousands):

	Year Ended December 31,	
	2022	2021
Net cash and cash equivalents (used in) provided by:		
Operating activities	$ (80,144)	$ (53,716)
Investing activities	57,008	(22,619)
Financing activities	42,678	1,393
Effect of exchange rate on cash, cash equivalents, and restricted cash	(106)	(15)
Net increase (decrease) in cash and cash equivalents	$ 19,436	$ (74,957)

Cash used in operating activities

Cash used in operating activities for the year ended December 31, 2022 was $80.1 million and reflected a net loss of $83.8 million. The cash impact of our net loss was offset by non-cash expenses of $7.1 million for stock-based compensation, $1.6 million for depreciation and amortization, $0.4 million for operating lease expense, and $0.1 million for net premium purchase and amortization on marketable securities. The net decrease in operating assets and liabilities of $5.5 million was primarily related to a $2.6 million decrease in accounts payable, a $1.1 million increase in prepaid expenses and other assets, a $0.9 million decrease in deferred revenue due to receiving payments under the Immedica Agreement offset by the recognition of revenue allocated to the license, PEACE Phase 3 trial and BLA filing, a $0.9 million decrease in accrued expenses and other liabilities, and a $0.4 million decrease in operating lease liabilities due to lease payments made during the year, partially offset by a $0.4 million increase in accounts receivable for incremental services provided to Immedica and not yet paid.

Cash used in operating activities for the year ended December 31, 2021 was $53.7 million and reflected a net loss of $65.8 million. The cash impact of our net loss was offset by non-cash expenses of $8.0 million for stock-based compensation, $1.6 million for depreciation and amortization, $0.4 million for operating lease expense, and $0.2 million for net premium purchase and amortization on marketable securities. The net change in operating assets and liabilities of $1.8 million was primarily related to a $3.6 million increase in deferred revenue due to receiving a $21.5 million upfront payment under the Immedica Agreement offset by the recognition of revenue allocated to the license, PEACE Phase 3 trial and BLA submission. Additional offsets included a $1.2 million increase in prepaid expenses and other assets due to advance payments for the Phase 1/2 trial of pegtarviliase and manufacturing activities for the Arginase 1 Deficiency program, a $0.8 million increase in license and development receivable for incremental services provided to Immedica and not yet paid, and a $0.4 million decrease in operating lease liabilities due to lease payments made during the year.

Cash used in investing activities

Cash used in investing activities for the year ended December 31, 2022 was $57.0 million and consisted of $39.5 million in purchases of marketable securities offset by $96.5 million in maturities of marketable securities.

Cash used in investing activities for the year ended December 31, 2021 was $22.6 million and consisted of $133.1 million in purchases of marketable securities and $0.5 million in purchases of property and equipment offset by $111.0 million in maturities of marketable securities.

Cash provided by financing activities

Cash provided by financing activities for the year ended December 31, 2022 was $42.7 million, which consisted of $42.9 million from issuance of Common Stock and pre-funded warrants in a registered direct offering, the

2022 RDO, net of offering costs and $0.2 million sale of common stock under our 2016 Employee Stock Purchase Plan offset by $0.4 million in principal payments made on finance lease obligations.

Cash provided by financing activities for the year ended December 31, 2021 was $1.4 million, which consisted of $1.9 million in stock option exercises and sale of common stock under our 2016 Employee Stock Purchase Plan offset by $0.5 million in principal payments made on finance lease obligations.

Contractual Obligations and Other Commitments

Effective June 30, 2023, we abandoned our leased corporate headquarters and laboratory space located in Austin, Texas. As a result, we recognized an impairment loss related to the operating right-of-use asset of $0.9 million. On August 7, 2023, we terminated our building lease in Austin, Texas. In exchange for releasing us of all further obligations under the lease, we paid the lessor a $2.0 million termination fee.

We have entered into agreements in the normal course of business with contract research organizations for clinical trials and contract manufacturing organizations, and with vendors for nonclinical research studies and other services and products for operating purposes. These contractual obligations are cancelable at any time by us, generally upon 30 to 60 days' prior written notice to the vendor.

Contingent contractual obligations

Through the Asset Acquisition, we received the Option to license the IPR&D rights related to four research programs. On July 12, 2023 and on December 14, 2023, we exercised the Option with respect to two of these research programs, respectively. The exercise of the Option allows for us to enter into an exclusive license agreement with Paragon for the respective research program. Upon license execution, we expect to be obligated to pay Paragon up to $22.0 million based on specific development, regulatory and clinical milestones for each licensed research program. As of December 31, 2023, none of the $22.0 million obligation was accrued for since the related license agreements are still being negotiated. As of the date of the filing of this prospectus, the Option remains unexercised with respect to the two remaining research programs under the Paragon Agreement. Should the Option for these research programs be exercised and upon entry into license agreements with respect to such research programs, we expect to be obligated to pay Paragon up to $22.0 million per research program based on certain development, regulatory and clinical milestones.

We expect to enter into a SPY001 license agreement (the "SPY001 License Agreement") and a SPY002 license agreement (the "SPY002 License Agreement"). Upon execution of each of the SPY001 License Agreement and the SPY002 License Agreement, we expect to pay Paragon a $1.5 million fee for nomination of a development candidate, as applicable, and we expect to be obligated to make a further milestone payment of $2.5 million upon the first dosing of a human patient in a Phase 1 trial. Subject to the execution of the Option with respect to the SPY003 or SPY004 research programs, we expect to be obligated to make similar payments upon and following the execution of license agreements with respect to these research programs.

In addition to the above, although the SPY001 License Agreement and the SPY002 License Agreement have not been entered into as of the date hereof, the following summarizes other key terms that we expect to be included in such agreements:

- Paragon will provide Spyre with an exclusive license to its patents covering the related antibody, the method of use and its method of manufacture.
- Paragon will not conduct any new campaigns that generate anti-α4ß7 or anti-TL1A monospecific antibodies for at least 5 years.
- Spyre will pay Paragon a low single-digit percentage royalty for single antibody products and a mid single-digit percentage royalty for products containing more than one antibody from Paragon.

- There is a royalty step-down of 1/3rd if there is no Paragon patent in effect during the royalty term.
- The royalty term ends on the later of (i) the last-to-expire licensed patent or Spyre patent directed to a derived antibody or (ii) 12 years from the date of first sale of a Spyre product.
- Agreement may be terminated on 60 days' notice by Spyre; on material breach without cure; and to the extent permitted by law, on a party's insolvency or bankruptcy.
- With respect to the SPY002 License Agreement only, on a product by product basis, Spyre will pay Paragon sublicensing fees of up to approximately $20 million upon the achievement of mostly commercial milestones.

Recently Adopted Accounting Pronouncements

We early adopted the Financial Accounting Standards Board's Accounting Standards Update 2020-06, Accounting for Convertible Instruments and Contracts in an Entity's Own Equity ("ASU 2020-06"), effective as of January 1, 2023 using the modified retrospective method. Among other amendments, ASU 2020-06 eliminates the cash conversion and beneficial conversion feature models in ASC 470-20 that required an issuer of certain convertible debt and preferred stock to separately account for embedded conversion features as a component of equity, as well as changes the accounting for diluted earnings-per-share for convertible instruments and contracts that may be settled in cash or stock. Additionally, ASU 2020-06 requires the if-converted method, which is more dilutive than the treasury stock method, be used for all convertible instruments. We applied ASU 2020-06 to all Series A Preferred Stock and Series B Preferred Stock during fiscal year 2023, and, accordingly, we did not apply the cash conversion or beneficial conversion feature models in its analysis of the Series A Preferred Stock and Series B Preferred Stock. The adoption of ASU 2020-06 did not have a material impact on our consolidated financial statements.

Recently Issued Accounting Pronouncements

In November 2023, the FASB issued ASU 2023-07, Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures to update reportable segment disclosure requirements, primarily through enhanced disclosures about significant segment expenses and information used to assess segment performance and requires companies to disclose all annual disclosures about segments in interim periods. The ASU also requires companies with a single reportable segment to provide all disclosures required by Topic 280 – Segment Reporting. This update is effective beginning with the Company's 2024 fiscal year annual reporting period and interim periods beginning thereafter. The Company is currently evaluating the impact that the adoption of this standard will have on its consolidated financial statements.

In December 2023, the FASB issued ASU 2023-09, Income Taxes (Topic 740): Improvements to Income Tax Disclosures. This ASU expands disclosures in an entity's income tax rate reconciliation table and disclosures regarding taxes paid both in the U.S. and foreign jurisdictions. This update is effective beginning with the Company's 2025 fiscal year annual reporting period. This ASU will have no impact on the Company's consolidated financial condition or results of operations. The Company is currently evaluating the impact to its income tax disclosures.

CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to market risks in the ordinary course of our business. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of United States interest rates, particularly because our investments are in marketable securities. Our marketable securities are subject to interest rate risk and could fall in value if market interest rates increase. However, we believe that our exposure to interest rate risk is not significant as the majority of our investments are short-term in duration and have a low risk profile. A hypothetical 10% change in interest rates is not expected to have a material effect on the total market value of our investment portfolio. We have the ability to hold our marketable securities until maturity, and therefore, we would not expect our operating results or cash flows to be materially impacted by a change in market interest rates on our investments.

As of December 31, 2023, we held $339.6 million in cash, cash equivalents, marketable securities, and restricted cash, predominately all of which was denominated in U.S. dollars, and consisted primarily of investments in money market funds, commercial paper, U.S. government obligations and corporate bonds.

We are also exposed to market risk related to changes in foreign currency exchange rates as a result of our entering into transactions denominated in currencies other than U.S. dollars. Due to the uncertain timing of expected payments in foreign currencies, we do not utilize any forward exchange contracts. All foreign transactions settle on the applicable spot exchange basis at the time such payments are made. For the twelve months ended December 31, 2023, a majority of our expenditures were denominated in U.S. dollars. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

BUSINESS

Company Overview

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

Through the Asset Acquisition, we received the Option pursuant to the Paragon Agreement. On July 12, 2023, we exercised the Option with respect to one of these research programs to exclusively license intellectual property rights related to such research program directed to antibodies that selectively bind to α4ß7 integrin and methods of using these antibodies, including methods of treating IBD using the SPY001 program. If this research program is pursued non-provisionally and matures into issued patents, we would expect those patents to expire no earlier than 2044 subject to any disclaimers or extensions. On December 14, 2023, we exercised the Option under the Paragon Agreement to be granted an exclusive license to all of Paragon's rights, title and interest in and to intellectual property rights, including inventions, patents, sequence information and results, under SPY002, our TL1A program, to develop and commercialize antibodies and products worldwide in all therapeutics disorders. If this research program is pursued non-provisionally and matures into issued patents, we would expect those patents to expire no earlier than 2044, subject to any disclaimers or extensions. The license agreements pertaining to such research programs are currently being finalized. Furthermore, as of the date of this registration statement, the Option remains unexercised with respect to the intellectual property rights related to the two remaining research programs under the Paragon Agreement. For more information on the Paragon Agreement, see discussion under the heading "*Paragon Agreement*" below.

On July 27, 2023, we announced that we entered into an agreement to sell the global rights to pegzilarginase, an investigational treatment for the rare metabolic disease Arginase 1 Deficiency, to Immedica for $15.0 million in upfront cash proceeds and up to $100.0 million in contingent milestone payments. The sale of pegzilarginase to Immedica supersedes and terminates the license agreement between us and Immedica dated March 2021. See the section titled "*Recent Developments*" below for more information regarding the Immedica APA.

Following the Asset Acquisition and the entry into the Immedica APA, we have significantly reshaped the business into a preclinical stage biotechnology company focused on developing next generation therapeutics for patients living with IBD, including UC and CD. Through the Paragon Agreement, our portfolio of novel and proprietary monoclonal antibody product candidates has the potential to address unmet needs in IBD care by improving efficacy, safety, and/or dosing convenience relative to products currently available or product candidates in development. We have engineered our product candidates with the aim to bind potently and selectively to their target epitopes and to exhibit extended pharmacokinetic half-lives through modifications in the Fc domain that increase affinity to human FcRn and increase antibody recycling. We anticipate that half-life extension will enable less frequent administration compared to marketed or development-stage mAbs that do not incorporate half-life extension modifications. In addition to development of our product candidates as potential monotherapies, we plan to investigate combinations of our proprietary antibodies in preclinical and clinical studies to evaluate whether combination therapy (co-administration or co-formulation of multiple monoclonal antibodies) can lead to greater efficacy compared to monotherapies in IBD. We also intend to examine patient selection strategies via complementary diagnostics in our clinical studies to evaluate whether patients can be matched to the optimal therapy based on genetic background and/or other biomarker signatures. We intend to deliver our product candidates through convenient, infrequently dosed, self-administered, SC injection, although the specific delivery mechanism or technology has not been selected given our early stage.

Our Strategy

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

- Advancing novel, long-acting antibodies against validated IBD targets,

- Evaluating rational therapeutic combinations of our long-acting antibodies, and
- Developing genetic- or biomarker-based complementary diagnostics (e.g., a medical device that provides valuable information about whether a treatment might be beneficial, but is not required for the administration of the drug) to match treatment targets to IBD sub-populations. See the heading "*Our Precision Immunology Approach*" below for additional information.

Our Half-Life Extension Approach

A drug's half-life is an indicator of how long the therapy remains in the body and is a measure of the period of time it takes for the concentration of a drug in the blood to be reduced by half. The half-life determines how frequently a drug needs to be administered to maintain its therapeutic effect. Technologies that extend half-life for injectable products reduce the frequency of injections, or number of injections per applicable time period, needed to provide a therapeutic benefit.

All of our antibody programs are engineered to increase FcRn binding in order to prolong the half-life via increased FcRn-mediated endosomal recycling (rather than catabolism) efficiency. Mutagenesis of the antibody Fc domain, such as the YTE and LS mutations, has been shown to increase binding affinity to human FcRn by more than ten-fold and result in >two-fold the half-life in cynomolgus monkeys (Haraya and Tachibana 2022). Additionally, several antibodies incorporating YTE or LS mutations have been tested in humans and exhibit prolonged half-lives, including at least two FDA-approved products (Beyfortus ®, Evushield ®).

Engineered mAbs with increased half-life have the potential to confer more favorable dosing profiles, including lower dosing frequencies and/or lower required doses administered. In our head-to-head NHP studies, SPY001 and SPY002 exhibited a greater than three-fold and two to three-fold increase in half-life, respectively, relative to comparator antibodies that lack half-life extension modifications. Allometric scaling of the NHP pharmacokinetics to humans support the potential for every other month or quarterly SC dosing for these antibodies, which we believe is a significant improvement over every two week or monthly SC dosing of competitor programs.

Our Combination Therapy Approach

In addition to the development of our product candidates as potential monotherapies, we also plan to investigate combinations of our proprietary antibodies in preclinical studies in 2024 and in a clinical study that will include combinations in 2025, subject to approval of an IND or equivalent foreign regulatory submission, to evaluate whether combination therapy (co-administration or co-formulation of multiple monoclonal antibodies) can lead to greater efficacy compared to monotherapies in IBD. This is expected to initially include SPY120, which combines SPY001 (α4ß7) and SPY002 (TL1A), following approval of an IND or equivalent foreign regulatory submission anticipated in 2025. This is anticipated to be followed by combinations that include SPY003 (IL-23), SPY130 (a combination of SPY001 and SPY003) and SPY230 (a combination of SPY002 and SPY003). We believe that combinations targeting distinct pathways could lead to greater efficacy in IBD. To support our plans, this year we intend to evaluate our combination regimens in preclinical *in vitro* and i*n vivo* pharmacology models and to conduct combination toxicology studies.

Our Precision Immunology Approach

We aim to develop genetic- or biomarker-based patient selection approaches such as complementary diagnostics that utilize a genomic or proteomic signature across our portfolio of therapeutics to aid patients and physicians in selecting the optimal treatment regimen. We are in discussions with potential partners to develop patient selection strategies for each of our targets, and if successful, we would intend to evaluate such approaches in Phase 2 studies in IBD patients. Depending on their performance, one or more of such approaches could be utilized in Phase 3 studies and potentially commercially as complementary diagnostics.

A complementary diagnostic is a medical device, often an in vitro device, which provides information that is valuable for the safe and effective use of a corresponding therapeutic drug or biologic product. In contrast, a

companion diagnostic is considered *essential* for the safe and effective use of a corresponding drug or biological product. A complementary diagnostic can be used to identify patients or subsets of patients who are most likely to benefit from the therapeutic product, but unlike a companion diagnostic, is not required prior to administration or prescription of a drug. A complementary diagnostic is generally developed in conjunction with the clinical program for an associated therapeutic product and would require additional subgroup analysis as a secondary or exploratory endpoint from patient samples (e.g., blood, saliva) provided in the trial. The development path of a complementary diagnostic may include additional meetings with regulatory authorities, such as a pre-submission meeting and the requirement to submit an investigational device exemption application. As a result, the overall timing and cost of our clinical development program, and ultimately our commercial strategy, may be impacted by our pursuit of complementary diagnostics.

Commercial use of a complementary diagnostic may require additional regulatory approvals, but we do not expect the approval and commercialization of any of our therapeutic product candidates to be dependent on regulatory approval or the commercialization of a diagnostic. A complementary diagnostic could be useful in a commercial setting to facilitate first line use of a therapeutic for patients who are diagnostic-positive and are deemed more likely to respond, as long as diagnostic-negative patients (e.g., false-negatives) are not unduly burdened with access restrictions.

Inflammatory Bowel Disease

IBD is a chronic condition characterized by inflammation within the gastrointestinal tract. It encompasses two main disorders: UC and CD. UC primarily affects the colon and the rectum. Inflammation occurs in the innermost lining of the colon. Symptoms include bloody diarrhea, abdominal pain, bowel urgency, and frequent bowel movements. CD can affect any part of the gastrointestinal tract, from the mouth to the anus. It is characterized by inflammation that extends through multiple layers of the bowel wall. Symptoms include abdominal pain, diarrhea, weight loss, fatigue, and complications such as strictures or fistulas. Both conditions can significantly impact patients' quality of life in terms of physical health, emotional well-being, and the unpredictability of symptom onset.

IBD affects millions of individuals worldwide, with increasing prevalence and incidence in both developed and developing countries. In the United States, it is estimated that approximately 2.4 million individuals currently have IBD, with approximately 70,000 patients newly diagnosed every year. Based on research from the Crohn's and Colitis Foundation of America, the market for IBD therapeutics is expected to experience steady growth, driven by rising disease prevalence, increasing diagnosis rates, and evolving treatment paradigms.

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

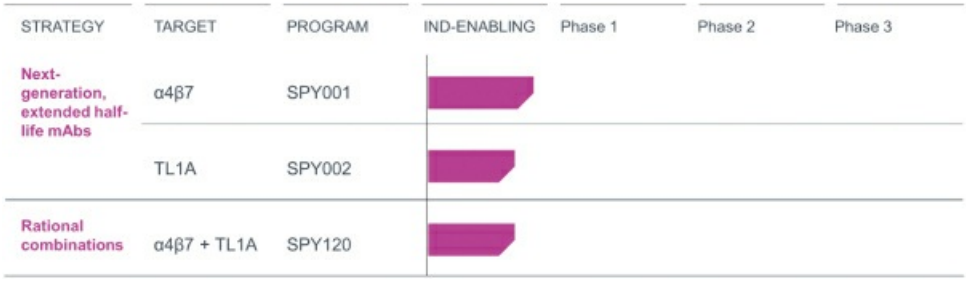
Despite available treatments, there remain substantial unmet needs in IBD management, including:

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

Our Portfolio

We are advancing a pipeline of mAbs for the treatment of IBD (UC and CD) in connection with the research programs with respect to which we have exercised the Option to exclusively license all of Paragon's right, title, and

interest in, including all intellectual property license rights to, or have the Option to acquire such intellectual property and other rights to pursuant to the Paragon Agreement and plan to develop patient selection approaches for each program. The following table summarizes the programs that have been exercised to date pursuant to the Paragon Agreement:



Other early-stage programs:

- SPY003 – anti-IL-23 mAb
- SPY004 – novel MOA mAb
- SPY130 – combination anti-α4ß7 and anti-IL-23 mAbs
- SPY230 – combination anti-TL1A and anti-IL-23 mAbs

We have nominated development candidates for SPY001 and SPY002. We have exercised our Option to license worldwide rights from Paragon for the SPY001 and SPY002 programs and the SPY001 License Agreement and SPY002 License Agreement are currently being finalized with execution expected to occur in the first half of 2024. We continue to hold the Option to license similar rights from Paragon for certain other programs. We expect the SPY003 license to be restricted to IBD, and we expect other potential program licenses related to the Option to be indication agnostic. We additionally have an exclusive option under the agreement for a discovery stage program targeting a novel MOA that also incorporates half-life extension (SPY004). See the section titled “Paragon Agreement” for more information on the Paragon Agreement, including the Option.

Although we hold the Option to acquire intellectual property license rights related to the SPY003 and SPY004 programs, such Option remains unexercised.

The drug and/or device development process is inherently uncertain, our development approach is unproven, the preclinical evidence that supports our proposed development program is preliminary and limited, and we have not yet tested any product candidate in humans. Notwithstanding our efforts to develop safe and effective monotherapies and combination therapies, there can be no guarantee that we will be able to develop product candidates that will be found to be safe and effective so as to obtain the necessary regulatory approvals to market our product candidates.

For a discussion of the risks associated with our portfolio, see the section of this prospectus entitled “ *Risk Factors*.”

SPY001 – anti-α4ß7 mAb

Our most advanced product candidate, SPY001, is a highly potent, highly selective, and fully human monoclonal immunoglobulin G1 antibody designed to bind selectively to the α4ß7 integrin being developed for the treatment of IBD (UC and CD). The α4ß7 integrin is a protein found on the surface of immune cells known as lymphocytes. This integrin regulates the migration of lymphocytes to the gut where they contribute to the

inflammatory process in IBD. By selectively binding to the α4ß7 integrin, SPY001 is designed to prevent the interaction of these lymphocytes with MAdCAM-1, a molecule expressed on endothelial cells lining the blood vessels in the gut. This interaction is responsible for guiding lymphocytes from the bloodstream into the gut tissue, where they cause inflammation. By blocking the interaction between α4ß7 integrin and MAdCAM-1, SPY001 aims to reduce the recruitment of lymphocytes to the gut, leading to a decrease in inflammation. Since it specifically targets the gut immune system, SPY001 is designed to minimize systemic immunosuppressive effects unrelated to IBD pathology.

SPY001 is being developed by us and our research partners at Paragon. Prior to the closing of the Asset Acquisition, Paragon had sole leadership in conducting *in vitro* and *in vivo* studies for SPY001 clones, including the potency, selectivity, and NHP PK data supporting development candidate nomination for the SPY001 program. Following the closing of the Asset Acquisition and the exercise of the Option with respect to the SPY001 program, Spyre and Paragon established a Joint Development Committee ("JDC") comprised of two employees from Spyre and two employees from Paragon and jointly directed research and development work, with Spyre having final decision rights on the budget for any research program. The JDC is the decision-making body for SPY001 and our other pipeline programs prior to the execution of the SPY001 License Agreement and, in addition to SPY001, we will also control and lead the development process for each of SPY002, non-optioned programs SPY003 and SPY004, and each of the combination programs once the respective license agreements are executed.

SPY001 preclinical characterization studies were conducted in-house with support from third party vendors. SPY001 demonstrates similar potency and selectivity as vedolizumab in preclinical *in vitro* models including surface plasmon residence (n=5 concentrations, study completed September 2023) and cellular adhesion assays (see Figure 1, n=6 replicates per group, study completed in August 2023). It also incorporates a half-life extending modification resulting in an increase in half-life of >three-fold in Tg276 transgenic mice that express human FcRn (n=5 per group, studies completed in August 2023) and an increase in half-life of >three-fold in NHPs (n=6 per group, studies completed in December 2023), compared to vedolizumab (see Figure 2).

SPY001 is currently progressing through IND-enabling studies (chemistry, manufacturing, and controls ("CMC") scale-up complete, IND-enabling toxicology studies initiating), and we expect to submit an IND or equivalent foreign regulatory submission and enter a Phase 1 first-in-human ("FIH") study in healthy volunteers in the first half of 2024, pending health agency approval. Interim data from the Phase 1 healthy volunteer study are expected by the end of 2024. If successful, SPY001 would then advance to Phase 2 clinical studies and, pending further success, Phase 3 clinical studies to support global regulatory submissions and commercial approval.

Figure 1. Potency and selectivity of SPY001 relative to vedolizumab in cellular assays.

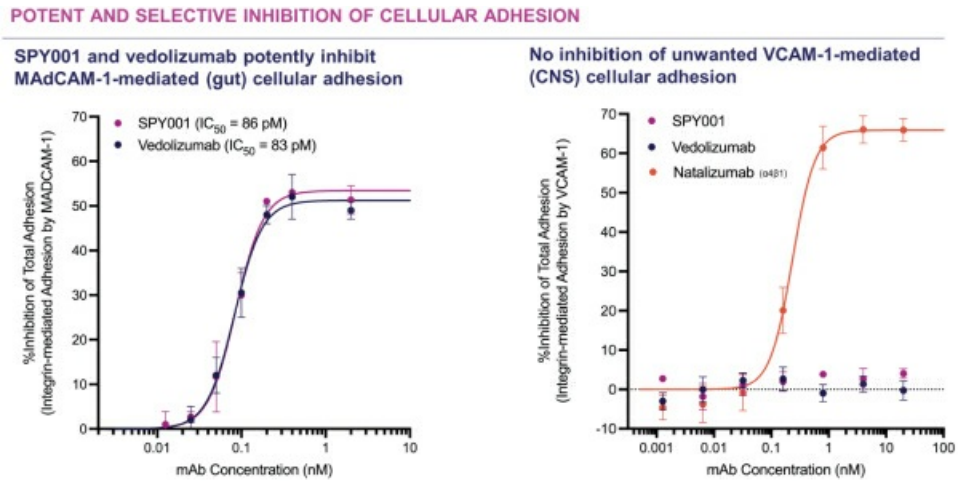
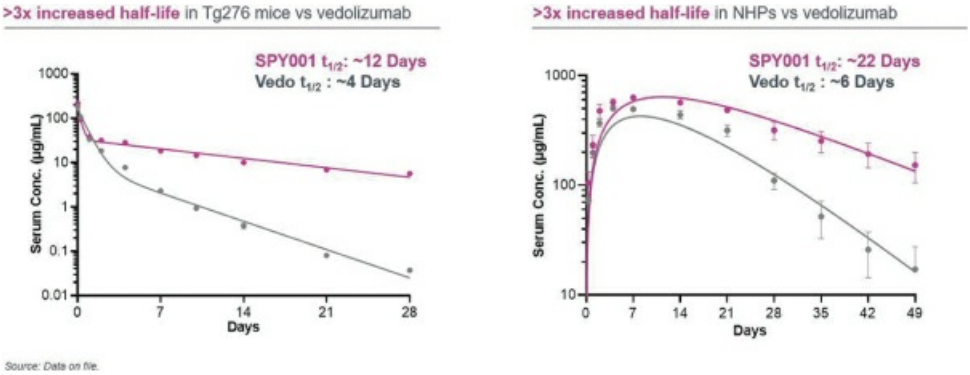


Figure 2. Pharmacokinetic concentration-time curves of SPY001 compared to vedolizumab in Tg276 transgenic mice and non-human primates (n=3-5 per group shown, removing primates that developed anti-drug antibodies).

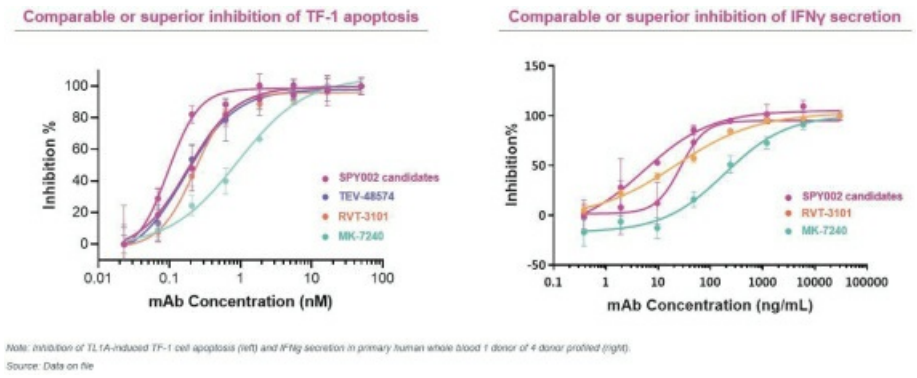


SPY002 – anti-TL1A mAb

For our co-lead program, SPY002, we have nominated two highly potent, highly selective, and fully human mAb candidates designed to bind to tumor necrosis factor-like ligand 1A (“TL1A”), both of which are in preclinical development for the treatment of IBD (UC and CD). TL1A is a protein that plays a role in regulating the immune system and is elevated in the gut tissue of individuals with IBD. TL1A interacts with its receptor, death receptor 3 (“DR3”), which is expressed in various immune cells, including T cells. This interaction triggers signaling pathways that contribute to inflammation and immune system activation, leading to IBD symptomology. The SPY002 candidates have been designed to block the interaction between TL1A and DR3 and thereby inhibit the downstream signaling events and dampen the inflammatory response. By neutralizing TL1A, we believe SPY002 candidates have the potential to modulate the immune response in IBD patients, potentially reducing disease activity and promoting mucosal healing.

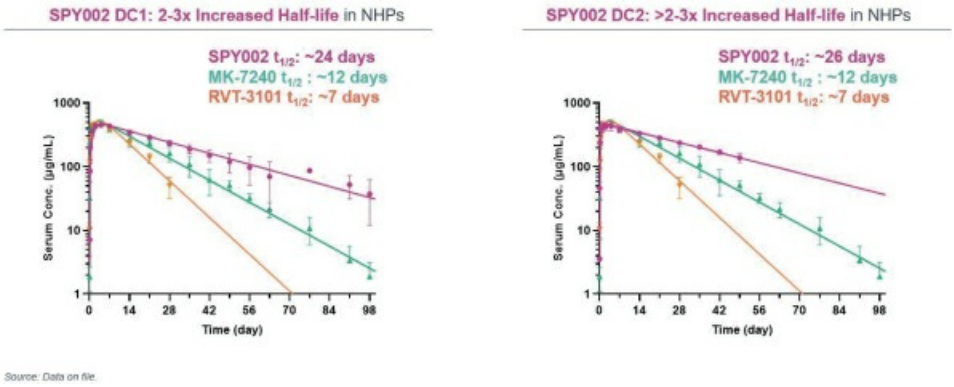
SPY002 preclinical characterization studies were conducted in-house with support from third party vendors. Our extensive discovery campaign has identified two lead candidates which bind TL1A monomers and trimers and have subnanomolar potency in cellular assays (see Figure 3, n=4 replicates per group per study, studies completed in Q4 2023 and Q1 2024). The candidates also exhibited extended pharmacokinetic half-lives of greater than two to three-fold relative to competitive molecules in clinical development that do not incorporate half-life extending modifications, based on head-to-head preclinical studies in NHPs (see Figure 4, n=5 per group, studies completed in Q4 2023 and Q1 2024). SPY002 candidates are currently progressing through IND-enabling studies (CMC scale-up ongoing) and we expect to submit an IND or equivalent foreign regulatory submission and enter a Phase 1 FIH study in healthy volunteers in the second half of 2024, with one or both of our SPY002 candidates pending additional preclinical data and pending health agency approval. Interim data from the Phase 1 healthy volunteer study are expected in the first half of 2025. If successful, one SPY002 candidate would then advance to Phase 2 clinical studies and, pending further success, Phase 3 clinical studies to support global regulatory submissions and commercial approval.

Figure 3. Inhibition of TL1-A induced TF-1 cell apoptosis (left) and IFN g secretion in primary human whole blood 1 donor of 4 donors profiled (right).



Note: Inhibition of TL1A-induced TF-1 cell apoptosis (left) and IFNg secretion in primary human whole blood 1 donor of 4 donor profiled (right).
Source: Data on file

Figure 4. Pharmacokinetic concentration-time curves of SPY002 candidates compared to competing anti-TL1A molecules in non-human primates.



Source: Data on file.

SPY003 – anti-IL-23 mAb

SPY003 is a discovery stage program focused on designing antibodies to bind to Interleukin 23 ("IL-23") and incorporates half-life extending modifications. IL-23 is a cytokine that is produced by immune cells and is involved in immune response regulation. IL-23 promotes the survival, expansion, and activity of Th17 cells. Th17 cells produce inflammatory cytokines, such as IL-17, which contribute to the inflammation seen in IBD. IL-23 also helps in the recruitment and activation of other immune cells, such as neutrophils, which further contribute to tissue damage in the gut. To date, we have identified several promising clones that meet our target product profile, and we are in the process of narrowing down the potential clones to select a development candidate based on pharmacokinetic performance and CMC developability. We are continuing our preclinical development efforts with the SPY003 program and expect to nominate a development candidate in mid-2024 and move into IND-enabling studies in the second half of 2024. Upon development candidate nomination, we intend to exercise our Option to acquire intellectual property rights for the SPY003 program pursuant to the Paragon Agreement.

SPY004 – novel MOA mAb

SPY004 is an undisclosed novel mechanism of action ("MOA") and incorporates half-life extension modifications. Upon development candidate nomination, we intend to exercise our Option to acquire intellectual property rights for the SPY004 program pursuant to the Paragon Agreement.

SPY120 – combination anti-α4ß7 and anti-TL1A mAbs

SPY120 combines SPY001 (anti-α4ß7) and SPY002 (anti-TL1A) antibodies, pairing two mechanisms studied in third-party clinical trials targeting non-overlapping sites of action. We are currently evaluating SPY120 in preclinical studies and plan to initiate combination toxicology studies in 2024. We expect to initiate clinical studies for SPY120 in 2025, pending approval of an IND or equivalent foreign regulatory submission anticipated in 2025.

SPY130 – combination anti-α4ß7 and anti-IL-23 mAbs

SPY130 combines SPY001 (anti-α4ß7) and SPY003 (anti-IL-23) antibodies, pairing two commercially validated mechanisms targeting non-overlapping sites of action. We are currently evaluating SPY130 in preclinical studies and plan to initiate combination toxicology studies in 2025.

SPY230 – combination anti-TL1A and anti-IL-23 mAbs

SPY230 combines SPY002 (anti-TL1A) and SPY003 (anti-IL-23) antibodies, pairing two complementary mechanisms of action with potential to address overlapping and non-overlapping triggers of inflammation. We are currently evaluating SPY230 in preclinical studies and plan to initiate combination toxicology studies in 2025.

Intellectual Property

Overview

We strive to protect the proprietary programs and technologies that we believe are important to our business, including seeking and maintaining patent protection intended to cover the composition of matter of our programs, their methods of use and manufacture, related technologies, diagnostics, and other inventions.

Patent Rights Relating to Our a4b7 Program

As of March 25, 2024, Paragon owns provisional patent applications directed to antibodies that target a4b7, including SPY001, pharmaceutical formulations, and methods of using those antibodies, which are subject to our

exercised option right and future licensed rights. If the provisional patent applications are pursued non-provisionally and mature into one or more issued patents, we would expect those patents to expire in 2044, absent any applicable patent term extensions.

Patent Rights Relating to Our TL1A Program

As of March 25, 2024, Paragon owns provisional patent applications directed to antibodies that target TL1A, including two lead SPY002 development candidates, pharmaceutical formulations, and methods of using those antibodies, which are subject to our exercised option right and future licensed rights. If the provisional patent applications are pursued non-provisionally and mature into one or more issued patents, we would expect those patents to expire in 2044, absent any applicable patent term extensions.

Patent Rights Relating to Our IL-23 Program

As of March 25, 2024, Paragon has filed a provisional patent application for antibodies that target IL-23 and intends to file one or more provisional patent applications directed to additional antibodies that target IL-23, including SPY003, pharmaceutical formulations, and methods of using those antibodies. We have not yet exercised our option to acquire exclusive rights to any IL-23 patent applications, but retain the option to do so. If the provisional patent applications are pursued non-provisionally and mature into one or more issued patents covering SPY003, we would expect those patents to expire in 2045, absent any applicable patent term extensions.

As indicated above, some of patent applications we intend to license and others that we may own outright are provisional patent applications. Provisional patent applications are not eligible to become issued patents until, among other things, we file a non-provisional patent application within 12 months of filing of the first of related provisional patent applications. If we do not timely file such non-provisional patent applications, we may lose our priority date with respect to our provisional patent applications and may be unable to obtain patent protection on inventions disclosed in such provisional patent applications. While we intend to timely file non-provisional patent applications relating to our provisional patent applications, we cannot predict whether any such patent applications will result in the issuance of patents that provide us with any competitive advantage. Moreover, the patent application and approval processes are expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries in which we have filed, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and issuing a patent, or may be shortened if a patent is terminally disclaimed over an earlier-issued patent. When FDA approval is granted for a product covered by a patent, the term of a patent that covers a drug or biological product may also be eligible for patent term extension for a portion of the term effectively lost as a result of the FDA regulatory review period, subject to certain limitations and provided statutory and regulatory requirements are met. Any such patent term extension can be for no more than five years, only one patent per approved product can be extended, the extension cannot extend the total patent term beyond 14 years from approval, and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. We may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents, or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. In the future, if and when our product candidates receive approval from the FDA or foreign regulatory authorities, we expect to apply for patent term extensions or the equivalent in foreign countries based on issued patents we may obtain in the future covering those products, depending upon the length of the clinical trials for each product and other factors. There can be no assurance that any of our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustment to the term of any of our patents.

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our product candidates will depend on our success in obtaining effective patent claims and enforcing those claims if issued. However, our owned and licensed pending patent applications, and any patent applications that we may in the future file or license from third parties, may not result in the issuance of patents. We also cannot predict the breadth of claims that may be allowed or enforced in our patents. Any issued patents that we may receive in the future may be invalidated or circumvented, or we may be unable to prove or not become aware of infringement such issued patents. In addition, because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting the protection such patent would afford the respective product and any competitive advantage such patent may provide. For more information, see the section titled “Risk Factors – Risks Related to our Intellectual Property”.

Other IP Rights

In addition to patents, we rely upon unpatented trade secrets, know-how and continuing technological innovation to develop and maintain our competitive position. However, trade secrets and know-how can be difficult to protect. We seek to protect our proprietary information, in part by executing confidentiality agreements with our collaborators and scientific advisors, and non-competition, non-solicitation, confidentiality and invention assignment agreements with our employees and consultants. We have also executed agreements requiring assignment of inventions with selected scientific advisors and collaborators. The confidentiality agreements we enter into are designed to protect our proprietary information and the agreements or clauses requiring assignment of inventions to us are designed to grant us ownership of technologies that are developed through our relationship with the respective counterparty. We cannot guarantee, however, that we have executed such agreements with all applicable counterparties, that such agreements will not be breached, or that these agreements will afford us adequate protection of our intellectual property and proprietary rights. For more information, see the section entitled “Risk Factors – Risks Related to our Intellectual Property”.

Employees and Human Capital Resources

As of December 31, 2023, we had 30 employees, all of whom were employed full time. We also engage temporary employees and consultants to augment our existing workforce. None of our employees are represented by a labor union or covered under a collective bargaining agreement. We consider our relationship with our employees to be good.

We recognize that attracting, motivating, and retaining talent at all levels is vital to continuing our success. We invest in our employees through high-quality benefits, professional development opportunities, and various health and wellness initiatives and offer competitive compensation packages (base salary and incentive plans), ensuring fairness in internal compensation practices. The principal purposes of our incentive plans (bonus and equity) are to align with the long-term interests of our stakeholders and stockholders.

Commercial

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

Manufacturing

We do not currently own or operate facilities for product manufacturing, testing, storage, and distribution. We are currently in the process of novating certain agreements with third parties for the performance of future clinical

manufacturing and development activities from Paragon to us. The initial forms of these agreements are generally non-specific master services agreements that allow an entity to begin the process of future manufacturing or development services, respectively. As clinical development activities are commenced by us, the agreements will be revised to provide for the specific deliverables and associated costs that are needed under our development plan.

Pursuant to a Novation Agreement dated September 19, 2023 (the "Novation Agreement"), by and between us, Paragon and WuXi Biologics (Hong Kong) Limited ("WuXi Biologics"), we novated (i) a Biologics Master Services Agreement (the "WuXi Biologics MSA") and (ii) a Cell Line License Agreement (the "Cell Line License Agreement").

In light of the recently introduced BIOSECURE Act, which would prohibit federal agencies from entering into procurement contracts with an entity that uses biotechnology equipment or services from a biotechnology company of concern, we have taken several measures to strengthen our supply chain in the event that WuXi Biologics or one of our other manufacturers is impacted. We intend to establish domestic inventory of key materials and are accelerating our clinical resupply campaigns to ensure we have a sufficient stockpile of drug substance in the United States. We will also continue to closely monitor geopolitical risk and implement additional mitigations and supply chain redundancies, as needed. See the risk factor entitled "*We currently rely, and plan to rely in the future, on third parties to conduct and support our preclinical studies and clinical trials. If these third parties do not properly and successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our product candidates.*"

Biologics Master Services Agreement

In April 2023, Paragon and WuXi Biologics entered into the WuXi Biologics MSA, which was subsequently novated to us by Paragon on September 19, 2023 pursuant to the Novation Agreement. The WuXi Biologics MSA governs certain development activities and GMP manufacturing and testing for the SPY001 program, as well as potential future programs, on a work order basis. Under the WuXi Biologics MSA, we are obligated to pay WuXi Biologics a service fee and all non-cancellable obligations in the amount specified in each work order associated with the agreement for the provision of services.

The WuXi Biologics MSA terminates on the later of (i) June 20, 2027 or (ii) the completion of services under all work orders executed by the parties prior to June 20, 2027, unless terminated earlier. The term of each work order terminates upon completion of the services under such work order, unless terminated earlier. We can terminate the WuXi Biologics MSA or any work order at any time upon 30 days' prior written notice and immediately upon written notice if WuXi Biologics fails to obtain or maintain required material governmental licenses or approvals. Either party may terminate a work order (i) at any time upon six months' prior notice with reasonable cause, provided however that if WuXi Biologics terminates a work order in such manner, no termination or cancellation fees shall be paid by us and (ii) immediately for cause upon (a) the other party's material breach that remains uncured for 30 days after notice of such breach, (b) the other party's bankruptcy or (c) a force majeure event that prevents performance for a period of at least 90 days.

Cell Line License Agreement

In April 2023, Paragon and WuXi Biologics entered into the Cell Line License Agreement, which was subsequently novated to us by Paragon pursuant to the Novation Agreement. Under the Cell Line License Agreement, we received a non-exclusive, worldwide, sublicensable license to certain of WuXi Biologics's know-how, cell line, biological materials (the "WuXi Biologics Licensed Technology") and media and feeds to make, have made, use, sell and import certain therapeutic products produced through the use of the cell line licensed by WuXi Biologics under the Cell Line License Agreement (the "WuXi Biologics Licensed Products"). Specifically, the WuXi Biologics Licensed Technology is used in certain manufacturing activities in support of the SPY001 program.

In consideration for the license, we agreed to pay WuXi Biologics a non-refundable license fee of $150,000. Additionally, if we manufacture all of our commercial supplies of bulk drug product with a manufacturer other than WuXi Biologics or its affiliates, we are required to make royalty payments to WuXi Biologics in an amount equal to a less than one percent of global net sales of WuXi Biologics Licensed Products manufactured by a third-party manufacturer (the "Royalty"). If we manufacture part of our commercial supplies of the WuXi Biologics Licensed Products with WuXi Biologics or its affiliates, then the Royalty will be reduced accordingly on a pro rata basis.

The Cell Line License Agreement will continue indefinitely unless terminated (i) by us upon six months' prior written notice and our payment of all undisputed amounts due to WuXi Biologics through the effective date of termination, (ii) by WuXi Biologics for a material breach by us that remains uncured for 60 days after written notice, (iii) by WuXi Biologics if we fail to make a payment and such failure continues for 30 days after receiving notice of such failure, or (iv) by either party upon the other party's bankruptcy.

Paragon Agreement

In May 2023, Pre-Merger Spyre entered into the Paragon Agreement with Paragon and Parapyre. Pursuant to the Paragon Agreement, the Option provided for the right to acquire the IPR&D rights related to four research programs from Paragon in accordance with a license agreement to be entered into following each exercise of the Option. Under the Paragon Agreement, the terms of such license agreement would be consistent with the economics and other terms set out in the Paragon Agreement and, in the event of failure to reach an agreement on the definitive terms, the matter would be resolved via arbitration. In consideration for the Option granted under the Paragon Agreement, Pre-Merger Spyre was obligated to pay Paragon an upfront cash amount of $3.0 million in research initiation fees. In addition, Pre-Merger Spyre was 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, which included the $3.0 million research initiation fee and $16.0 million of historical reimbursable expenses owed to Paragon. As of June 22, 2023, $19.0 million was unpaid and was assumed by us through the Asset Acquisition.

As a result of the Asset Acquisition, we assumed the rights and obligations of Pre-Merger Spyre under the Paragon Agreement, including the Parapyre Option Obligation. For more information on the Parapyre Option Obligation, see the section titled "*Our Relationship with Paragon and Parapyre.*" Pursuant to the Paragon Agreement, on a research program-by-research program basis following the finalization of the research plan for each respective research program, we are required to pay Paragon a nonrefundable fee in cash of $0.8 million.

On July 12, 2023 and December 14, 2023, we exercised our Option available under the Paragon Agreement with respect to the SPY001 and SPY002 research programs, respectively, and expect to enter into the SPY001 License Agreement and the SPY002 License Agreement. Our Option available under the Paragon Agreement with respect to the SPY003 and SPY004 programs remains unexercised.

Following the execution of each of the SPY001 License Agreement and SPY002 License Agreement, we will be obligated to pay Paragon up to $22.0 million upon the achievement of specific development, regulatory and clinical milestones for the first product under each agreement, respectively, that achieves such specified milestones. Upon execution of each of the SPY001 License Agreement and the SPY002 License Agreement, we expect to pay Paragon a $1.5 million fee for nomination of a development candidate, as applicable, and we expect to be obligated to make a further milestone payment of $2.5 million upon the first dosing of a human patient in a Phase 1 trial. Subject to the execution of the Option with respect to the SPY003 or SPY004 research programs, we expect to be obligated to make similar payments upon and following the execution of license agreements with respect to these research programs, respectively.

Competition

We expect to face intense competition from other biopharmaceutical companies that are developing agents for the treatment of inflammatory diseases. If approved for the treatment of patients with moderate-to-severe IBD, our portfolio of products would compete with TNF antibodies including Humira (AbbVie), Remicade (Johnson & Johnson), and Simponi (Johnson & Johnson); Omvoh (Lilly) IL-12/23 and IL-23 antibodies including Stelara (Johnson & Johnson) and Skyrizi (AbbVie); α4ß7 antibody Entyvio (Takeda); JAK inhibitors including Xeljanz (Pfizer), Rinvoq (AbbVie); and S1P1 receptor modulating therapies including Zeposia (Bristol Myers Squibb) and Velsipity (Pfizer).

We are aware of several companies with product candidates in development for the treatment of patients with IBD, including Merck's MK-7240, Roche/Roivant's RVT-3101, and Sanofi/Teva's TEV-48574 TL1A antibodies; additional IL-23/IL-23Rs including Tremfya and JNJ-2113 (Johnson & Johnson); and oral anti-integrin agents including Morphic Therapeutic's MORF-057, and Gilead's GS-1427, and a discovery program at Dice Therapeutics (Lilly).

Government Regulation

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of biologics such as those we are developing. We, along with our third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates.

United States Biologics Regulation

In the United States, biological products are subject to regulation under the FDCA, the Public Health Service Act ("PHSA") and other federal, state, local, and foreign statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, and local statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or following approval may subject an applicant to administrative action and judicial sanctions. The process required by the FDA before biologic product candidates may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's current Good Laboratory Practices ("GLP") regulation;
- submission to the FDA of an IND, which must become effective before clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an independent IRB, or ethics committee at each clinical site before the trial is commenced;
- manufacture of the proposed biologic candidate in accordance with current Good Manufacturing Practices ("cGMPs");
- performance of adequate and well-controlled human clinical trials in accordance with current Good Clinical Practice ("GCP") requirements to establish the safety, purity and potency of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of a BLA, after completion of all pivotal clinical trials;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;

- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMPs, and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of a BLA to permit commercial marketing of the product for particular indications for use in the United States.

Preclinical and Clinical Development

Prior to beginning any clinical trial with a product candidate, in the United States, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol or protocols for preclinical studies and clinical trials. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology and pharmacodynamic characteristics of the product, chemistry, manufacturing and controls information, and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

In addition to the IND submission process, supervision of human gene transfer trials includes evaluation and assessment by an institutional biosafety committee ("IBC"), a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment and such review may result in some delay before initiation of a clinical trial.

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

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

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

- Phase 1. The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance,

absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.

- Phase 2. The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3. The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the BLA. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain FDA regulatory requirements in order to use the study as support for an IND or application for marketing approval or licensure, including that the study was conducted in accordance with GCP, including review and approval by an independent ethics committee and use of proper procedures for obtaining informed consent from subjects, and the FDA is able to validate the data from the study through an onsite inspection if the FDA deems such inspection necessary. The GCP requirements encompass both ethical and data integrity standards for clinical studies.

BLA Submission and Review

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

In addition, under the Pediatric Research Equity Act ("PREA"), a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The Food and Drug Administration Safety and Innovation Act requires that a sponsor who is planning to submit a marketing application for a biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit

an initial pediatric study plan ("PSP") within sixty days after an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. Once a BLA has been accepted for filing, the FDA's goal is to review standard applications within ten months after the filing date, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process may also be extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may convene an advisory committee to provide clinical insight on application review questions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

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

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

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

Expedited Development and Review Programs

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

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

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

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

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

Combination Therapy

Combination therapy is a treatment modality that involves the use of two or more drugs to be used in combination to treat a disease or condition. If those drugs are combined in one dosage form, such as one pill, that is known as a fixed dose combination product and it is reviewed pursuant to the FDA's Combination Rule at 21 CFR 300.50. The rule provides that two or more drugs may be combined in a single dosage form when each component contributes to the claimed effects and the dosage of each component (amount, frequency, duration) is such that the combination is safe and effective for a significant patient population requiring such concurrent therapy as defined in the labeling for the drug.

But not all combination therapy falls under the category of a fixed dose combination. For example, the FDA recognizes that two drugs in separate dosage forms and in separate packaging, that otherwise might be administered as monotherapy for an indication, also may be used in combination for the same indication. In 2013, the FDA issued guidance to assist sponsors that were developing the range of combination therapies that fall outside the category of fixed dose combinations. That guidance provides recommendations and advice on such topics as: (1) assessment at the outset whether two or more therapies are appropriate for use in combination; (2) guiding principles for nonclinical and clinical development of the combination; (3) options for regulatory pathways to seek marketing approval of the combination; and (4) post-marketing safety monitoring and reporting obligations. Given the wide range of potential combination therapy variations, the FDA indicated it intends to assess each potential combination on a case-by case basis and encouraged sponsors to engage in early and regular consultation with the relevant review division at the agency throughout the development process for its proposed combination.

Regulation of Combination Products

Certain therapeutic products are comprised of multiple components, such as drug components and device components, that would normally be subject to different regulatory frameworks by the FDA and frequently regulated by different centers at the FDA. These products are known as combination products. Under the FDCA, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. The determination of which center will be the lead center is based on the "primary mode of action" of the combination product. Thus, if the primary mode of action of a drug-device combination product is attributable to the drug product, the FDA center responsible for premarket review of the drug product would have primary jurisdiction for the combination product. The FDA has also established the Office of Combination Products to address issues surrounding combination products and provide more certainty to the regulatory review process. That office serves as a focal point for combination product issues for agency reviewers and industry. It is also responsible for developing guidance and regulations to clarify the regulation of combination products, and for assignment of the FDA center that has primary jurisdiction for review of combination products where the jurisdiction is unclear or in dispute. A combination product with a primary mode of action attributable to the drug or biologic component generally would be reviewed and approved pursuant to the drug or biologic approval processes set forth in the FDCA. In reviewing the NDA or BLA for such a product, however, FDA reviewers would consult with their counterparts in the FDA's Center for Devices and Radiological Health to ensure that the device component of the combination product met applicable requirements regarding safety, effectiveness, durability and performance. In addition, under FDA regulations, combination products are subject to cGMP requirements applicable to both drugs and devices, including the Quality System Regulation applicable to medical devices.

Complementary Diagnostics

The success of our product candidates may depend, in part, on the development and commercialization of a complementary diagnostic. Complementary diagnostics can identify patients who are most likely to benefit from a particular therapeutic product; identify patients likely to be at increased risk for serious side effects as a result of treatment with a particular therapeutic product; or monitor response to treatment with a particular therapeutic

product for the purpose of adjusting treatment to achieve improved safety or effectiveness. Complementary diagnostics are regulated as medical devices by the FDA. The level of risk associated with a new diagnostic test combined with available controls to mitigate risk determines whether a complementary diagnostic device requires Premarket Approval ("PMA") from the FDA or if it can be cleared by the agency through the 510(k) premarket notification process based on a showing of substantial equivalence to a commercially available device. The use of the complementary diagnostic device will be stipulated in the labeling of the therapeutic product, and vice versa.

Post-Approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing user fee requirements, under which the FDA assesses an annual program fee for each product identified in an approved BLA. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMPs, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMPs and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMPs and other aspects of regulatory compliance.

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

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

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in

accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Biosimilars and Reference Product Exclusivity

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

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

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

A reference biologic is granted twelve years of exclusivity from the time of first licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against other biologics submitted under the abbreviated approval pathway for the lesser of (i) one year after the first commercial marketing, (ii) 18 months after approval if there is no legal challenge, (iii) 18 months after the resolution in the applicant's favor of a lawsuit challenging the biologics' patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs

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

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

Other Healthcare Laws and Compliance Requirements

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

The AKS prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, to induce, or in return for, either the referral of an individual, or the purchase or recommendation of an item or service for which payment may be made under any federal healthcare program. The term remuneration has been interpreted broadly to include anything of value.

The AKS has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand, and prescribers and purchasers on the other. The government often takes the position that to violate the AKS, only one purpose of the remuneration need be to induce referrals, even if there are other legitimate purposes for the remuneration. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from AKS prosecution, but they are drawn narrowly and practices that involve remuneration, such as consulting agreements, that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the AKS. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Civil and criminal false claims laws, including the FCA, and civil monetary penalty laws, which can be enforced through civil whistleblower or qui tam actions, prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment of federal government funds, including in federal healthcare programs, that are false or fraudulent. Pharmaceutical and other healthcare companies have been prosecuted under these laws for engaging in a variety of different types of conduct that "caused" the submission of false claims to federal healthcare programs. Under the AKS, for example, a claim resulting from a violation of the AKS is deemed to be a false or fraudulent claim for purposes of the FCA.

HIPAA created additional federal criminal statutes that prohibit, among other things, executing a scheme to defraud any healthcare benefit program, including private third-party payors, and making false statements relating to healthcare matters. A person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate the statute in order to have committed a violation.

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

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

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

Data Privacy and Security

Numerous state, federal, and foreign laws govern the collection, dissemination, use, access to, confidentiality, and security of personal information, including health-related information. In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations, govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. For example, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health ("HITECH"), and their respective implementing regulations imposes data privacy, security, and breach notification obligations on certain health care providers, health plans, and health care clearinghouses, known as covered entities, as well as their business associates and their covered subcontractors that perform certain services that involve using, disclosing, creating, receiving, maintaining, or transmitting individually identifiable protected health information ("PHI") for or on behalf of such covered entities. These requirements imposed by HIPAA and the HITECH Act on covered entities and business associates include entering into agreements that require business associates protect PHI provided by the covered entity against improper use or disclosure, among other things; following certain standards for the privacy of PHI, which limit the disclosure of a patient's past, present, or future physical or mental health or condition or information about a patient's receipt of health care if the information identifies, or could reasonably be used to identify, the individual; ensuring the confidentiality, integrity, and availability of all PHI created, received, maintained, or transmitted in electronic form, to identify and protect against reasonably anticipated threats or impermissible uses or disclosures to the security and integrity of such PHI; and reporting of breaches of PHI to individuals and regulators. Entities that are found to be in violation of HIPAA may be subject to significant civil, criminal, and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with the U.S. Department of Health and Human Services ("HHS") to settle allegations of HIPAA non-compliance. A covered entity or business associate is also liable for civil money penalties for a violation that is based on an act or omission of any of its agents, which may include a downstream business associate, as determined according to the federal common law of agency. HITECH also increased the civil and criminal penalties applicable to covered entities and business associates and gave state attorneys general new authority to

file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions. To the extent that we submit electronic healthcare claims and payment transactions that do not comply with the electronic data transmission standards established under HIPAA and HITECH, payments to us may be delayed or denied.

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

In addition, certain state laws, such as the California Consumer Privacy Act of 2018 ("CCPA"), as amended by the California Privacy Rights Act of 2020 ("CPRA"), govern the privacy and security of personal information, including health-related information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. The CCPA/CPRA applies to personal data of consumers, business representatives, and employees, and imposes obligations on certain businesses that do business in California, including to provide specific disclosures in privacy notices, rights to California residents in relation to their personal information. Health information falls under the CCPA/CPRA's definition of personal information where it identifies, relates to, describes, or is reasonably capable of being associated with or could reasonably be linked with a particular consumer or household — unless it is subject to HIPAA — and is included under a new category of personal information, "sensitive personal information," which is offered greater protection. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing. Additionally, our use of artificial intelligence and machine learning may be subject to laws and evolving regulations regarding the use of artificial intelligence/machine learning, controlling for data bias, and antidiscrimination.

In addition, the CPRA expands the CCPA's requirements, including by adding a new right for individuals to correct their personal information and establishing a new regulatory agency to implement and enforce the law. Other states, such as Virginia, Colorado, Connecticut and Utah, have also passed comprehensive privacy laws, and similar laws are being considered in several other states, as well as at the federal and local levels. While the laws in these states, like the CCPA, also exempt some data processed in the context of clinical trials, such developments further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties upon whom we rely.

Coverage and Reimbursement

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

Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical or biological products, medical

devices and medical services, in addition to questioning safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product that receives approval. Decreases in third-party reimbursement for any product or a decision by a third-party not to cover a product could reduce physician usage and patient demand for the product.

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

In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. The IRA provides CMS with significant new authorities intended to curb drug costs and to encourage market competition. For the first time, CMS will be able to directly negotiate prescription drug prices and to cap out-of-pocket costs. Each year, CMS will select and negotiate a preset number of high-spend drugs and biologics that are covered under Medicare Part B and Part D that do not have generic or biosimilar competition. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations. These price negotiations will begin in 2023, although the Medicare drug price negotiation program is currently subject to legal challenges. The IRA also provides a new “inflation rebate” covering Medicare patients that took effect in 2023 and is intended to counter certain price increases in prescriptions drugs. The inflation rebate provision will require drug manufacturers to pay a rebate to the federal government if the price for a drug or biologic under Medicare Part B and Part D increases faster than the rate of inflation. To support biosimilar competition, beginning in October 2022, qualifying biosimilars may receive a Medicare Part B payment increase for a period of five years. Separately, if a biologic drug for which no biosimilar exists delays a biosimilar’s market entry beyond two years, CMS will be authorized to subject the biologics manufacturer to price negotiations intended to ensure fair competition. Notwithstanding these provisions, the IRA’s impact on commercialization and competition remains largely uncertain.

Healthcare Reform

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

The ACA, which was enacted in March 2010, substantially changed the way healthcare is financed by both governmental and private insurers in the United States, and significantly affected the pharmaceutical industry. The ACA contains a number of provisions of particular import to the pharmaceutical and biotechnology industries, including, but not limited to, those governing enrollment in federal healthcare programs, a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and annual fees based on pharmaceutical companies’ share of sales to federal health care programs. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, the IRA, among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also

eliminates the “donut hole” under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program.

Other legislative changes have been proposed and adopted since the ACA was enacted, including automatic aggregate reductions of Medicare payments to providers of on average 2% per fiscal year as part of the federal budget sequestration under the Budget Control Act of 2011. These reductions went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect until 2032 unless additional action is taken by Congress.

In addition, the Bipartisan Budget Act of 2018, among other things, amended the Medicare Act (as amended by the ACA) to increase the point-of-sale discounts that manufacturers must agree to offer under the Medicare Part D coverage discount program from 50% to 70% off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs being covered under Medicare Part D.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state measures designed to, among other things, reduce the cost of prescription drugs, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, in May 2019, CMS adopted a final rule allowing Medicare Advantage Plans the option to use step therapy for Part B drugs, permitting Medicare Part D plans to apply certain utilization controls to new starts of five of the six protected class drugs, and requiring the Explanation of Benefits for Part D beneficiaries to disclose drug price increases and lower cost therapeutic alternatives, which went into effect on January 1, 2021. In response to the Biden administration’s October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. Further, on December 7, 2023, the Biden administration announced an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework.

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

Other Government Regulation Outside of the United States

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

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

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

Regulation in the European Union

European Data Laws

The collection and use of personal health data and other personal data in the EU is governed by the provisions of the European General Data Protection Regulation (EU) 2016/679 ("GDPR"), which came into force in May 2018, and related data protection laws in individual EU Member States. The GDPR imposes a number of strict obligations and restrictions on the ability to process, including collecting, analyzing and transferring, personal data of individuals, in particular with respect to health data from clinical trials and adverse event reporting. The GDPR includes requirements relating to the legal basis of the processing (such as consent of the individuals to whom the personal data relates), the information provided to the individuals prior to processing their personal data, the notification obligations to the national data protection authorities, and the security and confidentiality of the personal data. EU Member States may also impose additional requirements in relation to health, genetic and biometric data through their national legislation.

In addition, the GDPR imposes specific restrictions on the transfer of personal data to countries outside of the European Economic Area ("EEA") that are not considered by the European Commission ("EC") to provide an adequate level of data protection. Appropriate safeguards are required to enable such transfers. Among the appropriate safeguards that can be used, the data exporter may use the standard contractual clauses ("SCCs"). With regard to the transfer of data from the EEA to the United States, on July 10, 2023, the EC adopted its adequacy decision for the EU-US Data Privacy Framework. On the basis of the new adequacy decision, personal data can flow from the EEA to U.S. companies participating in the framework.

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

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

With regard to the transfer of personal data from the EEA to the UK, personal data may now freely flow from the EEA to the UK since the UK is deemed to have an adequate data protection level.

However, the adequacy decisions include a 'sunset clause' which entails that the decisions will automatically expire four years after their entry into force. Additionally, following the UK's withdrawal from the EU and the EEA, companies also have to comply with the UK's data protection laws (including the UK GDPR (as defined in section 3(10) (as supplemented by section 205(4)) of the Data Protection Act 2018 (the "DPA 2018")), the DPA 2018, and related data protection laws in the UK). Separate from the fines that can be imposed by the GDPR, the UK regime has the ability to fine up to the greater of £17.5 million or 4% of global turnover.

Following the UK's withdrawal from the EU and the EEA, companies are subject to specific transfer rules under the UK regime; personal data may flow freely from the UK to the EEA, since the EEA is deemed to have an adequate data protection level for purposes of the UK regime. These UK international transfer rules broadly mirror the GDPR rules. On February 2, 2022, the UK Secretary of State laid before the UK Parliament the international data transfer agreement ("IDTA") and the international data transfer addendum to the EC's standard contractual clauses for international data transfers (Addendum) and a document setting out transitional provisions. The IDTA and Addendum came into force on March 21, 2022 and replaced the old SCCs for the purposes of the UK regime. However, the transitional provisions, adopted with the IDTA and the Addendum, provide that contracts concluded on or before September 21, 2022 on the basis of any old SCCs continue to provide appropriate safeguards for the purpose of the UK regime until March 21, 2024, provided that the processing operations that are the subject matter of the contract remain unchanged and reliance on those clauses ensures that the transfer of personal data is subject to appropriate safeguards.

With regard to the transfer of personal data from the UK to the United States, the UK government has adopted an adequacy decision for the United States, the UK-US Data Bridge, which came into force on October 12, 2023. The UK-US Data Bridge recognizes the United States as offering an adequate level of data protection where the transfer is to a U.S. company participating in the EU-US Data Privacy Framework and the UK Extension.

Drug and Biologic Development Process

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

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

A more unified procedure will apply under the new CTR. A sponsor will be able to submit a single application for approval of a clinical trial through a centralized EU clinical trials portal (the "CTIS"). One national regulatory

authority (the reporting EU member state proposed by the applicant) will take the lead in validating and evaluating the application and consult and coordinate with the other concerned EU Member States. If an application is rejected, it may be amended and resubmitted through the EU clinical trials portal. If an approval is issued, the sponsor may start the clinical trial in all concerned EU Member States. However, a concerned EU member state may in limited circumstances declare an "opt-out" from an approval and prevent the clinical trial from being conducted in such member state. The CTR also aims to streamline and simplify the rules on safety reporting, and introduces enhanced transparency requirements such as mandatory submission of a summary of the clinical trial results to the EU Database. The CTR foresees a three-year transition period. EU Member States will work in CTIS immediately after the system has gone live. Since January 31, 2023, submission of initial clinical trial applications via CTIS is mandatory, and by January 31, 2025, all ongoing trials approved under the former Clinical Trials Directive will need to comply with the CTR and have to be transitioned to CTIS. On July 19, 2023, the EC published guidance concerning the steps to be taken in this transition. This guidance provides, among other things, that (i) documentation which was previously assessed will not be reassessed, (ii) templates that were developed and endorsed by the EU Clinical Trials Expert Group to provide compliance with the CTR do not need to be updated and (iii) there is no need to retrospectively create a site suitability form, which are only necessary for new trial sites.

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

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

Drug Marketing Authorization

In the EEA, after completion of all required clinical testing, pharmaceutical products may only be placed on the market after obtaining a MA. To obtain a MA of a drug under European Union regulatory systems, an applicant can submit an MAA through, amongst others, a centralized or decentralized procedure.

To be used or sold in the UK, a drug must have an effective MA obtained by a centralized application through EMA or a national application. National applications are governed by the Human Medicines Regulations (SI 2012/1916). Applications are made electronically through the Medicines and Healthcare products Regulatory Agency ("MHRA") Submissions Portal. The process from application to authorizations generally takes up to 210 days, excluding time taken to provide any additional information or data required by the MHRA.

On August 30, 2023, the MHRA published detailed guidance on its recently announced new International Reliance Procedure ("IRP") for MAAs. The IRP applies since January 1, 2024 and replaces existing EU reliance procedures to apply for authorizations from seven international regulators (e.g. Health Canada, Swiss Medic, FDA, EMA, among others). The IRP allows medicinal products approved in other jurisdictions that meet certain criteria to undergo a fast-tracked MHRA review to obtain and/or update a MA in the UK or Great Britain.

Applicants can submit initial MAAs to the IRP but the procedure can also be used throughout the lifecycle of a product for post-authorization procedures including line extensions, variations and renewals.

Centralized Authorization Procedure

The centralized procedure provides for the grant of a single MA that is issued by the EC following the scientific assessment of the application by the EMA that is valid for all EU Member States as well as in the three additional EEA Member States. The centralized procedure is compulsory for certain types of medicinal products, including for medicines developed by means of certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products ("ATMP") and medicinal products with a new active substance indicated for the treatment of certain diseases (AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases). For medicinal products containing a new active substance not yet authorized in the EEA before May 20, 2004 and indicated for the treatment of other diseases, medicinal products that constitute significant therapeutic, scientific or technical innovations or for which the grant of a MA through the centralized procedure would be in the interest of public health at EU level, an applicant may voluntarily submit an application for a MA through the centralized procedure.

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

Decentralized Authorization Procedure

Medicines that fall outside the mandatory scope of the centralized procedure have three routes to authorization: (i) they can be authorized under the centralized procedure if they concern a significant therapeutic, scientific or technical innovation, or if their authorization would be in the interest of public health; (ii) they can be authorized under a decentralized procedure where an applicant applies for simultaneous authorization in more than one EU member state; or (iii) they can be authorized in an EU member state in accordance with that state's national procedures and then be authorized in other EU countries by a procedure whereby the countries concerned agree to recognize the validity of the original, national MA (mutual recognition procedure).

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

Risk Management Plan

All new MAAs must include a Risk Management Plan ("RMP") describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the

product. RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available. An updated RMP must be submitted: (i) at the request of EMA or a national competent authority, or (ii) whenever the risk-management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit-risk profile or as a result of an important pharmacovigilance or risk-minimization milestone being reached. The regulatory authorities may also impose specific obligations as a condition of the MA. Since October 20, 2023, all RMPs for centrally authorized products are published by the EMA, subject only to limited redactions.

MA Validity Period

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

Additionally, the holder of a MA for an ATMP must put in place and maintain a system to ensure that each individual product and its starting and raw materials, including all substances coming into contact with the cells or tissues it may contain, can be traced through the sourcing, manufacturing, packaging, storage, transport and delivery to the relevant healthcare institution where the product is used.

Any authorization which is not followed by the actual placing of the drug on the EU market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid.

For the UK, the period of three years during which the drug has not been marketed in Great Britain will be restarted from the date of conversion to a Great Britain MA. Conversion refers to the procedure by which, as of January 1, 2021, MAs granted on the basis of a centralized procedure in the EU are only valid in Norther Ireland but not in Great Britain, whereas, prior EU authorizations have all been automatically converted into UK MAs effective in Great Britain only.

On the other hand, for the EU, in the case the drug has been marketed in the UK, the placing on the UK market before the end of the period starting when the UK left the EU on January 31, 2020 and ending on December 31, 2020 (the “Brexit Transition Period”) will be taken into account. If, after the end of the Brexit Transition Period, the drug is not placed on any other market of the remaining member states of the EU, the three year period will start running from the last date the drug was placed on the UK market before the end of the Brexit Transition Period.

Advanced Therapy Medicinal Products

In the EU, medicinal products, including ATMPs are subject to extensive pre- and post-market regulation by regulatory authorities at both the EU and national levels. ATMPs comprise gene therapy products, somatic cell therapy products and tissue engineered products, which are genes, cells or tissues that have undergone substantial manipulation and that are administered to human beings in order to cure, diagnose or prevent diseases or regenerate, repair or replace a human tissue. Pursuant to the ATMP Regulation, the Committee on Advanced Therapies (“CAT”) is responsible in conjunction with the CHMP for the evaluation of ATMPs. The CHMP and CAT are also responsible for providing guidelines on ATMPs. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs. Although such guidelines are not legally binding, compliance with them is often necessary to gain and maintain approval for product candidates.

In addition to the mandatory RMP, the holder of a MA for an ATMP must put in place and maintain a system to ensure that each individual product and its starting and raw materials, including all substances coming into

contact with the cells or tissues it may contain, can be traced through the sourcing, manufacturing, packaging, storage, transport and delivery to the relevant healthcare institution where the product is used.

Exceptional Circumstances/Conditional Approval

Similar to accelerated approval regulations in the United States, conditional MAs can be granted in the EU in exceptional circumstances. A conditional MA can be granted for medicinal products where, although comprehensive clinical data referring to the safety and efficacy of the medicinal product have not been supplied, a number of criteria are fulfilled: (i) the benefit/risk balance of the product is positive, (ii) it is likely that the applicant will be in a position to provide the comprehensive clinical data, (iii) unmet medical needs will be fulfilled by the grant of the MA and (iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional MA must be renewed annually.

Data and Market Exclusivity

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

An additional non-cumulative one-year period of marketing exclusivity is possible if during the data exclusivity period (the first eight years of the 10-year marketing exclusivity period), the MA holder obtains an authorization for one or more new therapeutic indications that are deemed to bring a significant clinical benefit compared to existing therapies.

The data exclusivity period begins on the date of the product's first MA in the EU. After eight years, a generic product application may be submitted and generic companies may rely on the MA holder's data. However, a generic product cannot launch until two years later (or a total of 10 years after the first MA in the EU of the innovator product), or three years later (or a total of 11 years after the first MA in the EU of the innovator product) if the MA holder obtains MA for a new indication with significant clinical benefit within the eight-year data exclusivity period. Additionally, another non-cumulative one-year period of data exclusivity can be added to the eight years of data exclusivity where an application is made for a new indication for a well-established substance, provided that significant pre-clinical or clinical studies were carried out in relation to the new indication.

Another year of data exclusivity may be added to the eight years, where a change of classification of a pharmaceutical product has been authorized on the basis of significant pre-trial tests or clinical trials (when examining an application by another applicant for or holder of MA for a change of classification of the same substance the competent authority will not refer to the results of those tests or trials for one year after the initial change was authorized).

Products may not be granted data exclusivity since there is no guarantee that a product will be considered by the EU's regulatory authorities to include a NCE. Even if a compound is considered to be a NCE and the MA applicant is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of the medicinal product if such company can complete a full MAA with their own complete database of pharmaceutical tests, preclinical studies and clinical trials and obtain MA of its product.

On April 26, 2023, the EC submitted a proposal for the reform of the European pharmaceutical legislation. The current draft envisages e.g., a shortening of the periods of data exclusivity, however, there is currently neither a final version of this draft nor a date for its entry into force.

Orphan Designation and Exclusivity

The criteria for designating an orphan medicinal product in the EU are similar in principle to those in the U.S. The EMA grants orphan drug designation if the medicinal product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting no more than five in 10,000 persons in the EU (prevalence criterion). In addition, orphan drug designation can be granted if, for economic reasons, the medicinal product would be unlikely to be developed without incentives and if there is no other satisfactory method approved in the EU of diagnosing, preventing, or treating the condition, or if such a method exists, the proposed medicinal product is a significant benefit to patients affected by the condition. An application for orphan drug designation (which is not a MA, as not all orphan-designated medicines reach the authorization application stage) must be submitted first before an application for MA of the medicinal product is submitted. The applicant will receive a fee reduction for the MAA if the orphan drug designation has been granted, but not if the designation is still pending at the time the MA is submitted, and sponsors must submit an annual report to EMA summarizing the status of development of the medicine. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Designated orphan medicines are eligible for conditional MA.

The EMA's Committee for Orphan Medicinal Products ("COMP") reassesses the orphan drug designation of a product in parallel with the review for a MA; for a product to benefit from market exclusivity it must maintain its orphan drug designation at the time of MA review by the EMA and approval by the EC. Additionally, any MA granted for an orphan medicinal product must only cover the therapeutic indication(s) that are covered by the orphan drug designation. Upon the grant of a MA, orphan drug designation provides up to ten years of market exclusivity in the orphan indication.

During the 10-year period of market exclusivity, with a limited number of exceptions, the regulatory authorities of the EU Member States and the EMA may not accept applications for MA, accept an application to extend an existing MA or grant a MA for other similar medicinal products for the same therapeutic indication. A similar medicinal product is defined as a medicinal product containing a similar active substance or substances as contained in a currently authorized orphan medicinal product, and which is intended for the same therapeutic indication. An orphan medicinal product can also obtain an additional two years of market exclusivity for an orphan-designated condition when the results of specific studies are reflected in the Summary of Product Characteristics ("SmPC") addressing the pediatric population and completed in accordance with a fully compliant Pediatric Investigation Plan ("PIP"). No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

The 10-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, i.e. the condition prevalence or financial returns criteria under Article 3 of Regulation (EC) No. 141/2000 on orphan medicinal products. When the period of orphan market exclusivity for an indication ends, the orphan drug designation for that indication expires as well. Orphan exclusivity runs in parallel with normal rules on data exclusivity and market protection. Additionally, a MA may be granted to a similar medicinal product (orphan or not) for the same or overlapping indication subject to certain requirements.

In the UK, following the post-Brexit transition period, a system for incentivizing the development of orphan medicines was introduced. Overall, the requirements for orphan designation largely replicate the requirements in the EU and the benefit of market exclusivity has been retained. Products with an orphan designation in the EU can be considered for an orphan MA in Great Britain, but a UK-wide orphan MA can only be considered in the absence of an active EU orphan designation. The MHRA will review applications for orphan designation at the time of a MA, and will offer incentives, such as market exclusivity and full or partial refunds for MA fees to encourage the development of medicines in rare diseases.

Pediatric Development

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

In the UK, the MHRA has published guidance on the procedures for UK PIPs which, where possible, mirror the submission format and requirements of the EU system. EU PIPs remain applicable for Northern Ireland and EU PIPs agreed by the EMA prior to January 1, 2021 have been adopted as UK PIPs.

PRIME Designation

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

Post-Approval Regulation

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

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

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

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

These pharmacovigilance rules can impose on holders of MAs the obligation to conduct a labor intensive collection of data regarding the risks and benefits of marketed medicinal products and to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies or post-authorization safety studies to obtain further information on a medicine's safety, or to measure the effectiveness of risk-management measures, which may be time consuming and expensive and could impact our profitability. MA holders must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of Periodic Safety Update Reports ("PSURs") in relation to medicinal products for which they hold MAs. The EMA reviews PSURs for medicinal products authorized through the centralized procedure. If the EMA has concerns that the risk benefit profile of a product has varied, it can adopt an opinion advising that the existing MA for the product be suspended, withdrawn or varied. The agency can advise that the MA holder be obliged to conduct post-authorization Phase IV safety studies. If the EC agrees with the opinion, it can adopt a decision varying the existing MA. Failure by the MA holder to fulfill the obligations for which the EC's decision provides can undermine the ongoing validity of the MA.

More generally, non-compliance with pharmacovigilance obligations can lead to the variation, suspension or withdrawal of the MA for the product or imposition of financial penalties or other enforcement measures.

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

Sales and Marketing Regulations

The advertising and promotion of our products is also subject to EU laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other national legislation of individual EU Member States may apply to the advertising and promotion of medicinal products and may differ from one country to another. These laws require that promotional materials and

advertising in relation to medicinal products comply with the product's SmPC as approved by the competent regulatory authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the MA granted for the medicinal product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. All advertising and promotional activities for the product must be consistent with the approved SmPC and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription-only medicines is also prohibited in the EU. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on its promotional activities with healthcare professionals.

EU regulation with regards to dispensing, sale and purchase of medicines has generally been preserved in the UK following Brexit, through the Human Medicines Regulations 2012. However, organizations wishing to sell medicines online need to register with the MHRA. Following Brexit, the requirements to display the common logo no longer apply to UK-based online sellers, except for those established in Northern Ireland.

Anti-Corruption Legislation

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

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

In the UK, the pharmaceutical sector is recognized as being particularly vulnerable to corrupt practices, some of which fall within the scope of the Bribery Act 2010. Due to the Bribery Act 2010's far-reaching territorial application, the potential penalized act does not have to occur in the UK to become within its scope. If the act or omission does not take place in the UK, but the person's act or omission would constitute an offense if carried out there and the person has a close connection with the UK, an offense will still have been committed.

The Bribery Act 2010 is comprised of four offenses that cover (i) individuals, companies and partnerships that give, promise or offer bribes, (ii) individuals, companies and partnerships that request, agree to receive or accept bribes, (iii) individuals, companies and partnerships that bribe foreign public officials, and (iv) companies and partnerships that fail to prevent persons acting on their behalf from paying bribes. The penalties imposed under the Bribery Act 2010 depend on the offence committed, harm and culpability and penalties range from unlimited fines to imprisonment for a maximum term of ten years and in some cases both.

Regulations in the UK and Other Markets

The UK formally left the EU on January 31, 2020 and EU laws now only apply to the UK in respect of Northern Ireland as laid out in the Protocol on Ireland and Northern Ireland and as amended by the Windsor Framework sets out a long-term set of arrangements for the supply of medicines into Northern Ireland. The EU and the UK agreed on a trade and cooperation agreement ("TCA"), which includes provisions affecting the life sciences

sector (including on customs and tariffs). There are some specific provisions concerning pharmaceuticals, including the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP issued documents. The TCA does not, however, contain wholesale mutual recognition of UK and EU pharmaceutical regulations and product standards.

The UK government has adopted the Medicines and Medical Devices Act 2021 (the "MMDA") to enable the UK's regulatory frameworks to be updated following the UK's departure from the EU. The MMDA introduces regulation-making, delegated powers covering the fields of human medicines, clinical trials of human medicines, veterinary medicines and medical devices. The MHRA has since been consulting on future regulations for medicines and medical devices in the UK.

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

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

Properties and Facilities

We are a fully remote company and do not maintain physical corporate offices. Our employees work remotely. We believe these arrangements support our current needs. We maintain a mailing address at 221 Crescent St., Building 23, Suite 105, Waltham, MA. As we expand, we believe that suitable additional alternative spaces will be available in the future on commercially reasonable terms, if required.

Legal Proceedings

From time to time, we may become involved in legal proceedings relating to claims arising from the ordinary course of business. Our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations, financial condition or cash flows.

MANAGEMENT

Directors

Our board of directors currently consists of eight directors and is divided into three classes. Each class serves for three years, with the terms of office of the respective classes expiring in successive years. Directors in Class I will stand for election at our Annual Meeting expected to be held in June 2026. The terms of office of directors in Class II and Class III do not expire until the annual meetings of stockholders held in 2024 and 2025, respectively. Peter Harwin and Tomas Kiselak were designated by entities affiliated with Fairmount.

Our current directors, and their ages, occupations and length of board service as of April 1, 2024, are provided in the table below. Additional biographical descriptions of each director are set forth in the text below the table. These descriptions include the primary individual experience, qualifications, qualities and skills of each of our directors.

Name of Director	Age	Principal Occupation	Director Since
Class I Directors:			
Mark McKenna	48	Chief Investment Officer and Managing Director, McKenna Capital Partners; Chairman, Apogee Therapeutics, Inc.	2024
Cameron Turtle	34	Chief Executive Officer of Spyre Therapeutics, Inc.	2023
Laurie Stelzer (1)(2)	56	Chief Financial Officer of ReNAgade Therapeutics, Inc.	2023
Class II Directors:			
Russell J. Cox (1)(3)	60	President and Chief Executive Officer, Epirium Bio, Inc.	2015
Jeffrey W. Albers (2)(3)	52	Chairman of Blueprint Medicines Corporation and Venture Partner at Atlas Venture	2023
Tomas Kiselak (3)	37	Managing Member, Fairmount Funds Management LLC; Director, Dianthus Therapeutics, Inc.; Director, Viridian Therapeutics, Inc.; Director, Apogee Therapeutics, Inc.; and Director, Paragon Therapeutics, Inc.	2023
Class III Directors:			
Peter Harwin (1)	37	Managing Member, Fairmount Funds Management LLC; Director, Cogent Biosciences, Inc.; Director, Viridian Therapeutics, Inc.; Director, Apogee Therapeutics, Inc.; and Director, Paragon Therapeutics, Inc.	2023
Michael Henderson (2)	34	Chief Executive Officer of Apogee Therapeutics, Inc.	2023

(1) Member of the nominating and corporate governance committee.
(2) Member of the audit committee.
(3) Member of the compensation committee.

Cameron Turtle, DPhil. Dr. Turtle joined us as Chief Operating Officer in June 2023, and was appointed as our Chief Executive Officer and 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 biotechnology 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 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, San Francisco Business Times 40 Under 40, and the Biocom Life Sciences Catalyst Award.

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

Russell J. Cox. Mr. Cox has served as a director since June 2015 and has served as Chair of our board of directors since January 2019. Mr. Cox has served as President and Chief Executive Officer of Epirium Bio, Inc. since July 2019. Mr. Cox previously served as Chief Executive Officer at Vital Therapies, Inc. from January 2018 to January 2019. Additionally, Mr. Cox served as Executive Vice President and Chief Operating Officer at Jazz
Pharmaceuticals plc, a publicly traded biopharmaceutical company, from May 2014 to January 2018, where he also served as Executive Vice President and Chief Commercial Officer from March 2012 to May 2014 and as Senior Vice President, Sales and Marketing from July 2010 until February 2012. Prior to that, Mr. Cox served in a variety of senior management roles since joining Jazz Pharmaceuticals, Inc. (the predecessor to Jazz Pharmaceuticals plc) in July 2010. From January 2009 to January 2010, he served as Senior Vice President and Chief Commercial Officer of Ipsen Group, a publicly traded pharmaceutical company, and from 2007 until December 2008, he served as Vice President of Marketing at Tercica, Inc. (acquired by Ipsen Group), a biotechnology company. From 2003 to 2007, Mr. Cox was with Scios Inc. (acquired by Johnson and Johnson in 2003), where he also served as Vice President, Marketing. Prior to 2003, Mr. Cox was with Genentech, Inc. for 12 years, where he was a Product Team Leader responsible for the Growth Hormone franchise and led numerous product launches as a Group Product Manager. Mr. Cox currently serves on the boards of directors of Epirium Bio, Inc. and Gossamer Bio, Inc. Mr. Cox received a B.S. in Biomedical Science from Texas A&M University.

We believe Mr. Cox is qualified to serve on our board of directors due to his commercial and operating experience in the biopharmaceutical industry.

Jeffrey W. Albers. 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 is currently Chairman of Blueprint Medicines Corporation (Nasdaq: BPMC), a global precision therapy company, since January 2023, 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 commercial and business functions. 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 that Mr. Albers is qualified to serve on our board of directors due to his extensive leadership experience in the biopharmaceutical industry.

Mark McKenna. Mr. McKenna has served as a director since February 2024. Mr. McKenna currently serves as Chief Investment Officer and Managing Director of McKenna Capital Partners, a family office dedicated to investing in breakthrough treatments for debilitating diseases, since June 2023. Mr. McKenna most recently served as the President and Chief Executive Officer and as 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, he served as President of Salix Pharmaceuticals, Inc., a pharmaceutical company and wholly-owned subsidiary of Bausch Health Companies, Inc., from March 2016 through August 2019. Prior to Salix, 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. Before joining Bausch + Lomb, he held several positions with Johnson & Johnson. Mr. McKenna has served as chair of the board of directors of Apogee Therapeutics, Inc. (Nasdaq: APGE) since August 2023. Mr. McKenna received a B.S. in Marketing from Arizona State University and an M.B.A. from Azusa Pacific University.

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

Laurie Stelzer. Ms. Stelzer has served as Chief Financial Officer of ReNAgade Therapeutics, Inc., a biotechnology company focused on RNA therapeutics, since September 2023. Prior to joining ReNAgade, Ms. Stelzer served as Chief Financial Officer of Mirati Therapeutics, Inc. (Nasdaq: MRTX), a commercial-stage targeted oncology company ("Mirati"), 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 Halozyme 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 Halozyme 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 PMV Pharmaceuticals, Inc. (Nasdaq: PMVP), a precision oncology company, since 2020, Surface Oncology, Inc. (Nasdaq: SURF), a clinical-stage immuno-oncology 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 of directors because of her financial expertise and experience within the biopharmaceutical industry.

Peter Harwin. Peter 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 Viridian Therapeutics, Inc. (Nasdaq: VRDN), Apogee Therapeutics, Inc. (Nasdaq: APGE) and Paragon Therapeutics, Inc. Mr. Harwin holds a B.B.A. from Emory University.

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

Tomas Kiselak. Tomas 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 currently 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), Dianthus Therapeutics, Inc. (Nasdaq: DNTH) as well as several private companies. He received a B.S. in neuroscience and economics from Amherst College.

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

Michael Henderson, M.D. Michael Henderson, M.D. has served as a director since June 2023. Dr. Henderson is 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 has served on the board of directors of ARYA Sciences Acquisition Corp IV (Nasdaq: ARYD), a special purpose acquisition company focused on the healthcare industry, since February 2021. 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 of directors because of his experience in business leadership, drug development, and commercial strategy in the area of life sciences.

Director Independence

Our board of directors determines the independence of our directors by applying the applicable rules, regulations and listing standards of 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 of directors, would interfere with the exercise of his or her independent judgment in carrying out the responsibilities of a director. They also specify various relationships that preclude a determination of director independence. Such relationships may include employment, commercial, accounting, family and other business, professional and personal relationships.

Applying these standards, the board reviews the independence of our directors, taking into account all relevant facts and circumstances. After considering the foregoing factors, our board of directors has determined that the following members of our board are currently independent as determined under applicable rules, regulations and listing standards of Nasdaq: Mr. Russell Cox, Ms. Laurie Stelzer, Mr. Jeffrey W. Albers, Mr. Peter Harwin, Mr. Tomas Kiselak and Dr. Michael Henderson.

All members of our audit committee, compensation committee and nominating and corporate governance committee must be independent directors under the applicable rules, regulations and listing standards of Nasdaq. Members of the audit committee also must satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act. Members of the compensation committee also must satisfy the independence criteria set forth in Rule 10C under the Exchange Act, and related Nasdaq listing standards with respect to their affiliation with us and any consulting, advisory or other fees they may have received from us. Our board of directors has determined that all members of our audit committee, compensation committee and nominating and corporate governance committee are independent and satisfy the relevant SEC, Exchange Act and Nasdaq independence requirements for such committees.

Executive Officers

The names of our current executive officers, their ages as of April 1, 2024, and their positions are shown below.

Name	Age	Position
Cameron Turtle, DPhil(1)	34	Chief Executive Officer
Scott Burrows	47	Chief Financial Officer
Heidy King-Jones	41	Chief Legal Officer and Corporate Secretary

(1) For Dr. Turtle's biographical information, see "Directors" above.

Our board of directors chooses executive officers, who then serve at the board's discretion.

Scott Burrows. Mr. Burrows joined as our Chief Financial Officer in September 2023. Prior to becoming Chief Financial Officer, Mr. Burrows most recently served as the Chief Financial Officer of Arcutis Biotherapeutics, Inc. ("Arcutis") (Nasdaq: ARQT) 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 based in Switzerland. 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. 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. through various financings, the approval of Tzield®, the companies 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. 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., 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.

Family Relationships

There are no family relationships among our directors and executive officers.

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 principal executive officer during any part of fiscal year 2023, and each of our two other most highly compensated executive officers (collectively, our "Named Executive Officers" or "NEOs") during fiscal year 2023. The compensation provided to our Named Executive Officers for fiscal year 2023 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 fiscal year 2023 were:

Name	Title
Cameron Turtle	Chief Executive Officer(1)
Scott Burrows	Chief Financial Officer(2)
Heidy King-Jones	Chief Legal Officer and Corporate Secretary (3)
Jeffrey M. Goldberg	Former President and Chief Executive Officer (4)
Jonathan Alspaugh	Former Chief Financial Officer(5)

(1) In connection with the Asset Acquisition, Dr. Turtle was appointed Chief Operating Officer of the Company effective June 22, 2023. On November 22, 2023, Dr. Turtle was promoted to Chief Executive Officer of the Company.
(2) Mr. Burrows was appointed Chief Financial Officer of the Company effective September 1, 2023.
(3) Ms. King-Jones was appointed Chief Legal Officer and Corporate Secretary effective September 1, 2023.
(4) Mr. Goldberg's employment with the Company as President and Chief Executive Officer was terminated effective May 16, 2023, and he was succeeded by Mr. Alspaugh as the principal executive officer. Mr. Alspaugh's employment with the Company was terminated effective August 31, 2023.

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 fiscal years ended December 31, 2023 and 2022.

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 *Chief Executive Officer*	2023	272,850	141,000	—	15,500,492	—	5,203	15,919,545
Scott Burrows *Chief Financial Officer*	2023	154,589	175,700	2,452,096	4,767,637	—	1,517	7,551,539
Heidy King-Jones *Chief Legal Officer and Corporate Secretary*	2023	168,724	62,700	—	6,356,857	—	—	6,588,281
Jeffrey M. Goldberg	2023	248,471	—	—	—	—	581,736	830,207
Former President and Chief Executive Officer	2022	54,616	—	—	1,774,952	—	2,917	1,832,485
Jonathan Alspaugh	2023	329,767	735,647	—	7,059,923	—	234,692	8,360,029
Former Chief Financial Officer	2022	425,001	—	—	443,285	130,560	12,994	1,011,840

(1) For 2023, the amounts reported in this column include: (i) discretionary annual bonuses of $141,000 for Mr. Turtle, $60,700 for Mr. Burrows, and $62,700 for Ms. King-Jones; (ii) a sign-on bonus for Mr. Burrows

in connection with the commencement of his employment with the Company during 2023 of $115,000; (iii) retention bonuses totaling $168,247 for Mr. Alspaugh in accordance with his June 21, 2023 incentive agreement, as described in more detail under "*Narrative Disclosure to Summary Compensation Table—Transaction and Retention Bonuses*" below; and (iv) transaction success bonuses totaling $567,400 for Mr. Alspaugh, as described in more detail under "*Narrative Disclosure to Summary Compensation Table—Transaction and Retention Bonuses*" below.

(2) Amounts reported in this column represent the aggregate grant date fair value of restricted stock units ("RSUs") granted to our NEOs, as computed in accordance with ASC 718 based on the closing price of our common stock on the applicable date of grant.

(3) Amounts reported in this column 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 included herein for the fiscal year ended December 31, 2023 for more information regarding the assumptions used in calculating the grant date fair value of stock options.

(4) Amounts reported in this column for 2023 include: (i) matching contributions under our 401(k) plan made during 2023 of $5,203 to Mr. Turtle, $1,517 to Mr. Burrows, $5,092 to Mr. Goldberg, and $13,200 to Mr. Alspaugh, (ii) severance payments and benefits totaling $563,384 for Mr. Goldberg and $211,617 for Mr. Alspaugh as described in more detail under "*Narrative Disclosure to Summary Compensation Table—Separation Agreements*" below; (iii) consulting fees of $9,875 paid to Mr. Alspaugh during 2023 as described in more detail under "*Narrative Disclosure to Summary Compensation Table—Separation Agreements* " below; and (iv) housing allowances and home office expense reimbursements for Mr. Goldberg.

Narrative Disclosure to Summary Compensation Table

In October 2023, our compensation committee adopted a compensation philosophy to frame future compensation decisions for the Company. Under this 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 biopharma companies (with priority places on companies with a similar therapeutic focus) with a market capitalization ranging from $250M to $2B and less than 100 employees. The peer group, which was used in making compensation decisions in connection with Dr. Turtle's promotion to Chief Executive Officer, includes the following companies:

ACELYRIN, Inc.	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.

Elements of Compensation

Base Salary

Each NEOs 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 of directors for approval for our Chief Executive Officer) each NEO's base salary. The base salaries for the NEOs hired during 2023 were established in connection with their appointments, and Dr. Turtle's base salary was subsequently adjusted in connection with his promotion. The table below sets forth the base salary as of December 31, 2023 for each NEO that was employed with us at such time:

Named Executive Officer	Base Salary as of 12/31/2023
Cameron Turtle	$ 625,000
Scott Burrows	$ 455,000
Heidy King-Jones	$ 470,000

Annual Bonus Program

In light of the strategic process and the Asset Acquisition, our compensation committee and the board of directors determined not to utilize an annual bonus program for 2023. Instead, our compensation committee determined that each NEO who was employed as of the payment date would receive an annual bonus for 2023 equal to their target bonus, pro-rated for any partial years of service.

Long-Term Incentive Compensation

In connection with his appointment as Chief Operating Officer of the Company, on June 22, 2023, Dr. Turtle received an initial grant of stock options to purchase 47,297,197 shares of our common stock (1,891,887 shares following our reverse stock split), which vest in equal monthly installments through the fourth anniversary of the grant date. As a result of his promotion to Chief Executive Officer, on November 22, 2023, Dr. Turtle received an additional grant of stock options to purchase 374,000 shares of our common stock, which 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.

In connection with his appointment as Chief Financial Officer of the Company, (i) on September 1, 2023, Mr. Burrows received an initial grant of stock options to purchase 10,121,441 shares of our common stock (404,857 shares following our reverse stock split), which 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, and (ii) on December 22, 2023, Mr. Burrows received an initial grant of 134,953 RSUs, which vest in equal annual installments through the fourth anniversary of the grant date.

In connection with her appointment as Chief Legal Officer of the Company, on September 1, 2023, Ms. King-Jones received an initial grant of stock options to purchase 13,495,255 shares of our common stock (539,810 shares following our reverse stock split), which 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.

As part of the Company's annual grants, Mr. Alspaugh received a grant of stock options to purchase 640,000 shares of our common stock (15,999 shares following our reverse split), which vest in equal monthly installments through the fourth anniversary of the grant date. In connection with the Asset Acquisition, on June 22, 2023, Mr. Alspaugh receive a grant of stock options to purchase 19,787,969 shares of our common stock (791,518 shares following our reverse split), which vest in equal monthly installments through the fourth anniversary of the grant date.

Transaction and Retention Bonuses

Prior to the Asset Acquisition, the Company entered into an incentive agreement with Mr. Alspaugh that provided for (i) a retention bonus equal to Mr. Alspaugh's annual salary pro-rated for the period of time between

April 15, 2023 and the earlier of October 25, 2023 or a termination of employment by the Company without cause and (ii) a transaction bonus equal to (A) 0.5% of the equity value of the Company in a transaction if the equity value is greater than or equal to $15 million but less than $20 million or (B) 1.0% of the equity value of the Company in a transaction if the equity value is greater than or equal to $20 million. In accordance with the incentive agreement, in connection with the Asset Acquisition, Mr. Alspaugh received a transaction bonus of $274,400, and in connection with his separation, he received a retention bonus of $168,247.

In August 2023, our compensation committee approved a bonus to Mr. Alspaugh of $293,000 in recognition of the successful consummation of the transaction to sell assets relating to pegzilarginase to Immedica.

Offer Letters

In connection with their appointments (and, for Dr. Turtle, his promotion to Chief Executive Officer), we entered into offer letters with each of Dr. Turtle, Mr. Burrows and Ms. King-Jones (collectively, the "Offer Letters"). The Offer Letters provide 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 or Change in Control* " below. Mr. Burrow's Offer Letter also provides for a sign-on bonus of $115,000, which is subject to repayment in the event of a termination for cause or resignation without good reason prior to September 1, 2024.

Each of Dr. Turtle, Mr. Burrows and Ms. King-Jones are 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.

Separation Agreements

Jeffrey M. Goldberg

In connection with his termination in May 2023, Mr. Goldberg entered into a separation agreement that provided for the following severance benefits in consideration for a release of claims: (i) $600,000, reflecting 12 months of base salary; (ii) $300,000, reflecting 100% of his annual target bonus; (iii) $15,801, reflecting the estimated amount of his premiums under COBRA for 12 months; (iv) $50,000 as an additional severance payment; and (v) accelerated vesting of 667,756 stock options, representing the stock options that would have vested within the 12-month period following the termination date, which had a value of $1,636,002 on the date of termination.

Jonathan Alspaugh

In connection with his termination in August 2023, Mr. Alspaugh entered into a separation and consulting agreement and general release of claims (the "Separation Agreement") that provided for the following severance benefits in consideration for a release of claims: (i) aggregate severance payments of $623,000 payable in installments over 12 months; (ii) $15,801, reflecting the estimated amount of fully subsidized COBRA coverage for up to 12 months; (iii) a retention bonus of $168,247; (iv) accelerated vesting of all stock options that were scheduled to vest during the 12-month period following the last day of the consulting period described below; (v) extension of the post-termination exercise period of outstanding stock options to six months; and (vi) the opportunity to earn potential transaction bonuses in the event the Company consummates any sale, licensing, disposition or monetization transaction relating to pegtarviliase or any of the Company's legacy development-stage assets prior to June 23, 2024, which had not become earned as of December 31, 2023.

The Separation Agreement also provides that Mr. Alspaugh will provide consulting services to the Company through February 29, 2024 (which consulting period may be extended by mutual agreement of the parties or may be earlier terminated by Mr. Alspaugh, by the Company for cause or as a result of Mr. Alspaugh's death or disability). During the consulting period, Mr. Alspaugh will receive a consulting fee of $500 per hour and will continue to vest in any outstanding stock options.

Outstanding Equity Awards at December 31, 2023

The following table presents information regarding outstanding stock options, RSUs and restricted stock held by each Named Executive Officer as of December 31, 2023. The equity awards reflected below give effect to our 1-for-25 reverse stock split on September 8, 2023.

		Option Awards				Stock Awards	
Name	Grant Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested ($)(1)
Cameron Turtle	6/22/2023	236,485	1,655,402(2)	$ 7.50	6/22/2033		
	11/22/2023(4)	—	374,000(3)	10.39	11/22/2033		
						508,073(5)	10,933,731
Scott Burrows	9/1/2023	—	404,857(3)	$ 14.50	9/1/2033		
	12/22/2023					134,953(6)	2,904,189
Heidy King-Jones	9/1/2023	—	539,810(3)	$ 14.50	9/1/2033		
Jeffrey M. Goldberg	—	—	—	—	—	—	—
Jonathan Alspaugh	7/6/2021	3,866	2,534(2)	$175.75	7/5/2031		
	2/17/2022	3,114	3,685(2)	$ 79.25	2/16/2032		
	8/23/2022	1,732	3,467(2)	$ 17.00	8/22/2032		
	2/23/2023	3,334	12,665(2)	$ 11.00	2/22/2033		
	11/21/2023	98,939	692,579(2)	$ 7.50	6/22/2033		

(1) The market value was determined by multiplying the number of shares by $21.52, the closing price of our common stock as reported on the Nasdaq Capital Market on December 29, 2023, the last trading day of 2023.
(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 was 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 Code. 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 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; (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).

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; (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.

Director Compensation

The following table provides information for the fiscal year ended December 31, 2023 regarding all compensation awarded to, earned by or paid to each person who served as a non-employee director for some portion of 2023. Employees who served on our board during 2023 did not receive additional compensation for such service.

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)(1)	Total ($)
Jeffrey W. Albers(2)	6,250	427,315	433,565
Russell J. Cox	112,500	633,508	746,008
Peter Harwin(3)	27,773	633,508	661,281
Michael Henderson(3)	27,276	633,508	660,784
Tomas Kiselak(3)	24,924	633,508	658,432
V. Bryan Lawlis, Ph.D.(3)	36,264	—	36,264
Alison Lawton	62,500	633,508	696,008
Ivana Magovčević-Liebisch, Ph.D.(4)	62,690	633,508	696,198
Armen Shanafelt, Ph.D.(3)	32,637	—	32,637
Hunter C. Smith(4)	78,478	633,508	711,986
Marcio Souza(3)	38,077	—	38,077
Laurie Stelzer(2)	7,065	427,315	434,380

(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, 2023, 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 See Note 15 to our consolidated financial statements included herein for the fiscal year ended December 31, 2023. 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, 2023, our non-employee directors held the following number of outstanding stock options: (i) Mr. Albers, 50,000; (ii) Mr. Cox, 86,228; (iii) Mr. Harwin, 78,000; (iv) Dr. Henderson, 78,000; (v) Mr. Kiselak, 78,000; (vi) Dr. Lawlis, 0; (vii) Ms. Lawton, 83,208; (viii) Dr. Magovčević-Liebisch, 84,412; (ix) Dr. Shanafelt, 0; (x), Mr. Smith. 73,620; (xi) Mr. Souza, 0; and (xii) Ms. Stelzer, 50,000.

(2) Mr. Albers and Ms. Stelzer were appointed to our board of directors effective as of November 22, 2023.

(3) In connection with the Asset Acquisition, effective as of June 22, 2023, Drs. Lawlis and Shanafelt and Mr. Souza resigned from our board of directors and Messrs. Harwin and Kiselak and Dr. Henderson were appointed to our board of directors.

(4) Dr. Magovčević-Liebisch and Mr. Smith resigned from our board of directors effective as of November 22, 2023.

Non-Employee Director Compensation Arrangements

Each of our non-employee directors receives compensation pursuant to the non-employee director cash and equity compensation program adopted by our board of directors. This program provides for the following annual cash retainers:

Annual Cash Retainer	$40,000
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

In addition, each non-employee director who initially joins our board of directors receives an initial grant of stock options to purchase 50,000 shares of our common stock; however, Messrs. Harwin and Kiselak and Dr. Henderson did not receive an initial grant as a result of their appointments in connection with the Asset Acquisition. The initial stock option grants vest in equal monthly installments over three years.

In connection with the Asset Acquisition, and in lieu of grants made in connection with the 2023 annual meeting, each non-employee director serving immediately following the Asset Acquisition (including Messrs. Harwin, Henderson and Kiselak) received a grant of stock options to purchase 1,950,000 shares of our common stock (or 78,000 shares following our reverse stock split) in June 2023, which stock options vest in equal monthly installments over one year or, if earlier, upon the date of the 2024 annual meeting of stockholders.

Each non-employee director who is serving as of the date of the annual meeting in 2024 will receive a grant of stock options to purchase 20,000 shares of our common stock. Annual stock option grants vest in equal monthly installments over one year or, if earlier, upon the next annual meeting of stockholders.

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

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 April 15, 2024 by:

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

The column entitled “Shares Beneficially Owned” is based on a total of 36,639,734 shares of our Common Stock outstanding as of April 15, 2024.

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 April 15, 2024 are considered outstanding and beneficially owned by the person holding the options for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Due to the conversion limitations on the Series A Preferred Stock and Series B Preferred Stock, shares of underlying Common Stock have been excluded from beneficial ownership set forth below. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our Common Stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise indicated in the table below, addresses of named beneficial owners are in care of Spyre Therapeutics, Inc., 221 Crescent Street, Building 23, Suite 105, Waltham, MA 02453.

	Shares beneficially owned	
Name and address of beneficial owner	Number	Percentage
5% Stockholders:		
FMR LLC (1)	6,206,451	17.2%
Perceptive Life Sciences Master Fund, Ltd. (2)	2,606,679	7.2%
Entities associated with RTW Investments, LP (4)	2,232,760	6.2%
Entities associated with Venrock Healthcare Capital Partners (3)	1,912,538	5.2%
Commodore Capital Master LP (6)	1,884,084	5.2%
Avoro Life Sciences Fund LLC (5)	1,839,138	5.0%
Named Executive Officers and Directors:		
Jonathan Alspaugh (7)	99,603	*
Scott Burrows (8)	5,833	*
Jeffrey M. Goldberg	—	*
Heidy King-Jones (9)	5,250	*
Russell J. Cox (10)	80,008	*
Jeffrey W. Albers (11)	42,693	*
Laurie Stelzer (12)	8,333	*
Mark McKenna (13)	4,444	*
Peter Harwin (14)	855,959	2.3%
Tomas Kiselak (15)	855,959	2.3%
Michael Henderson, M.D. (16)	71,500	*
Cameron Turtle, DPhil (17)	1,203,609	3.3%
All current executive officers and directors as a group (10 persons) (18)	3,133,588	8.6%

* Represents beneficial ownership of less than one percent.

(1) 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 13G/A filed on February 14, 2024. Represents shares of Common Stock held by Perceptive Life Sciences Master Fund, Ltd ("Perceptive Fund"). The address of Perceptive Fund is 51 Astor Place, 10th Floor, New York, NY 10003.

(3) Based upon a Schedule 13G/A filed on February 14, 2024 and on information provided by Venrock Healthcare Capital Partners. Represents shares of Common Stock held by Venrock Healthcare Capital Partners III, LP ("VHCP III"), VHCP III Co-Investment Holdings III, LLC ("VHCP III Co") and Venrock Healthcare Capital Partners EG, L.P. ("VHCP EG"). VHCP Management III, LLC ("VHCPM") is the sole general partner of VHCP III and the sole manager of VHCP III Co. VHCP Management EG, LLC ("VHCPM EG") is the sole general partner of VHCP EG. Dr. Bong Koh and Nimish Shah are the voting members of VHCPM and VHCPM EG. The address of each of these persons and entities is 7 Bryant Park, 23rd Floor, New York, NY 10018.

(4) Based solely upon a Schedule 13G filed on February 13, 2024. Represents shares of Common Stock held by RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd. and RTW Biotech Opportunities Operating LTD (collectively, the "RTW Funds"). RTW Investments, LP ("RTW"), in its capacity as the investment manager of 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 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.

(5) Based upon a Schedule 13G filed on February 14, 2024 and on information provided by Avoro Capital Advisors LLC ("Avoro"). Represents shares of Common Stock held by Avoro. The address of Avoro is 110 Greene Street, Suite 800, New York, NY 10012.

(6) Based solely upon a Schedule 13G/A filed on February 14, 2024. Represents shares of Common Stock held by Commodore Capital Master LP ("Commodore Capital"). Commodore Capital LP is the investment manager to Commodore Capital and may be deemed to beneficially own the shares held by Commodore Capital. Michael Kramarz and Robert Egen Atkinson are the managing partners of Commodore Capital LP and exercise investment discretion with respect to these shares. The address of Commodore Capital LP and Commodore Capital Master LP is 444 Madison Avenue, 35th Floor, New York, NY 10022.

(7) Represents (i) 7,254 shares of Common Stock held by Mr. Alspaugh and (ii) options exercisable for 92,349 shares of Common Stock within 60 days of April 15, 2024.

(8) Represents options exercisable for 5,833 shares of Common Stock within 60 days of April 15, 2024.

(9) Represents options exercisable for 5,250 shares of Common Stock within 60 days of April 15, 2024.

(10) Represents (i) 280 shares of Common Stock held by Mr. Cox and (ii) options exercisable for 79,728 shares of Common Stock within 60 days of April 15, 2024.

(11) Represents (i) 34,360 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 8,333 shares of Common Stock within 60 days of April 15, 2024.

(12) Represents options exercisable for 8,333 shares of Common Stock within 60 days of April 15, 2024.

(13) Represents options exercisable for 4,444 shares of Common Stock within 60 days of April 15, 2024.

(14) Represents (i) 378,421 shares of Common Stock held by Fairmount Healthcare Fund II L.P. ("Fund II") that may be deemed to be beneficially owned by Mr. Harwin; (ii) 406,038 shares of Common Stock held by Mr. Harwin; and (iii) options exercisable for 71,500 shares of Common Stock within 60 days of April 15, 2024.

(15) Represents (i) 378,421 shares of Common Stock held by Fund II that may be deemed to be beneficially owned by Mr. Kiselak; (ii) 406,038 shares of Common Stock held by Mr. Kiselak; and (iii) options exercisable for 71,500 shares of Common Stock within 60 days of April 15, 2024.
(16) Represents options exercisable for 58,500 shares of Common Stock within 60 days of April 15, 2024.
(17) Represents (i) 746,907 shares of Common Stock held by Dr. Turtle and (ii) options exercisable for 456,702 shares of Common Stock within 60 days of April 15, 2024.
(18) Represents (i) 1,972,044 shares of Common Stock and (ii) options exercisable for 783,123 shares of Common Stock within 60 days of April 15, 2024.

CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

Other than the executive officer and director compensation arrangements discussed above under "Executive Compensation," below we describe the transactions to which we were a party since January 1, 2022, in which the amount involved exceeded the lesser of $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:

- On May 5, 2022, we entered into a placement agent agreement with JonesTrading Institutional Services LLC, as placement agent, relating to a registered direct offering of an aggregate of 430,107 shares of our Common Stock at a public purchase price of $40.00 per share and pre-funded warrants to purchase up to 694,892 shares of our Common Stock at a public purchase price of $39.99 per pre-funded warrant with an exercise price of $0.0025 per share. This registered direct offering closed on May 9, 2022. Pursuant to this offering, on the closing date:

i. Baker Brothers Life Sciences, L.P. and 667, L.P. (together, the "Baker Funds") purchased 251,351 and 29,898 pre-funded warrants to purchase Common Stock, respectively, for an aggregate purchase price of approximately $11.2 million;

ii. Averill Master Fund, Ltd., an entity affiliated with Suvretta, purchased 250,000 pre-funded warrants to purchase Common Stock for an aggregate purchase price of approximately $10.0 million; and

iii. Entities affiliated with Nantahala purchased 132,071 pre-funded warrants to purchase Common Stock for an aggregate purchase price of approximately $5.3 million.

- On March 16, 2021, we entered into a registration rights agreement (the "Baker RRA") with the Baker Funds, pursuant to which the Baker Funds are entitled to certain resale registration rights with respect to shares of our Common Stock held by the Baker Funds (the "Baker Registrable Securities"). Under the Baker RRA, following a request by the Baker Funds, we are obligated to file a resale registration statement on Form S-3, or other appropriate form, covering Baker Registrable Securities. Under the Baker RRA, the Baker Funds also have the right to up to two underwritten public offerings or block trades per calendar year, but no more than three underwritten public offerings and eight block trades in total, to effect the sale or distribution of their Baker Registrable Securities, subject to specified exceptions, conditions and limitations. The Baker RRA also includes customary indemnification obligations in connection with registrations conducted pursuant to the Baker RRA. The Baker RRA has terminated and is no longer in effect.

- Paragon and Parapyre each beneficially owns less than 5% of our capital stock through their respective holdings of our common stock. Fairmount beneficially owns more than 5% of our capital stock, has two seats on our Board and beneficially owns more than 5% of Paragon, which is a joint venture between Fairmount and Fair Journey Biologics. Fairmount appointed Paragon's board of directors and has the contractual right to approve the appointment of any executive officers. Parapyre is an entity formed by Paragon as a vehicle to hold equity in Pre-Merger Spyre in order to share profits with certain employees of Paragon. In connection with the Asset Acquisition, we assumed the rights and obligations of Pre-Merger Spyre under 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 acquisition date, $19.0 million was unpaid and was assumed by us through the Asset Acquisition. Furthermore, following our amendment and restatement of the Paragon Agreement on September 29, 2023, we are obligated to provide certain equity grants to Parapyre pursuant to the Parapyre Option Obligation 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. Following the execution of each of the SPY001 License Agreement and SPY002 License Agreement, we expect to be obligated to pay Paragon up to $22.0 million upon the achievement of specific development, regulatory and clinical milestones for the first product under each agreement, respectively, that achieves such specified milestones. Upon execution of each of the SPY001 License Agreement and SPY002 License Agreement, we expect to pay Paragon a $1.5 million fee for nomination of a development candidate and we expect to be obligated to make a further milestone payment of $2.5 million upon the first dosing of a human patient in a Phase 1 trial. Subject to the execution of the Option with respect to the SPY003 or SPY004 research programs pursuant to the Paragon Agreement, we expect to be obligated to make similar payments upon and following the execution of license agreements with respect to the these research programs, respectively. For additional detail regarding our arrangements with Paragon and Parapyre, see the sections titled "*Paragon Agreement*" and "*Our Relationship with Paragon and Parapyre* ."

- 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 expect to enter into the SPY001 License Agreement and the SPY002 License Agreement. Our option available under the Paragon Agreement with respect to the SPY003 and SPY004 programs remains unexercised.
- Concurrently with the Asset Acquisition, we entered into the June 2023 SPA with the June 2023 Investors for gross proceeds of approximately $210 million, pursuant to which the June 2023 Investors purchased an aggregate of 721,452 shares of Series A Preferred Stock at a price of $291.08 per share. In connection with the June 2023 Transactions, issued to Fairmount (i) 378,421 shares of Common Stock and 265,263 shares of Series A Preferred Stock in exchange for shares of Pre-Merger Spyre based on a fixed exchange ratio of 0.5494488 to 1 pursuant to the Asset Acquisition and (ii) 257,661 shares of Series A Preferred Stock at a price of $291.08 per share pursuant to the June 2023 PIPE. On June 22, 2023, we also entered into a registration rights agreement (the "June 2023 RRA") with the June 2023 Investors, including Fairmount, pursuant to which the June 2023 Investors are entitled to certain resale registration rights with respect to shares of our Common Stock held by such investors. For additional detail regarding the June 2023 Transactions, see "*Prospectus Summary – Recent Developments.* "
- On December 7, 2023, we entered into the December 2023 SPA with the December 2023 Investors for gross proceeds of approximately $180 million, pursuant to which the December 2023 Investors purchased an aggregate of 6,000,000 shares of common stock at a price of $15.00 per share and 150,000 shares of Series B Preferred Stock at a price of $600.00 per share. In connection with the December 2023 PIPE, we issued (i) 16,667 shares of Series B Preferred Stock to Fairmount, (ii) 1,666,666 shares of Common Stock to entities associated with FMR LLC, (iii) 710,000 shares of Common Stock and 18,083 shares of Series B Preferred Stock to Perceptive Life Sciences Master Fund, Ltd., (iv) 250,000 shares of Common Stock and 35,417 shares of Preferred Stock to entities associated with Venrock Healthcare Capital Partners, (v) 515,000 shares of Common Stock and 12,125 shares of Series B Preferred Stock to entities associated with RTW Investments, LP, (vi) 235,000 shares of Common Stock and 5,792 shares of Series B Preferred Stock to Deep Track Biotechnology Master Fund, Ltd., and (vii) 50,000 shares of Common Stock and 1,250 shares of Series B Preferred Stock to Commodore Capital Master LP, at a price of $15.00 per share of Common Stock and $600.00 per share of Series B Preferred Stock. On December 7, 2023, we also entered into the December 2023 RRA with the December 2023 Investors, including the above-named investors, pursuant to which the December 2023 Investors are entitled to certain resale registration rights with respect to shares of our Common Stock held by such investors. For additional detail regarding the December 2023 PIPE and the December 2023 RRA, see "*Prospectus Summary – Recent Developments*" and "*Risk Factors—Future sales of shares by existing stockholders could cause our stock price to decline* ," respectively.
- In November 2023, we entered into a consulting agreement with Mr. McKenna, who subsequently 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 Common Stock under the 2016 Plan, vesting over four years with an exercise price of $10.39 per share.

- On March 18, 2024, we entered into the March 2024 SPA with 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 PIPE, 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 (the "March 2024 RRA") 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. For additional detail regarding the March 2024 PIPE and the March 2024 RRA, see "*Prospectus Summary – Recent Developments*" and "*Selling Stockholders – Registration Rights Agreements,*" respectively.

Review, Approval or Ratification of Transactions with Related Parties

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.

SELLING STOCKHOLDERS

This prospectus covers the resale or other disposition from time to time by the Selling Stockholders identified in the table below of up to an aggregate of 33,361,402 shares of our Common Stock. The Selling Stockholders may from time to time offer and sell any or all of the Resale Shares set forth below pursuant to this prospectus and any accompanying prospectus supplement.

On June 22, 2023, we entered into the June 2023 SPA, pursuant to which we sold an aggregate of 721,452 shares of our Series A Preferred Stock, each of which automatically converted into 40 shares of Common Stock, subject to stockholder approval and certain beneficial ownership limitations set by each holder, pursuant to the Series A Certificate of Designation, at an aggregate purchase price of approximately $210 million. Also on June 22, 2023, we completed our acquisition of Pre-Merger Spyre in accordance with the Acquisition Agreement, pursuant to which we issued an aggregate of 517,809 shares of Common Stock and 364,887 shares of Series A Preferred Stock to certain of the Selling Stockholders.

On December 7, 2023, we entered into the December 2023 SPA, pursuant to which we sold an aggregate of 6,000,000 shares of our Common Stock and 150,000 shares of our Series B Preferred Stock, which will automatically convert into 40 shares of Common Stock, subject to stockholder approval and certain beneficial ownership limitations set by each holder, pursuant to the Series B Certificate of Designation, at an aggregate purchase price of $180 million.

On March 18, 2024, we entered into the March 2024 SPA, pursuant to which we sold an aggregate of 121,625 shares of our Series B Preferred Stock, which will automatically convert into 40 shares of Common Stock, subject to stockholder approval and certain beneficial ownership limitations set by each holder, pursuant to the Series B Certificate of Designation, at an aggregate purchase price of approximately $180 million.

This prospectus covers the resale or other disposition by the Selling Stockholders or their pledgees, donees, transferees or other successors-in-interest that receive their shares after the date of this prospectus of up to the total number of shares of Common Stock, shares of Common Stock issued upon the conversion of the Series A Preferred Stock and shares of Common Stock issuable upon the conversion of the Series B Preferred Stock issued to the Selling Stockholders pursuant to the Acquisition Agreement, the June 2023 SPA, the December 2023 SPA and the March 2024 SPA, as applicable, that remain unsold by such Selling Stockholders. Throughout this prospectus, when we refer to the “Selling Stockholders,” we are referring to the purchasers under the June 2023 SPA, the December 2023 SPA and the March 2024 SPA and certain of the securityholders under the Acquisition Agreement and certain of our employees listed in the table below.

We are registering the resale of the Resale Shares to permit the Selling Stockholders and their pledgees, donees, transferees or other successors-in interest that receive their shares after the date of this prospectus to resell or otherwise dispose of the shares in the manner contemplated under “Plan of Distribution” herein.

Except as otherwise disclosed herein, the Selling Stockholders do not have, and within the past three years have not had, any position, office or other material relationship with us.

The following table sets forth the names of the Selling Stockholders, the number of shares of our Common Stock beneficially owned by the Selling Stockholders, the number of shares of our Common Stock that may be offered under this prospectus and the number of shares of our Common Stock that will be owned after this offering by the Selling Stockholders assuming all of the shares registered for resale hereby are sold.

The Selling Stockholders may sell some, all or none of their Resale Shares. We do not know how long the Selling Stockholders will hold the Resale Shares before selling them, and we currently have no agreements, arrangements or understandings with the Selling Stockholders regarding the sale or other disposition of any of the Resale Shares. The Resale Shares covered hereby may be offered from time to time by the Selling Stockholders, provided that Resale Shares issued upon conversion of Series B Preferred Stock may only be offered after such shares of Series B Preferred Stock are converted to Common Stock pursuant to the terms of the Series B Certificate of Designation.

The information set forth below is based upon information obtained from the Selling Stockholders and upon information in our possession regarding the issuance of the Merger Common Shares, the Merger Preferred Shares and June 2023 Private Placement Preferred Shares in connection with the June 2023 Transactions, the December 2023 Private Placement Common Shares and the December 2023 Private Placement Preferred Shares in connection with the December 2023 PIPE and the March 2024 Private Placement Preferred Shares in connection with the March 2024 PIPE. The percentages of Common Stock owned after the offering by each Selling Stockholder below are based on 36,639,734 shares of Common Stock outstanding as of April 15, 2024, and, for each Selling Stockholder, assumes the conversion of only the Series B Preferred Stock owned by such Selling Stockholder but not the Series B Preferred Stock owned by any other Selling Stockholder. The numbers of shares of Common Stock beneficially owned before and after the offering presented in the table below do not give effect to any Beneficial Ownership Limitations with respect to the Series B Preferred Stock.

Name of Selling Stockholders(1)	Common Stock Beneficially Owned Before Offering (2)	Common Stock that May Be Offered Pursuant to Prospectus	Common Stock Beneficially Owned After Offering (2)	
			Number	Percentage (%)
Perceptive Life Sciences Master Fund, Ltd. (3)	3,600,199	3,421,280	178,919	*
Entities associated with Venrock Healthcare Capital Partners (4)	3,329,218	3,329,218	—	*
Entities associated with RTW Investments, LP (5)	3,258,360	3,258,360	—	*
AI Biotechnology LLC (6)	2,000,000	2,000,000	—	*
Commodore Capital Master LP (7)	1,988,084	1,871,760	116,324	*
Deep Track Capital, LP (8)	1,985,700	1.985,700	—	*
Avoro Life Sciences Fund LLC (9)	1,839,138	1,827,680	11,458	*
Fidelity Growth Company Commingled Pool (10)	1,376,763	1,376,763	—	*
Braidwell Partners Master Fund LP (11)	1,313,000	1,108,000	205,000	*
Adage Capital Partners LP (12)	1,140,200	270,200	870,000	2.4
Fidelity Mt. Vernon Street Trust: Fidelity Growth Company Fund (10)	1,070,184	1,070,184	—	*
Fairmount Healthcare Fund II L.P. (13)	1,045,101	666,680	378,421	1.0
Entities associated with EcoR1 Capital (14)	887,076	687,080	199,996	*
Entities associated with Franklin Biotechnology (15)	741,880	687,080	54,800	*
Boxer Capital, LLC (16)	696,480	696,480	—	*
Entities associated with BVF Partners L.P. (17)	687,080	687,080	—	*
Entities associated with Driehaus Capital Management LLC (18)	687,080	687,080	—	*
RA Capital Healthcare Fund, L.P. (19)	687,080	687,080	—	*
Affinity Healthcare Fund, LP (20)	550,920	337,334	213,586	*
Entities associated with Logos Global Master Fund LP (21)	514,800	514,800	—	*
Polar Capital Funds Plc — Biotechnology Fund (22)	500,000	233,320	266,680	*
Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund (10)	479,168	479,168	—	*
Entities associated with Darwin Global (23)	473,200	473,200	—	*
Entities associated with Farallon Capital Management, L.L.C. (24)	473,200	473,200	—	*
Cormorant Global Healthcare Master Fund, LP (25)	466,680	466,680	—	*
Citadel CEMF Investments Ltd. (26)	412,240	412,240	—	*
Avidity Master Fund LP (27)	405,400	405,400	—	*
Entities advised or subadvised by T. Rowe Price Associates, Inc. (28)	405,400	405,400	—	*

Name of Selling Stockholders(1)	Common Stock Beneficially Owned Before Offering (2)	Common Stock that May Be Offered Pursuant to Prospectus	Common Stock Beneficially Owned After Offering (2)	
			Number	Percentage (%)
Entities associated with Great Point Partners LLC (29)	341,320	341,320	—	*
Fidelity Mt. Vernon Street Trust: Fidelity Growth Company K6 Fund (10)	332,531	332,531	—	*
Entities associated with Blackstone Alternative Asset Management Associates LLC (30)	315,431	295,440	19,991	*
Stempoint Capital Master Fund LP (31)	306,981	130,080	176,901	*
Fidelity Mt. Vernon Street Trust: Fidelity Series Growth Company Fund (10)	294,104	294,104	—	*
CDK Associates, L.L.C. (32)	264,180	264,180	—	*
Walleye Opportunities Master Fund Ltd. (33)	229,385	67,600	161,785	*
Atlas Diversified Master Fund, Ltd. (34)	202,600	202,600	—	*
Woodline Master Fund LP (35)	181,000	181,000	—	*
Fidelity Select Portfolios: Pharmaceuticals Portfolio (10)	148,742	148,742	—	*
Andrew Spencer (36)	146,665	91,387	55,278	*
Janet Gunzner-Toste (37)	146,665	91,387	55,278	*
Justin LaFountaine (38)	106,671	74,650	32,021	*
Wedbush Healthcare Partners 2023 Fund, LLC (39)	68,720	68,720	—	*
Quantum Partners LP (40)	67,600	67,600	—	*
Salthill Partners, L.P. (41)	50,075	50,075	—	*
Salthill Investors (Bermuda) L.P. (41)	43,185	43,185	—	*
Sessions LLC (42)	34,360	34,360	—	*
Fidelity Select Portfolios: Biotechnology Portfolio (10)	33,334	33,334	—	*
Third Street Holdings LLC (43)	16,900	16,900	—	*
Harry Turtle (44)	13,760	13,760	—	*

* Less than 1%

(1) To our knowledge, unless otherwise indicated, all persons named in the table above have sole voting and investment power with respect to their shares of Common Stock. Unless an address is provided below, the address for the holder is 221 Crescent Street, Building 23, Suite 105, Waltham MA 02453.

(2) "Beneficial ownership" is a term broadly defined by the SEC in Rule 13d-3 under the Exchange Act, and includes more than the typical form of stock ownership, that is, stock held in the person's name. The term also includes what is referred to as "indirect ownership," meaning ownership of shares as to which a person has or shares investment power. Notwithstanding the foregoing, the beneficial ownership amounts assume the sale of all Common Stock that may be offered pursuant to this prospectus without taking into account certain limitations, including that a holder of Series B Preferred Stock is prohibited from converting shares of Series B Preferred Stock into shares of Common Stock (i) prior to the affirmative vote of the holders of a majority of the then outstanding shares of the Series B Preferred Stock, or (ii) if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (established by the holder between 0.00% and 19.99%) (the "Beneficial Ownership Limitation") of the total number of shares of Common Stock issued and outstanding immediately after giving effect to such conversion.

(3) Consists of (i) 993,520 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Perceptive Life Sciences Master Fund, Ltd ("Perceptive Fund") and (ii) 2,606,679 shares of Common Stock held by Perceptive Fund. Perceptive Advisors LLC ("Perceptive Advisors") is the investment advisor of Perceptive Fund and may be deemed to have beneficial ownership of the shares

beneficially owned thereby. Joseph Edelman is the controlling person of each of Perceptive Fund and Perceptive Advisors and, accordingly, may be deemed to have beneficial ownership of the shares beneficially owned by each of Perceptive Fund and Perceptive Advisors. Mr. Edelman disclaims beneficial ownership of such shares except to the extent of his pecuniary interest therein. The address of Perceptive is 51 Astor Place, 10th Floor, New York, NY 10003. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by Perceptive Life Sciences Master Fund, Ltd. are subject to a Beneficial Ownership Limitation of 9.99%.

(4) Consists of (i) 1,403,560 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Venrock Healthcare Capital Partners EG, L.P. ("VHCP EG"), (ii) 1,429,360 shares of Common Stock held by VHCP EG, (iii) 11,960 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Venrock Healthcare Capital Partners III, L.P. ("VHCP III"), (iv) 439,194 shares of Common Stock held by VHCP III, (v) 1,160 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by VHCP Co-Investment Holdings III, LLC ("VHCP III Co"), and (vi) 43,984 shares of Common Stock held by VHCP III Co. VHCP Management III, LLC ("VHCPM") is the sole general partner of VHCP III and the sole manager of VHCP III Co. VHCP Management EG, LLC ("VHCPM EG") is the sole general partner of VHCP EG. Dr. Bong Koh and Nimish Shah are the voting members of VHCPM and VHCPM EG. The address of each of these persons and entities is 7 Bryant Park, 23rd Floor, New York, NY 10018. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by VHCP EG, VHCP III, and VHCP III Co are subject to a Beneficial Ownership Limitation of 9.99%.

(5) Consists of an aggregate of (i) 1,025,600 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd. and RTW Biotech Opportunities Operating Ltd. (collectively, the "RTW Funds") and (ii) 2,232,760 shares of Common Stock held by RTW Funds. RTW Investments, LP ("RTW"), in its capacity as the investment manager of 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. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by the RTW Funds are subject to a Beneficial Ownership Limitation of 9.99%.

(6) Consists of (i) 1,000,000 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by AI Biotechnology LLC and (ii) 1,000,000 shares of Common Stock held by AI Biotechnology LLC. Access Industries Holdings LLC, or AIH, directly controls all of the outstanding voting interest in AI Biotechnology LLC. Access Industries Management, LLC, or AIM, controls AIH. Len Blavatnik controls AIM and holds a majority of the outstanding voting interests in AIH. Each of Len Blavatnik, AIM and AIH may be deemed to have voting and investment power over the shares held by AI Biotechnology LLC. The address of each of AI Biotechnology LLC, AIM, AIH and Len Blavatnik is c/o Access Industries, Inc. 40 West 57th Street, 28th Floor, New York, NY 10019.

(7) Consists of (i) 104,000 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Commodore Capital Master LP and (ii) 1,884,084 shares of Common Stock held by Commodore Capital Master LP. Commodore Capital LP is the investment manager to Commodore Capital Master LP and may be deemed to beneficially own the shares held by Commodore Capital Master LP. Michael Kramarz and Robert Egen Atkinson are the managing partners of Commodore Capital LP and exercise investment discretion with respect to these shares. Commodore Capital LP and Commodore Capital Master LP have shared voting and dispositive power with respect to these shares. The address of Commodore Capital LP and Commodore Capital Master LP is 444 Madison Avenue, 35th Floor, New York, NY 10022. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by Commodore Capital Master LP are subject to a Beneficial Ownership Limitation of 9.99%.

(8) Consists of (i) 772,280 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Deep Track Biotechnology Master Fund, Ltd. ("Deep Track Biotech") and (ii) 1,213,420 shares of Common Stock held by Deep Track Biotech. Deep Track Capital, LP ("Deep Track Capital") and David Kroin have shared voting power and shared dispositive power over the shares held by the Deep Track Biotech. Mr. Kroin may be considered a control person for Deep Track Capital. The address of Deep Track Capital and Mr. Kroin is 200 Greenwich Ave, 3rd Floor, Greenwich, CT 06830, and the address for Deep Track Biotech is 190 Elgin Avenue, George Town, KY1-9001, Cayman Islands. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by Deep Track Biotech are subject to a Beneficial Ownership Limitation of 9.99%.

(9) Consists of 1,839,138 shares of Common Stock held by Avoro Life Sciences Fund LLC. Avoro Capital Advisors LLC ("Avoro") is the investment advisor for Avoro Life Sciences Fund LLC. Behzad Aghazadeh serves as the portfolio manager and controlling person of Avoro and may be deemed to have investment discretion and voting power over the shares held by Avoro. Mr. Aghazadeh disclaims beneficial ownership of these shares, except to the extent of his pecuniary interest in such shares, if any. The address of Avoro Life Sciences Fund LLC is 110 Greene Street, Suite 800, New York, NY 10012.

(10) These funds and accounts are 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.

(11) Consists of (i) 593,000 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Braidwell Partners Master Fund LP ("Braidwell Partners") and (ii) 720,000 shares of Common Stock held by Braidwell Partners. Braidwell LP (the "Braidwell Investment Manager") is the investment manager of Braidwell Partners, Braidwell GP LLC (the "Braidwell GP") is the general partner of Braidwell Partners, and Braidwell Management LLC (the "Braidwell IM GP") is the general partner of the Braidwell Investment Manager and the managing member of the Braidwell GP. Messrs. Alexander T. Karnal and Brian J. Kreiter (together with Braidwell Partners, the Braidwell Investment Manager, the Braidwell GP and the Braidwell IM GP, the "Braidwell Parties") together own, directly or indirectly, the Braidwell Investment Manager, the Braidwell GP and the Braidwell IM GP. The address of Braidwell Partners is c/o Maples Corporate Services Limited, P.O Box 309, Ugland House, Grand Cayman, KY1-1104 Cayman Islands. The principal address of the Braidwell Investment Manager, the Braidwell GP and the Co-Founders is One Harbor Point, 2200 Atlantic Street, 4th Floor, Stamford, Connecticut 06902. The Braidwell Parties may be deemed to have shared voting and dispositive powers with respect to the shares of Common Stock held by Braidwell Partners and the shares of Common Stock issuable upon conversion of Series B Preferred Stock held by Braidwell Partners. Each of the Braidwell Parties disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The shares of Common Stock issuable upon the conversion of the shares of Series B Preferred Stock held by Braidwell Partners purchased in the December 2023 PIPE and the March 2024 PIPE are subject to a Beneficial Ownership Limitation of 9.99% and 4.90%, respectively.

(12) Consists of (i) 270,200 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Adage Capital Partners LP ("Adage") and (ii) 870,000 shares of Common Stock held by Adage. Bob Atchinson and Phillip Gross are the managing members of Adage Capital Advisors, L.L.C., which is the managing member of Adage Capital Partners GP, L.L.C., which is the general partner of Adage, and each such person or entity, as the case may be, has shared voting and/or investment power over the securities held by Adage Capital Partners, LP and may be deemed the beneficial owner of such shares, and each such person or entity, as the case may be, disclaims beneficial ownership of such securities except to

the extent of their respective pecuniary interest therein. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by Adage are subject to a Beneficial Ownership Limitation of 9.90%.

(13) Consists of (i) 666,680 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Fairmount Healthcare Fund II, L.P. ("Fund II"); and (ii) 378,421 shares of Common Stock held by Fund II. Fairmount Funds Management LLC ("Fairmount") serves as investment manager for Fund II. Fund II has delegated to 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 the entities listed is 200 Barr Harbor Drive, Suite 400, West Conshohocken, PA 19428. The shares of Common Stock issuable upon the conversion of the shares of Preferred Stock held by Fund II are subject to a Beneficial Ownership Limitation of 0.00%. Shares of Series A Preferred Stock held by Fund II are omitted from this footnote because the conversion of such shares is subject to a Beneficial Ownership Limitation of 0.00%.

(14) Consists of (i) 39,520 shares of Common Stock held by EcoR1 Capital Fund, L.P. ("Capital"), (ii) 647,560 shares of Common Stock held by EcoR1 Capital Fund Qualified, L.P. ("Qualified"), and (iii) 199,996 shares of Common Stock held by Capital and Qualified. EcoR1 Capital LLC ("EcoR1") is the general partner and investment advisor of Capital and Qualified, which disclaims beneficial ownership of the shares. Oleg Nodelman is the control person of EcoR1 Capital. EcoR1 Capital is the general partner and investment advisor of EcoR1 and Qualified, which disclaims beneficial ownership of the shares. Mr. Nodelman, EcoR1, Capital and Qualified each disclaim beneficial ownership of the shares except to the extent of their pecuniary interest therein. The address of each of EcoR1, Capital, Qualified and Mr. Nodelman is 357 Tehama Street #3, San Francisco, CA 94103.

(15) Consists of (i) 220,100 shares of Common Stock held by Franklin Strategic Series – Franklin Biotechnology Discovery Fund ("Franklin Strategic") and (ii) 486,780 shares of Common Stock held by Franklin Templeton Investment Funds – Franklin Biotechnology Discovery Fund ("Franklin Templeton"). Franklin Advisers, Inc., a SEC registered broker-dealer, is the investment adviser to both Franklin Strategic and Franklin Templeton. Evan McCulloch is the portfolio manager for both Franklin Strategic and Franklin Templeton. Mr. McCulloch may be deemed to have voting and investment power over the common stock held by Franklin Strategic and Franklin Templeton. Mr. McCulloch disclaims beneficial ownership of such shares, except to the extent of any pecuniary interest therein. The address of the Franklin entities is c/o Franklin Advisers, Inc., One Franklin Parkway, San Mateo, CA 94403.

(16) Consists of (i) 446,480 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Boxer Capital, LLC ("Boxer Capital") and (ii) 250,000 shares of Common Stock held by Boxer Capital. Boxer Asset Management Inc. ("Boxer Asset Management") is the managing member of Boxer Capital. Joseph C. Lewis, as the sole indirect owner of Boxer Asset Management, may be deemed to have shared power to vote (or direct vote) and/or to dispose (or direct the disposition) of the securities held by Boxer Capital. Boxer Asset Management and Joseph C. Lewis disclaim beneficial ownership over the shares owned by Boxer Capital except to the extent of their pecuniary interests therein. The principal address for Boxer Capital is 12860 El Camino Real, Ste 300, San Diego, CA 92130 and the principal address for Boxer Asset Management and Mr. Lewis is Cay House, EP Taylor Drive N7776, Lyford Cay, New Providence, Bahamas. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by Boxer Capital are subject to a Beneficial Ownership Limitation of 4.99%.

(17) Consists of (i) 367,080 shares of Common Stock held by Biotechnology Value Fund, L.P. ("BVF LP"), (ii) 278,240 shares of Common Stock held by Biotechnology Value Fund II, L.P. ("BVF2 LP"), (iii) 32,360 shares of Common Stock held by Biotechnology Value Trading Fund OS LP ("BVF OS"), and (iv) 9,400 shares of Common Stock held by MSI BVF SPV, LLC ("MSI BVF" and together with BVF LP, BVF2 LP and BVF OS, the "BVF Entities"). BVF I GP LLC ("BVF GP"), as general partner of BVF LP, may be

deemed to beneficially own the shares beneficially owned by BVF LP. BVF II GP LLC ("BVF2 GP"), as general partner of BVF2 LP, may be deemed to beneficially own the shares beneficially owned by BVF2 LP. BVF Partners OS Ltd. ("Partners OS"), as general partner of BVF OS, may be deemed to beneficially own the shares beneficially owned by BVF OS. BVF GP Holdings LLC ("BVF GPH"), as the sole member of BVF GP and BVF2 GP, may be deemed to beneficially own the shares beneficially owned in the aggregate by BVF GP and BVF2 GP. BVF Partners L.P. ("Partners"), as investment manager of BVF LP, BVF2 LP, BVF OS and MSI BVF, and the sole member of Partners OS, may be deemed to beneficially own the shares beneficially owned in the aggregate by the BVF Entities. BVF Inc., as the general partner of Partners, may be deemed to beneficially own the shares beneficially owned by Partners. Mark N. Lampert as director and officer of BVF Inc., may be deemed to beneficially own the shares beneficially owned by BVF Inc. Each of BVF GP, BVF2 GP, Partners OS, BVF GPH, Partners, BVF Inc. and Mark N. Lampert disclaims beneficial ownership of securities beneficially owned by the BVF Entities. The address of each of these entities is 44 Montgomery Street, Suite 4000, San Francisco, CA 94104.

(18) Consists of (i) 507,720 shares of Common Stock held by Driehaus Life Sciences Master Fund, L.P. ("Driehaus Master Fund") and (ii) 179,360 shares of Common Stock held by Driehaus Life Sciences (QP) Fund, L.P. ("Driehaus QP Fund"). Driehaus Capital Management (USVI) LLC is the general partner of both Driehaus Life Sciences Master Fund, L.P. and Driehaus Life Sciences (QP) Fund, L.P. By virtue of such relationship, Driehaus Capital Management (USVI) LLC may be deemed to have beneficial ownership over such securities. Driehaus Capital Management LLC is the investment advisor to both Driehaus Life Sciences Master Fund, L.P. and Driehaus Life Sciences (QP) Fund. Driehaus Capital Management LLC exercises voting and investment power through portfolio managers comprised of Michael Caldwell and Alex Munns, each of whom disclaims beneficial ownership of the shares held by Driehaus Life Sciences Master Fund, L.P. and Driehaus Life Sciences (QP) Fund, L.P.. The address for these entities is c/o Driehaus Capital Management LLC, 25 East Erie Street, Chicago, IL 60611.

(19) Consists of 687,080 shares of Common Stock held by RA Capital Healthcare Fund, L.P. ("RACHF"). RA Capital Management, L.P. is the investment manager for RACHF. The general partner of RA Capital Management, L.P. is RA Capital Management GP, LLC, of which Peter Kolchinsky and Rajeev Shah are the managing members. Each of Mr. Kolchinsky and Mr. Shah may be deemed to have voting and investment power over the ordinary shares held by RACHF. Mr. Kolchinsky and Mr. Shah disclaim beneficial ownership of such shares, except to the extent of any pecuniary interest therein. The principal business address of these persons and entities is 200 Berkeley Street, 18th Floor, Boston, MA 02116.

(20) Consists of (i) 400,000 shares of Common Stock held by Affinity Healthcare Fund, LP (the "Affinity Fund") and (ii) 150,920 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Affinity Fund. Affinity Asset Advisors, LLC (the "Affinity Advisor") is the investment manager of Affinity Fund and exercises investment discretion with regard to the shares of Common Stock owned by Affinity Fund. Affinity Fund and Affinity Advisor have the shared power to vote or to direct the vote and to dispose or direct the disposition of such shares of Common Stock owned by Affinity Fund. Affinity Advisor may be deemed to be the beneficial owner of such shares of Common Stock owned by Affinity Fund by virtue of its position as investment manager of Affinity Fund. The address of each of these entities is 767 3rd Avenue, Floor 15, New York, NY 10017. The shares of Common Stock issuable upon the conversion of the shares of Series B Preferred Stock held by Affinity Fund is subject to a Beneficial Ownership Limitation of 9.99%.

(21) Consists of (i) 285,000 shares of Common Stock held by Logos Global Master Fund LP ("Global Fund"), and (iii) 229,800 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Global Fund. Logos GP LLC ("Logos GP") is the general partner of Global Fund. Logos Global Management LP ("Logos Global") is the investment advisor to Global Fund. Logos Global Management GP LLC ("Logos Global GP") is the general partner of Logos Global. Arsani William and Graham Walmsley are the members of Logos GP and Mr. William is a control person of Logos Global and Logos Global GP. Mr. William and Mr. Walmsley each disclaim beneficial ownership of these shares, except to the extent of each's pecuniary interest in such shares, if any. The principal address of Global Fund is 1 Letterman Drive,

Building C, Suite C3-350, San Francisco, CA 94129. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by Global Fund is subject to a Beneficial Ownership Limitation of 9.99%.

(22) Consists of (i) 108,320 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Polar Capital Funds plc – Biotechnology Fund, Polar Capital Funds plc is a company with variable capital and segregated liability between sub-funds incorporated in Ireland and authorized by the Central Bank of Ireland pursuant to the European Communities (Undertakings for Investment in Transferable Securities) Regulations 2011, as amended and with the address George's Court, 54-62 Townsend Street, Dublin 2, Ireland and (ii) 391,680 shares of Common Stock held by Polar Capital Funds plc – Biotechnology Fund. The investment manager of Polar Capital Funds plc is Polar Capital LLP, an FCA and SEC regulated fund manager/investment advisor, which has the ability to make decisions with respect to the voting and disposition of the shares and has overall responsibility for directing the investments of the entities in accordance with their investment objectives, policies and limitations. Polar Capital LLP is 100% owned by Polar Capital Partners Ltd, which is in turn 100% owned by Polar Capital Holdings plc, a London AIM listed holding company. Certain directors/employees are beneficial owners of Polar Capital Holdings plc but each such individual disclaims any beneficial ownership of the reported shares, other than to the extent they may or may not hold shares directly of the entities. The address for the investment manager is 16 Palace Street, London, United Kingdom, SW1E 5JD. The shares of Common Stock issuable upon the conversion of the shares of Series B Preferred Stock held by Polar Capital Funds plc – Biotechnology Fund is subject to a Beneficial Ownership Limitation of 9.99%.

(23) Consists of (i) 452,040 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Darwin Global Master Fund, Ltd ("Darwin Master Fund") and (ii) 21,160 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Darwin Global Private Fund Client ("Darwin Global Private Fund"). Darwin Global Management, Ltd., a limited company incorporated under the laws of Jersey ("Darwin Global"), serves as an investment manager to Darwin Master Fund and Darwin Global Private Fund. Dr. Abhishek Trehan is the Chief Investment Officer and the controlling person of Darwin Global. Dr. Trehan specifically disclaims beneficial ownership of these securities, which he does not directly own. The address for each of these Darwin entities and Dr. Trehan is Whiteley Chambers, Don Street, St. Helier, Jersey JE2 4TR. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by each of Darwin Master Fund and Darwin Global Private Fund are subject to a Beneficial Ownership Limitation of 9.90%.

(24) Consists of (i) 216,680 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Cormorant Global Healthcare Master Fund, LP ("Cormorant Global Healthcare") and (ii) 250,000 shares of Common Stock held by Cormorant Global Healthcare. Cormorant Global Healthcare GP, LLC ("Global Healthcare GP") is the general partner of Cormorant Global Healthcare. Cormorant Asset Management, LP serves as the investment manager to Cormorant Global Healthcare. Bihua Chen serves as the managing member of both Global Healthcare GP and Cormorant Asset Management, LP and accordingly may be deemed to have voting and dispositive power with respect to shares held by Cormorant Global Healthcare. Each of Global Healthcare GP, Cormorant Asset Management, LP and Ms. Chen disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The principal address for the Cormorant Asset Management, LP entities is 200 Clarendon Street 52nd Floor, Boston, MA 02116. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by Cormorant Global Healthcare are subject to a Beneficial Ownership Limitation of 9.99%.

(25) Consists of (i) 93,640 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Farallon Capital Partners, L.P. ("FCP"), (ii) 85,760 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Farallon Capital Institutional Partners, L.P. ("FCIP"), (iii) 19,040 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Farallon Capital Institutional Partners II, L.P. ("FCIP II"), (iv) 680 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Farallon Capital Institutional Partners III, L.P. ("FCIP III"), (v) 14,240 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Four Crossings Institutional Partners V, L.P. ("FCIP V"), (vi) 194,000 shares of Common Stock issuable upon

the conversion of Series B Preferred Stock held by Farallon Capital Offshore Investors II, L.P. (“FCOI II”), (vii) 54,720 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Farallon Capital F5 Master I, L.P. (“F5MI”) and (viii) 11,120 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Farallon Capital (AM) Investors, L.P. (“FCAMI” and, together with FCP, FCIP, FCIP II, FCIP III, FCIP V, FCOI II and F5MI, the “Farallon Funds”),). Farallon Partners, L.LC. (the “Farallon General Partner”), as the general partner of each of FCP, FCIP, FCIP II, FCIP III, FCOI II and FCAMI, may be deemed a beneficial owner of the shares of Common Stock held by, and the shares of Common Stock acquirable upon the conversion of the Series B Preferred Stock held by, FCP, FCIP, FCIP II, FCIP III, FCOI II and FCAMI. Farallon Institutional (GP) V, L.L.C. (the “FCIP V General Partner”), as the general partner of FCIP V, may be deemed a beneficial owner of the shares of Common Stock held by, and the shares of Common Stock acquirable upon the conversion of the Series B Preferred Stock held by, FCIP V. Farallon F5 (GP), L.L.C. (the “F5MI General Partner”), as the general partner of F5MI, may be deemed a beneficial owner of the shares of Common Stock held by, and the shares of Common Stock acquirable upon the conversion of the Series B Preferred Stock held by, F5MI. Farallon Healthcare Partners (GP), L.L.C. (the “FHPM General Partner”), as the general partner of FHPM, may be deemed a beneficial owner of the shares of Common Stock held by, and the shares of Common Stock acquirable upon the conversion of the Series B Preferred Stock held by, FHPM. Each of Joshua J. Dapice, Philip D. Dreyfuss, Hannah E. Dunn, Richard B. Fried, Varun N. Gehani, Nicolas Giauque, David T. Kim, Michael G. Linn, Rajiv A. Patel, Thomas G. Roberts, Jr., Edric C. Saito, William Seybold, Daniel S. Short, Andrew J. M. Spokes, John R. Warren and Mark C. Wehrly (collectively, the “Farallon Managing Members”), as a senior managing member or managing member, as the case may be, of the Farallon General Partner, and a manager or senior manager, as the case may be, of the FCIP V General Partner, the F5MI General Partner and the FHPM General Partner, in each case with the power to exercise investment discretion, may be deemed a beneficial owner of all such shares of Common Stock held by, and all such shares of Common Stock acquirable upon the conversion of the Series B Preferred Stock held by, the Farallon Funds. Each of the Farallon General Partner, the FCIP V General Partner, the F5MI General Partner, the FHPM General Partner, and the Farallon Managing Members hereby disclaims any beneficial ownership of any such shares. The principal business address of these persons and entities is c/o Farallon Capital Management, L.L.C., One Maritime Plaza, Suite 2100, San Francisco, CA 94111. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by the Farallon Funds are subject to a Beneficial Ownership Limitation of 9.90%.

(26) Consists of 412,240 shares of Common Stock held by Citadel CEMF Investments Ltd. (“Citadel CEMF”). Citadel Advisors LLC (“Citadel Advisors”) is the portfolio manager of Citadel CEMF. Citadel Advisors Holdings LP (“Citadel Holdings”) is the sole member of Citadel Advisors. Citadel GP LLC (“Citadel GP”) is the General Partner of Citadel Holdings. Kenneth Griffin owns a controlling interest in Citadel GP LLC. Mr. Griffin, as the owner of a controlling interest in Citadel GP LLC, may be deemed to have shared power to vote and/or shared power to dispose of the securities held by Citadel CEMF. This disclosure shall not be construed as an admission that Mr. Griffin or any of the Citadel related entities listed above is the beneficial owner of any of the Company’s securities other than the securities actually owned by such person (if any). The address of Citadel CEMF is Southeast Financial Center, 200 S. Biscayne Blvd., Suite 3300, Miami, FL 33131.

(27) Consists of 405,400 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Avidity Master Fund LP (“Avidity Master”). Avidity Master is a Cayman exempted limited partnership. The general partner of Avidity Master is Avidity Capital Partners Fund (GP) LP, a Delaware limited partnership, whose general partner is Avidity Capital Partners (GP) LLC, a Delaware limited liability company. Avidity Partners Management LP is the investment manager of Avidity Master. Avidity Partners Management (GP) LLC is the general partner of Avidity Partners Management LP. David Witzke and Michael Gregory are the managing members of Avidity Capital Partners (GP) LLC and Avidity Partners Management (GP) LLC. Each of the entities and individuals referenced in this paragraph may be deemed to beneficially own the shares held by the Avidity entities. Certain affiliates of the Avidity entities, which are not Selling Stockholders, may also own shares. The business address of these Avidity entities and

individuals is 2828 N. Harwood Street, Suite 1220, Dallas, TX 75201. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by Avidity Master is subject to a Beneficial Ownership Limitation of 9.90%.

(28) Consists of (i) 386,880 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by T. Rowe Price Health Sciences Fund, Inc., (ii) 18,480 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by T. Rowe Price Health Sciences Portfolio, and (iii) 40 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by T. Rowe Price Multi-Strategy Total Return Fund, Inc. T. Rowe Price Associates, Inc. ("TRPA"), as investment adviser, has dispositive and voting power with respect to the shares held by these funds and accounts. For purposes of the Securities Exchange Act of 1934, TRPA may be deemed to be the beneficial owner of these aforementioned shares; however, TRPA expressly disclaims that it is, in fact, the beneficial owner of such securities. TRPA is a wholly owned subsidiary of T. Rowe Price Group, Inc., which is a publicly traded financial services holding company. The principal business address of TRPA is 100 East Pratt Street, Baltimore, MD 21202. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by these TRPA entities is subject to a Beneficial Ownership Limitation of 19.90%.

(29) Consists of (i) 121,120 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Biomedical Value Fund, L.P. ("BMVF"), (ii) 71,000 shares of Common Stock held by BMVF, (iii) 80,480 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Biomedical Offshore Value Fund, Ltd. ("BOVF"), (iv) 45,500 shares of Common Stock held by BOVF, (v) 14,720 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Cheyne Select Master Fund ICAV – Cheyne Global Equity Fund ("CGEF" and together with BMVF and BOVF, the "GPP Entities"), and (vi) 8,500 shares of Common Stock held by CGEF. Great Point Partners LLC ("GPP LLC") is the investment manager of BMVF and BMOVF and the sub-advisor to CGEF, and by virtue of such status may be deemed to be the beneficial owner of the securities held by the GPP Entities. Each of Dr. Jeffrey R. Jay, M.D., as Senior Managing Member of GPP LLC, and Mr. Ortav Yehudai, as Managing Director of GPP LLC, has voting and investment power with respect to securities held by the GPP Entities, and therefore may be deemed to be the beneficial owner of the securities held by the GPP Entities. Notwithstanding the above, GPP LLC, Dr. Jay and Mr. Yehudai disclaim beneficial ownership of the securities held by the GPP Entities except to the extent of their respective pecuniary interests. The address of the GPP Entities is 165 Mason Street, 3rd Floor, Greenwich, CT 06830. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by each of the GPP Entities are subject to a Beneficial Ownership Limitation of 9.99%.

(30) Consists of (i) 184,920 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Blackstone Annex Master Fund L.P. ("Annex Fund"), (ii) 77,997 shares of Common Stock held by Annex Fund, (iii) 28,360 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Spruce Street Aggregator L.P – ECDF A1 ("ECDF A1"), (iv) 8,396 shares of Common Stock held by ECDF A1, (v) 12,160 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Spruce Street Aggregator L.P – ECDF A2 ("ECDF A2", and together with ECDF A1, the "Aggregator Fund"), and (vi) 3,598 shares of Common Stock held by ECDF A2. Blackstone Alternative Asset Management Associates LLC is the general partner of Annex Fund and the Aggregator Fund. Blackstone Holdings II L.P. is the sole member of Blackstone Alternative Asset Management Associates LLC. Blackstone Holdings I/II GP L.L.C. is the general partner of Blackstone Holdings II L.P. Blackstone Inc. is the sole member of Blackstone Holdings I/II GP L.L.C. Blackstone Group Management L.L.C. is the sole holder of the Series II preferred stock of Blackstone Inc. Blackstone Group Management L.L.C. is wholly owned by its senior managing directors and controlled by its founder, Stephen A. Schwarzman. Each of such Blackstone entities and Mr. Schwarzman may be deemed to beneficially own the securities beneficially owned by the Annex Fund and the Aggregator Fund directly or indirectly controlled by it or him, but each (other than each of the Annex Fund and the Aggregator Fund to the extent of their respective direct holdings) disclaims beneficial ownership of such securities. The address of each of the entities listed is c/o Blackstone Inc., 345 Park Avenue, New York, New York 10154. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by Annex Fund and Aggregator Fund are subject to a Beneficial Ownership Limitation of 4.90%.

(31) Consists of (i) 103,080 shares of Common Stock held by StemPoint Capital Master Fund LP ("StemPoint Fund"), (ii) 27,000 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by StemPoint Fund, (iii) 87,530 shares of Common Stock held by Jefferies Strategic Investments, LLC ("JSI") and (iv) 89,371 shares of Common Stock held by Titan Biotech Dislocation Fund SP ("TBDF"). StemPoint Capital LP ("Stempoint") serves as investment advisor to StemPoint Fund and JSI, and as sub-advisor to TBDF. StemPoint exercises voting and investment power over the shares held by each of StemPoint Fund and JSI pursuant to investment management agreements and StemPoint exercises investment power over the shares held by TBDF pursuant to its sub-advisory agreement. StemPoint hereby disclaims beneficial ownership of the shares held by StemPoint Fund, JSI and TBDF. The total number of shares that StemPoint exercises investment power over is [176,901], as of April 15, 2024. The total number of shares that StemPoint exercises voting and investment power over is [87,530], as of April 15, 2024. The address of these funds and accounts is 520 Madison Avenue, 19th Floor, New York, NY 10022. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by StemPoint are subject to a Beneficial Ownership Limitation of 9.90%.

(32) Consists of (i) 165,480 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by CDK Associates, L.L.C. ("CDK") and (ii) 98,700 shares of Common Stock held by CDK. Bruce Kovner has voting and/or dispositive power over the holdings of CDK. The address of CDK is c/o CAM Capital 731 Alexander Road, Bldg 2, Suite 500, Princeton, NJ 08540. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by CDK is subject to a Beneficial Ownership Limitation of 4.90%.

(33) Consists of (i) 67,600 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Walleye Opportunities Master Fund Ltd. ("Walleye Opportunities Fund"), (ii) 161,285 shares of Common Stock held by Walleye Opportunities Fund and (iii) 500 shares of Common Stock held by Sea Hawk Multi-Strategy Master Fund Ltd. Walleye Opportunities Fund is a private investment fund managed by Walleye Capital LLC. William England is the chief executive officer of Walleye Capital LLC. As a result, Walleye Capital LLC and Mr. England may be deemed to have shared voting and dispositive power with respect to the securities held by Walleye Opportunities Fund. The business address of these entities is 2800 Lane N., Plymouth, MN 55447. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by Walleye Opportunities Fund is subject to a Beneficial Ownership Limitation of 4.99%.

(34) Consists of 202,600 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Atlas Diversified Master Fund, Ltd. ("ADMF"). Balyasny Asset Management L.P. ("BAM") is the investment manager of ADMF. Dmitry Balyasny indirectly controls the general partner of BAM and shall be deemed to have voting and investment control over the shares held by ADMF and may be deemed to beneficially own the shares beneficially owned by ADMF. The business address of ADMF is c/o Maples Corporate Services Limited, P.O. Box 309, Ugland House, George Town, Grand Cayman KY1-1104, Cayman Islands, and the business address of BAM and Dmitry Balyasny is 444 W. Lake Street, 50th Floor, Chicago, IL 60606. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by ADMF are subject to a Beneficial Ownership Limitation of 9.90%.

(35) Consists of (i) 131,000 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Woodline Master Fund LP (the "Woodline Fund"), and (ii) 50,000 shares of Common Stock held by Woodline Fund. Woodline Partners LP serves as the investment manager of Woodline Fund and may be deemed to be the beneficial owner of the shares. Woodline Partners LP disclaims any beneficial ownership of these shares. The address of this fund and account is 4 Embarcadero Center, Suite 34590, San Francisco, CA 94111. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by Woodline Fund is subject to a Beneficial Ownership Limitation of 9.99%.

(36) Consists of (i) 91,387 shares of Common Stock and (ii) 55,278 shares of Common Stock issuable upon the exercise of options that are or will become exercisable within 60 days of April 15, 2024, held by Dr. Spencer.

(37) Consists of (i) 91,387 shares of Common Stock and (ii) 55,278 shares of Common Stock issuable upon the exercise of options that are or will become exercisable within 60 days of April 15, 2024, held by Dr. Gunzner-Toste.

(38) Consists of (i) 74,650 shares of Common Stock and (ii) 32,021 shares of Common Stock issuable upon the exercise of options that are or will become exercisable within 60 days of April 15, 2024, held by Mr. LaFountaine.
(39) Consists of 68,720 shares of Common Stock held by Wedbush Healthcare Partners 2023 Fund, LLC. The address for Wedbush Healthcare Partners 2023 Fund, LLC is Wedbush Center, 1000 Wilshire Blvd., Los Angeles, CA 90017.
(40) Consists of 67,600 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Quantum Partners LP ("Quantum Partners"). The address of Quantum Partners is 103 Mount Street, London, W1K 2TJ, United Kingdom. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by Quantum Partners is subject to a Beneficial Ownership Limitation of 9.99%.
(41) Consists of (i) 43,185 shares of Common Stock held by Salthill Investors (Bermuda) L.P. ("Salthill Investors") and (ii) 50,075 shares of Common Stock held by Salthill Partners, L.P. ("Salthill Partners" and together with Salthill Investors, the "Wellington Selling Stockholders"). Wellington Management Company LLP ("WMC") has the power to vote and dispose of the securities pursuant to WMC's capacity as investment advisor on behalf of the Wellington Selling Stockholders. WMC is a subsidiary of Wellington Management Group LLP ("WMG"). WMG is a Massachusetts limited liability partnership, privately held by 204 partners (as of January 1, 2024). There are no external entities with any ownership interest in the firm. No single partner owns or has the right to vote more than 5% of WMC's capital. Additional information about WMC is available in its Form ADV filed with the SEC. The address of the Wellington entities is 280 Congress Street, Boston, MA 02210.
(42) Consists of 34,360 shares of Common Stock held by Sessions LLC. The address for Sessions LLC is 96 Fairbanks Ave, Wellesley, MA 02481.
(43) Consists of (i) 10,600 shares of Common Stock issuable upon the conversion of Series B Preferred Stock held by Third Street Holdings LLC ("Third Street") and (ii) 6,300 shares of Common Stock held by Third Street. Peter P. D'Angelo has voting and/or dispositive power over the holdings of Third Street Holdings, LLC. The address of Third Street is c/o CAM Capital 731 Alexander Road, Bldg 2, Suite 500, Princeton, NJ 08540. The shares of Common Stock issuable upon conversion of the shares of Series B Preferred Stock held by Third Street is subject to a Beneficial Ownership Limitation of 4.90%.
(44) Consists of 13,760 shares of Common Stock held by Harry Turtle.

Relationship with the Selling Stockholders

In addition to the June 2023 SPA, in connection with the June 2023 PIPE, we entered into the June 2023 RRA on June 22, 2023 with certain Selling Stockholders. Andrew Spencer is our SVP, Preclinical R&D, Janet Gunzner-Toste is our SVP, Operations and Justin LaFountaine is our VP, Corporate Development. Wedbush PacGrow served as lead financial advisor to our board of directors with respect to the Asset Acquisition. See "*Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters*" and "*Certain Relationships and Related Transactions.*"

In addition to the December 2023 SPA, in connection with the December 2023 PIPE, we entered into the December 2023 RRA on December 7, 2023 with the Selling Stockholders. Certain of the December 2023 Investors were, immediately prior to the closing of the December 2023 PIPE, or became holders of more than 5% of our Common Stock and were parties to the June 2023 SPA and the June 2023 RRA. See "*Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters* " and "*Certain Relationships and Related Transactions.*"

In addition to the March 2024 SPA, in connection with the March 2024 PIPE, we entered into the March 2024 RRA on March 18, 2024 with the Selling Stockholders. Certain of the March 2024 Investors were, immediately prior to the closing of the March 2024 PIPE, or became holders of more than 5% of our Common Stock and were parties to the March 2024 SPA and the March 2024 RRA. See "*Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters*" and "*Certain Relationships and Related Transactions.* "

Registration Rights Agreements

Pursuant to the terms of each of our registration rights agreements with certain groups of investors, including the March 2024 RRA with the March 2024 Investors, we agreed to prepare and file with the SEC resale a registration statement to register the Registrable Securities (as defined in the respective registration rights agreement) and, subject to certain exceptions, use commercially reasonable efforts to keep the registration statement effective under the Securities Act for so long as such securities registered for resale thereunder retain their character as Registrable Securities. This registration statement is being filed in order to satisfy our obligations under the March 2024 RRA.

We have also agreed, among other things, to indemnify the Selling Stockholders, and each of their respective officers, directors, members, employees, partners, managers, stockholders, affiliates, investment advisors and agents, each person who controls any such Selling Stockholder and the officers, directors, members, employees, partners, managers, stockholders, affiliates, investment advisors and agents of each such controlling person from certain liabilities and pay all fees and expenses (excluding any legal fees of the selling holder(s), and any underwriting discounts and selling commissions) incident to our obligations under the June 2023 RRA, the December 2023 RRA and the March 2024 RRA, respectively.

PLAN OF DISTRIBUTION

We are registering the Resale Shares issued to the Selling Stockholders to permit the sale, transfer or other disposition of these shares by the Selling Stockholders or their donees, pledgees, transferees or other successors-in-interest from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the Selling Stockholders of the Resale Shares. We will, or will procure to, bear all fees and expenses incident to our obligation to register the Resale Shares.

The Selling Stockholders may sell all or a portion of the Resale Shares beneficially owned by them and offered hereby from time to time, and in the case of the December 2023 Private Placement Conversion Shares and the March 2024 Private Placement Conversion Shares, may only be offered after such shares are converted to Common Stock pursuant to the terms of the Series B Certificate of Designation, directly or through one or more underwriters, broker-dealers or agents. If the Resale Shares are sold through underwriters or broker-dealers, the Selling Stockholders will be responsible for underwriting discounts (it being understood that the Selling Stockholders shall not be deemed to be underwriters solely as a result of their participation in this offering) or commissions or agent's commissions. The Resale Shares may be sold on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale, in the over-the-counter market or in transactions otherwise than on these exchanges or systems or in the over-the-counter market and in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions. The Selling Stockholders may use any one or more of the following methods when selling Resale Shares:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- to or through underwriters or purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part;
- broker-dealers may agree with the Selling Stockholders to sell a specified number of such shares at a stipulated price per share;
- through the writing or settlement of options or other hedging transactions, whether such options are listed on an options exchange or otherwise;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

The Selling Stockholders also may resell all or a portion of the Resale Shares in open market transactions in reliance upon Rule 144, as permitted by that rule, or Section 4(a)(1) under the Securities Act, if available, rather than under this prospectus, provided that they meet the criteria and conform to the requirements of those provisions.

Broker-dealers engaged by the Selling Stockholders may arrange for other broker-dealers to participate in sales. If the Selling Stockholders effect such transactions by selling Resale Shares to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the Selling Stockholders or commissions from purchasers of the Resale Shares for whom they may act as agent or to whom they may sell as principal. Such commissions will be in amounts to

be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction will not be in excess of a customary brokerage commission in compliance with FINRA Rule 2121; and in the case of a principal transaction a markup or markdown in compliance with FINRA IM-2121.01.

In connection with sales of the Resale Shares or otherwise, the Selling Stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the Resale Shares in the course of hedging in positions they assume. The Selling Stockholders may also sell Resale Shares short and if such short sale takes place after the date that this registration statement is declared effective by the SEC, the Selling Stockholders may deliver Resale Shares covered by this prospectus to close out short positions and to return borrowed Resale Shares in connection with such short sales. The Selling Stockholders may also loan or pledge Resale Shares to broker-dealers that in turn may sell such shares, to the extent permitted by applicable law. The Selling Stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). Notwithstanding the foregoing, the Selling Stockholders have been advised that they may not use Resale Shares the resale of which has been registered on this registration statement to cover short sales of our Common Stock made prior to the date the registration statement, of which this prospectus forms a part, has been declared effective by the SEC.

The Selling Stockholders may, from time to time, pledge or grant a security interest in some or all of the Resale Shares owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the Resale Shares from time to time pursuant to this prospectus or any amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending, if necessary, the list of Selling Stockholders to include the pledgee, transferee or other successors in interest as Selling Stockholders under this prospectus. The Selling Stockholders also may transfer and donate the Resale Shares in other circumstances in which case the transferees, donees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The Selling Stockholders and any broker-dealer or agents participating in the distribution of the Resale Shares may be deemed to be “underwriters” within the meaning of Section 2(11) of the Securities Act in connection with such sales. In such event, any commissions paid, or any discounts or concessions allowed to, any such broker-dealer or agent and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Selling Stockholders who are “underwriters” within the meaning of Section 2(11) of the Securities Act will be subject to the applicable prospectus delivery requirements of the Securities Act including Rule 172 thereunder and may be subject to certain statutory liabilities of, including but not limited to, Sections 11, 12 and 17 of the Securities Act and Rule 10b-5 under the Exchange Act.

Each Selling Stockholder has informed us that it is not a registered broker-dealer and does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the Resale Shares. Upon us being notified in writing by a Selling Stockholder that any material arrangement has been entered into with a broker-dealer for the sale of Common Stock through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker or dealer, a supplement to this prospectus will be filed, if required, pursuant to Rule 424(b) under the Securities Act, disclosing (i) the name of each such Selling Stockholder and of the participating broker-dealer(s), (ii) the number of Resale Shares involved, (iii) the price at which such the Resale Shares were sold, (iv) the commissions paid or discounts or concessions allowed to such broker-dealer(s), where applicable, (v) that such broker-dealer(s) did not conduct any investigation to verify the information set out in this prospectus, and (vi) other facts material to the transaction. In no event shall any broker-dealer receive fees, commissions and markups, which, in the aggregate, would exceed eight percent (8.0%).

Under the securities laws of some U.S. states, the Resale Shares may be sold in such states only through registered or licensed brokers or dealers. In addition, in some U.S. states the Resale Shares may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with.

There can be no assurance that any Selling Stockholder will sell any or all of the Resale Shares registered pursuant to the shelf registration statement, of which this prospectus forms a part.

Each Selling Stockholder and any other person participating in such distribution will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including, without limitation, to the extent applicable, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the Resale Shares by the Selling Stockholder and any other participating person. To the extent applicable, Regulation M may also restrict the ability of any person engaged in the distribution of the Resale Shares to engage in market-making activities with respect to the Resale Shares. All of the foregoing may affect the marketability of the Resale Shares and the ability of any person or entity to engage in market-making activities with respect to the Resale Shares.

We will pay all expenses of the registration of the Resale Shares pursuant to the June 2023 RRA, the December 2023 RRA and the March 2024 RRA, including, without limitation, SEC filing fees and expenses of compliance with state securities or “blue sky” laws; provided, however, that each Selling Stockholder will pay all underwriting discounts and selling commissions, if any and any related legal expenses incurred by it. We will indemnify the Selling Stockholders against certain liabilities, including some liabilities under the Securities Act, in accordance with the June 2023 RRA, the December 2023 RRA and the March 2024 RRA, or the Selling Stockholders will be entitled to contribution. We may be indemnified by the Selling Stockholders against certain civil liabilities set forth in the June 2023 RRA, the December 2023 RRA or the March 2024 RRA, as applicable, including liabilities under the Securities Act, that may arise from any written information furnished to us by the Selling Stockholders specifically for use in this prospectus, in accordance with the related registration rights agreements, or we may be entitled to contribution.

DESCRIPTION OF CAPITAL STOCK

General

The following description summarizes the material terms of our capital stock, as well as other material terms of our amended and restated certificate of incorporation ("Certificate of Incorporation") and amended and restated bylaws ("Bylaws") and certain provisions of Delaware law. This summary does not purport to be complete and is qualified in its entirety by the provisions of our Certificate of Incorporation and Bylaws, copies of which are filed as exhibits to our Annual Report on Form 10-K, to which this exhibit is also appended.

Our authorized capital stock consists of 400,000,000 shares of Common Stock, $0.0001 par value per share, and 10,000,000 shares of preferred stock, $0.0001 par value per share ("Preferred Stock"), of which 1,086,341 shares have been designated as Series A Preferred Stock, $0.0001 par value per share and 271,625 shares have been designated as Series B Preferred Stock, $0.0001 par value per share.

As of April 15, 2024, there were 36,639,734 shares of our Common Stock, 271,625 shares of Series A Preferred Stock and 150,000 shares of Series B Preferred Stock outstanding.

Common Stock

Our Certificate of Incorporation authorizes the issuance of up to 400,000,000 shares of Common Stock. All outstanding shares of Common Stock are validly issued, fully paid and nonassessable.

Dividend rights

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

Voting rights

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

No preemptive or similar rights

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

Right to receive liquidation distributions

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

Preferred Stock

Under the terms of our Certificate of Incorporation, our board of directors is authorized, subject to limitations prescribed by Delaware law, to issue up to 10,000,000 shares of Preferred Stock in one or more series, to

establish from time to time the number of shares to be included in each series and to fix the designation, powers, preferences and rights of the shares of each series and any of their qualifications, limitations or restrictions, in each case without further vote or action by our stockholders. Subject to any certificates of designation, our board of directors can also increase or decrease the number of shares of any series of Preferred Stock, but not below the number of shares of that series then outstanding, without any further vote or action by our stockholders. Our board of directors may authorize the issuance of Preferred Stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our Common Stock. The issuance of Preferred Stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in control of our company and might adversely affect the market price of our Common Stock and the voting and other rights of the holders of our Common Stock. We have no current plan to issue any shares of Preferred Stock other than the shares of our Series A Preferred Stock and shares of our Series B Preferred Stock that were issued in connection with the June 2023 Transactions, the December 2023 PIPE and the March 2024 PIPE, as applicable.

Series A Preferred Stock

Holders of Series A Preferred Stock are entitled to receive dividends on shares of Series A Preferred Stock equal to, on an as-if-converted-to-common-stock basis, and in the same form as dividends actually paid on shares of our Common Stock. Except as provided in the Series A Certificate of Designation or as otherwise required by law, the Series A Preferred Stock does not have voting rights. However, as long as any shares of Series A Preferred Stock are outstanding, we will not, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series A Preferred Stock: (a) alter or change adversely the powers, preferences or rights given to the Series A Preferred Stock, or alter or amend the Series A Certificate of Designation, amend or repeal any provision of, or add any provision to, our Certificate of Incorporation or its Bylaws, or file any articles of amendment, certificate of designations, preferences, limitations and relative rights of any series of Preferred Stock, if such action would adversely alter or change the preferences, rights, privileges or powers of, or restrictions provided for the benefit of the Series A Preferred Stock, regardless of whether any of the foregoing actions will be by means of amendment to the Certificate of Incorporation or by merger, consolidation, recapitalization, reclassification, conversion or otherwise, (b) issue further shares of Series A Preferred Stock or increase or decrease (other than by conversion) the number of authorized shares of Series A Preferred Stock, (c) prior to the stockholder approval of the conversion of the Series A Preferred Stock into shares of Common Stock in accordance with Nasdaq Stock Market Rules (the “Series A Conversion Proposal”) or at any time while at least 30% of the originally issued Series A Preferred Stock remains issued and outstanding, consummate (x) any Fundamental Transaction (as defined in the Series A Certificate of Designation) or (y) any merger or consolidation of the Company with or into another entity or any stock sale to, or other business combination in which the stockholders of the Company immediately before such transaction do not hold at least a majority of our capital stock immediately after such transaction or (d) enter into any agreement with respect to any of the foregoing. The Series A Preferred Stock does not have a preference upon any liquidation, dissolution or winding-up of the Company.

Following stockholder approval of the Series A Conversion Proposal, each share of Series A Preferred Stock automatically converted into 40 shares of Common Stock, subject to certain limitations, including that a holder of Series A Preferred Stock is prohibited from converting shares of Series A Preferred Stock into shares of Common Stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (established by the holder between 0% and 19.9%) of the total number of shares of Common Stock issued and outstanding immediately after giving effect to such conversion.

Series B Preferred Stock

Certain holders of our Common Stock, Series B Preferred Stock are entitled to receive dividends on shares of Series B Preferred Stock equal to, on an as-if-converted-to-common-stock basis, and in the same form as dividends actually paid on shares of our Common Stock. Except as provided in the Series B Certificate of Designation or as otherwise required by law, the Series B Preferred Stock does not have voting rights. However,

as long as any shares of Series B Preferred Stock are outstanding, we will not, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series B Preferred Stock alter or change adversely the powers, preferences or rights given to the Series B Preferred Stock, or alter or amend the Series B Certificate of Designation, amend or repeal any provision of, or add any provision to, our Certificate of Incorporation or its Bylaws, or file any articles of amendment, certificate of designations, preferences, limitations and relative rights of any series of Preferred Stock, if such action would adversely alter or change the preferences, rights, privileges or powers of, or restrictions provided for the benefit of the Series B Preferred Stock, regardless of whether any of the foregoing actions will be by means of amendment to the Certificate of Incorporation or by merger, consolidation, recapitalization, reclassification, conversion or otherwise. The Series B Preferred Stock does not have a preference upon any liquidation, dissolution or winding-up of the Company.

Following stockholder approval of the conversion of the Series B Preferred Stock into shares of Common Stock in accordance with Nasdaq Stock Market Rules (the "Series B Conversion Proposal"), each share of Series B Preferred Stock will automatically convert into 40 shares of Common Stock, subject to certain limitations, including that a holder of Series B Preferred Stock is prohibited from converting shares of Series B Preferred Stock into shares of Common Stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (established by the holder between 0% and 19.9%) of the total number of shares of Common Stock issued and outstanding immediately after giving effect to such conversion.

Registration Rights

Holders of our Series A Preferred Stock and Series B Preferred Stock are entitled to certain rights with respect to the registration of such securities as further provided under the heading "*Selling Stockholders – Registration Rights Agreements*."

Anti-Takeover Provisions

The provisions of Delaware law, our Certificate of Incorporation and our Bylaws could have the effect of delaying, deferring or discouraging another person from acquiring control of our company. These provisions, which are summarized below, may have the effect of discouraging takeover bids. They are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging a proposal to acquire us because negotiation of these proposals could result in an improvement of their terms.

Delaware law

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

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

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

- at or subsequent to the date of the transaction, the business combination is approved by the board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a “business combination” to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an “interested stockholder” as an entity or person who, together with the person’s affiliates and associates, beneficially owns, or within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

Certificate of Incorporation and Bylaw Provisions

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

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

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

- ***Stockholder action; special meetings of stockholders***. Our Certificate of Incorporation and Bylaws provide that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. As a result, a holder controlling a majority of our capital stock would not be able to amend our Bylaws or remove directors without holding a meeting of our stockholders called in accordance with our Bylaws. Further, our Certificate of Incorporation and Bylaws provide that special meetings of our stockholders may be called only by a majority of our entire board of directors, the chairperson of our board of directors, our Chief Executive Officer or our President, thus prohibiting a stockholder from calling a special meeting. These provisions might delay the ability of our stockholders to force consideration of a proposal or for stockholders controlling a majority of our capital stock to take any action, including the removal of directors.

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

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

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

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

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

- ***Choice of forum***. Our Certificate of Incorporation and Bylaws provide that the Court of Chancery of the State of Delaware is the sole and exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the DGCL, our Certificate of Incorporation or our Bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. In addition, our Bylaws also provide that the federal district courts of the United States is the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. These choice of forum provisions will not apply to claims brought to enforce a duty or liability created by the Exchange Act.

Transfer Agent and Registrar

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

Exchange Listing

Our Common Stock is listed on The Nasdaq Global Select Market under the symbol "SYRE."

LEGAL MATTERS

Certain legal matters, including the legality of the securities offered, has been passed upon for us by Gibson, Dunn & Crutcher LLP, San Francisco, California. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements of Spyre Therapeutics, Inc. as of December 31, 2023 and 2022 and for each of the three years in the period ended December 31, 2023 included in this prospectus have been so included in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

The audited Statement of Assets Acquired and Liabilities Assumed from Spyre Therapeutics, Inc. by Aeglea BioTherapeutics, Inc., as of June 22, 2023 included in this prospectus have been so included in reliance on the report (which contains an emphasis of matter relating to the basis of presentation as described in Note 1 and an explanatory paragraph relating to the Company's ability to continue as a going concern as described in Note 1 to the financial statement) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the informational requirements of the Exchange Act and are required to file annual, quarterly and other reports, proxy statements and other information with the SEC. The SEC maintains an Internet site (http://www.sec.gov) that contains reports, proxy and information statements, and various other information about us.

Information about us is also available at our website at http://www.aeglea.com. You may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. However, the information on our website is not a part of this prospectus and is not incorporated by reference into this prospectus.

We have filed a registration statement on Form S-1 with the SEC relating to the securities covered by this prospectus. This prospectus is a part of the registration statement and does not contain all of the information in the registration statement. Whenever a reference is made in this prospectus to a contract or other document of ours, please be aware that the reference is only a summary and that you should refer to the exhibits that are part of the registration statement for a copy of the contract or other document. You may review a copy of the registration statement through the SEC's website or our website.

SPYRE THERAPEUTICS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

INDEX TO STATEMENT OF ASSETS ACQUIRED AND LIABILITIES ASSUMED FROM SPYRE THERAPEUTICS, INC. BY AEGLEA BIOTHERAPEUTICS, INC.

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Spyre Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Spyre Therapeutics, Inc. and its subsidiaries (the "Company") as of December 31, 2023 and 2022, and the related consolidated statements of operations, of comprehensive loss, of changes in convertible preferred stock and stockholders' equity and of cash flows for each of the three years in the period ended December 31, 2023, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2023 in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the consolidated financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Contingent Value Right (CVR) Liability

As described in Notes 1, 2, 3, and 8 to the consolidated financial statements, in connection with the asset acquisition of Pre-Merger Spyre, a non-transferable contingent value right was distributed to certain legacy stockholders of record as of the close of business on July 3, 2023 entitling holders of the contingent value right to

receive certain cash payments from proceeds received by the Company related to the disposition or monetization of the Company's legacy assets. Management determined that certain contingent payments under the Contingent Value Rights (CVR) Agreement qualified as derivatives, and as such, were recorded as a liability on the balance sheet. For derivative financial instruments accounted for as liabilities, the derivative instrument is initially recorded by management at its fair value and is then re-valued at each reporting date. The fair value of the CVR liability was determined using the probability weighted discounted cash flow method to estimate future cash flows associated with the sale of the legacy assets. The CVR liability value is based on significant inputs not observable in the market such as estimated cash flows, estimated probabilities of regulatory success, estimated reimbursement rates compared to the reimbursement target, and risk-adjusted discount rates. The CVR liability as of December 31, 2023 was $42.7 million and the Company recognized an increase in the CVR liability of $19.0 million for the year ended December 31, 2023 related to the change in fair value between the issuance of the CVR and December 31, 2023.

The principal considerations for our determination that performing procedures relating to the valuation of the CVR liability is a critical audit matter are (i) the significant judgment by management when developing the fair value estimate of the CVR liability; (ii) a high degree of auditor judgment, subjectivity, and effort in performing procedures and evaluating management's significant assumptions related to the estimated probabilities of regulatory success, estimated reimbursement rates compared to the reimbursement target, and risk-adjusted discount rates; and (iii) the audit effort involved the use of professionals with specialized skill and knowledge.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included, among others (i) reading and evaluating the terms of the CVR Agreement; (ii) testing management's process for developing the fair value estimate of the CVR liability; (iii) evaluating the appropriateness of the probability weighted discounted cash flow method used by management; (iv) testing the completeness and accuracy of underlying data used by management in the probability weighted discounted cash flow method; and (v) evaluating the reasonableness of the significant assumptions used by management related to the estimated probabilities of regulatory success, estimated reimbursement rates compared to the reimbursement target, and risk-adjusted discount rates. Evaluating management's assumptions related to estimated probabilities of regulatory success and estimated reimbursement rates compared to the reimbursement target involved evaluating whether the assumptions used by management were reasonable considering the consistency with (i) external market and industry data and (ii) evidence obtained in other areas of the audit. Professionals with specialized skill and knowledge were used to assist in evaluating (i) the appropriateness of the probability weighted discounted cash flow method and (ii) the reasonableness of the risk-adjusted discount rate assumption.

/s/ PricewaterhouseCoopers LLP
Austin, Texas
February 29, 2024

We have served as the Company's auditor since 2014.

Spyre Therapeutics, Inc.
Consolidated Balance Sheets
(In thousands, except share and per share amounts)

	December 31, 2023	December 31, 2022
ASSETS		
CURRENT ASSETS		
Cash and cash equivalents	$ 188,893	$ 34,863
Marketable securities	150,384	20,848
Development receivables	—	375
Prepaid expenses and other current assets	2,251	6,172
Total current assets	341,528	62,258
Restricted cash	322	1,553
Property and equipment, net	—	3,220
Operating lease right-of-use assets	—	3,430
Other non-current assets	9	683
TOTAL ASSETS	$ 341,859	$ 71,144
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES		
Accounts payable	$ 896	$ 677
CVR liability	1,390	—
Operating lease liabilities	—	625
Deferred revenue	—	517
Accrued and other current liabilities	13,108	12,837
Related party accounts payable and other current liabilities	16,584	—
Total current liabilities	31,978	14,656
Non-current CVR liability	41,310	—
Non-current operating lease liabilities	—	4,004
Deferred revenue, net of current portion	—	2,179
TOTAL LIABILITIES	73,288	20,839
Commitments and Contingencies (Note 9)		
Series B non-voting convertible preferred stock, $0.0001 par value; 150,000 and no shares authorized as of December 31, 2023 and December 31, 2022, respectively; 150,000 and no shares issued and outstanding as of December 31, 2023 and December 31, 2022, respectively.	84,555	—
STOCKHOLDERS' EQUITY		
Series A non-voting convertible preferred stock, $0.0001 par value; 1,086,341 and no shares authorized as of December 31, 2023 and December 31, 2022, respectively; 437,037 and no shares issued and outstanding as of December 31, 2023 and December 31, 2022, respectively.	184,927	—
Preferred stock, $0.0001 par value; 8,763,659 shares and 10,000,000 authorized as of December 31, 2023 and December 31, 2022, respectively; no shares issued and outstanding as of December 31, 2023 and December 31, 2022.	—	—
Common stock, $0.0001 par value; 400,000,000 and 20,000,000 shares authorized as of December 31, 2023 and December 31, 2022, respectively; 36,057,109 shares and 2,614,014 shares issued and outstanding as of December 31, 2023 and December 31, 2022, respectively.	10	6
Additional paid-in capital	763,191	475,971
Accumulated other comprehensive income (loss)	302	(48)
Accumulated deficit	(764,414)	(425,624)
TOTAL STOCKHOLDERS' EQUITY	184,016	50,305
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY	$ 341,859	$ 71,144

The accompanying notes are an integral part of these consolidated financial statements.

Spyre Therapeutics, Inc.
Consolidated Statements of Operations
(In thousands, except share and per share amounts)

	Year Ended December 31,		
	2023	2022	2021
Revenue:			
License	$ —	$ —	$ 12,000
Development fee and royalty	886	2,329	6,739
Total revenue	886	2,329	18,739
Operating expenses:			
Research and development [(1)]	89,504	58,579	57,069
General and administrative	39,946	28,531	27,319
Acquired in-process research and development	130,188	—	—
Gain on sale of in-process research and development asset	(16,449)	—	—
Total operating expenses	243,189	87,110	84,388
Loss from operations	(242,303)	(84,781)	(65,649)
Other (expense) income:			
Interest income	6,147	837	111
Change in fair value of forward contract liability	(83,530)	—	—
Other expense, net	(19,130)	(7)	(122)
Total other (expense) income	(96,513)	830	(11)
Loss before income tax expense	(338,816)	(83,951)	(65,660)
Income tax benefit (expense)	26	136	(141)
Net loss	$ (338,790)	$ (83,815)	$ (65,801)
Net loss per share, basic and diluted	$ (49.12)	$ (24.86)	$ (25.02)
Weighted-average common shares outstanding, basic and diluted	6,897,065	3,371,231	2,629,784

(1) Includes $48.5 million in related party expenses for the year ended December 31, 2023 and no related party expenses for the year ended months ended December 31, 2022 and 2021.

The accompanying notes are an integral part of these consolidated financial statements.

Spyre Therapeutics, Inc.
Consolidated Statements of Comprehensive Loss
(In thousands)

	Year Ended December 31,		
	2023	2022	2021
Net loss	$(338,790)	$(83,815)	$(65,801)
Other comprehensive income (loss):			
Foreign currency translation adjustment	37	(35)	(1)
Unrealized gain (loss) on marketable securities	313	7	(30)
Total comprehensive loss	$(338,440)	$(83,843)	$(65,832)

The accompanying notes are an integral part of these consolidated financial statements.

Spyre Therapeutics, Inc.
Consolidated Statements of Changes in Convertible Preferred Stock and Stockholders' Equity
(In thousands)

	Series B Non-Voting Convertible Preferred Stock		Series A Non-Voting Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount				
Balances—December 31, 2020	—	$ —	—	$ —	1,918	$ 5	$ 415,824	$ 11	$ (276,008)	$ 139,832
Issuance of common stock in connection with exercise of pre-funded warrants	—	—	—	—	40	—	—	—	—	—
Issuance of common stock in connection with exercise of stock options and employee stock purchase plan	—	—	—	—	16	—	1,903	—	—	1,903
Stock-based compensation expense	—	—	—	—	—	—	8,038	—	—	8,038
Foreign currency translation adjustment	—	—	—	—	—	—	—	(1)	—	(1)
Unrealized loss on marketable securities	—	—	—	—	—	—	—	(30)	—	(30)
Net loss	—	—	—	—	—	—	—	—	(65,801)	(65,801)
Balances—December 31, 2021	—	$ —	—	$ —	1,974	$ 5	$ 425,765	$ (20)	$ (341,809)	$ 83,941
Issuance of common stock and pre-funded warrants in connection with registered direct offering, net of offering costs	—	—	—	—	430	1	42,873	—	—	42,874
Issuance of common stock in connection with exercise of pre-funded warrants	—	—	—	—	204	—	—	—	—	—
Issuance of common stock in connection with employee stock purchase plan	—	—	—	—	6	—	222	—	—	222
Stock-based compensation expense	—	—	—	—	—	—	7,111	—	—	7,111
Foreign currency translation adjustment	—	—	—	—	—	—	—	(35)	—	(35)
Unrealized gain on marketable securities	—	—	—	—	—	—	—	7	—	7
Net loss	—	—	—	—	—	—	—	—	(83,815)	(83,815)
Balances—December 31, 2022	—	$ —	—	$ —	2,614	$ 6	$ 475,971	$ (48)	$ (425,624)	$ 50,305

	Series B Non-Voting Convertible Preferred Stock		Series A Non-Voting Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount				
Issuance of Series A non-voting convertible preferred stock in connection with private placement, net of financing costs	—	—	721	197,364	—	—	—	—	—	197,364
Issuance of Series A non-voting convertible preferred stock in connection with the asset acquisition of Spyre and settlement of related forward contract	—	—	365	189,741	—	—	—	—	—	189,741
Conversion of Series A non-voting convertible preferred stock into common stock	—	—	(649)	(202,178)	25,972	3	202,175	—	—	—
Issuance of Series B non-voting convertible preferred stock in connection with private placement, net of financing costs	150	84,555	—	—	—	—	—	—	—	—
Issuance of common stock in connection with private placement, net of financing costs	—	—	—	—	6,000	—	84,555			84,555
Issuance of common stock in connection with the asset acquisition of Spyre	—	—	—	—	518	1	3,767			3,768
Issuance of common stock in connection with exercise of pre-funded warrants	—	—	—	—	905	—	—	—	—	—
Issuance of common stock in connection with exercise of stock options and employee stock purchase plan	—	—	—	—	48	—	405	—	—	405
CVR distribution to common stockholders	—	—	—	—	—	—	(29,500)	—	—	(29,500)
Stock-based compensation expense	—	—	—	—	—	—	14,347	—	—	14,347
Issuance of Parapyre Option Obligation warrants	—	—	—	—	—	—	11,471	—	—	11,471
Foreign currency translation adjustment	—	—	—	—	—	—	—	37	—	37
Unrealized gain on marketable securities	—	—	—	—	—	—	—	313	—	313
Net loss	—	—	—	—	—	—	—	—	(338,790)	(338,790)
Balances—December 31, 2023	150	$84,555	437	$ 184,927	36,057	$ 10	$ 763,191	$ 302	$ (764,414)	$ 184,016

The accompanying notes are an integral part of these consolidated financial statements.

Spyre Therapeutics, Inc.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2023	2022	2021
CASH FLOWS FROM OPERATING ACTIVITIES			
Net loss	$(338,790)	$(83,815)	$ (65,801)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	744	1,567	1,576
Stock-based compensation	25,675	7,111	8,038
Acquired in-process research and development	130,188	—	—
Change in fair value of CVR liability	18,986	—	—
Change in fair value of forward contract liability	83,530	—	—
Gain on sale of in-process research and development asset	(16,449)	—	—
Lease ROU asset and leasehold improvement impairment loss	2,580	—	—
Loss on disposal of long-lived assets	915	—	—
Net (accretion of discount) amortization of premium on marketable securities	(2,318)	(327)	548
Amortization of operating lease assets	220	397	425
Other	15	426	(335)
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	3,245	(1,144)	(1,216)
Accounts payable	218	(2,641)	1,065
Deferred revenue	575	(880)	3,576
Development receivables	375	440	(815)
Operating lease liabilities	(2,326)	(435)	(404)
Accrued and other liabilities	(4,891)	(843)	(373)
Related party payable	(2,402)	—	—
Net cash used in operating activities	(99,910)	(80,144)	(53,716)
CASH FLOWS FROM INVESTING ACTIVITIES			
Cash assumed from asset acquisition of Spyre	3,035	—	—
Proceeds from sale of in-process research & development asset	15,000	—	—
Purchases of property and equipment	—	(38)	(573)
Proceeds from the sale of property plant and equipment	475	—	—
Purchases of marketable securities	(166,803)	(39,500)	(133,079)
Proceeds from maturities and sales of marketable securities	39,900	96,546	111,033
Net cash provided by (used in) investing activities	(108,393)	57,008	(22,619)
CASH FLOWS FROM FINANCING ACTIVITIES			
Proceeds from issuance of Series A non-voting convertible preferred stock in connection with private placement, net of placement and other offering costs	197,364	—	—
Proceeds from issuance of Series B non-voting convertible preferred stock in connection with private placement, net of placement and other offering costs	84,555	—	—
Proceeds from issuance of common stock in connection with private placement, net of placement and other offering costs	84,555	—	—
Payment of contingent value rights liability	(5,786)	—	—
Proceeds from issuance of common stock and pre-funded warrants in registered direct offering, net of offering costs	—	42,874	—
Proceeds from employee stock plan purchases and stock option exercises	405	222	1,903
Principal payments on finance lease obligation	(16)	(418)	(510)
Net cash provided by financing activities	361,077	42,678	1,393
Effect of exchange rate on cash, cash equivalents, and restricted cash	25	(106)	(15)
NET INCREASE (DECREASE) IN CASH, CASH EQUIVALENTS, AND RESTRICTED CASH	152,799	19,436	(74,957)
CASH, CASH EQUIVALENTS, AND RESTRICTED CASH			
Beginning of period	36,416	16,980	91,937
End of period	$ 189,215	$ 36,416	$ 16,980
Supplemental Disclosure of Non-Cash Investing and Financing Information:			
Settlement of forward contract liability and issuance of Series A non-voting convertible preferred stock in connection with the asset acquisition of Spyre	$ 189,741	$ —	$ —
Conversion of Series A non-voting convertible preferred stock into common stock	$ 202,178	$ —	$ —
Leased assets obtained in exchange for lease obligations	$ —	$ 21	$ 872

The accompanying notes are an integral part of these consolidated financial statements.

Spyre Therapeutics, Inc.
Notes to Consolidated Financial Statements

1. The Company and Basis of Presentation

Spyre Therapeutics, Inc., formerly Aeglea BioTherapeutics, Inc., ("Spyre" or the "Company") is a preclinical stage biotechnology company focused on developing next generation therapeutics for patients living with inflammatory bowel disease. The Company was formed as a Limited Liability Company ("LLC") in Delaware on December 16, 2013 under the name Aeglea BioTherapeutics Holdings, LLC and was converted from a Delaware LLC to a Delaware corporation on March 10, 2015. On November 27, 2023, the Company completed its corporate rebranding, changing the name of the Company to Spyre Therapeutics, Inc. The Company operates in one segment and has its principal offices in Waltham, Massachusetts.

On September 8, 2023, the Company effected a reverse stock split of its Common Stock at a ratio of 1-for-25 (the "Reverse Split"). Except as indicated otherwise, all share numbers related to the Company's Common Stock disclosed in these financial statements have been adjusted on a post-Reverse Split basis.

On April 12, 2023, based on the review of the inconclusive interim results from the Company's Phase 1/2 clinical trial of pegtarviliase for the treatment of Classical Homocystinuria and other business considerations, the Company announced that it had initiated a process to explore strategic alternatives to maximize stockholder value and engaged an independent exclusive financial advisor to support this process. As a result, in April 2023, the Company implemented a restructuring plan resulting in an approximate 83% reduction of the Company's existing headcount.

On June 22, 2023, the Company acquired, in accordance with the terms of the Agreement and Plan of Merger (the "Acquisition Agreement"), the assets of Spyre Therapeutics, Inc. ("Pre-Merger Spyre") as disclosed in Note 7 and 8, a privately held biotechnology company advancing a pipeline of antibody therapeutics with the potential to transform the treatment of inflammatory bowel disease through a research and development option agreement ("Paragon Agreement") with Paragon Therapeutics ("Paragon"). The asset acquisition was accomplished through a two-step reverse triangular merger whereby a wholly owned subsidiary of the Company merged with and into Pre-Merger Spyre, which existed at the time the Acquisition Agreement was entered into, became a wholly owned subsidiary of the Company in accordance with the terms of the Acquisition Agreement. Immediately following this merger, Pre-Merger Spyre merged with an into a second wholly subsidiary of the Company ("Merger Sub") in accordance with the terms of the Acquisition Agreement and Pre-Merger Spyre ceased to exist. Subsequently, Aeglea BioTherapeutics, Inc. was renamed Spyre Therapeutics, Inc. and is a different entity than Pre-Merger Spyre, which ceased to exist upon merging with Merger Sub. The transaction was structured as a stock-for-stock transaction pursuant to which all of Pre-Merger Spyre's outstanding equity interests were exchanged based on a fixed exchange ratio of 0.5494488 to 1 for consideration from the Company of 517,809 shares of common stock and 364,887 shares of Series A non-voting convertible preferred stock, par value of $0.0001 per share ("Series A Preferred Stock") (convertible on a 40 to 1 basis), in addition to the assumption of outstanding and unexercised stock options to purchase 2,734 shares of common stock from the Amended and Restated Spyre 2023 Equity Incentive Plan (the "Asset Acquisition"). The common stock and Series A Preferred Stock related to the Asset Acquisition were issued to the Pre-Merger Spyre stockholders on July 7, 2023. For additional information, see Note 8.

In connection with the Asset Acquisition, on June 26, 2023, the Company completed a private placement of shares of Series A Preferred Stock (the "Series A PIPE") to a group of investors (the "Series A Investors"). The Company sold an aggregate of 721,452 shares of Series A Preferred Stock (the "Series A PIPE Securities") for an aggregate purchase price of approximately $210.0 million before deducting approximately $12.7 million of placement agent and other offering expenses. For additional information, see Note 11.

In connection with the Asset Acquisition, a non-transferable contingent value right ("CVR") was distributed to stockholders of record of the Company as of the close of business on July 3, 2023 (the "Legacy Stockholders"), but was not distributed to the holders of shares of common stock or Series A Preferred Stock issued to the former stockholders of Pre-Merger Spyre or Investors in the Transactions. Holders of the CVRs will be entitled to receive cash payments from proceeds received by the Company for a 3-year period related to the disposition or monetization of its legacy assets for a period of one-year following the closing of the Asset Acquisition. For additional information, see Note 3.

On November 21, 2023, the Company's stockholders approved the conversion of the Company's Series A non-voting convertible preferred stock to Common Stock. For additional information, see Note 11.

On December 11, 2023, the Company completed a private placement of shares of common stock and Series B non-voting convertible preferred stock, par value of $0.0001 per share ("Series B Preferred Stock") (convertible on a 40 to 1 basis) (collectively, the "December 2023 PIPE") to a group of investors (the "December 2023 PIPE Investors"). The Company sold an aggregate of 6,000,000 shares of Common Stock and 150,000 shares of Series B Preferred Stock (the "December 2023 PIPE Securities") for an aggregate purchase price of approximately $180.0 million before deducting approximately $10.9 million of placement agent and other offering expenses. For additional information, see Note 11.

Liquidity

The Company is a preclinical stage biotechnology company with a limited operating history, and due to its significant research and development expenditures, the Company has generated operating losses since its inception and has not generated any revenue from the commercial sale of any products. There can be no assurance that profitable operations will ever be achieved, and, if achieved, whether profitability can be sustained on a continuing basis.

Since its inception and through December 31, 2023, the Company has funded our operations by raising an aggregate of approximately $896.2 million of gross proceeds from the sale and issuance of convertible preferred stock and common stock, pre-funded warrants, the collection of grant proceeds, and the licensing of its product rights for commercialization of pegzilarginase in Europe and certain countries in the Middle East. As of December 31, 2023, Spyre had an accumulated deficit of $764.4 million, and cash, cash equivalents, and marketable securities of $339.3 million.

Based on current operating plans, the Company has sufficient resources to fund operations for at least one year from the issuance date of these financial statements with existing cash, cash equivalents, and marketable securities. Spyre will need to secure additional financing in the future to fund additional research and development, and before a commercial drug can be produced, marketed and sold. If the Company is unable to obtain additional financing or generate license or product revenue, the lack of liquidity could have a material adverse effect on the Company.

Basis of Presentation

The consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States ("U.S. GAAP") as defined by the Financial Accounting Standards Board ("FASB") and include the accounts of the Company and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and

accompanying notes. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets, liabilities, and equity and the amount of revenues and expenses. Actual results could differ significantly from those estimates. The most significant estimates and assumptions that management considers in the preparation of the Company's financial statements relate to the valuation of consideration transferred in acquiring in-process research & development ("IPR&D"); the discount rate, probabilities of success, and timing of estimated cash flows in the valuation of the CVR liability; inputs used in the Black-Scholes model for stock-based compensation expense; estimated future cash flows used in calculating the impairment of right-of-use lease assets; and estimated cost to complete performance obligations related to revenue recognition. The consideration transferred in acquiring IPR&D in connection with the acquisition of Pre-Merger Spyre was comprised of shares of the Company's Common Stock and shares of Series A Preferred Stock. To determine the fair value of the equity transferred, the Company considered the per share value of the Series A PIPE securities, which was a financing event involving a group of accredited investors.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less from the date of purchase to be cash equivalents. Cash equivalents consist of money market funds and debt securities and are stated at fair value.

Marketable Securities

All investments have been classified as available-for-sale and are carried at estimated fair value as determined based upon quoted market prices or pricing models for similar securities. Management determines the appropriate classification of its investments in debt securities at the time of purchase. The Company may hold securities with stated maturities greater than one year until maturity. All available-for-sale securities are considered available to support current operations and are classified as current assets. The Company presents credit losses as an allowance rather than as a reduction in the amortized cost of the available-for-sale securities.

For available-for-sale debt securities in an unrealized loss position, the Company first assesses whether it intends to sell, or it is more likely than not that it will be required to sell the security before recovery of its amortized cost basis. If either of the criteria regarding intent or requirement to sell is met, the security's amortized cost basis is written down to fair value and recognized in other income (expense) in the results of operations. For available-for-sale debt securities that do not meet the aforementioned criteria, the Company evaluates whether the decline in fair value has resulted from credit losses or other factors. In making this assessment, management considers the extent to which fair value is less than amortized cost, any changes to the rating of the security by a rating agency, and adverse conditions specifically related to the security, among other factors. If this assessment indicates that a credit loss exists, an allowance is recorded for the difference between the present value of cash flows expected to be collected and the amortized cost basis of the security. Impairment losses attributable to credit loss factors are charged against the allowance when management believes an available-for-sale security is uncollectible or when either of the criteria regarding intent or requirement to sell is met.

Any unrealized losses from declines in fair value below the amortized cost basis as a result of non-credit loss factors is recognized as a component of accumulated other comprehensive (loss) income, along with unrealized gains. Realized gains and losses and declines in fair value, if any, on available-for-sale securities are included in other income (expense) in the results of operations. The cost of securities sold is based on the specific-identification method.

Restricted Cash

Restricted cash consisted of money market accounts held by financial institutions as collateral for the Company's obligations under a credit agreement and a facility lease for the Company's corporate headquarters in Austin, Texas. The lease was terminated in August 2023 and the cash was subsequently unrestricted. Remaining restricted cash balances relate to the Company's operations in the United Kingdom.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents, marketable securities, and restricted cash. The Company's investment policy limits investments to high credit quality securities issued by the U.S. government, U.S. government-sponsored agencies, highly rated banks, and corporate issuers, subject to certain concentration limits and restrictions on maturities. The Company's cash, cash equivalents, marketable securities, and restricted cash are held by financial institutions that management believes are of high credit quality. The financial instruments that potentially subject the Company to a concentration of credit risk consist principally of cash deposits. Accounts at each of the Company's two U.S. banking institutions are insured by the Federal Deposit Insurance Corporation ("FDIC") up to $250,000 per depositor. As of December 31, 2023 and 2022, balances at the Company's U.S. banking institutions exceeded the FDIC limits. The Company has not experienced any losses on its deposits of cash, cash equivalents, and restricted cash and its accounts are monitored by management to mitigate risk. The Company is exposed to credit risk in the event of default by the financial institutions holding its cash, cash equivalents, and restricted cash, and bond issuers.

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation and amortization. Depreciation and amortization are computed using the straight-line method over the estimated useful lives of the assets. Repairs and maintenance that do not extend the life or improve an asset are expensed as incurred. Upon retirement or sale, the cost of disposed assets and their related accumulated depreciation and amortization are removed from the balance sheet. Any gain or loss is credited or charged to operations.

The useful lives of the property and equipment are as follows:

Laboratory equipment	5 years
Furniture and office equipment	5 years
Computer equipment	3 years
Software	3 years
Leasehold improvements	Shorter of remaining lease term or estimated useful life

Impairment of Long-Lived Assets

Long-lived assets are reviewed for indications of possible impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparison of the carrying amounts to the future undiscounted cash flows attributable to these assets. An impairment loss is recognized to the extent an asset group is not recoverable, and the carrying amount exceeds the fair value. The Company recognized a $2.6 million impairment loss for the year ended December 31, 2023 related to its leased office space in Austin, Texas (see Note 17 for additional information). There were no impairments of long-lived assets for the years ended December 31, 2022 and 2021.

Accrued Research and Development Costs

The Company records the costs associated with research nonclinical studies, clinical trials, and manufacturing development as incurred. These costs are a significant component of the Company's research and

development expenses, with a substantial portion of the Company's on-going research and development activities conducted by third-party service providers, including contract research organizations ("CROs") and contract manufacturing organizations ("CMOs"), and the Company's related-party Paragon.

The Company accrues for expenses resulting from obligations under the Paragon Agreement and agreements with CROs, CMOs, and other outside service providers for which payment flows do not match the periods over which materials or services are provided to the Company. Accruals are recorded based on estimates of services received and efforts expended pursuant to agreements established with Paragon, CROs, CMOs, and other outside service providers. These estimates are typically based on contracted amounts applied to the proportion of work performed and determined through analysis with internal personnel and external service providers as to the progress or stage of completion of the services. The Company makes significant judgments and estimates in determining the accrual balance in each reporting period. In the event advance payments are made to Paragon, a CRO, CMO, or outside service provider, the payments will be recorded as a prepaid asset which will be amortized as the contracted services are performed. As actual costs become known, the Company adjusts its accruals. Inputs, such as the services performed, the number of patients enrolled, or the study duration, may vary from the Company's estimates, resulting in adjustments to research and development expense in future periods. Changes in these estimates that result in material changes to the Company's accruals could materially affect the Company's results of operations. Historically, the Company has not experienced any material deviations between accrued and actual research and development expenses.

Leases

The Company determines if an arrangement is a lease at inception. Right-of-use ("ROU") assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. The classification of the Company's leases as operating or finance leases along with the initial measurement and recognition of the associated ROU assets and lease liabilities is performed at the lease commencement date. The measurement of lease liabilities is based on the present value of future lease payments over the lease term. As the Company's leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at the lease commencement date in determining the present value of future lease payments. To determine the incremental borrowing rate, the Company uses the lease-term appropriate current treasury bond rates adjusted for collateral and inflation risks combined with quoted bank financing rates. The ROU asset is based on the measurement of the lease liability and also includes any lease payments made prior to or on lease commencement and excludes lease incentives and initial direct costs incurred, as applicable. The lease terms may include options to extend or terminate the lease when it is reasonably certain the Company will exercise any such options. Rent expense for the Company's operating leases is recognized on a straight-line basis over the lease term. Amortization expense for the ROU asset associated with its finance leases is recognized on a straight-line basis over the term of the lease and interest expense associated with its finance leases is recognized on the balance of the lease liability using the effective interest method based on the estimated incremental borrowing rate.

Prior to the Company's restructuring, as described in Note 17, the Company had lease agreements with lease and non-lease components. As allowed under Topic 842, the Company elected to not separate lease and non-lease components for any leases involving real estate and office equipment classes of assets and, as a result, accounted for the lease and non-lease components as a single lease component. The Company also elected to not apply the recognition requirement of Topic 842 to leases with a term of 12 months or less for all classes of assets.

Fair Value of Financial Instruments

The Company uses fair value measurements to record fair value adjustments to certain financial and non-financial assets and liabilities and to determine fair value disclosures. The accounting standards define fair value, establish a framework for measuring fair value, and require disclosures about fair value measurements. Fair value is defined as the price that would be received from selling an asset or paid to transfer a liability in an

orderly transaction between market participants at the measurement date. When determining the fair value measurements for assets and liabilities required to be recorded at fair value, the principal or most advantageous market in which the Company would transact are considered along with assumptions that market participants would use when pricing the asset or liability, such as inherent risk, transfer restrictions, and risk of nonperformance.

The accounting standard for fair value establishes a fair value hierarchy based on three levels of inputs, the first two of which are considered observable and the last unobservable, that requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. A financial instrument's categorization within the fair value hierarchy is based upon the lowest level of input that is significant to the fair value measurement.

The three levels of inputs that may be used to measure fair value are as follows:

Level 1:	Observable inputs, such as quoted prices in active markets for identical assets or liabilities.
Level 2:	Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
Level 3:	Valuations based on unobservable inputs to the valuation methodology and including data about assumptions that market participants would use in pricing the asset or liability based on the best information available under the circumstances.

Financial instruments carried at fair value include cash equivalents and marketable securities. The carrying amounts of accounts payable and accrued liabilities approximate fair value due to their relatively short maturities.

Revenue Recognition

Under ASC Topic 606, "Revenue from Contracts with Customers" ("Topic 606"), an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation.

The Company assesses its license arrangements within the scope of Topic 606 in accordance with this framework as follows:

License revenue

The Company assesses whether the goods or services promised within each contract are distinct to identify those that are performance obligations. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. In assessing whether a promised good or service is distinct, and therefore a performance obligation, the Company considers factors such as the research, stage of development of the licensed product, manufacturing and commercialization capabilities of the customer and the availability of the associated expertise in the general marketplace. The Company also considers the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, the Company is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is

distinct. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, they are considered performance obligations.

The transaction price is determined and allocated to the identified performance obligations in proportion to their stand-alone selling prices ("SSP") on a relative SSP basis. SSP is based on observable prices of the performance obligations or, when such prices are not observable, are estimated. The estimation of SSP may include factors such as forecasted revenues or costs, development timelines, discount rates, probabilities of technical and regulatory success, and considerations such as market conditions and entity-specific factors. In certain circumstances, the Company may apply the residual method to determine the SSP of a good or service if the SSP is considered highly variable or uncertain. The Company validates the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, the Company estimates the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. The Company determines the amount of variable consideration by using the expected value method or the most likely amount method. The Company includes the amount of estimated variable consideration in the transaction price to the extent that it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development, regulatory or commercial milestone payments, the Company evaluates whether the milestones are considered likely of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant cumulative revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are generally not considered likely of being achieved until those approvals are received.

In determining the transaction price, the Company adjusts consideration for the effects of the time value of money if the timing of payments provides the Company with a significant benefit of financing. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensee and the transfer of the promised goods or services to the licensees will be one year or less. For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and if the license is deemed to be the predominant item to which the royalties relate, the Company recognizes royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

The Company recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time, recognition is based on the use of an output or input method.

The Company's contracts may be modified for changes in the customer's requirements. If contract modifications are for additional goods and services that are distinct from the existing contract, the modification will be accounted for as either a separate contract or a termination of the existing contract, depending on whether the additional goods or services reflects the SSP.

If the additional goods or services in a contract modification are not distinct from the existing contract, they are accounted for as if they were part of the original contract. The effect of the contract modification on the transaction price and the measure of progress for the performance obligation to which it relates is recognized as

an adjustment to revenue on a cumulative catch-up basis. The cumulative catch-up adjustment is calculated using an updated measure of progress applied to the sum of (1) the remaining consideration allocated to the partially satisfied performance obligation and (2) the revenue already recognized on that performance obligation. The revenue recognized for fully satisfied goods or services and distinct from the remaining performance obligations is not altered by the modification.

Collaborative arrangements

The Company analyzes its license arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and therefore within the scope of ASC Topic 808, Collaborative Arrangements ("Topic 808"). This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For arrangements within the scope of Topic 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of Topic 808 and which elements of the collaboration are more reflective of a vendor-customer relationship and therefore within the scope of Topic 606. For elements of collaboration arrangements that are accounted for pursuant to Topic 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election. For those elements of the arrangement that are accounted for pursuant to Topic 606, the Company applies the five-step model described above.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development costs include, but are not limited to, salaries, benefits, travel, stock-based compensation, consulting costs, contract research service costs, laboratory supplies and facilities, contract manufacturing costs, and costs paid to other third parties that conduct research and development activities on the Company's behalf. Amounts incurred in connection with license agreements are also included in research and development expense.

Advance payments for goods or services to be rendered in the future for use in research and development activities are recorded as a prepaid asset and expensed as the related goods are delivered or the services are performed.

Stock-Based Compensation

The Company recognizes the cost of stock-based awards granted to employees and non-employees based on the estimated grant-date fair values of the awards. The fair values of stock options are estimated on the date of grant using the Black-Scholes option pricing model. The fair values of restricted stock units ("RSUs") are based on the fair value of the Company's common stock on the date of the grant. The value of the award is recognized as compensation expense on a straight-line basis over the requisite service period. Forfeitures are recognized when they occur, which may result in the reversal of compensation costs in subsequent periods as the forfeitures arise. Compensation expense for employee and non-employee share-based payment awards with performance conditions is recognized when the performance condition is deemed probable.

Convertible Preferred Stock Issued through PIPE

The Company records shares of convertible preferred stock at their respective fair values on the dates of issuance, net of issuance costs. The Company classified the Series B Preferred Stock outside of stockholders' equity because, if conversion to Common Stock is not approved by the stockholders, the Series B Preferred Stock will be redeemable at the option of the holders for cash equal to the closing price of the Common Stock on the last trading day prior to the holder's redemption request. The Company has determined that the conversion and redemption are outside of the Company's control. Additionally, the Company determined the Series B Preferred Stock did not contain any embedded derivatives and therefore the conversion and redemption features did not require bifurcation.

Contingent Milestone Proceeds

The Company recognizes contingent milestone proceeds associated from the sale of in-process research and development assets in earnings once the achievement of the milestone becomes probable and payment to the Company is contractually required.

Acquisitions

The Company evaluates acquisitions of assets and other similar transactions to assess whether or not the transaction should be accounted for as a business combination or asset acquisition by first applying a screen test to determine whether substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets. If so, the transaction is accounted for as an asset acquisition. If not, further determination is required as to whether or not the Company has acquired inputs and processes that have the ability to create outputs, which would meet the definition of a business. Significant judgment is required in the application of the test to determine whether an acquisition is a business combination or an acquisition of assets.

Acquisitions meeting the definition of business combinations are accounted for using the acquisition method of accounting, which requires that the purchase price be allocated to the net assets acquired at their respective fair values. In a business combination, any excess of the purchase price over the estimated fair values of the net assets acquired is recorded as goodwill.

The Company measures and recognizes asset acquisitions that are not deemed to be business combinations based on the cost to acquire the assets, which includes pre-acquisition direct costs recorded in accrued professional and consulting fees. Goodwill is not recognized in asset acquisitions. When a transaction accounted for as an asset acquisition includes an IPR&D asset, the IPR&D asset is only capitalized if it has an alternative future use other than in a particular research and development project. Otherwise, the cost allocated to acquire an IPR&D asset with no alternative future use is charged to expense at the acquisition date.

Contingent Value Rights

The Company evaluates its contracts to determine if those contracts qualify as derivatives under ASC 815, Derivatives and Hedging (“ASC 815”). For derivative financial instruments that are accounted for as liabilities, the derivative instrument is initially recorded at its fair value and is then re-valued at each reporting date. Any changes in fair value are recorded as other income or expense for each reporting period. Derivative instrument liabilities are classified in the balance sheet as current or non-current based on whether or not net-cash settlement of the derivative instrument is probable within the next 12 months from the balance sheet date. The Company determined that certain contingent payments under the CVR Agreement qualified as derivatives under ASC 815, and as such, were recorded as a liability on the balance sheet. This value is then remeasured for future expected payout as well as the increase in fair value due to the time value of money. These gains or losses, if any, are recognized in the consolidated statements of operations and comprehensive loss within Other (expense) income, net.

The Company applies a scenario-based method and weighs them based on the possible achievement of certain milestones. The milestone payments are contingent on formal reimbursement decisions by national authorities in key European markets and pegzilarginase approval by the U.S. Food and Drug Administration (“FDA”), among other events. This fair value measurement is based on significant inputs not observable in the market and thus represents a Level 3 measurement as defined in ASC 820, Fair Value Measurement. The key assumptions used include the discount rate, probability of regulatory success, and reimbursement rates from certain government agencies. The estimated value of the CVR consideration is based upon available information and certain assumptions which the Company’s management believes are reasonable under the circumstances. The ultimate payout under the CVRs may differ materially from the assumptions used in determining the fair value of the CVR consideration.

Income Taxes

The Company uses the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the financial statements and the tax bases of assets and liabilities. Additionally, any changes in income tax laws are immediately recognized in the year of enactment.

A valuation allowance is established against the deferred tax assets to reduce their carrying value to an amount that is more likely than not to be realized. The deferred tax assets and liabilities are classified as noncurrent along with the related valuation allowance. Due to a lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance.

The Company recognizes benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on the technical merits, as the largest amount of benefits that is more likely than not to be realized upon the ultimate settlement. The Company's policy is to recognize interest and penalties related to the unrecognized tax benefits as a component of income tax expense, if applicable. As of December 31, 2023 and 2022, the Company had no unrecognized tax benefits and there were no interest or penalties incurred by the Company in the years ended December 31, 2023, 2022, or 2021.

Comprehensive Loss

Comprehensive loss is the change in stockholders' equity from transactions and other events and circumstances other than those resulting from investments by stockholders and distributions to stockholders. The Company's other comprehensive income (loss) is currently comprised of changes in unrealized losses and gains on available-for-sale securities and foreign currency translation adjustments reflecting the cumulative effect of changes in exchange rates between the foreign entity's functional currency and the reporting currency.

Recently Adopted Accounting Pronouncement

The Company early adopted the Financial Accounting Standards Board's Accounting Standards Update 2020-06, Accounting for Convertible Instruments and Contracts in an Entity's Own Equity ("ASU 2020-06"), effective as of January 1, 2023 using the modified retrospective method. Among other amendments, ASU 2020-06 eliminates the cash conversion and beneficial conversion feature models in ASC 470-20 that required an issuer of certain convertible debt and preferred stock to separately account for embedded conversion features as a component of equity, as well as changes the accounting for diluted earnings-per-share for convertible instruments and contracts that may be settled in cash or stock. Additionally, ASU 2020-06 requires the if-converted method, which is more dilutive than the treasury stock method, be used for all convertible instruments. The Company applied ASU 2020-06 to all Series A Preferred Stock and Series B Preferred Stock during fiscal year 2023, and, accordingly, the Company did not apply the cash conversion or beneficial conversion feature models in its analysis of the Series A Preferred Stock and Series B Preferred Stock. The adoption of ASU 2020-06 did not have a material impact on the Company's consolidated financial statements.

Recently Issued Accounting Pronouncements

In November 2023, the FASB issued ASU 2023-07, Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures to update reportable segment disclosure requirements, primarily through enhanced disclosures about significant segment expenses and information used to assess segment performance and requires companies to disclose all annual disclosures about segments in interim periods. The ASU also requires companies with a single reportable segment to provide all disclosures required by Topic 280 – Segment Reporting. This update is effective beginning with the Company's 2024 fiscal year annual reporting period and interim periods beginning thereafter. The Company is currently evaluating the impact that the adoption of this standard will have on its consolidated financial statements.

In December 2023, the FASB issued ASU 2023-09, Income Taxes (Topic 740): Improvements to Income Tax Disclosures. This ASU expands disclosures in an entity's income tax rate reconciliation table and disclosures regarding taxes paid both in the U.S. and foreign jurisdictions. This update is effective beginning with the Company's 2025 fiscal year annual reporting period. This ASU will have no impact on the Company's consolidated financial condition or results of operations. The Company is currently evaluating the impact to its income tax disclosures.

3. Fair Value Measurements

The Company measures and reports certain financial instruments as assets and liabilities at fair value on a recurring basis. The following tables sets forth the fair value of the Company's financial assets and liabilities at fair value on a recurring basis based on the three-tier fair value hierarchy (in thousands):

	December 31, 2023			
	Level 1	Level 2	Level 3	Total
Financial Assets				
Money market funds	$150,648	$ —	$ —	$150,648
U.S. government treasury securities	32,843	—	—	32,843
U.S. government agency securities	—	16,257	—	16,257
Commercial paper	—	104,141	—	104,141
Corporate bonds	—	33,064	—	33,064
Total financial assets	$183,491	$153,462	$ —	$336,953
Liabilities:				
CVR liability	$ —	$ —	$42,700	$ 42,700
Total liabilities	$ —	$ —	$42,700	$ 42,700

	December 31, 2022			
	Level 1	Level 2	Level 3	Total
Financial Assets				
Money market funds	$ 15,250	$ —	$ —	$ 15,250
Commercial paper	—	23,641	—	23,641
U.S. government agency securities	—	4,230		4,230
Corporate bonds	—	3,732	—	3,732
Total financial assets	$ 15,250	$ 31,603	$ —	$ 46,853

The Company measures the fair value of money market funds on quoted prices in active markets for identical asset or liabilities. The Level 2 assets include U.S. government agency securities, commercial paper and corporate bonds, and are valued based on quoted prices for similar assets in active markets and inputs other than quoted prices that are derived from observable market data.

The Company evaluates transfers between levels at the end of each reporting period. There were no transfers between Level 1 and Level 2 during the periods presented.

As of December 31, 2022, the Company had no financial liabilities outstanding measured at fair value.

Forward Contract Liability

In connection with the Asset Acquisition, the Company entered into a contract for the issuance of 364,887 shares of Series A Preferred Stock as part of the consideration transferred. This forward contract was classified as a liability because the underlying preferred shares were contingently redeemable. Further, the forward contract

liability was considered a Level 2 liability based on observable market data for substantially the full term of the liability and was initially measured at its estimated fair value on the transaction date based on the underlying price per share on an as-converted basis of the Series A PIPE Securities issued in the Series A PIPE. Subsequent remeasurement of the fair value of the forward contract liability through its settlement date was based on the market price of the Company's Common Stock, which represents the redemption value of the Series A Preferred Stock.

The fair value of the forward contract at the transaction date, June 22, 2023, was $ 106.2 million. The liability was settled with the issuance of the Series A Preferred Stock on July 7, 2023 for $189.7 million. For the year ended December 31, 2023, $ 83.5 million was recorded as Other (expense) income in the consolidated statements of operations in connection with the change in fair value of the forward contract liability. There was no similar expense for the year ended December 31, 2022 and 2021.

The following table presents changes in the forward contract liability for the periods presented (in millions):

	Forward Contract Liability
Beginning balance as of June 22, 2023	$ 106.2
Change in fair value	83.5
Issuance of Series A Preferred Stock on July 7, 2023	(189.7)
Ending balance as of December 31, 2023	$ —

CVR Liability

In connection with the Asset Acquisition, a non-transferable contingent value right was distributed to the Legacy Stockholders, but was not distributed to holders of shares of Common Stock or Series A Preferred Stock issued to the Investors or former stockholders of Pre-Merger Spyre in connection with the Transactions. Holders of the CVR will be entitled to receive certain cash payments from proceeds received by the Company for a three-year period, if any, related to the disposition or monetization of the Company's legacy assets for a period of one year following the closing of the Asset Acquisition.

The fair value of the CVR liability was determined using the probability weighted discounted cash flow method to estimate future cash flows associated with the sale of the legacy assets. Analogous to a dividend being declared/approved in one period and paid out in another, the liability was recorded at the date of approval, June 22, 2023, as a Common Stock dividend, returning capital to the Legacy Stockholders. Changes in fair value of the liability will be recognized as a component of Other income (expense) in the consolidated statement of operations and comprehensive loss in each reporting period. The liability value is based on significant inputs not observable in the market such as estimated cash flows, estimated probabilities of regulatory success, and discount rates, which represent a Level 3 measurement within the fair value hierarchy. The significant inputs used to estimate the fair value of the CVR liability were as follows:

	December 31, 2023
Estimated cash flow dates	2/28/24 - 06/22/26
Estimated probability of success	39% - 100%
Estimated reimbursement rate compared to reimbursement target	81% - 100%
Risk-adjusted discount rates	5.91% - 6.32%

The change in fair value between the issuance of the CVR and December 31, 2023 was a $ 19.0 million increase, and was primarily driven by changes in the expected timing of achievement of certain milestones, changes in the likelihood of certain milestones related to the approval received from the European Medicines Agency by Immedica Pharma AB ("Immedica"), partially offset by a change in the likelihood of a successful disposition of pegtarviliase and updates to expenses and deductions.

The following table presents changes in the CVR liability for the periods presented (in thousands):

	CVR Liability
Beginning balance as of December 31, 2022	$ —
Fair value at CVR issuance	29,500
Changes in the fair value of the CVR liability since issuance	18,986
Payments	(5,786)
Ending Balance as of December 31, 2023	$ 42,700

4. Cash Equivalents and Marketable Securities

The following tables summarize the estimated fair value of the Company's cash equivalents and marketable securities and the gross unrealized gains and losses (in thousands):

	December 31, 2023			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Cash equivalents:				
Money market funds	$150,648	$ —	$ —	$150,648
Commercial paper	24,950	5	—	24,955
U.S. government treasury securities	10,965	1	—	10,966
Total cash equivalents	186,563	6	—	186,569
Marketable securities:				
Commercial paper	79,124	62	—	79,186
Corporate bonds	32,984	81	(1)	33,064
U.S. government treasury securities	21,846	31	—	21,877
U.S. government agency securities	16,147	110	—	16,257
Total marketable securities	$150,101	$ 284	$ (1)	$150,384

	December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Cash equivalents:				
Money market funds	$ 15,250	$ —	$ —	$ 15,250
Commercial paper	7,021	1	(2)	7,020
U.S. government agency securities	3,736	—	(1)	3,735
Total cash equivalents	$ 26,007	$ 1	$ (3)	$ 26,005
Marketable securities:				
Commercial paper	$ 16,644	$ 2	$ (25)	$ 16,621
Corporate bonds	3,738	—	(6)	3,732
U.S. government agency securities	495	—	—	495
Total marketable securities	$ 20,877	$ 2	$ (31)	$ 20,848

The following table summarizes the available-for-sale securities in an unrealized loss position for which an allowance for credit losses has not been recorded as of December 31, 2023 and 2022, aggregated by major security type and length of time in a continuous unrealized loss position:

	December 31, 2023					
	Less Than 12 Months		12 Months or Longer		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
Commercial paper	$ —	$ —	$ —	$ —	$ —	$ —
Corporate bonds	9,907	(1)	—	—	9,907	(1)
U.S. government treasury securities	4,831	—	—	—	4,831	—
Total marketable securities	$ 14,738	$ (1)	$ —	$ —	$ 14,738	$ (1)

	December 31, 2022					
	Less Than 12 Months		12 Months or Longer		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
Commercial paper	$ 17,699	$ (27)	$ —	$ —	$ 17,699	$ (27)
Corporate bonds	3,732	(6)	—	—	3,732	(6)
U.S. government agency securities	3,735	(1)	—	—	3,735	(1)
Total marketable securities	$ 25,166	$ (34)	$ —	$ —	$ 25,166	$ (34)

The Company evaluated its securities for credit losses and considered the decline in market value to be primarily attributable to current economic and market conditions and not to a credit loss or other factors. Additionally, the Company does not intend to sell the securities in an unrealized loss position and does not expect they will be required to sell the securities before recovery of the unamortized cost basis. As of December 31, 2023 and 2022, an allowance for credit losses had not been recognized. Given the Company's intent and ability to hold such securities until recovery, and the lack of significant change in credit risk of these investments, the Company does not consider these marketable securities to be impaired as of December 31, 2023 and 2022.

There were $0.3 million unrealized gains on marketable securities for the year ended December 31, 2023. There were no realized gains on marketable securities for the year ended December 31, 2023, 2022 and 2021. Interest on marketable securities is included in interest income. Accrued interest receivable on available-for-sale debt securities totaled $0.9 million and $0.1 million as of December 31, 2023 and 2022, respectively, and is excluded from the estimate of credit losses.

The following table summarizes the contractual maturities of the Company's marketable securities at estimated fair value (in thousands):

	December 31,	
	2023	2022
Due in one year or less	$115,784	$20,848
Due in 1 – 2 years	34,600	—
Total marketable securities	$150,384	$20,848

The Company may sell investments at any time for use in current operations even if they have not yet reached maturity. As a result, the Company classifies marketable securities, including securities with maturities beyond twelve months as current assets.

5. Property and Equipment, Net

Property and equipment, net consist of the following (in thousands):

	December 31,	
	2023	2022
Laboratory equipment	$—	$ 2,257
Furniture and office equipment	—	520
Computer equipment	—	73
Software	—	121
Leasehold improvements	—	4,393
Property and equipment, gross	—	7,364
Less: Accumulated depreciation and amortization	—	(4,144)
Property and equipment, net	$—	$ 3,220

Depreciation and amortization expense for the years ended December 31, 2023, 2022, and 2021 was $ 0.7 million, $1.4 million, and $1.4 million, respectively. All of the Company's long-lived assets were located in the United States.

Sale of Assets

On April 12, 2023, based on the review of the inconclusive interim results from the Company's Phase 1/2 clinical trial of pegtarviliase for the treatment of classical homocystinuria and other business considerations, the Company announced that it had initiated a process to explore strategic alternatives to maximize stockholder value and engaged an independent exclusive financial advisor to support this process. As a result, the Company implemented a restructuring plan resulting in an approximate 83% reduction of the Company's existing headcount by June 30, 2023.

During the second quarter of 2023, the Company sold various lab equipment, consumables, and furniture and fixtures for total consideration of $0.5 million. After recording the disposal of all the Company's property and equipment net of proceeds, the Company recorded a $0.7 million and $0.2 million loss on disposal of long lived assets which is included in Research and development and General and administrative expenses, respectively.

6. Accrued and Other Current Liabilities

Accrued and other current liabilities consist of the following (in thousands):

	December 31,	
	2023	2022
Accrued compensation	$ 4,054	$ 4,589
Accrued contracted research and development costs	7,092	6,972
Accrued professional and consulting fees	1,474	946
Other	488	330
Total accrued and other current liabilities	$13,108	$12,837

7. Related Party Transactions

Paragon and Parapyre Holding LLC ("Parapyre") each beneficially own less than 5% of the Company's capital stock through their respective holdings of the Company's common stock. Fairmount Funds Management

LLC (“Fairmount”) beneficially owns more than 5% of the Company’s capital stock on an as-converted basis, has two seats on the Board and beneficially owns more than 5% of Paragon, which is a joint venture between Fairmount and Fair Journey Biologics. Fairmount appointed Paragon’s board of directors and has the contractual right to approve the appointment of any executive officers. 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.

In connection with the Asset Acquisition, the Company assumed the rights and obligations of Pre-Merger Spyre under the Paragon Agreement. Under the Paragon Agreement, Spyre is obligated to compensate Paragon 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, which included the $3.0 million research initiation fee and $ 16.0 million of reimbursable expenses under the Paragon Agreement for historical costs owed to Paragon. As of the acquisition date, $19.0 million was unpaid and was assumed by the Company through the Asset Acquisition.

For the year ended December 31, 2023, the Company recognized expenses related to services provided by Paragon subsequent to the Asset Acquisition totaling $48.5 million, which included $11.4 million of stock-based compensation expense, and were recorded as Research and development expenses in the consolidated statements of operations. As of December 31, 2023, $16.6 million was unpaid and was included in Related party accounts payable and other current liabilities on the Company’s consolidated balance sheets.

For the year ended December 31, 2023, the Company made payments totaling $ 39.5 million to Paragon.

On July 12, 2023 and December 14, 2023, the Company exercised the Option available under the Paragon Agreement with respect to the SPY001 and SPY002 research programs, respectively, and expects to enter into the SPY001 License Agreement and the SPY002 License Agreement.

Following the execution of each of the SPY001 License Agreement and SPY002 License Agreement, the Company will be obligated to pay Paragon up to $22.0 million upon the achievement of specific development, regulatory and clinical milestones for the first product under each agreement, respectively, that achieves such specified milestones. Upon execution of each of the SPY001 License Agreement and the SPY002 License Agreement, we expect to pay Paragon a $1.5 million fee for nomination of a development candidate, as applicable, and the Company expects to be obligated to make a further milestone payment of $2.5 million upon the first dosing of a human patient in a Phase 1 trial.

The following is the summary of expenses related to the Paragon Agreement recognized within research and development expenses, which were ultimately settled in cash (in millions):

	December 31,		
	2023	2022	2021
Reimbursable costs under the Paragon Agreement	$37.1	$—	$—

Parapyre Option Obligation

As part of the Paragon Agreement, the Company is obligated to issue Parapyre a stock option grant on the last business day of 2023 and 2024 (the “Parapyre Option Obligation”). See Note 15 for additional information.

The following is the summary of Related party accounts payable and other current liabilities (in millions):

	December 31, 2023	December 31, 2022
Reimbursable costs under the Paragon Agreement	$ 16.6	$ —
Related party accounts payable and other current liabilities	$ 16.6	$ —

December 2023 PIPE

The December 2023 Investors included Fairmount, a related party. Fairmount's participation in the December 2023 PIPE was approved by the Company's board of directors. Fairmount's investment accounted for $10.0 million of the $180.0 million gross proceeds raised in the December 2023 PIPE.

Mark McKenna Option Grant

On February 1, 2024, the Board appointed Mark McKenna as a Class I director. Mr. McKenna and the Company are parties to a consulting agreement, pursuant to which Mr. McKenna agreed to continue to provide consulting services as an independent contractor to the Company, with an effective date of August 1, 2023 (the "Vesting Commencement Date"). As compensation for Mr. McKenna's consulting services, on November 22, 2023, he was granted non-qualified stock options to purchase 477,000 shares of the Company's common stock under the Company's equity incentive plan with an exercise price of $10.39 per share, which vest as to 25% on the one year anniversary of the Vesting Commencement Date and thereafter vest and become exercisable in 48th equal monthly installments, subject to Mr. McKenna's continued service to the Company through each applicable vesting date. For the twelve months ended December 31, 2023, the Company recognized $0.1 million in stock-based compensation expense related to Mr. McKenna's consulting agreement. There was no such expense for the twelve months ended December 31, 2022 and 2021.

8. Asset Acquisition

On June 22, 2023, the Company acquired Pre-Merger Spyre pursuant to the Acquisition Agreement, by and among the Company, Aspen Merger Sub I, Inc., a Delaware corporation and a wholly owned subsidiary of the Company ("First Merger Sub"), Sequoia Merger Sub II, LLC, a Delaware limited liability company and a wholly owned subsidiary of the Company ("Second Merger Sub"), and Pre-Merger Spyre. Pursuant to the Acquisition Agreement, First Merger Sub merged with and into Pre-Merger Spyre, pursuant to which Pre-Merger Spyre was the surviving corporation and became the Company's wholly owned subsidiary (the "First Merger"). Immediately following the First Merger, Pre-Merger Spyre merged with and into Second Merger Sub, pursuant to which Second Merger Sub became the surviving entity. Pre-Merger Spyre was a pre-clinical stage biotechnology company that was incorporated on April 28, 2023 under the direction of Peter Harwin, a Managing Member of Fairmount, for the purpose of holding rights to certain intellectual property being developed by Paragon. Fairmount is a founder of Paragon.

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

The Company completed the Asset Acquisition of Pre-Merger Spyre, in accordance with the terms of the Acquisition Agreement. Under the terms of the Acquisition Agreement, the Company issued 517,809 shares of Common Stock and 364,887 shares of Series A Preferred Stock to former Pre-Merger Spyre security holders. In addition, outstanding and unexercised stock options to purchase 2,734 shares of common stock were assumed from the Amended and Restated Spyre 2023 Equity Incentive Plan.

At the acquisition date, the Company recorded forward contracts to represent the obligation to issue shares of the Company's Common Stock and shares of Series A Preferred Stock. The forward contract related to the Common Stock was recorded as Additional paid-in capital as the instrument is indexed to the Company's Common Stock. The forward contract related to the Series A Preferred Stock was recorded as a liability, as the underlying stock has a cash redemption feature. On July 7, 2023, both the shares of Common Stock and Series A Preferred Stock were issued and the forward contract liability associated with the Series A Preferred Stock was settled accordingly.

The Company concluded that the arrangement meets the definition of an asset acquisition rather than a business combination, as substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset, the Option to exclusively license IPR&D. The Company determined that the Option to license IPR&D was a single asset as the Company's strategy relies on developing the entire portfolio of individual treatments to create combination treatments that simultaneously address different mechanisms of irritable bowel disease with a single treatment. The Company also determined that the pipeline candidates within the portfolio are similar in nature and risk profile. In addition, the Company did not obtain any substantive processes, assembled workforce, or employees capable of producing outputs in connection with the Asset Acquisition.

The Company determined that the cost to acquire the asset was $ 113.2 million which was recorded as acquired IPR&D. The fair value of the consideration issued consisted of the 364,887 shares of Series A Preferred Stock (14,595,480 shares of Common Stock on an as-converted basis) and 517,809 shares of Common Stock, valued at $ 291.08 per share and $ 7.277 per share, respectively.

The Asset Acquisition Costs are shown on the following table (in millions):

	June 22, 2023
Consideration transferred in Series A Preferred Stock and Common Stock	$ 110.0
Transaction costs incurred by the Company	3.2
Total cost to acquire asset	$ 113.2

The allocation of the purchase price to net assets acquired is as a follows:

	June 22, 2023
Acquired in-process research and development	$ 130.2
Cash acquired	3.0
Assumed liabilities	(20.0)
Total cost to acquire asset	$ 113.2

9. Paragon Agreement

In May 2023, Pre-Merger Spyre entered into the Paragon Agreement with Paragon and Parapyre. Pursuant to the Paragon Agreement, the Option provided for the right to acquire the intellectual property rights related to four research programs from Paragon in accordance with a license agreement to be entered into following each exercise of the Option. Under the Paragon Agreement, the terms of such license agreement would be consistent with the economics and other terms set out in the Paragon Agreement and, in the event of failure to reach an agreement on the definitive terms, the matter would be resolved via arbitration. In consideration for the Option granted under the Paragon Agreement, Pre-Merger Spyre was obligated to pay Paragon an upfront cash amount of $ 3.0 million in research initiation fees. In addition, Pre-Merger Spyre was 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, which included the $ 3.0 million research initiation fee and $16.0 million of historical reimbursable expenses owed to Paragon. As of June 22, 2023, $ 19.0 million was unpaid and was assumed by the Company through the Asset Acquisition. Furthermore, the Paragon Agreement provided for an annual equity grant of options to purchase 1% of the then outstanding shares of Spyre's common stock, on a fully diluted basis, on the last business day of each calendar year, during the term of the Paragon Agreement, at the fair market value determined by the board of directors of Spyre.

As a result of the Asset Acquisition, the Company assumed the rights and obligations of Pre-Merger Spyre under the Paragon Agreement, including the Parapyre Option Obligation. Pursuant to the Paragon Agreement, on a research program-by-research program basis following the finalization of the research plan for each respective research program, the Company is required to pay Paragon a nonrefundable fee in cash of $0.8 million. For the year ended December 31, 2023, the Company incurred $ 48.5 million, in costs reimbursable to Paragon, which were recorded as Research and development expenses in the consolidated statements of operations.

For the year ended December 31, 2023, the Company made payments totaling $ 39.5 million to Paragon.

On July 12, 2023 and December 14, 2023, the Company exercised the Option available under the Paragon Agreement with respect to the SPY001 and SPY002 research programs, respectively, and expects to enter into the SPY001 License Agreement and the SPY002 License Agreement. Our Option available under the Paragon Agreement with respect to the SPY003 and SPY004 programs remains unexercised.

Following the execution of each of the SPY001 License Agreement and SPY002 License Agreement, the Company will be obligated to pay Paragon up to $22.0 million upon the achievement of specific development, regulatory and clinical milestones for the first product under each agreement, respectively, that achieves such specified milestones. Upon execution of each of the SPY001 License Agreement and the SPY002 License Agreement, the Company expects to pay Paragon a $1.5 million fee for nomination of a development candidate, as applicable, and the Company expects to be obligated to make a further milestone payment of $2.5 million upon the first dosing of a human patient in a Phase 1 trial. Subject to the execution of the Option with respect to the SPY003 or SPY004 research programs, the Company expects to be obligated to make similar payments upon and following the execution of license agreements with respect to these research programs, respectively.

10. Leases

Prior to the Company's restructuring, as described in Note 17, the Company leased certain office space, laboratory facilities, and equipment. These leases required monthly lease payments that were subject to annual increases throughout the lease term. Certain of these leases also included renewal options at the election of the Company to renew or extend the lease for an additional three to five years. These optional periods were not considered in the determination of the right-of-use assets or lease liabilities associated with these leases as the Company did not consider it reasonably certain it would exercise the options. The Company performed evaluations of its contracts and determined it has both operating and finance leases. Variable lease expense for these leases primarily consisted of common area maintenance and other operating costs.

In April 2019, the Company entered into a lease agreement (the "Las Cimas Lease") for its corporate headquarters and laboratory space located in Austin, Texas. The Las Cimas Lease included approximately 30,000 square feet and commenced on April 30, 2019, with an expiration on April 30, 2028. The Company posted a customary letter of credit in the amount of $1.5 million as security, which is subject to automatic reductions per the terms of the Las Cimas Lease. A tenant allowance of up to $1.0 million was provided by the lessor and fully reimbursed to the Company.

In August 2023, the Company terminated its building lease in Austin, Texas. The negotiated termination agreement obligated the Company to pay the lessor a $2.0 million termination fee in exchange for releasing the Company of all further obligations under the lease including terminating the associated letter of credit.

The following table summarizes the Company's recognition of its operating and finance leases (in thousands):

	Classification	December 31, 2023	2022
Assets			
Operating	Operating lease right-of-use assets	$—	$3,430
Finance	Other non-current assets	—	597
Total leased assets		—	4,027
Leases			
Current			
Operating	Operating lease liabilities	—	625
Finance	Accrued and other current liabilities	—	16
Non-current			
Operating	Non-current operating lease liabilities	—	4,004
Total lease liabilities		$—	$4,645

The following table summarizes the weighted-average remaining lease term and discount rates for the Company's operating and finance leases:

	December 31, 2023	2022
Lease term (years)		
Operating leases	0.0	5.3
Finance leases	0.0	0.6
Discount rate		
Operating leases	— %	10.6%
Finance leases	— %	10.2%

The following table summarizes the lease costs pertaining to the Company's operating leases (in thousands):

	Year Ended December 31, 2023	2022	2021
Operating lease cost	$455	$ 910	$ 991
Variable lease cost	471	472	519
Total lease cost	$926	$1,382	$1,510

Cash paid for amounts included in the measurement of operating lease liabilities during the years ended December 31, 2023 and 2022 was $0.5 million and $0.9 million, respectively, and was included within net cash used in operating activities in the cash flows.

As of December 31, 2023, the Company had no operating or finance lease obligations.

11. Convertible Preferred Stock and Stockholders' Equity

The Company is authorized to issue 410,000,000 shares of capital stock of which 400,000,000 shares are designated as Common Stock and 10,000,000 shares are designated as preferred stock, all with a par value of $ 0.0001 per share. Each holder of Common Stock is entitled to one vote for each share of Common Stock held. The Common Stock is not entitled to preemptive rights, and is not subject to conversion, redemption or sinking

fund provisions. Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of Common Stock are entitled to receive dividends out of funds legally available if the board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that the board of directors may determine.

As of December 31, 2023 and 2022, no Common Stock dividends had been declared by the board of directors. As of December 31, 2023 there were 437,037 shares of Series A preferred stock and 150,000 shares of Series B preferred stock outstanding. There were no shares of Series A preferred stock or shares of Series B preferred stock outstanding as of December 31, 2022.

Registered Direct Offering

In May 2022, the Company issued and sold 430,107 shares of Common Stock at an offering price of $ 40.00 per share and pre-funded warrants to purchase up to 694,892 shares of Common Stock at an offering price of $ 39.9975 per warrant (representing the price per share of Common Stock sold in the offering minus the $0.0025 exercise price per warrant) in a registered direct offering pursuant to a shelf registration statement on Form S-3. The net proceeds to the Company from this offering were approximately $ 42.9 million, after deducting placement agent fees and offering costs of $2.1 million.

June 2023 PIPE

In June 2023, in connection with the Asset Acquisition, the Company issued and sold 721,452 shares of Series A Preferred Stock at approximately $291.08 per share through a private placement to a group of accredited investors. The net proceeds from this offering were approximately $197.3 million, after deducting placement agent fees and offering costs of $ 12.7 million.

December 2023 PIPE

In December 2023, the Company issued and sold 6,000,000 shares of Common Stock at an offering price of $ 15.00 per share and 150,000 shares of Series B Preferred Stock at $ 600 per share through a private placement to a group of accredited investors. The net proceeds from this offering were approximately $169.1 million, after deducting placement agent fees and offering costs of $ 10.9 million.

Parapyre Warrants

The Company settled its 2023 obligations under the Parapyre Option Obligation by issuing Parapyre 684,407 warrants to purchase the Company's common stock, less the $21.52 per share exercise price of each warrant. As of December 31, 2023, none of the warrants issued under the Parapyre Option Obligation have been exercised. See Note 15 for additional information on the Parapyre Option Obligation.

Pre-Funded Warrants

In May 2022, the Company issued pre-funded warrants to purchase shares of Common Stock in underwritten public offerings at the offering price of the Common Stock, less the $0.0025 per share exercise price of each warrant. The warrants were recorded as a component of stockholders' equity within additional paid-in capital and have no expiration date. Per the terms of the warrant agreements, the outstanding warrants to purchase shares of Common Stock may not be exercised if the holder's ownership of the Common Stock would exceed 4.99% ("Maximum Ownership Percentage") or 9.99% for certain holders. By written notice to the Company, each holder may increase or decrease the Maximum Ownership Percentage to any other percentage (not in excess of 19.99% for the majority of such warrants). The revised Maximum Ownership Percentage would be effective 61 days after the notice is received by the Company.

As of December 31, 2023, the following pre-funded warrants to purchase Common Stock were issued and outstanding:

Issue Date	Expiration Date	Exercise Price	Number of Warrants Outstanding
May 2022	None	$ 0.0025	250,000
Total pre-funded warrants			250,000

Series A Non-Voting Convertible Preferred Stock

On June 22, 2023, the Company filed a Certificate of Designation of Preferences, Rights and Limitations of the Series A Preferred Stock with the Secretary of State of the State of Delaware (the "Certificate of Designation") in connection with the Asset Acquisition and the PIPE.

Pursuant to the Certificate of Designation, holders of Series A Preferred Stock are entitled to receive dividends on shares of Series A Preferred Stock equal to, on an as-if-converted-to-Common Stock basis, and in the same form as, dividends actually paid on shares of Common Stock. Except as provided in the Certificate of Designation or as otherwise required by law, the Series A Preferred Stock does not have voting rights. However, as long as any shares of Series A Preferred Stock are outstanding, the Company will not, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series A Preferred Stock: (a) alter or change adversely the powers, preferences or rights given to the Series A Preferred Stock, or alter or amend the Certificate of Designation, amend or repeal any provision of, or add any provision to, the Company's Certificate of Incorporation or its Bylaws, or file any articles of amendment, certificate of designations, preferences, limitations and relative rights of any series of Preferred Stock, if such action would adversely alter or change the preferences, rights, privileges or powers of, or restrictions provided for the benefit of the Series A Preferred Stock, regardless of whether any of the foregoing actions will be by means of amendment to the Certificate of Incorporation or by merger, consolidation, recapitalization, reclassification, conversion or otherwise, (b) issue further shares of Series A Preferred Stock or increase or decrease (other than by conversion) the number of authorized shares of Series A Preferred Stock, (c) prior to the stockholder approval of the conversion of the Series A Preferred Stock into shares of Common Stock in accordance with Nasdaq Stock Market Rules (the "Conversion Proposal") or at any time while at least 30% of the originally issued Series A Preferred Stock remains issued and outstanding, consummate (x) any Fundamental Transaction (as defined in the Certificate of Designation) or (y) any merger or consolidation of the Company with or into another entity or any stock sale to, or other business combination in which our stockholders immediately before such transaction do not hold at least a majority of our capital stock immediately after such transaction or (d) enter into any agreement with respect to any of the foregoing. The Series A Preferred Stock does not have a preference upon any liquidation, dissolution or winding-up of the Company.

The Company held a stockholders' meeting to submit the following matters to its stockholders for their consideration: (i) the approval of the Conversion Proposal, and (ii) if deemed necessary or appropriate by the Company or as otherwise required by law or contract, the approval of an amendment to the Certificate of Incorporation to authorize sufficient shares of Common Stock for the conversion of the Series A Preferred Stock issued pursuant to the Acquisition Agreement. In connection with these matters, the Company filed with the SEC a definitive proxy statement and other relevant materials.

Following stockholder approval of the Conversion Proposal, each share of Series A Preferred Stock automatically converted into 40 shares of Common Stock, subject to certain limitations, including that a holder of Series A Preferred Stock is prohibited from converting shares of Series A Preferred Stock into shares of Common Stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (established by the holder between 0.0% and 20.0%) of the total number of shares of Common Stock issued and outstanding immediately after giving effect to such conversion.

On June 26, 2023, the Company completed a private placement of 721,452 shares of Series A PIPE Securities in exchange for gross proceeds of $210.0 million, or net proceeds of $197.3 million, after deducting placement agent and other offering costs.

On July 7, 2023, the Company issued 364,887 shares of Series A Preferred Stock as part of its consideration transferred in connection with the Asset Acquisition that closed on June 22, 2023 which settled the related forward contract liability. For additional information, see Note 3.

On November 21, 2023, the Company's stockholders approved the Conversion Proposal, among other matters, at a special meeting of stockholders. As a result of the approval of the Conversion Proposal, all conditions that could have required cash redemption of the Series A Preferred Stock were satisfied. Since the Series A Preferred Stock is no longer redeemable, the associated balances of the Series A Preferred Stock were reclassified from mezzanine equity to permanent equity during the fourth quarter of 2023. In addition, 649,302 shares of Series A Preferred Stock automatically converted to 25,972,080 shares of Common Stock; 437,037 shares of Series A Preferred Stock did not automatically convert and remain outstanding as of December 31, 2023 due to beneficial ownership limitations. This conversion was recorded as a reclassification between Series A Preferred Stock and Common Stock based on the historical per-share contributed capital amount, inclusive of any forward-contract valuation adjustments, of the Series A Preferred Stock.

Series B Non-Voting Convertible Preferred Stock

On December 8, 2023, the Company filed a Certificate of Designation of Preferences, Rights and Limitations of Series B Non-Voting Convertible Preferred Stock with the Secretary of State of the State of Delaware (the "Series B Certificate of Designation") in connection with the December 2023 PIPE.

Pursuant to the Series B Certificate of Designation, holders of Series B Preferred Stock are entitled to receive dividends on shares of Series B Preferred Stock equal to, on an as-if-converted-to-Common Stock basis, and in the same form as, dividends actually paid on shares of Common Stock. Except as provided in the Series B Certificate of Designation or as otherwise required by law, the Series B Preferred Stock does not have voting rights. However, as long as any shares of Series B Preferred Stock are outstanding, the Company will not, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series B Preferred Stock, alter or change adversely the powers, preferences or rights given to the Series B Preferred Stock, or alter or amend the Series B Certificate of Designation, amend or repeal any provision of, or add any provision to, the Company's Certificate of Incorporation or its Bylaws, or file any articles of amendment, certificate of designations, preferences, limitations and relative rights of any series of Preferred Stock, if such action would adversely alter or change the preferences, rights, privileges or powers of, or restrictions provided for the benefit of the Series B Preferred Stock, regardless of whether any of the foregoing actions will be by means of amendment to the Certificate of Incorporation or by merger, consolidation, recapitalization, reclassification, conversion or otherwise. The Series B Preferred Stock does not have a preference upon any liquidation, dissolution or winding-up of the Company.

The Company has agreed to use its best efforts to obtain stockholder approval of the conversion of all issued and outstanding Series B Preferred Stock into shares of Common Stock in accordance with the Nasdaq Stock Market Rules (the "Series B Conversion Proposal") at its 2024 annual meeting of stockholders, which the Company agreed to hold no later than May 15, 2024. The Series B Preferred Stock is recorded outside of stockholders' equity because, if conversion to Common Stock is not approved by the stockholders, the Series B Preferred Stock will be redeemable at the option of the holders for cash equal to the closing price of the Common Stock per share of Common Stock underlying the Series B Preferred Stock, on the last trading day prior to the holder's redemption request. As of December 31, 2023, the redemption value of the Company's outstanding Series B Preferred Stock was $129.1 million based on the closing stock price of the Company's Common Stock on December 31, 2023 of $21.52 per share. The Company has determined that the Series B Preferred Stock did not contain any embedded derivatives and therefore the conversion and redemption features did not require bifurcation.

Following stockholder approval of the Series B Conversion Proposal, each share of Series B Preferred Stock will automatically convert into 40 shares of the Common Stock, subject to certain limitations, including that a holder of Series B Preferred Stock is prohibited from converting shares of Series B Preferred Stock into shares of Common Stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (established by the holder between 0% and 19.99%) of the total number of shares of Common Stock issued and outstanding immediately after giving effect to such conversion.

On December 11, 2023, as part of the December 2023 PIPE, the Company completed a private placement of 150,000 shares of Series B Preferred Stock in exchange for gross proceeds of $90.0 million.

12. Strategic License Agreements

Immedica Pharma AB License and Development Agreement

On March 21, 2021, the Company entered into an exclusive license and supply agreement with Immedica Pharma AB ("Immedica"). By entering into this agreement, the Company agreed to provide Immedica the following goods and services:

i. Deliver an exclusive, sublicensable, license and know-how (the "License") to develop and commercialize pegzilarginase (the "Product") in the territory comprising the members states of the European Economic Area, United Kingdom, Switzerland, Andorra, Monaco, San Marino, Vatican City, Turkey, Saudi Arabia, United Arab Emirates, Qatar, Kuwait, Bahrain, and Oman (the "Territory");

ii. Complete the global pivotal PEACE (Pegzilarginase Effect on Arginase 1 Deficiency Clinical Endpoints) Phase 3 trial ("PEACE Trial") and related Biologics License Application ("BLA") package to file with the United States Food and Drug Administration ("FDA"), which will be leveraged by Immedica in obtaining the necessary regulatory approvals in the Territory; and

iii. Perform a Pediatric Investigation Plan trial ("PIP Trial") in order for Immedica to be able to receive certain regulatory approvals within the Territory.

In addition, the Company and Immedica formed a Joint Steering Committee ("JSC") to provide oversight to the activities performed under the agreement; however, the substance of the Company's participation in the JSC does not represent an additional promised service, but rather, a right of the Company to protect its own interests in the arrangement.

Further, the Company agreed to supply to Immedica, and Immedica agreed to purchase from the Company, substantially all commercial requirements of the Product. The terms of the agreement do not provide for either (i) an option to Immedica to purchase the Product from the Company at a discount from the standalone selling price or (ii) minimum purchase quantities. Finally, Immedica will bear (i) all costs and expenses for any development or commercialization of the Product in the Territory subject to the License exclusive of the Company's promised goods and services summarized above and (ii) all costs and fees associated with applying for regulatory approval of the Product in the Territory. In July 2021, the Company modified the agreement with Immedica to provide certain additional services in relation to the PEACE Phase 3 Trial and BLA package performance obligation in exchange for the reimbursement of up to $3.0 million of the actual costs incurred in relation to such incremental services.

The Company received a non-refundable payment of $21.5 million and Immedica agreed to provide payment of 50% of the Company's costs incurred in performing the PIP Trial up to a maximum of $1.8 million. In addition, the Company has the ability to receive additional payments under the agreement of up to approximately $120.8 million in regulatory and commercial milestone payments, assuming an exchange rate of $1.07 to €1.00. The Company is also entitled to receive royalties in the mid-20 percent range on net sales of the Product in the Territory.

The Company concluded that Immedica meets the definition to be accounted for as a customer because the Company is delivering intellectual property and other services within the Company's normal course of business, in which the parties are not jointly sharing the risks and rewards. Therefore, the Company concluded that the promises summarized above represent transactions with a customer within the scope of ASC 606. The Company determined that the following promises represent distinct promised services, and therefore, performance obligations: (i) the License, (ii) the PEACE Trial and BLA package, and (iii) the PIP Trial.

Specifically, in making these determinations, the Company considered the following factors:

- As of inception of the agreement, the Company had completed the Phase 1/2 clinical trial related to the Product and were conducting the ongoing PEACE Trial. Accordingly, the Company is not promising, nor expecting, to perform additional research and development activities pursuant to the agreement that would either significantly modify, customize or be considered highly interdependent or interrelated with pegzilarginase.
- The License represents functional intellectual property given the functionality of the License is not expected to change substantially as a result of the company's ongoing activities.
- The services necessary to complete the PEACE Trial, BLA package and PIP Trial could be performed by other parties.

Given that Immedica was not obligated to purchase any minimum amount or quantities of the Product, the supply of the Product for commercial use to Immedica was determined to be an option for Immedica, rather than a performance obligation of the Company at contract inception and will be accounted for if and when exercised. The Company also determined that Immedica's option to purchase the Product does not create a material right as the expected pricing is not at a discount.

The Company determined that the upfront fixed payment amount of $ 21.5 million must be included in the transaction price. Additionally, the Company determined at inception of the arrangement that 50% of the estimated costs to be incurred in relation to the PIP Trial exceeded $1.8 million and included the full reimbursement amount of $ 1.8 million in the transaction price. Upon subsequent re-evaluation due to changing facts and circumstances, the Company determined the estimated costs are now less than the maximum allowable reimbursement and a portion of the variable consideration was constrained, which did not materially impact the revenue recognized to date. Additionally, upon the modification of the agreement in July 2021, the Company determined that the estimated costs to perform the additional services related to the PEACE Trial and BLA package exceeds the maximum allowable reimbursement of $3.0 million. Therefore, the Company included an estimated total of $3.6 million that will be due in relation to the PIP Trial, PEACE Trial, and BLA package in the transaction price and it is probable that a significant reversal will not occur in the future. In total, the modified transaction price was determined to be $25.1 million.

The Company has allocated $ 9.6 million and $3.5 million of the modified transaction price to the PEACE Trial and BLA package and PIP Trial performance obligations, respectively, based on the stand-alone selling prices ("SSP"), which was based on the estimated costs that a third-party would charge in performing such services on a stand-alone basis. The SSP for the License was established at inception of the arrangement using a residual value approach due to the uniqueness of and lack of observable data related to the License, and without a specific analog from which to make reliable estimates, resulting in an allocation of $12.0 million.

The potential regulatory milestone payments that the Company is eligible to receive were excluded from the transaction price, as the milestone amounts were fully constrained based on the probability of achievement, since the milestones relate to successful achievement of certain regulatory approvals, which might not be achieved. The Company determined that the royalties and commercial milestone payments relate predominantly to the license of intellectual property and are therefore excluded from the transaction price under the sales- or usage-based royalty exception of ASC 606. The Company will reevaluate the transaction price, including all constrained amounts, at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, the Company will adjust its estimate of the transaction price as necessary. The Company

will recognize the royalties and commercial milestone payments as revenue when the associated sales occur, and relevant sales-based thresholds are met. The Company assessed the arrangement with Immedica and concluded that a significant financing component does not exist.

The Company recognized revenue allocated to the License performance obligation at a point in time and upon transfer of the License. The Company completed the transfer of the know-how necessary for Immedica to benefit from the License in June 2021 and recognized $12.0 million of revenue at that time. The development fee allocated to the PEACE Trial, BLA package and PIP Trial performance obligations will be recognized over time using an input method of costs incurred related to the performance obligations.

For the years ended December 31, 2023 and 2022, the Company recognized revenue of $ 0.9 million and $2.3 million, respectively, related to the PEACE Trial and BLA package performance obligation using a cost to cost model. The Company recognized revenue of $6.7 million related to the PEACE Trial and BLA package performance obligation using a cost to cost model and $ 12.0 million related to the transfer of the License for the year ended December 31, 2021. As of December 31, 2022, the Company recorded deferred revenue of $2.7 million associated with the license and supply agreement with Immedica, of which $ 0.5 million was classified as current.

On July 27, 2023, the Company announced that it had entered into an agreement to sell the global rights to pegzilarginase to Immedica for $15.0 million in upfront cash proceeds and up to $100.0 million in contingent milestone payments. The sale of pegzilarginase to Immedica superseded and terminated the previous license agreement between the Company and Immedica. On July 27, 2023, the carrying value of the asset was zero as it was internally developed. Accordingly, the Company recognized a $ 16.4 million gain within Gain on Sale of in-process research and development, which is comprised of $15.0 million in upfront cash proceeds and the reimbursement of $ 1.8 million in pre-paid manufacturing costs that was contingent upon a favorable opinion being received by the CHMP, net of transaction costs and the derecognition of pegzilarginase related nonfinancial assets and liabilities totaling $0.4 million.

The milestone payments are contingent on formal reimbursement decisions by national authorities in key European markets and pegzilarginase approval by the FDA, among other events. The upfront payment and contingent milestone payments if paid, net of expenses and adjustments, will reduce the CVR liability and will be distributed to CVR holders pursuant to the CVR Agreement resulting from the Asset Acquisition.

Contract Balances from Customer Contract

The timing of revenue recognition, billings and cash collections results in contract assets and contract liabilities on the balance sheets. The Company recognizes license and development receivables based on billed services, which are derecognized upon reimbursement. When consideration is received, or such consideration is unconditionally due, from a customer prior to transferring goods or services to the customer under the terms of a contract, a contract liability is recorded. Contract liabilities are recognized as revenue after control of the goods or services is transferred to the customer and all revenue recognition criteria have been met.

The following table presents changes in the Company's contract liabilities for the periods presented (in thousands):

Year Ended December 31, 2022	December 31, 2022	Additions	Deductions	December 31, 2023
Contract liabilities:				
Deferred revenue	$ 2,696	$ 575	$ (3,271)	$ —

The Company had no contract assets during the years ended December 31, 2023 and 2022.

13. Sale of Pegzilarginase to Immedica

On July 27, 2023, the Company announced that it had entered into an agreement to sell the global rights to pegzilarginase to Immedica for $15.0 million in upfront cash proceeds and up to $100.0 million in contingent milestone payments. The sale of pegzilarginase to Immedica superseded and terminated the previous license agreement between the Company and Immedica. On July 27, 2023, the carrying value of the asset was zero as it was internally developed. Accordingly the Company recognized a $ 16.4 million gain within Gain on sale of in-process research and development, which is comprised of $15.0 million in upfront cash proceeds and the reimbursement of $ 1.8 million in pre-paid manufacturing costs that was contingent upon a favorable opinion being received by the Committee for Medicinal Products for Human Use, net of transaction costs and the derecognition of pegzilarginase related nonfinancial assets and liabilities totaling $0.4 million.

The milestone payments are contingent on formal reimbursement decisions by national authorities in key European markets and pegzilarginase approval by the FDA, among other events. Accordingly, the Company will recognize any future milestone payments once the contingency is resolved and payment is contractually required. The upfront payment and contingent milestone payments if paid, net of expenses and adjustments, will be distributed to CVR holders pursuant to the CVR Agreement resulting from the Asset Acquisition.

14. Novation of Manufacturing Agreements

Pursuant to a Novation Agreement dated September 19, 2023 (the “Novation Agreement”), by and between the Company, Paragon and WuXi Biologics (Hong Kong) Limited (“WuXi Biologics”), the Company novated (i) a Biologics Master Services Agreement (the “WuXi Biologics MSA”) and (ii) a Cell Line License Agreement (the “Cell Line License Agreement”).

Biologics Master Services Agreement

In April 2023, Paragon and WuXi Biologics entered into the WuXi Biologics MSA, which was subsequently novated to the Company by Paragon on September 19, 2023 pursuant to the Novation Agreement. The WuXi Biologics MSA governs certain development activities and GMP manufacturing and testing for the SPY001 program, as well as potential future programs, on a work order basis. Under the WuXi Biologics MSA, the Company is obligated to pay WuXi Biologics a service fee and all non-cancellable obligations in the amount specified in each work order associated with the agreement for the provision of services.

The WuXi Biologics MSA terminates on the later of (i) June 20, 2027 or (ii) the completion of services under all work orders executed by the parties prior to June 20, 2027, unless terminated earlier. The term of each work order terminates upon completion of the services under such work order, unless terminated earlier. The Company can terminate the WuXi Biologics MSA or any work order at any time upon 30 days’ prior written notice and immediately upon written notice if WuXi Biologics fails to obtain or maintain required material governmental licenses or approvals. Either party may terminate a work order (i) at any time upon six months prior notice with reasonable cause, provided however that if WuXi Biologics terminates a work order in such manner, no termination or cancellation fees shall be paid by the Company and (ii) immediately for cause upon (a) the other party’s material breach that remains uncured for 30 days after notice of such breach, (b) the other party’s bankruptcy or (c) a force majeure event that prevents performance for a period of at least 90 days.

Cell Line License Agreement

In April 2023, Paragon and WuXi Biologics entered into the Cell Line License Agreement, which was subsequently novated to the Company by Paragon pursuant to the Novation Agreement. Under the Cell Line License Agreement, the Company received a non-exclusive, worldwide, sublicensable license to certain of WuXi Biologics’s know-how, cell line, biological materials (the “WuXi Biologics Licensed Technology”) and media and feeds to make, have made, use, sell and import certain therapeutic products produced through the use of the

cell line licensed by WuXi Biologics under the Cell Line License Agreement (the “WuXi Biologics Licensed Products”). Specifically, the WuXi Biologics Licensed Technology is used in certain manufacturing activities in support of the SPY001 program.

In consideration for the license, the Company agreed to pay WuXi Biologics a non-refundable license fee of $0.2 million. Additionally, if the Company manufactures all of its commercial supplies of bulk drug product with a manufacturer other than WuXi Biologics or its affiliates, the Company is required to make royalty payments to WuXi Biologics of less than one percent of global net sales of WuXi Biologics Licensed Products manufactured by a third-party manufacturer (the “Royalty”). If the Company manufactures part of its commercial supplies of the WuXi Biologics Licensed Products with WuXi Biologics or its affiliates, then the Royalty will be reduced accordingly on a pro rata basis.

The Cell Line License Agreement will continue indefinitely unless terminated (i) by the Company upon six months prior written notice and our payment of all undisputed amounts due to WuXi Biologics through the effective date of termination, (ii) by WuXi Biologics for a material breach by the Company that remains uncured for 60 days after written notice, (iii) by WuXi Biologics if the Company fails to make a payment and such failure continues for 30 days after receiving notice of such failure, or (iv) by either party upon the other party’s bankruptcy.

15. Stock-Based Compensation

2015 Equity Incentive Plan

In March 2015, the Company adopted the 2015 Equity Incentive Plan (“2015 Plan”), administered by the board of directors, and provides for the Company to sell or issue share of Common Stock or restricted Common Stock, or to grant incentive stock options or nonqualified stock options for the purchase of Common Stock, to employees, members of the board of directors and consultants of the Company. Under the terms of the 2015 Plan, the exercise prices, vesting and other restrictions may be determined at the discretion of the board of directors, or their committee if so delegated, except that the exercise price per share of stock options may not be less than 100% of the fair market value of the share of common stock on the date of grant, the term of stock options may not be greater than ten years for all grants, and for grantees holding more than 10% of the total combined voting power of all classes of stock, the term may not be greater than five years.

The Company granted options under the 2015 Plan until April 2016 when it was terminated as to future awards, although it continues to govern the terms of options that remain outstanding under the 2015 Plan.

As of December 31, 2023, a total of 3,029 shares of Common Stock are subject to options outstanding under the 2015 Plan and will become available under the 2016 Equity Incentive Plan (“2016 Plan”) to the extent the options are forfeited or lapse unexercised.

2016 Equity Incentive Plan

The 2016 Plan became effective in April 2016 and serves as the successor to the 2015 Plan. Under the 2016 Plan, the Company may grant stock options, stock appreciation rights, restricted stock awards, restricted stock units, performance awards, and stock bonuses. The 2016 Plan provides for an initial reserve of 44,000 shares of Common Stock, plus 20,395 shares of Common Stock remaining under the 2015 Plan, and any share awards that subsequently are forfeited or lapse unexercised under the 2015 Plan. The shares reserved exclude shares of Common Stock reserved for issuance under the 2015 Plan.

In October 2018, the 2016 Plan was amended to increase the number of shares of Common Stock reserved for issuance thereunder by 70,384 shares, extend the term of the 2016 Plan through August 7, 2028, and provide for an automatic increase in the number of shares reserved for issuance thereunder on January 1 of each year for

the remaining term of the plan equal to (a) 4.0% 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 (the "Evergreen Provision"). As a result of the operation of each of these provisions, on January 1, 2023, 2022, and 2021, an additional 104,561, 78,968, and 76,735 shares, respectively, became available for issuance under the 2016 Plan.

In November 2023, the 2016 Plan was amended to (i) increase the number of shares of Common Stock reserved for issuance thereunder by 4,481,152 shares, (ii) revise the annual limit on non-employee director compensation from 4,000 shares to (a) $750,000 in total value or (b) $1,000,000 in the year of the director's initial service as a non-employee director or in any year a director serves as chairman of the Board of Directors, in either case, applicable to fees paid in both cash and equity, (iii) remove the fixed termination date of the 2016 Plan and, (iv) revise the Evergreen Provision from 4% to 5% of issued and outstanding shares of Common Stock on December 31 of the preceding calendar year and to include shares issuable upon the exercise of pre-funded warrants and the conversion of outstanding shares of non-voting convertible preferred stock in the calculation.

As of December 31, 2023, the total number of shares reserved for issuance under the 2016 Plan was 5,019,177, of which 3,294,962 shares were subject to outstanding option awards and restricted unit awards.

2018 Equity Inducement Plan

In February 2018, the board of directors approved and adopted the 2018 Equity Inducement Plan ("2018 Plan"), which became effective on the same date. The board of directors approved an initial reserve of 44,000 shares of Common Stock to be used exclusively for individuals who were not previously employees or directors, or following a bona fide period of non-employment, as an inducement material to the individual entering into employment with the Company. Nonqualified stock options or restricted stock units may be granted under the 2018 Plan at the discretion of the Compensation Committee or the board of directors. The Company did not seek stockholder approval of the 2018 Plan pursuant to Nasdaq Rule 5635(c)(4).

During 2023, the 2018 Plan was amended to increase the number of shares of Common Stock reserved for issuance by 6,000,000.

Under the 2016 Plan and 2018 Plan, the Company may grant stock-based awards with service conditions ("service-based" awards), performance conditions ("performance-based" awards), and market conditions ("market-based" awards). Service-based awards granted under the 2018 Plan, 2016 Plan, and 2015 Plan generally vest over four years and expire after ten years, although awards have been granted with vesting terms less than four years.

The Company granted 153,865 service-based restricted stock units ("RSUs") during the year ended December 31, 2023 to certain employees under the 2018 Plan.

As of December 31, 2023, the total number of shares reserved for issuance under the 2018 Plan was 6,044,000, of which 5,350,595 shares were subject to outstanding awards.

Spyre 2023 Equity Incentive Plan

On June 22, 2023, in connection with the Asset Acquisition, the Company assumed the Amended and Restated Spyre 2023 Equity Incentive Plan (the "Spyre Equity Plan") and its outstanding and unexercised stock options, which were converted to options to purchase 2,734 shares of Common Stock. The acquisition-date fair value of these grants will be recognized as an expense on a pro-rata basis over the vesting period.

Parapyre Option Obligation

On June 22, 2023, in connection with the Asset Acquisition, the Company assumed the Parapyre Option Obligation which provided for an annual equity grant of warrants for Parapyre to purchase 1% of the then outstanding shares of Pre-Merger Spyre's common stock, on a fully diluted basis, on the last business day of each calendar year during the term of the Paragon Agreement, at the fair market value determined by the board of directors of Pre-Merger Spyre.

On September 29, 2023, the Company amended the Paragon Agreement to amend and restate certain terms of the option grant pertaining to the Parapyre Option Obligation, including but not limited to (i) defining that the annual equity grant of warrants is based on the outstanding shares of the Company's Common Stock, (ii) establishing the grant date as the last business day of 2023 and 2024, and (iii) defining the term of the warrants granted as ten years. The Company determined that the 2023 and 2024 grants are two separate grants, as there would be no obligation for the 2024 grant had the Company exercised or terminated all of the options under the Paragon Agreement prior to December 31, 2023. The service inception period for the grant precedes the grant date, with the full award being vested as of the grant date with no post-grant date service requirement. Accordingly, a liability related to the Parapyre Option Obligation was recorded pursuant to the amended Paragon Agreement during 2023 interim periods. The Company determined that the grant date of the award was December 31, 2023, as all terms of the award, including number of shares and exercise price, were known by all parties. Accordingly, the Company measured the grant-date fair value of the warrants granted at approximately $11.5 million as an equity-classified award, of which $0.1 million was recognized as part of the liabilities assumed with the Asset Acquisition on June 22, 2023. For the year ended December 31, 2023, $11.4 million was recognized as stock compensation expense related to the Parapyre Option Obligation. There was no similar expense for the years ended December 31, 2022 and 2021.

As of December 31, 2023, the unamortized expense related to the Parapyre Option Obligation was nil.

The following table summarizes employee and non-employee stock option activity for the year ended December 31, 2023:

	Shares Issuable Under Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2022	405,082	$ 113.75	6.72	$ 2
Granted	8,776,245	9.67		
Exercised	(46,246)	8.22		
Forfeited	(637,686)	43.00		
Outstanding as of December 31, 2023	8,497,395	$ 12.13	8.40	$ 98,928
Options vested and expected to vest as of December 31, 2023	8,497,395	$ 12.13	8.40	$ 98,928
Options exercisable as of December 31, 2023	1,065,700	$ 24.72	5.62	$ 13,328

The aggregate intrinsic value of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the fair value of the Company's Common Stock as of the reporting date.

For the years ended December 31, 2023, 2022, and 2021, the weighted-average grant date fair value of options granted was $ 9.67, $1.80, and $4.96, per share, respectively. The total intrinsic value of options exercised during the years ended December 31, 2023, and 2021 was $0.4 million and $0.7 million, respectively. No options were exercised in the year ended December 31, 2022.

There were 477,000 stock options issued to non-employees during the years ended December 31, 2023. There were no stock options issued to non-employees during the years ended December 31, 2022 and 2021. For the years ended December 31, 2023, 2022 and 2021, no non-employee stock options vested in the period.

2016 Employee Stock Purchase Plan

The 2016 Employee Stock Purchase Plan ("2016 ESPP") became effective in April 2016. A total of 6,600 shares of Common Stock were reserved for issuance under the 2016 ESPP. Eligible employees may purchase shares of Common Stock under the 2016 ESPP at 85% of the lower of the fair market value of the Common Stock as of the first or the last day of each offering period. Employees are limited to contributing 15% of the employee's eligible compensation and may not purchase more than $ 25,000 of stock during any calendar year. The 2016 ESPP will terminate ten years from the first purchase date under the plan, unless terminated earlier by the board of directors.

In June 2018, the 2016 ESPP was amended to provide for an automatic annual increase in the number of shares reserved for issuance thereunder on January 1 of each year for the remaining term of the year equal to (a) 1.0% 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 of directors each year. As a result of the operation of this provision, on January 1, 2023, 2022 and 2021, an additional 26,140, 19,742, and 19,184 shares, respectively, became available for issuance under the 2016 ESPP. As of December 31, 2023, the reserve remaining and available for future issuance under the 2016 ESPP was 72,404 shares.

In February 2023, the 2016 ESPP was amended to increase the maximum shares purchased during any one period from 80 shares to 400 shares or a lesser amount determined by the board of directors.

For the year ended December 31, 2023, stock-based compensation expense related to the 2016 ESPP plan was di minimis. For the years ended 2022 and 2021, stock-based compensation expense related to the 2016 ESPP plan was $0.1 million and $0.2 million, respectively.

Restricted Common Stock Units

In July 2020, the Company granted 9,128 restricted stock units to certain employees, with vesting terms subject to regulatory, commercial, and clinical milestones, in addition to a service condition. As of December 31, 2023 none of these restricted stock units had vested and all restricted stock units were forfeited since the performance milestones were not met within the required time frame. No stock-based compensation expense was recognized on these awards.

The Company granted 153,865 service-based restricted stock units during the year ended December 31, 2023. There were no restricted stock units granted during the years ended December 31, 2022 and 2021.

The following table summarizes employee restricted stock activity for the year ended December 31, 2023:

	Shares	Weighted Average Grant Date Fair Value
Unvested restricted stock units as of December 31, 2022	5,660	$ 203.25
Granted	153,865	18.17
Vested	—	—
Forfeited	(5,660)	203.25
Unvested restricted stock units as of December 31, 2023	153,865	$ 18.17

There were no restricted stock units granted to non-employees during the years ended December 31, 2023, 2022, and 2021.

Stock-Based Compensation Expense

Total stock-based compensation expense recognized from the Company's equity incentive plans, 2018 Plan, and the 2016 ESPP for the years ended December 31, 2023, 2022, and 2021 was as follows (in thousands):

	Year Ended December 31,					
	2023		2022		2021	
	Employees	Non-Employees	Employees	Non-Employees	Employees	Non-Employees
Research and development	$ 2,910	$ 11,328	$ 2,591	$ —	$ 2,723	$ —
General and administrative	11,327	109	4,520	—	5,315	—
Total stock-based compensation expense	$ 14,237	$ 11,437	$ 7,111	$ —	$ 8,038	$ —

No related tax benefits were recognized for the years ended December 31, 2023, 2022, and 2021 (see Note 18).

The employee and non-employee awards contain both performance and service-based vesting conditions. No expense was recognized for the unvested employee and non-employee awards with only a performance condition for the years ended December 31, 2023, 2022, and 2021. The performance-based vesting conditions represent specific performance targets. Compensation expense for employee and non-employee share-based payment awards with performance conditions is recognized when the performance condition is deemed probable of achievement.

As of December 31, 2023, the Company had an aggregate of $ 64.4 million of unrecognized stock-based compensation expense for options outstanding, which is expected to be recognized over a weighted average period of 3.5 years.

In determining the fair value of the stock-based awards, the Company uses the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Expected Term

The Company's expected term represents the period that the Company's stock-based awards are expected to be outstanding and is determined using the simplified method (based on the midpoint between the vesting date and the end of the contractual term). The Company utilizes this method due to lack of historical exercise data and the plain-vanilla nature of the Company's stock-based awards.

Expected Volatility

Since the Company was privately held through April 2016 and transitioned from a clinical stage company to a pre-clinical stage company in 2023, it alone does not have the relevant company-specific historical data to support its expected volatility. As such, the Company has used an average of expected volatilities based on the volatilities of a representative group of publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. Subsequent to the Company's initial public offering, it began to consider the Company's own historic volatility. However, due to the transition from a clinical stage company to a pre-clinical stage company, the Company still uses peer company data to assist in this analysis. For purposes of identifying comparable companies, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. The Company intends to consistently apply this process using the same or

similar comparable entities until a sufficient amount of historical information regarding the volatility of the Company's own share price post transition becomes available.

Risk-Free Interest Rate

The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend

The Company has never paid dividends on its Common Stock and has no plans to pay dividends on its Common Stock. Therefore, the Company used an expected dividend yield of zero.

Valuation of Stock Options and 2016 ESPP

The fair value of the stock options granted under the the Company's equity incentive plans, as well as the shares available for purchase under the 2016 ESPP were determined using the Black-Scholes option-pricing model. The following table summarizes the weighted-average assumptions used in calculating the fair value of the awards:

	Year Ended December 31,		
	2023	2022	2021
Stock Options Granted			
Expected term (in years)	5.88	6.00	5.99
Expected volatility	107%	84%	83%
Risk-free interest	4.37%	2.93%	0.88%
Dividend yield	0%	0%	0%
2016 ESPP			
Expected term (in years)	0.49	0.49	0.50
Expected volatility	181%	84%	86%
Risk-free interest	4.99%	1.95%	0.08%
Dividend yield	0%	0%	0%

16. Defined Contribution Plan

The Company sponsors a 401(k) retirement plan in which substantially all of its full-time employees are eligible to participate. Participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. During the years ended December 31, 2023, 2022, 2021, the Company provided $0.2 million, $0.6 million, and $0.6 million, respectively, in contributions to the plan.

17. Restructuring Charges

Severance and Stock Compensation

On April 12, 2023, based on the review of the inconclusive interim results from the Company's Phase 1/2 clinical trial of pegtarviliase for the treatment of classical homocystinuria and other business considerations, the Company announced that it had initiated a process to explore strategic alternatives to maximize stockholder value and engaged an independent exclusive financial advisor to support this process.

As a result, the Company implemented a restructuring plan resulting in an approximate 83% reduction of the Company's existing headcount by June 30, 2023. The Company recognized restructuring expenses consisting of cash severance payments and other employee-related costs of $6.4 million during the year ended December 31, 2023. Cash payments for employee related restructuring charges of $5.3 million were paid as of December 31, 2023. In addition, the Company recognized $ 1.0 million in non-cash stock-based compensation

expense related to the accelerated vesting of stock-based awards for certain employees. The Company recorded these restructuring charges based on each employee's role to the respective research and development and general and administrative operating expense categories on its consolidated statements of operations and comprehensive loss.

The following table summarizes the changes in the Company's accrued restructuring balance (in thousands):

	Beginning Balance December 31, 2022	Charges	Payments	Ending Balance December 31, 2023
Severance liability	$ —	$ 6,448	$ (5,325)	$ 1,123

Sale of Assets

During the second quarter of 2023, the Company sold various lab equipment, consumables, and furniture and fixtures for total consideration of $0.5 million. After recording the disposal of all the Company's property and equipment net of proceeds, the Company recorded a $0.7 million and $0.2 million loss on disposal of long lived assets which is included in Research and development and General and administrative expenses, respectively.

Lease Right-of-use Asset and Leasehold Improvement Impairment

Effective June 30, 2023, the Company abandoned its leased office space in Austin, Texas. As a result, the Company recognized an impairment loss of $0.9 million related to the operating lease right-of-use asset and $1.7 million related to leasehold improvements. On August 7, 2023, the Company terminated its building lease in Austin, Texas. The negotiated termination agreement obligated the Company to pay the lessor a $2.0 million termination fee in exchange for releasing the Company of all further obligations under the lease.

All charges related to the restructuring activities were recognized during the second quarter of 2023. No further restructuring charges will be incurred under the restructuring plan. A summary of the charges related to the restructuring activities is as follows (in thousands):

	Severance Related Expenses	Stock Compensation Expenses	Loss on Disposal of Long Lived Assets	Lease Asset Impairment	Total Restructuring Costs
Research and development	$ 3,182	$ 123	$ 749	$ 1,405	$ 5,459
General and administrative	3,266	870	182	1,175	5,493
Total	$ 6,448	$ 993	$ 931	$ 2,580	$ 10,952

18. Income Taxes

The following table summarizes the (loss) income before income tax expense by jurisdiction for the periods indicated:

	Year Ended December 31,		
	2023	2022	2021
Domestic	$(338,942)	$(84,113)	$(65,940)
Foreign	126	162	280
Loss before income tax expense	$(338,816)	$(83,951)	$(65,660)

For the year ended December 31, 2023, the Company recognized no provision or benefit from income taxes. For both the years ended December 31, 2022 and 2021, the Company recognized an income tax expense of $0.1 million, related to foreign subsidiaries income tax expense and the Texas margins tax. The difference between the Company's provision for income taxes and the amounts computed by applying the statutory federal income tax rate to income before income taxes is as follows (in thousands):

	Year Ended December 31,		
	2023	2022	2021
Tax provision derived by applying the federal statutory rate to income before income taxes	$(71,151)	$(17,630)	$(13,789)
Loss on forward contract valuation	17,541	—	—
Acquired IPR&D	27,340	—	—
Loss on CVR revaluation	3,987	—	—
Other permanent differences	4,472	1,042	1,002
Federal tax credits	(1)	(3,559)	(3,815)
State tax credits	—	(640)	(152)
Effect of tax rate on foreign jurisdiction	(53)	42	(5)
Change in the valuation allowance	17,839	20,609	16,900
Income tax (benefit) expense	$ (26)	$ (136)	$ 141

The components of the deferred tax assets and liabilities consist of the following (in thousands):

	December 31,	
	2023	2022
Deferred tax assets		
Net operating loss carryforward	$ 74,454	$ 68,917
Capitalized 174 R&D costs	22,532	11,097
Intangible assets	47	52
Deferred revenue	—	566
Accrued expense	579	668
Stock-based compensation	4,246	3,293
Federal tax credits	21,914	21,914
State tax credits	1,631	1,631
Other	88	190
Total deferred tax assets	125,491	108,328
Deferred tax liabilities		
Depreciable assets	—	(676)
Total deferred tax liabilities	—	(676)
Less: Valuation allowance	(125,491)	(107,652)
Deferred tax assets, net	$ —	$ —

The Company has established a full federal and state valuation allowance equal to the net deferred tax assets due to uncertainties regarding the realization of the deferred tax asset based on the Company's lack of earnings history. The valuation allowance increased by $17.8 million, $20.6 million, and $16.9 million during the years ended December 31, 2023, 2022, and 2021, respectively, primarily due to continuing loss from operations.

As of December 31, 2023 and 2022, the Company had U.S. net operating loss carryforwards ("NOL") of $ 354.5 million and $328.2 million, respectively. For both the years ended December 31, 2023 and 2022, the Company had U.S. tax credit carryforwards and state tax credit carryforwards of $21.9 million and $1.6 million, respectively. Of the net operating loss and tax credit carryforwards $ 58.4 million and $21.9 million, respectively, will expire in 2033, if not utilized. Any remaining net operating loss will carry forward indefinitely and can be

utilized to offset up to 80% of the taxable income in any tax year. The net operating loss and credit carryforwards are subject to Internal Revenue Service adjustments until the statute closes on the year the net operating loss or tax credits are utilized.

The Company has not completed a study to assess whether an ownership change has occurred or whether there have been multiple ownership changes since the Company's formation due to the complexity and cost associated with such a study, and the fact that there may be additional such ownership changes in the future. If the Company has experienced an ownership change at any time since its formation, utilization of the NOL or research and development credit carryforwards would be subject to an annual limitation under Section 382 or 383 of the Internal Revenue Code, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term, tax-exempt rate, and then could be subject to additional adjustments, as required. Additionally, the separate return limitation year ("SRLY") rules may apply to losses of the Company's eight wholly owned U.S. subsidiary corporations. The SRLY rules limit the consolidated group's use of a subsidiary corporation's net operating losses to the amount of income generated by the subsidiary corporation after it becomes a member of the group. Any limitation may result in expiration of a portion of the NOL or research and development credit carryforwards before utilization. Further, until a study is completed and any limitation known, no amounts are being considered as an uncertain tax position or disclosed as an unrecognized tax benefit. Additionally, the Company does not expect any unrecognized tax benefits to change significantly over the next twelve months. Due to the existence of the valuation allowance, future changes in the Company's unrecognized tax benefits will not impact its effective tax rate. Any carryforwards that will expire prior to utilization as a result of such limitations will be removed from deferred tax assets with a corresponding reduction of the valuation allowance.

The Company is subject to examination by taxing authorities in its significant jurisdictions for the 2019 and subsequent years. However, due to NOL and tax attribute carryovers, the taxing authorities have the ability to adjust the NOLs and other tax attributes related to closed years. As of December 31, 2023 and 2022, there were no amounts recorded for uncertain tax positions. As of December 31, 2023, undistributed earnings of the Company's incorporated foreign subsidiaries are immaterial. Under the Global Intangible Low-Taxed Income ("GILTI") provisions of the 2017 Tax Cuts and Jobs Act, U.S. income taxes have been incurred on the undistributed earnings of the foreign subsidiaries and therefore, the tax impact upon distribution is limited to state income and withholding taxes and is not material.

19. Net Loss Per Share

The Company computes net loss attributable per common stockholder using the two-class method required for participating securities. The Company considers convertible preferred stock to be participating securities. In the event that the Company paid out distributions, holders of convertible preferred stock would participate in the distribution.

The two-class method is an earnings (loss) allocation method under which earnings (loss) per share is calculated for Common Stock and participating security considering a participating security's rights to undistributed earnings (loss) as if all such earnings (loss) had been distributed during the period. The holders of Series A Preferred Stock and Series B Preferred Stock do not have an obligation to fund losses and therefore the Series A Preferred Stock and the Series B Preferred Stock were excluded from the calculation of basic net loss per share.

Basic and diluted net loss per share is computed by dividing the net loss by the weighted-average number of Common Stock and pre-funded warrants outstanding during the period, without consideration of potential dilutive securities. The pre-funded warrants are included in the computation of basic net loss per share as the exercise price is negligible and they are fully vested and exercisable. For periods in which the Company generated a net loss, the Company does not include the potential impact of dilutive securities in diluted net loss per share, as the impact of these items is anti-dilutive. The Company has generated a net loss for all periods presented, therefore diluted net loss per share is the same as basic net loss per share since the inclusion of potentially dilutive securities would be anti-dilutive.

The following weighted-average equity instruments were excluded from the calculation of diluted net loss per share because their effect would have been anti-dilutive for the periods presented:

	Year Ended December 31,		
	2023	2022	2021
Options to purchase Common Stock	2,583,226	346,331	264,858
Unvested restricted stock units	4,240	6,983	7,975
Outstanding Parapyre Warrants	5,625	—	—

The following is a reconciliation of the shares used as the denominator for the calculation of basic and diluted net loss per share:

	Year Ended December 31,		
	2023	2022	2021
Weighted average Common Shares	6,201,954	2,307,668	1,956,933
Weighted average pre-funded warrants	695,111	1,063,563	672,851
Total basic and diluted weighted average shares	6,897,065	3,371,231	2,629,784

Report of Independent Registered Public Accounting Firm

To the Board of Directors of Aeglea BioTherapeutics, Inc.

Opinion

We have audited the accompanying statement of assets acquired and liabilities assumed from Spyre Therapeutics, Inc. ("Spyre") by Aeglea BioTherapeutics, Inc. ("Aeglea") as of June 22, 2023, including the related notes (collectively referred to as the "financial statement").

In our opinion, the accompanying financial statement presents fairly, in all material respects, the assets acquired and liabilities assumed from Spyre by Aeglea as of June 22, 2023 in accordance with accounting principles generally accepted in the United States of America.

Basis for Opinion

We conducted our audit in accordance with auditing standards generally accepted in the United States of America (US GAAS). Our responsibilities under those standards are further described in the Auditors' Responsibilities for the Audit of the Financial Statement section of our report. We are required to be independent of Aeglea and to meet our other ethical responsibilities, in accordance with the relevant ethical requirements relating to our audit. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Substantial Doubt about the Company's Ability to Continue as a Going Concern

The accompanying financial statement has been prepared assuming that Aeglea will continue as a going concern. As discussed in Note 1 to the financial statement, holders of Aeglea Series A Preferred Stock are entitled to require Aeglea to settle their shares of Series A Preferred Stock for cash, and the cash redemption is not in Aeglea's control, and Aeglea has stated that substantial doubt exists about it's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The financial statement does not include any adjustments that might result from the outcome of the uncertainty. Our opinion is not modified with respect to this matter.

Emphasis of Matter

As described in Note 1 to the accompanying financial statement, the financial statement was prepared in connection with Aeglea's acquisition of Spyre in accordance with a Securities and Exchange Commission (SEC) waiver received by Aeglea, for the purpose of Aeglea complying with Rule 3-05 of the SEC's Regulation S-X. The financial statement is not intended to be a complete presentation of the financial position, results of operations, or cash flows of Spyre. Our opinion is not modified with respect to this matter.

Responsibilities of Management for the Financial Statement

Management is responsible for the preparation and fair presentation of the financial statement in accordance with accounting principles generally accepted in the United States of America, and for the design, implementation, and maintenance of internal control relevant to the preparation and fair presentation of the financial statement that is free from material misstatement, whether due to fraud or error.

In preparing the financial statement, management is required to evaluate whether there are conditions or events, considered in the aggregate, that raise substantial doubt about Aeglea's ability to continue as a going concern for one year after the date the financial statement is available to be issued.

Auditors' Responsibilities for the Audit of the Financial Statement

Our objectives are to obtain reasonable assurance about whether the financial statement as a whole is free from material misstatement, whether due to fraud or error, and to issue an auditors' report that includes our opinion. Reasonable assurance is a high level of assurance but is not absolute assurance and therefore is not a guarantee that an audit conducted in accordance with US GAAS will always detect a material misstatement when it exists. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control. Misstatements are considered material if there is a substantial likelihood that, individually or in the aggregate, they would influence the judgment made by a reasonable user based on the financial statement.

In performing an audit in accordance with US GAAS, we:

- Exercise professional judgment and maintain professional skepticism throughout the audit.
- Identify and assess the risks of material misstatement of the financial statement, whether due to fraud or error, and design and perform audit procedures responsive to those risks. Such procedures include examining, on a test basis, evidence regarding the amounts and disclosures in the financial statement.
- Obtain an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of Aeglea's internal control. Accordingly, no such opinion is expressed.
- Evaluate the appropriateness of accounting policies used and the reasonableness of significant accounting estimates made by management, as well as evaluate the overall presentation of the financial statement.
- Conclude whether, in our judgment, there are conditions or events, considered in the aggregate, that raise substantial doubt about Aeglea's ability to continue as a going concern for a reasonable period of time.

We are required to communicate with those charged with governance regarding, among other matters, the planned scope and timing of the audit, significant audit findings, and certain internal control-related matters that we identified during the audit.

/s/ PricewaterhouseCoopers LLP

Austin, Texas
October 6, 2023

Aeglea BioTherapeutics, Inc.
Statement of Assets Acquired and Liabilities Assumed
from Spyre Therapeutics, Inc. by Aeglea BioTherapeutics, Inc.
(in thousands)

	As of June 22, 2023
ASSETS ACQUIRED	
Current assets:	
Cash and cash equivalents	$ 3,035
Total current assets	3,035
Total assets acquired	$ 3,035
LIABILITIES ASSUMED	
Current liabilities:	
Accrued liabilities	$ 20,047
Total current liabilities	20,047
Total liabilities assumed	20,047
Net liabilities assumed	**$ (17,012)**

See accompanying notes to the Statement of Assets Acquired and Liabilities Assumed from Spyre Therapeutics, Inc. by Aeglea BioTherapeutics, Inc.

Aeglea BioTherapeutics, Inc.
Notes to Statement of Assets Acquired and Liabilities Assumed
from Spyre Therapeutics, Inc. by Aeglea BioTherapeutics, Inc.

1. Description of the Business and Summary of Significant Accounting Policies

On June 22, 2023, Aeglea BioTherapeutics, Inc. ("Aeglea", the "Company", and "our") acquired, in accordance with the terms of the Agreement and Plan of Merger (the "Acquisition Agreement"), the assets from Spyre Therapeutics, Inc ("Spyre"), a privately held biotechnology company advancing a pipeline of antibody therapeutics through a research and development option agreement ("Paragon Agreement") with Paragon Therapeutics ("Paragon"). Spyre was incorporated on April 28, 2023, for the purpose of holding rights to certain intellectual property being developed by Paragon.

On September 8, 2023, Aeglea effected a reverse stock split of its Common Stock at a ratio of 1-for-25 (the "Reverse Split"). Except as indicated otherwise, all share numbers related to our Common Stock disclosed in this statement have been adjusted on a post-Reverse Split basis.

The transaction (the "Asset Acquisition") was structured as a stock-for-stock transaction pursuant to which all of Spyre's outstanding equity interests were exchanged based on a fixed exchange ratio of 0.5494488 to 1 for consideration from Aeglea of 517,809 shares of common stock and 364,887 shares of Series A non-voting convertible preferred stock, par value of $ 0.0001 per share ("Series A Preferred Stock") (convertible on a 40 to 1 basis) in addition to the assumption of outstanding and unexercised stock options to purchase 2,734 shares of common stock from the Amended and Restated Spyre 2023 Equity Incentive Plan. The Aeglea common stock and the Aeglea Series A Preferred Stock related to the Asset Acquisition were issued to the Spyre stockholders on July 7, 2023.

The Company concluded that the arrangement meets the definition of an asset acquisition rather than a business combination, as substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset, Spyre's option (the "Option") to exclusively license certain in-process research and development ("IPR&D"). The Company determined that the Option to license IPR&D was a single asset as the Company's strategy relies on developing a portfolio of combination treatments that simultaneously address different mechanisms of irritable bowel disease. The Company also determined that the pipeline candidates within the portfolio are similar in nature and risk profile. In addition, the Company did not obtain any substantive processes, assembled workforce, or employees capable of producing outputs in connection with the Asset Acquisition.

The Company determined that the cost to acquire the asset was $ 113.2 million, which was recorded as acquired IPR&D. The fair value of the consideration issued consisted of the 364,887 shares of Series A Preferred Stock (14,595,480 shares of common stock on an as-converted basis) and 517,809 shares of common stock, valued at $ 291.08 per share and $ 7.277 per share, respectively.

The Paragon Agreement provided for an annual equity grant of options to purchase 1% of the then outstanding shares of Spyre's common stock, on a fully diluted basis, on the last business day of each calendar year during the term of the Option, at the fair market value determined by the board of directors of Spyre (the "Parapyre Option Obligation"). In connection with the Asset Acquisition, the Company assumed the rights and obligations of Spyre under the Paragon Agreement, including the Parapyre Option Obligation. As a result, the Parapyre Option Obligation shall continue and Parapyre shall be entitled to receive the equivalent shares of common stock of the Company on the same terms. For additional information, see Note 3.

The Asset Acquisition costs are shown on the following table (in thousands):

	As of June 22, 2023
Consideration transferred in Series A Preferred Stock and common stock	$ 109,979
Transaction costs incurred by Aeglea	3,197
Total cost to acquire asset	$ 113,176

The Company's allocation of the purchase price to net assets acquired is as follows (in thousands):

	As of June 22, 2023
Acquired in-process research and development	$ 130,188
Cash acquired	3,035
Accrued liabilities	(20,047)
Total cost to acquire asset	$ 113,176

In accordance with ASC 730-10-25-2(c), intangible assets used in research and developmental activities acquired in an asset acquisition should be expensed at the acquisition date if there is no alternative future use in other R&D projects or otherwise (i.e., if they have no economic value). The Company determined that product candidates pertaining to Spyre had no alternative future use at the time of acquisition and recorded $130.2 million to Acquired In-process Research and Development Expenses as of the date of acquisition. The difference between this amount and the $113.2 million cost to acquire Spyre represents the net liabilities assumed of $ 17.0 million.

Basis of Presentation

As a result of acquiring Spyre, and based on the criteria in Rule 3-05 of the Securities and Exchange Commission's (the "SEC") Regulation S-X, the Company would ordinarily be required to file certain historical audited financial statements for Spyre and corresponding pro forma financial information pursuant to Article 11 of Regulation S-X. Further, the historical financial statements could require the inclusion of predecessor entity information, if warranted. However, because the Company believes that Spyre's full financial statements are not material to the Company's shareholders and would be of limited value to investors, the Company requested relief from the SEC from the requirements under Rule 3-05 and Article 11 of Regulation S-X to file audited financial statements and pro forma financial information in connection with the acquisition of Spyre. In response to the waiver request, the SEC provided the Company with a waiver that it could file an audited Statement of Assets Acquired and Liabilities Assumed from Spyre Therapeutics, Inc. on the basis of the allocation of the Company's purchase price as of the acquisition date of June 22, 2023. Stand-alone full financial statements related to the assets acquired have not been prepared previously. This financial statement is not intended to be a complete presentation of the financial position, results of operations, or cash flows of Spyre.

The Company determined that it was the acquirer of Spyre under ASC 805 due to the relative voting rights in the combined entity, the composition of the governing body of the combined entity, and the composition of the senior management of the combined entity remaining relatively the same before and after the consummation of the transaction. The Company determined that the future conversion of the Series A Preferred Stock, if approved by the Company's voting shareholders, was an independent event based on it being outside of the control of the Company and therefore substantive. The Company did not succeed to substantially all of Paragon's business nor acquire from Paragon any separately identifiable line of business, the Company concluded that Paragon did not meet the definition of predecessor.

The Company evaluates acquisitions of assets and other similar transactions to assess whether or not the transaction should be accounted for as a business combination or asset acquisition by first applying a screen test to determine whether substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets. If so, the transaction is accounted for as an asset acquisition. If not, further determination is required as to whether or not the Company has acquired inputs and processes that have the ability to create outputs, which would meet the definition of a business. Significant judgment is required in the application of the screen test to determine whether an acquisition is a business combination or an acquisition of assets.

The Company concluded that the arrangement meets the definition of an asset acquisition rather than a business combination, as substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset, Spyre's option to exclusively license IPR&D.

The Company measures and recognizes asset acquisitions that are not deemed to be business combinations based on the cost to acquire the assets, which includes pre-acquisition direct costs recorded in accrued professional and consulting fees. Goodwill is not recognized in asset acquisitions. When a transaction accounted for as an asset acquisition includes an IPR&D asset, the IPR&D asset is only capitalized if it has an alternative future use other than in a particular research and development project. Otherwise, the cost allocated to acquire an IPR&D asset with no alternative future use is charged to expense at the acquisition date.

The Company has not generated any product revenues and has not achieved profitable operations. There is no assurance that profitable operations will ever be achieved, and, if achieved, could be sustained on a continuing basis. In addition, development activities, clinical and nonclinical testing, and commercialization of the Company's product candidates will require significant additional financing before a commercial drug can be produced and marketed.

The Company is subject to a number of risks similar to other life science companies, including, but not limited to, risks related to the successful discovery, development, and commercialization of product candidates, raising additional capital, development of competing drugs and therapies, protection of proprietary technology and market acceptance of the Company's product candidates. As a result of these and other factors and the related uncertainties, there can be no assurance of the Company's future success.

In April 2023, the Board of Directors approved a restructuring of the Company's workforce pursuant to which the Company's workforce was reduced by approximately 83%, retaining approximately 10 employees. Additionally, the Company announced interim results from its ongoing Phase 1/2 clinical trial of pegtarviliase for the treatment of classical homocystinuria. Following a review of the interim results and other business considerations, the Company explored strategic alternatives with the goal of maximizing stockholder value, including possible business combinations and/or a divestiture of the Company's clinical programs.

On June 22, 2023, the Company acquired the net liabilities from Spyre. Additionally, on June 26, 2023, the Company completed a private placement of shares of Series A Preferred Stock and sold an aggregate of 721,452 shares of Series A Preferred Stock for an aggregate purchase price of approximately $210.0 million before deducting approximately $12.7 million placement agent and other offering expenses. In accordance with ASC 205-40, Going Concern, in connection with the preparation of the statement of assets acquired and liabilities assumed of Spyre, the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date the financial statement is available to be issued. Our Series A Preferred Stock agreement requires us to seek stockholder approval for the conversion of the Series A Preferred Stock to Common Stock. The Company has agreed to hold a stockholders' meeting to submit this matter to its stockholders for their consideration. In connection with this, the Company filed with the SEC a preliminary proxy statement and other relevant materials. The stockholder meeting has not occurred as of October 6, 2023. If our stockholders do not timely approve the conversion of our Series A Preferred Stock, then the holders of our Series A Preferred Stock

are entitled to require us to settle their shares of Series A Preferred Stock for cash at a price per share equal to the fair value of the Series A Preferred Stock, as described in our Certificate of Designation relating to the Series A Preferred Stock. The cash redemption is not in our control and raises substantial doubt about our ability to continue as a going concern. The accompanying financial statement assumes the Company will continue as a going concern through the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and certain financial statement disclosures. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets, liabilities, and equity and the amount of revenues and expenses. Actual results could differ significantly from those estimates. Key estimates that management considers in the preparation of the Company's financial statements relate to accrued option costs payable to Paragon and the valuation of consideration transferred. The consideration transferred in acquiring IPR&D in connection with the acquisition of Spyre was comprised of the Company's common stock and shares of Series A preferred stock. To determine the fair value of the equity transferred, the Company considered the per share value of its concurrent private financing transaction, which was an over-subscribed financing event involving a group of investors.

Cash and Cash Equivalents

As of June 22, 2023, Spyre held $3.0 million in cash and cash equivalents, which consisted of a single deposit account denominated in U.S. dollars. At June 22, 2023, U.S. cash deposits in excess of the Federal Deposit Insurance Corporation's insured limit were $2.8 million.

Accrued Liabilities

Accrued liabilities primarily consist of research initiation fees, reimbursable expenses under the Paragon Agreement for historical costs incurred by Paragon, professional and consulting fees, and the fair of assumed Parapyre Option Obligation.

2. Accrued liabilities

In connection with the Asset Acquisition, the Company assumed the rights and obligations of Spyre under the Paragon Agreement. Under the Paragon Agreement, Spyre is 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, 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 historical reimbursable expenses owed to Paragon. As of June 22, 2023, $19.0 million was unpaid and was assumed by the Company through the Asset Acquisition.

Accrued liabilities consist of the following (in thousands):

	As of June 22, 2023
Accrued option cost payable to Paragon	$ 18,987
Accrued professional and consulting fees	917
Fair value of assumed Parapyre Option Obligation (Note 3)	143
Accrued liabilities	$ 20,047

3. Parapyre Option Obligation

On June 22, 2023, in connection with the Asset Acquisition, the Company assumed the Parapyre Option Obligation which provided for an annual equity grant of options for Parapyre to purchase 1% of the then outstanding shares of Spyre's common stock, on a fully diluted basis, on the last business day of each calendar year during the term of the Paragon Agreement, at the fair market value determined by the board of directors of Spyre. As a result of the Asset Acquisition the Parapyre Option Obligation shall continue and Parapyre shall be entitled to receive the equivalent shares of the Company with the same terms. The Parapyre Option Obligation is considered a Level 2 liability based on observable market data for substantially the full term of the liabilities. The Parapyre Option Obligation is measured each period using a Black-Scholes model to estimate the fair value of the option grant. Changes in the fair value of the Parapyre Option Obligation are recorded as stock-based compensation within Research and development expenses for non-employees who provided pre-clinical testing services within Research and development expenses. As of June 22, 2023, the estimated liability of the Parapyre Option Obligation was $0.1 million and was included in accrued liabilities.

4. Related Party Transactions

Paragon and Parapyre Holding LLC each beneficially owns less than 5% of the Company's capital stock through their respective holdings of Common Stock and Series A Preferred Stock of the Company. Fairmount Funds Management LLC ("Fairmount") beneficially owns more than 5% of our capital stock, has two seats on the Company's board of directors and beneficially owns more than 5% of Paragon, which is a joint venture between Fairmount and Fair Journey Biologics. Fairmount has appointed Paragon's board of directors and has the contractual right to approve the appointment of any executive officers. 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.

5. Subsequent Events

The Company's management has evaluated subsequent events up to October 6, 2023, the date the Statement of Assets Acquired and Liabilities Assumed from Spyre, Inc. was available to be issued. There have been no subsequent events that require recognition or disclosure in this financial statement except for the following described below.

On July 7, 2023, the Company issued 517,809 shares of common stock and 364,887 shares of Series A Preferred Stock as part of its consideration transferred in connection with the Asset Acquisition.

On August 8, 2023, the Company filed a preliminary proxy statement with the SEC to solicit approval of the conversion of the Series A Preferred Stock into shares of Common Stock in connection with the Asset acquisition, among other matters, at a special meeting of stockholders.

On September 8, 2023, the Company's Board of Directors approved a reverse stock split of the Company's common stock, par value $0.0001 per share, at a ratio of 1-for-25 and a reduction in the total number of authorized shares of Common Stock from 500,000,000 shares to 20,000,000 shares.

On September 29, 2023, the Company amended the Paragon Agreement to amend and restate certain terms of the option grant pertaining to the Parapyre Option Obligation, including but not limited to (i) defining that the annual equity grant of options is based on the outstanding shares of Aeglea's common stock, (ii) establishing the grant date as the last business day of each applicable calendar year, and (iii) defining the term of the options granted is ten years. The liability related to the Parapyre Option Obligation will be recorded pursuant to the amended Paragon Agreement on a go forward basis. The Company determined that these amendments would not have materially impacted the liability as of June 22, 2023.

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution

The expenses payable by us in connection with the issuance and distribution of the securities being registered hereunder on Form S-1 (other than underwriting discounts and commissions, if any) are set forth below. The Selling Stockholders will not bear any portion of such expenses. Each item listed is estimated, except for the SEC registration fee:

SEC registration fee	$ 24,551
Printing and engraving	25,000
Legal fees and expenses	50,000
Accounting fees and expenses	50,000
Miscellaneous expenses	449
Total	$150,000

Item 14. Indemnification of Officers and Directors

Section 145 of the DGCL authorizes a court to award, or a corporation's board of directors to grant, indemnity to directors and officers under certain circumstances and subject to certain limitations. The terms of Section 145 of the DGCL are sufficiently broad to permit indemnification under certain circumstances for liabilities, including reimbursement of expenses incurred, arising under the Securities Act.

As permitted by the DGCL, the Registrant's Certificate of Incorporation contains provisions that eliminate the personal liability of its directors for monetary damages for any breach of fiduciary duties as a director, except liability for the following:

- any breach of the director's duty of loyalty to the Registrant or its stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- under Section 174 of the DGCL (regarding unlawful dividends and stock purchases); or
- any transaction from which the director derived an improper personal benefit.

As permitted by the DGCL, the Registrant's Bylaws provide that:

- the Registrant is required to indemnify its directors and executive officers to the fullest extent permitted by the DGCL, subject to very limited exceptions;
- the Registrant may indemnify its other employees and agents as set forth in the DGCL;
- the Registrant is required to advance expenses, as incurred, to its directors and executive officers in connection with a legal proceeding to the fullest extent permitted by the DGCL, subject to very limited exceptions; and
- the rights conferred in the Bylaws are not exclusive.

The Registrant has entered, and intends to continue to enter, into separate indemnification agreements with its directors and executive officers to provide these directors and executive officers additional contractual assurances regarding the scope of the indemnification set forth in the Registrant's Certificate of Incorporation and Bylaws and to provide additional procedural protections. At present, there is no pending litigation or proceeding involving a director or executive officer of the Registrant regarding which indemnification is sought.

The indemnification provisions in the Registrant's Certificate of Incorporation, Bylaws and the indemnification agreements entered into or to be entered into between the Registrant and each of its directors and executive officers may be sufficiently broad to permit indemnification of the Registrant's directors and executive officers for liabilities arising under the Securities Act.

The Registrant currently carries liability insurance for its directors and officers. Two of the Registrant's directors, Peter Harwin and Tomas Kiselak, are also indemnified by their employer with regard to their service on the Registrant's board of directors.

Item 15. Recent Sales of Unregistered Securities

On June 22, 2023, we entered into the June 2023 SPA, pursuant to which we sold an aggregate of 721,452 shares of our Series A Preferred Stock, which will automatically convert into 40 shares of Common Stock, subject to stockholder approval and certain beneficial ownership limitations set by each holder, pursuant to the Series A Certificate of Designation, at an aggregate purchase price of approximately $210 million. The shares issued pursuant to the June 2023 SPA were offered and sold in transactions exempt from registration under the Securities Act, in reliance on Section 4(a)(2) thereof and Rule 506 of Regulation D thereunder. Each of the June 2023 Investors represented that it was an "accredited investor,"; as defined in Regulation D, and acquired the securities for investment only and not with a view towards, or for resale in connection with, the public sale or distribution thereof. The shares of Series A Preferred Stock issued pursuant to the June 2023 SPA have not been registered under the Securities Act and such securities may not be offered or sold in the United States absent registration or an exemption from registration under the Securities Act and any applicable state securities laws.

Also on June 22, 2023, we completed our acquisition of Pre-Merger Spyre in accordance with the Acquisition Agreement, pursuant to which we issued an aggregate of 517,809 shares of Common Stock and 364,887 shares of Series A Preferred Stock to certain of the Previous Selling Stockholders. Such issuances were exempt from registration pursuant to Section 4(a)(2) of the Securities Act and Regulation D promulgated thereunder.

On December 7, 2023, we entered into the December 2023 SPA, pursuant to which we sold an aggregate of 6,000,000 shares of our Common Stock and 150,000 shares of our Series B Preferred Stock, which will automatically convert into 40 shares of Common Stock, subject to stockholder approval and certain beneficial ownership limitations set by each holder, pursuant to the Series B Certificate of Designation, at an aggregate purchase price of $180.0 million. The December 2023 Private Placement Common Shares and the December 2023 Private Placement Preferred Shares were offered and sold in transactions exempt from registration under the Securities Act, in reliance on Section 4(a)(2) thereof and Rule 506 of Regulation D thereunder. Each of the December 2023 Investors represented that it was an "accredited investor,"; as defined in Regulation D, and acquired the securities for investment only and not with a view towards, or for resale in connection with, the public sale or distribution thereof. The December 2023 Private Placement Preferred Shares have not been registered under the Securities Act and such securities may not be offered or sold in the United States absent registration or an exemption from registration under the Securities Act and any applicable state securities laws.

Effective December 29, 2023, we issued to one of our existing investors a warrant to purchase up to an aggregate of up to 684,407 shares of Common Stock, with an exercise price equal to $21.52 per share and an expiration date of December 29, 2033. Such issuance was exempt from registration pursuant to Section 4(a)(2) of the Securities Act and Regulation D promulgated thereunder.

On March 20, 2024, we entered into the March 2024 SPA, pursuant to which we sold an aggregate of 121,625 shares of our Series B Preferred Stock, which will automatically convert into 40 shares of Common Stock, subject to stockholder approval and certain beneficial ownership limitations set by each holder, pursuant to the Series B Certificate of Designation, at an aggregate purchase price of approximately $180.0 million. The March 2024 Private Placement Preferred Shares were offered and sold in transactions exempt from registration under the Securities Act, in reliance on Section 4(a)(2) thereof and Rule 506 of Regulation D thereunder. Each of the

March 2024 Investors represented that it was an “accredited investor,”; as defined in Regulation D, and acquired the securities for investment only and not with a view towards, or for resale in connection with, the public sale or distribution thereof. The March 2024 Private Placement Preferred Shares have not been registered under the Securities Act and such securities may not be offered or sold in the United States absent registration or an exemption from registration under the Securities Act and any applicable state securities laws.

Item 16. Exhibits and Financial Statement Schedules

(a) Exhibits

EXHIBIT NUMBER	DESCRIPTION OF EXHIBIT
2.1	Agreement and Plan of Merger, dated June 22, 2023, by and among the Company, Aspen Merger Sub I, Inc., Sequoia Merger Sub II, LLC and Spyre Therapeutics, Inc. (incorporated by reference to Exhibit 2.1 to the Company’s registration statement on Form S-1/A filed with the SEC on March 1, 2024).
3.1	Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company’s registration statement on Form S-1/A filed with the SEC on March 1, 2024).
3.2	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
3.3	Certificate of Designation of Series A Non-Voting Convertible Preferred Stock (incorporated by reference to Exhibit 3.3 to the Company’s registration statement on Form S-1/A filed with the SEC on March 1, 2024).
3.4	Certificate of Designation of Series B Non-Voting Convertible Preferred Stock (incorporated by reference to Exhibit 3.4 to the Company’s registration statement on Form S-1/A filed with the SEC on March 1, 2024).
3.5	Certificate of Amendment to Certificate of Designation of Series B Non-Voting Convertible Preferred Stock (incorporated by reference to Exhibit 3.2 to the Company’s Current Report on Form 8-K filed with the SEC on March 18, 2024).
4.1	Form of Registration Rights Agreement (December 2023 PIPE) (incorporated by reference to Exhibit 4.1 to the Company’s registration statement on Form S-1/A filed with the SEC on March 1, 2024).
4.2	Form of Common Stock Certificate (incorporated by reference to Exhibit 4.2 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
4.3	Securities Purchase Agreement, dated December 7, 2023, by and among the Company and each purchaser identified on Annex A thereto (incorporated by reference to Exhibit 4.3 to the Company’s registration statement on Form S-1/A filed with the SEC on March 1, 2024).
4.4	Form of Registration Rights Agreement (June 2023 PIPE) (incorporated by reference to Exhibit 4.4 to the Company’s registration statement on Form S-1/A filed with the SEC on March 1, 2024).
4.5	Form of Pre-Funded Warrants 2022 (incorporated by reference to Exhibit 4.5 to the Company’s registration statement on Form S-1/A filed with the SEC on March 1, 2024).
4.6	Form of Registration Rights Agreement (March 2024 PIPE) (incorporated by reference to Exhibit 10.2 to the Company’s Current Report on Form 8-K filed with the SEC on March 18, 2024).
5.1	Opinion of Gibson, Dunn & Crutcher LLP .

EXHIBIT NUMBER	DESCRIPTION OF EXHIBIT
10.1#	Biologics Master Services Agreement, effective June 20, 2022, by and between Paragon Therapeutics, Inc. and WuXi Biologics (Hong Kong) Limited (incorporated by reference to Exhibit 10.1 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.2#	Cell Line License Agreement, effective June 20, 2022, by and between Paragon Therapeutics, Inc. and WuXi Biologics (Hong Kong) Limited (incorporated by reference to Exhibit 10.2 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.3	Novation Agreement, dated September 19, 2023, by and between Paragon Therapeutics, Inc., the Company and WuXi Biologics (Hong Kong) Limited (incorporated by reference to Exhibit 10.3 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.4†	Amended and Restated Offer Letter, dated November 22, 2023 and as amended on February 1, 2024, by and between the Company and Cameron Turtle (incorporated by reference to Exhibit 10.4 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.5#	Amended and Restated Antibody Discovery and Option agreement, dated September 29, 2023, by and between Paragon Therapeutics, Inc., Parapyre Holding LLC and Spyre Therapeutics, LLC (incorporated by reference to Exhibit 10.5 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.6†	2015 Equity Incentive Plan and forms of award agreements (incorporated by reference to Exhibit 10.6 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.7†	Spyre Therapeutics, Inc. 2016 Equity Incentive Plan, As Amended and Restated Effective November 21, 2023 (incorporated by reference to Exhibit 10.7 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.8†	Spyre Therapeutics, Inc. 2016 Employee Stock Purchase Plan, as amended by the First Amendment on January 31, 2024 (incorporated by reference to Exhibit 10.8 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.9†	Spyre Therapeutics, Inc. 2018 Equity Inducement Plan and the First Amendment, Second Amendment, Third Amendment and Fourth Amendment thereto (incorporated by reference to Exhibit 10.9 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.10†	Form of Stock Option Agreement under the Amended and Restated 2018 Equity Inducement Plan (incorporated by reference to Exhibit 10.10 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.11†	Spyre Therapeutics, Inc. 2023 Equity Incentive Plan (incorporated by reference to Exhibit 10.11 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.12†	Form of Stock Restriction Agreement (incorporated by reference to Exhibit 10.12 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.13†	Form of Severance Agreement (incorporated by reference to Exhibit 10.13 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.14†	Separation and Consulting Agreement and General Release of Claims by and between the Company and Jonathan Alspaugh, dated as of September 22, 2023 (incorporated by reference to Exhibit 10.14 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).

EXHIBIT NUMBER	DESCRIPTION OF EXHIBIT
10.15†	Offer Letter, dated August 10, 2023, by and between the Company and Scott Burrows (incorporated by reference to Exhibit 10.15 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.16	Asset Purchase Agreement, dated July 27, 2023, by and between the Company and Immedica Pharma AB (incorporated by reference to Exhibit 10.16 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.17	Lease Termination Agreement dated August 7, 2023, between the Company and Las Cimas Owner LP (incorporated by reference to Exhibit 10.17 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.18	2024 Form of Indemnification Agreement (incorporated by reference to Exhibit 10.18 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.19†	Offer Letter, dated August 18, 2023, by and between the Company and Heidy King-Jones (incorporated by reference to Exhibit 10.19 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.20	Consulting Agreement by and between the Company and Mark McKenna, effective August 1, 2023 (incorporated by reference to Exhibit 10.20 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
10.21	Securities Purchase Agreement, dated March 18, 2024, by and among the Company and each purchaser identified on Annex A thereto (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on March 18, 2024).
21.1	Subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 to the Company's registration statement on Form S-1/A filed with the SEC on March 1, 2024).
23.1	Consent of PricewaterhouseCoopers LLP
23.2	Consent of PricewaterhouseCoopers LLP
23.3	Consent of Gibson, Dunn & Crutcher LLP (included in Exhibit 5.1)
24.1*	Power of Attorney (included on the signature page to the registration statement)
101.INS	Inline XBRL Instance Document.
101.SCH	Inline XBRL Taxonomy Extension Schema Document.
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document.
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).
107	Filing Fee Table.

† Indicates a management contract or compensatory plan.
# Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

(b) Financial statement schedules

None.

Item 17. Undertakings

(a) The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) to include any prospectus required by Section 10(a)(3) of the Securities Act;

(ii) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the "Filing Fee Table" in the effective registration statement; and

(iii) to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act to any purchaser, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. *Provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

(5) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers, and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer, or controlling person of the Registrant in the successful defense of any action, suit, or proceeding) is asserted by such director, officer, or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act, the Registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Waltham, Commonwealth of Massachusetts, on April 18, 2024.

SPYRE THERAPEUTICS, INC.

By: /s/ Cameron Turtle, DPhil
Cameron Turtle, DPhil
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Dr. Cameron Turtle and Mr. Scott Burrows, as his or her true and lawful attorneys-infact, proxies and agents, each with full power of substitution, for him or her in any and all capacities, to sign any and all amendments to this registration statement (including post-effective amendments or any abbreviated registration statement and any amendments thereto filed pursuant to Rule 462(b) increasing the number of securities for which registration is sought), and to file the same, with all exhibits thereto and other documents in connection therewith, with the SEC, granting unto said attorneys-in-fact, proxies and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact, proxies and agents, or their or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Cameron Turtle, DPhil Cameron Turtle, DPhil	Chief Executive Officer & Director (Principal Executive Officer)	April 18, 2024
/s/ Scott Burrows Scott Burrows	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	April 18, 2024
/s/ Russell J. Cox Russell J. Cox	Chairman of the Board	April 18, 2024
/s/ Jeffrey W. Albers Jeffrey W. Albers	Director	April 18, 2024
/s/ Peter Harwin Peter Harwin	Director	April 18, 2024
/s/ Michael Henderson, M.D. Michael Henderson, M.D.	Director	April 18, 2024
/s/ Tomas Kiselak Tomas Kiselak	Director	April 18, 2024

Signature	Title	Date
/s/ Mark McKenna Mark McKenna	Director	April 18, 2024
/s/ Laurie Stelzer Laurie Stelzer	Director	April 18, 2024

***

Exhibit 5.1

GIBSON DUNN

Gibson, Dunn & Crutcher LLP

One Embarcadero Center, Suite 2600
San Francisco, CA 94111-3715
Tel 415.393.8200
gibsondunn.com

Client: 06759-00004

April 18, 2024

Spyre Therapeutics, Inc.
221 Crescent Street
Building 23, Suite 105
Waltham, MA 02453

Re: Spyre Therapeutics, Inc.
Registration Statement on Form S-1

Ladies and Gentlemen:

We have acted as counsel to Spyre Therapeutics, Inc., a Delaware corporation (the " Company"), in connection with the preparation and filing with the Securities and Exchange Commission (the "Commission") of a Registration Statement on Form S-1 (the "Registration Statement") pursuant to the Securities Act of 1933, as amended (the "Securities Act"), relating to the resale from time to time by the selling stockholders named therein of (i) up to 22,496,402 shares (the "Common Shares") of the Company's common stock, par value $0.0001 per share ("Common Stock") and (ii) 10,865,000 shares (the "Conversion Shares") of Common Stock issuable upon the conversion of 271,625 shares of the Company's Series B preferred stock, par value $0.0001 per share (the "Preferred Stock").

In arriving at the opinion expressed below, we have examined originals, or copies certified or otherwise identified to our satisfaction as being true and complete copies of the originals, of the specimen common stock certificates and such other documents, corporate records, certificates of officers of the Company and of public officials and other instruments as we have deemed necessary or advisable to enable us to render these opinions. In our examination, we have assumed the genuineness of all signatures, the legal capacity and competency of all natural persons, the authenticity of all documents submitted to us as originals and the conformity to original documents of all documents submitted to us as copies.

Based on the foregoing, and subject to the assumptions, exceptions, qualifications and limitations set forth herein, we are of the opinion that the Common Shares are validly issued, fully paid and non-assessable and the Conversion Shares, when issued upon the conversion of the Preferred Stock, will be validly issued, fully paid and non-assessable.

We consent to the filing of this opinion as an exhibit to the Registration Statement, and we further consent to the use of our name under the caption “Legal Matters” in the Registration Statement and the prospectus that forms a part thereof. In giving these consents, we do not thereby admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission.

Very truly yours,

/s/ Gibson, Dunn & Crutcher LLP

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the use in this Registration Statement on Form S-1 of Spyre Therapeutics, Inc. of our report dated February 29, 2024 relating to the financial statements of Spyre Therapeutics, Inc., which appears in this Registration Statement. We also consent to the reference to us under the heading “Experts” in such Registration Statement.

/s/ PricewaterhouseCoopers LLP

Austin, Texas
April 18, 2024

Exhibit 23.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the use in this Registration Statement on Form S-1 of Spyre Therapeutics, Inc. of our report dated October 6, 2023 relating to the Statement of Assets Acquired and Liabilities Assumed from Spyre Therapeutics, Inc. by Aeglea BioTherapeutics, Inc., which appears in this Registration Statement. We also consent to the reference to us under the heading “Experts” in such Registration Statement.

/s/ PricewaterhouseCoopers LLP

Austin, Texas
April 18, 2024

Exhibit 107

CALCULATION OF FILING FEE TABLES
Form S-1
(Form Type)

Spyre Therapeutics, Inc.
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee
Fees to Be Paid	Equity	Common stock, par value $0.0001 per share(1)	457(c)	4,865,000(2)	$34.19(3)	$166,334,350.00	$0.0001476	$24,550.95
		Total Offering Amounts				$166,334,350.00		$24,550.95
		Total Fees Previously Paid						—
		Total Fee Offsets						—
		Net Fee Due						$24,550.95

(1) Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), this registration statement also covers an indeterminate number of shares of common stock, par value $0.0001 per share (the "common stock"), of Spyre Therapeutics, Inc. (the "Registrant"), that may be offered or issued to prevent dilution resulting from stock splits, stock dividends and similar events.
(2) Represents 4,865,000 shares of common stock issuable upon conversion of 150,000 shares of Series B Preferred Stock held by certain selling stockholders.
(3) Estimated solely for the purpose of calculating the registration fee, based on the average of the high and low prices of the shares of common stock on The Nasdaq Global Select Market on April 17, 2024 (such date being within five business days of the date that this registration statement was first filed with the Securities and Exchange Commission, in accordance with Rule 457(c) under the Securities Act).

Table 3: Combined Prospectuses

Security Type	Security Class Title	Amount of Securities Previously Registered(1)	Maximum Aggregate Offering Price of Securities Previously Registered	Form Type	File Number	Initial Effective Date
Equity	Common stock, $0.0001 par value per share(2)	16,496,424(3)	$147,807,959.04	S-1	333-273769	November 20, 2023
Equity	Common stock, $0.0001 par value per share(2)	11,999,978(4)	$181,679,666.92	S-1	333-276251	April 1, 2024

(1) Pursuant to Rule 416 under the Securities Act, this registration statement also covers an indeterminate number of securities of common stock of the Registrant that may be offered or issued to prevent dilution resulting from stock splits, stock dividends and similar events.

(2) No registration fee is payable in connection with these shares that were previously registered under (i) the registration statement on Form S-1 (No. 333-273769), initially filed by the Registrant on Form S-3 on August 7, 2023, and declared effective on November 20, 2023, as most recently amended by Post-Effective Amendment No. 3 to Form S-1, filed on March 27, 2024 and declared effective on April 1, 2024 (the "Prior Registration Statement #1," as amended and/or supplemented) and (ii) the registration statement on Form S-1 (No. 333-276251), initially filed by the Registrant on December 22, 2023, and declared effective on April 1, 2024 (the "Prior Registration Statement #2," as amended and/or supplemented), because such shares are being transferred from the Prior Registration Statement #1 and the Prior Registration Statement #2 pursuant to Rule 429 under the Securities Act. Pursuant to Rule 429(b) under the Securities Act, this registration statement, upon effectiveness, will constitute a post-effective amendment to each of the Prior Registration Statement #1 and the Prior Registration Statement #2, which post-effective amendments shall hereafter become effective concurrently with the effectiveness of this registration statement and in accordance with Section 8(c) of the Securities Act.

(3) Represents an aggregate of 16,496,424 shares of common stock registered for resale by the selling securityholders named in the Prior Registration Statement #1, consisting of (i) 8,864 shares of common stock and (ii) 16,239,000 shares of common stock that were issued upon the conversion of 412,189 shares of Series A preferred stock, par value $0.0001 per share. If securities previously registered under the Prior Registration Statement #1 are offered and sold before the effective date of this registration statement, the amount of previously registered securities so sold will not be included in the prospectus hereunder.

(4) Represents an aggregate of 11,999,978 shares of common stock registered for resale by the selling securityholders named in the Prior Registration Statement #2, consisting of (i) 5,999,978 shares of common stock, and (ii) 6,000,000 shares of common stock issuable upon the conversion of 150,000 shares of Series B preferred stock, par value $0.0001. If securities previously registered under the Prior Registration Statement #2 are offered and sold before the effective date of this registration statement, the amount of previously registered securities so sold will not be included in the prospectus hereunder.