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Filed Pursuant to Rule 424(b)(5)
Registration Statement No. 333-297063

PROSPECTUS SUPPLEMENT
(To Prospectus dated June 26, 2026)

4,117,648 Shares

Common Stock

We are offering 4,117,648 shares of our common stock, par value $0.0001 per share ("common stock"). The public offering price for each share of common stock is $85.00.

Our common stock is traded on the Nasdaq Global Select Market under the symbol "SYRE." On October 2, 2026, the last reported sale price per share of our common stock was $93.19.

	Per Share of Common Stock	Total
Public offering price	$ 85.00	$ 350,000,080.00
Underwriting discounts and commissions (1)	$ 5.10	$ 21,000,004.80
Proceeds to Company before expenses	$ 79.90	$ 329,000,075.20

(1) See "Underwriting" beginning on page S-16 of this prospectus supplement for additional information regarding underwriting compensation.

We have granted the underwriters an option to purchase up to an additional 617,647 shares of our common stock from us, at the public offering price, less underwriting discounts and commissions, within 30 days of the date of this prospectus supplement.

Investing in our securities involves a high degree of risk. You should carefully consider the risks and uncertainties described under the heading "Risk Factors" on page S-7 of this prospectus supplement and in the accompanying prospectus, as well as those contained in the other documents that are incorporated by reference. You should carefully read this entire prospectus supplement and the accompanying prospectus, including any information incorporated by reference, before deciding whether to purchase shares of our common stock.

Neither the U.S. Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock on or about October 7, 2026.

Joint Book-Running Managers

Jefferies **TD Cowen** **Leerink Partners** **Stifel**

Passive Bookrunner

LifeSci Capital

October 5, 2026

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Prospectus

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 (File No. 333-297063) that we filed with the U.S. Securities and Exchange Commission (the "SEC") on June 26, 2026, as a "well-known seasoned issuer" as defined in Rule 405 under the Securities Act of 1933, as amended (the "Securities Act"), utilizing a "shelf" registration process. Under this shelf registration process, we may, from time to time, sell common stock and other securities, including in this offering. This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part consists of the accompanying prospectus, which provides more general information, some of which may not apply to this offering. Generally, when we refer only to the "prospectus," we are referring to both parts combined. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus, or any documents incorporated by reference, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus, including the documents incorporated by reference therein. Information in any document we subsequently file that is incorporated by reference shall modify or supersede the information in this prospectus supplement, the accompanying prospectus and documents incorporated by reference prior to such subsequent filing. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents we have referred you to in the section entitled "Where You Can Find More Information" below in this prospectus supplement.

We are responsible for the information contained and incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not authorized anyone to give you any other information, and we take no responsibility for any other information that others may give you. We are not making offers to sell the securities in any jurisdiction in which an offer or solicitation is not authorized or permitted or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. The information contained and incorporated by reference in this prospectus supplement or the accompanying prospectus speaks only as of the date of this document, unless the information specifically indicates that another date applies. Neither the delivery of this prospectus supplement or the accompanying prospectus, nor any sale of securities made under these documents, will, under any circumstances, create any implication that there has been no change in our affairs since the date of this prospectus supplement or the accompanying prospectus, nor that the information contained or incorporated by reference is correct as of any time subsequent to the date of such information. You should assume that the information contained and incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of the date of the documents containing the information, unless the information specifically indicates that another date applies. Our business, financial condition, results of operations and prospects may have changed since those dates.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in this prospectus supplement or the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus supplement and the accompanying prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the shares of common stock to which it relates, nor do this prospectus supplement and the accompanying prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

Unless otherwise indicated, information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus concerning our industry and the markets in which we operate, including market position and market opportunity, is based on information from our management's estimates, as well as from industry publications and research, surveys and studies conducted by third parties. Management

estimates are derived from publicly available information, our knowledge of our industry and assumptions based on such information and knowledge, which we believe to be reasonable. However, assumptions and estimates of our future performance, and the future performance of our industry are subject to numerous known and unknown risks and uncertainties, including those described under the heading "Risk Factors" beginning on page S-7 of this prospectus supplement and the risk factors incorporated by reference into this prospectus supplement and the accompanying prospectus. These and other important factors could result in our estimates and assumptions being materially different from future results. You should read the information contained in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus completely and with the understanding that future results may be materially different and worse from what we expect. See the information included under the heading "Cautionary Note Concerning Forward-Looking Statements."

"Spyre" and all product candidate names are our common law trademarks. This prospectus supplement contains additional trade names, trademarks and service marks of other companies, which are the property of their respective owners. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies. Solely for convenience, trademarks and trade names referred to in this prospectus supplement may appear without the ® or TM symbols.

All references to "our product candidates," "our programs" and "our pipeline" in this prospectus supplement refer to the research programs with respect to which we have signed a license agreement for, 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 and May 14, 2024, by and among us, Paragon Therapeutics, Inc. and Parapyre Holding LLC.

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 supplement 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 NOTE CONCERNING FORWARD-LOOKING STATEMENTS

This prospectus supplement contains "forward-looking statements" within the meaning of Section 27A of 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 contained in this prospectus supplement, other than statements of historical fact, including, without limitation, statements regarding: any future payouts under our contingent value rights issued in connection with the acquisition of Spyre Therapeutics, Inc. (the "Asset Acquisition"); our future results of operations and financial position; our business strategy, including our ability to elevate the standard in immunology by delivering more complete disease control, greater durability, and a simpler treatment experience for patients and to develop potential first-in-class and best-in-class therapeutics for inflammatory bowel disease ("IBD"), rheumatoid arthritis ("RA"), psoriatic arthritis ("PsA"), axial spondyloarthritis ("axSpA"), hidradenitis suppurativa ("HS") and other immune-mediated diseases and rheumatic diseases ("RD") that meaningfully improve both efficacy and convenience compared to today's standard of care; our plans to expand the development of our product candidates to indications beyond IBD, RD and HS; our plans to develop a new program to advance SPY072 into late-stage development for HS; our plans to develop a SPY072 monotherapy for the treatment of HS; our ability to achieve the expected benefits or opportunities with respect to our product candidates, including their potential commercialization; the potential consistency of the SPY001, SPY002, SPY072 and SPY003 Phase 1 trial and Phase 2 trial final data readouts with previously disclosed data for our programs; expectations regarding the drug delivery of our product candidates, including in the form of a subcutaneous injection; the planned dosing regimen for SPY001, SPY002, SPY072 and SPY003, as well as rational combination programs, including the potential for a Q3M-Q6M dosing profile and the potential for such dosing profile to be the leading product profile in IBD, RD and HS; our current and planned non-clinical and clinical development activities, including our plans for and timing of cohort initiation and data readouts for the ongoing SKYWAY Phase 2 basket trial, SKYLINE Phase 2 platform trial and SKYLIGHT Phase 2 trial, and the number of data readouts expected to be delivered in 2026 and 2027; estimated market sizes and potential growth opportunities; statements regarding the Company's cash guidance; the potential efficacy, tolerability, convenience, commercial viability and safety profile of our product candidates, including rational combination programs; the potential therapeutic benefits and economic value of our product candidates as monotherapies or our rational combination programs and their extended half-life; our ability to achieve the expected benefits or opportunities and related timing with respect to the Asset Acquisition; the expected impact of macroeconomic conditions, including inflation, increasing interest rates and volatile market conditions, and current or potential bank failures, as well as global events, including the ongoing military conflict between the United States and Iran and Ukraine and Russia, the conflicts in the Middle East, and geopolitical tensions between the United States and other countries, including China, on our operations, and the implementation of changes in law, tariffs, sanctions, export or import controls, and other government measures that could impact our business operations, including restricting international trade by the United States, China or other countries; are forward-looking statements. 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 include the risks set forth under the caption "Risk Factors" in this prospectus supplement and the accompanying prospectus and in the documents incorporated by reference herein and therein. You should evaluate all forward-looking statements made in this prospectus supplement, the accompanying prospectus and in the documents incorporated by reference herein and therein in the context of these risks and uncertainties. We caution you that the risks, uncertainties and other factors referred to in this prospectus supplement, the accompanying prospectus and in the documents

incorporated by reference herein and therein 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 supplement. 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. This prospectus supplement also contains or incorporates by reference estimates, projections, and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained such industry, business, market, and other data from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources.

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 supplement 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 SUPPLEMENT SUMMARY

The items in the following summary are described in more detail later in this prospectus supplement and the accompanying prospectus. This summary provides an overview of selected information and does not contain all of the information you should consider before buying our common stock. Therefore, you should read the entire prospectus supplement and the accompanying prospectus carefully, including the information in our filings with the SEC incorporated by reference herein and therein, before deciding to invest in our common stock. Investors should carefully consider the information set forth under "Risk Factors" beginning on page S-7 of this prospectus supplement and page 5 of the accompanying prospectus and those risks identified in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q. In this prospectus supplement, unless the context otherwise requires, references to "Spyre," the "Company," "we," "us," and "our" refer to Spyre Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries and the term "securities" refers to shares of our common stock.

Company Overview

We are a clinical stage biotechnology company committed to developing next-generation therapies that elevate the standard in immunology by delivering more complete disease control, greater durability, and a simpler treatment experience for patients. Our pipeline includes extended half-life antibodies targeting α4β7, TL1A, IL-23, IL-17A/F as well as rational combination programs. The expected global market in 2030 for the diseases that our next-generation therapies aim to address is, (i) with respect to ulcerative colitis ("UC") and Crohn's disease ("CD"), approximately $40 billion, (ii) with respect to PsA and axSpA, approximately $10 billion, and (iii) with respect to HS, approximately $5 billion.

As of June 30, 2026, we had a cash balance of approximately $1.1 billion (inclusive of cash, cash equivalents and marketable securities), which we anticipate will be sufficient for us to fund our operating expenses and capital expenditure requirements into the second half of 2029.

Our Portfolio and Development Plan

We are advancing a pipeline of monoclonal antibodies ("mAbs") for the treatment of immune-mediated diseases. The following table (Figure 1) summarizes our pipeline and development strategy, including our SKYLINE Phase 2 platform trial evaluating SPY120, SPY130, SPY230, and monotherapy components thereof in subjects with moderately to severely active UC, our SKYWAY basket trial evaluating SPY072 in three rheumatic diseases: RA, PsA, and axSpA, and our SKYLIGHT trial evaluating SPY072 as an add-on to bimekizumab as a proof-of-concept trial for the dual inhibition of anti-TL1A and IL-17A/F, as well as our SPY772 combination program in HS.

In addition to these ongoing clinical trials, we intend to initiate a clinical program evaluating SPY072 as a monotherapy for the treatment of HS.

Figure 1. Spyre Portfolio

*SKYLIGHT proof-of concept study with SPY072 + bimekizumab, serving as a surrogate for internal SPY007 long-acting IL-17A/F antibody.

Our Assets

SPY001 – anti-α4ß7 mAb

SPY001 is a highly potent, highly selective, and humanized monoclonal immunoglobulin G1 investigational 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. This integrin regulates the migration of immune cells 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 immune cells with MAdCAM-1, a molecule expressed on endothelial cells lining the blood vessels in the gut. By blocking the interaction between α4ß7 integrin and MAdCAM-1, SPY001 aims to reduce the recruitment of immune cells 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.

SPY002 and SPY072 – anti-TL1A mAbs

For our anti-TL1A program, we nominated two highly potent, highly selective, and fully human mAb candidates designed to bind to tumor necrosis factor-like ligand 1A ("TL1A"). SPY002 (formerly SPY002-091) is being developed for the treatment of IBD (UC and CD) and SPY072 (formerly SPY002-072) is being developed for the treatment of RD and we plan to initiate late-stage development of SPY072 as a monotherapy for the treatment of HS.

TL1A is a protein that plays a role in regulating the immune system and is elevated in gut tissue of individuals with immune-mediated diseases. TL1A interacts with its receptor, death receptor 3 ("DR3"), which is expressed in various immune cells, including T cells and fibroblast-like synoviocytes. This interaction triggers signaling pathways that contribute to inflammation and joint injury in RD, leading to symptomology, such as pain and swelling. SPY002 and SPY072 have been designed to block the interaction between TL1A and DR3, and thereby inhibit the downstream signaling events to dampen the inflammatory response. By neutralizing TL1A, we believe that SPY002 and SPY072 have the potential to modulate the immune response in patients with immune-mediated diseases, potentially reducing disease activity.

SPY003 – anti-IL-23 mAb

SPY003 is a clinical-stage program designed 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.

SPY003 binds to the p19 subunit of IL-23 with subnanomolar potency in cellular assays. SPY003 also exhibited extended PK half-life of greater than three-fold relative to a synthesized risankizumab comparator that does not incorporate half-life extending modifications, based on head-to-head preclinical studies in non-human primates.

SPY120 - combination, anti-α4β7 and anti-TL1A mAbs

SPY120 combines SPY001 (anti-α4β7) and SPY002 (anti-TL1A) antibodies, pairing two complementary mechanisms studied in third-party clinical trials targeting non-overlapping sites of action.

In February and May 2025, we presented preclinical data demonstrating that combinations resulted in additive or greater than additive in vivo biological activity relative to either monotherapy in mouse hapten reagent 2,4,6-trinitrobenzene sulfonic acid ("TNBS") and anti-CD40 colitis models. In October 2025, we presented preclinical data further demonstrating that combined inhibition resulted in superior efficacy relative to constituent monotherapies in a mouse TNBS-induced colitis model. In addition, combination toxicology studies have been completed with no drug-related adverse findings observed.

SPY130 - combination anti-α4β7 and anti-IL-23 mAbs

SPY130 combines SPY001 (anti-α4β7) and SPY003 (anti-IL-23) antibodies, pairing two commercially validated mechanisms targeting non-overlapping sites of action.

In October 2024, we presented preclinical data, demonstrating in a T-cell transfer model of IBD, that combinations with anti-IL-23 and anti-α4ß7 improved body weight and reduced colonic CD4+ infiltration and IL-17 levels relative to monotherapy. In March and October 2025, we presented additional preclinical data, demonstrating that combinations resulted in superior in vivo biological activity relative to either monotherapy in mouse TNBS model. In addition, combination toxicology studies have been completed with no drug-related adverse findings observed.

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.

In October 2024, we presented preclinical data, demonstrating that anti-IL-23 and anti-TL1A have a synergistic effect on promoting IL-17 secretion from human and mouse cells, and that the combination of anti-IL-23 and anti-TL1A suppressed IL-17 secretion more effectively than either agent alone. In March and October 2025, we presented additional preclinical data, demonstrating that combinations resulted in superior in vivo biological activity relative to either monotherapy in mouse TNBS model. In addition, combination toxicology studies have been completed with no drug-related adverse findings observed.

SPY772 – combination anti-TL1A and anti-IL-17A/F mAbs

SPY772 combines SPY072 (anti-TL1A) and SPY007 (anti-IL-17A/F) antibodies, pairing two complementary mechanisms of action with potential to address overlapping and non-overlapping triggers of inflammation. By combining an IL-17A/F mAb with an anti-TL1A mAb, we aim to target multiple inflammatory pathways involved in HS, with the potential to improve efficacy over single-mechanism therapies.

SPY007 – anti-IL-17A/F mAb

SPY007 is a preclinical program designed to bind to interleukin 17A ("IL-17A") and interleukin 17F ("IL-17F") while incorporating half-life extending modifications. SPY007 is being developed for the treatment of HS in combination with our anti-TL1A mAb (SPY072). IL-17A and IL-17F are closely related cytokines produced by Th17

cells and other immune cells. Both are elevated in the skin lesions of individuals with HS. IL-17A and IL-17F act on keratinocytes and other cells in the skin, driving the production of pro-inflammatory cytokines, chemokines,

and antimicrobial peptides. These signals recruit neutrophils and other immune cells to the skin, which contributes to the painful nodules, abscesses, and draining tunnels seen in HS. SPY007 is designed to neutralize both IL-17A and IL-17F, and thereby inhibit the downstream signaling events to dampen the inflammatory response.

Corporate History and Information

We were formed as a limited liability company ("LLC") in Delaware on December 16, 2013 under the name Aeglea BioTherapeutics Holdings, LLC and were converted from a Delaware LLC to a Delaware corporation on March 10, 2015. On June 22, 2023, we completed the Asset Acquisition, and on November 27, 2023, we completed our corporate rebranding, changing our name to Spyre Therapeutics, Inc.

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. Our website is *www.spyre.com*. The information on, or that can be accessed through, our website is not part of this prospectus supplement and is not incorporated by reference herein. We have included our website address in this prospectus supplement solely as an inactive textual reference.

THE OFFERING

Common stock offered by us	4,117,648 shares of common stock.
Option to purchase additional shares of common stock	We have granted the underwriters a 30-day option to purchase up to 617,647 additional shares of common stock at the public offering price, less underwriting discounts and commissions.
Common stock to be outstanding immediately after this offering	92,181,781 shares (or 106,023,581 shares on an as-converted-basis, giving effect to the conversion of all of our outstanding shares of preferred stock into shares of common stock without regard to any beneficial ownership limitations). If the underwriters' option to purchase additional shares of common stock is exercised in full, there will be 92,799,428 shares outstanding immediately after this offering (or 106,641,228 shares on an as-converted basis, giving effect to the conversion of all of our outstanding shares of preferred stock into shares of common stock without regard to any beneficial ownership limitations).
Use of proceeds	We intend to use the net proceeds of the offering to continue to advance our programs in Gastroenterology, Rheumatology, and Dermatology, including to fund preclinical studies, clinical trials, manufacturing, and Phase 3 readiness, as well as a new program to advance SPY072 into late-stage development for HS. We also intend to use a portion of the net proceeds to further develop and support our general infrastructure. Finally, we may use a portion of the net proceeds to in-license, acquire, or invest in additional businesses, technologies, products, or assets, and to fund the development of such new acquired or in-licensed products and technologies. Any remaining proceeds will be used for other ongoing research and development, working capital and other general corporate purposes.
Risk Factors	You should read and consider the information set forth under the heading "Risk Factors" in this prospectus supplement and in the accompanying prospectus, together with the risk factors and cautionary statements described in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, incorporated by reference herein, before deciding to invest in shares of our common stock.
Nasdaq Global Select Market Symbol	"SYRE."

The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 101,905,933 shares of common stock outstanding as of June 30, 2026, after giving effect to the conversion of all of our outstanding shares of preferred stock into 13,841,800 shares of common stock without regard to any beneficial ownership limitations, but otherwise excludes:

- 12,660,773 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of $19.76 per share;
- 197,032 shares of common stock issuable upon the vesting of restricted stock units outstanding;
- 8,207,770 shares of common stock reserved for issuance pursuant to future equity awards under our 2016 Equity Incentive Plan (the "2016 Plan"), as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2016 Plan;

- 500,884 shares of common stock reserved for issuance pursuant to future equity awards under our 2018 Equity Inducement Plan (the "2018 Plan"), as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2018 Plan;

- 952,808 shares of common stock reserved for future issuance under our 2016 Employee Stock Purchase Plan (the "2016 ESPP"), as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2016 ESPP; and
- 1,532,591 shares of common stock issuable upon the exercise of outstanding warrants having an exercise price of $22.49 per share.

As of June 30, 2026, 346,045 shares of Series A Non-Voting Convertible Preferred Stock ("Series A Preferred Stock") were issued and outstanding, convertible into 13,841,800 shares of common stock as of such date. After June 30, 2026, 527,502 shares of common stock have been sold pursuant to our Sales Agreement with TD Securities (USA) LLC, dated June 26, 2026 (the "Sales Agreement") through the date of this prospectus supplement. On September 22, 2026, 1,160,620 shares of common stock were issued in connection with the cashless net exercise of 1,532,591 outstanding warrants.

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

Unless otherwise indicated, all information in this prospectus supplement (i) assumes no exercise of outstanding stock options and warrants or vesting of restricted stock units as of June 30, 2026, (ii) assumes no exercise of the underwriters' option to purchase additional shares of common stock and (iii) does not reflect the potential issuance of up to approximately $451.6 million of shares of common stock that remains available for sale as of the date of this prospectus supplement under the Sales Agreement.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should consider carefully the risks described below, together with the other information contained in this prospectus supplement or incorporated by reference in this prospectus supplement, including the risks and uncertainties discussed under "Risk Factors" in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference herein in their entirety. If any of the risks incorporated by reference herein or set forth below occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks Relating to this Offering

We have broad discretion as to the use of proceeds from this offering and may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds to us from this offering, including to use them for any of the purposes described in the section entitled "Use of Proceeds," and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds to us from this offering, their ultimate use may vary from their currently intended use. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds to us from this offering in interest-bearing, investment-grade securities, certificates of deposit or government securities. These investments may not yield a favorable return to our stockholders.

If you purchase shares of our common stock in this offering, you may incur immediate and substantial dilution. In addition, we may issue additional equity or convertible securities in the future, which may result in additional dilution to you.

If you purchase shares of our common stock in this offering, you will incur immediate and substantial dilution in the amount of $71.51 per share of common stock because the public offering price of $85.00 per share of common stock is substantially higher than the pro forma as-adjusted net tangible book value per share of our outstanding common stock. In addition, you may also experience additional dilution after this offering on any future equity issuances, including the issuance of common stock under our 2016 Plan, 2018 Plan, and 2016 ESPP or upon conversion of outstanding Series A Preferred Stock. To the extent we raise additional capital by issuing equity securities under the Sales Agreement or otherwise, our stockholders will experience substantial additional dilution. See "Dilution" for additional information.

Future sales of our common stock in the public market, or the perception that such sales could occur, could cause our common stock price to fall.

Our common stock price could decline as a result of sales of a large number of shares of common stock after this offering or the perception that these sales could occur. These sales, or the possibility that these sales may occur, might also make it more difficult for us to sell equity securities in the future at a time and price that we deem appropriate. Upon the completion of this offering, shares of our common stock (or shares of our common stock on an as-converted-basis, giving effect to the conversion of all of our Series A Preferred Stock into shares of common stock without regard to any beneficial ownership limitations) will be outstanding (or shares of our common stock if the underwriters exercise their option to purchase additional shares from us in full (or shares of our common stock on an as-converted basis, giving effect to the conversion of all of our Series A Preferred Stock into shares of common stock without regard to any beneficial ownership limitations)), based on the number of shares outstanding as of June 30, 2026, all of which will be freely tradable without restriction in the public market immediately following this offering, except for those shares that are subject to lock-up restrictions or restricted pursuant to Rule 144. We may also sell large quantities of our common stock in one or more separate offerings. If we or our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and other legal restrictions on sale discussed in this prospectus supplement lapse, the trading price of our common stock could decline.

If securities or industry analysts either do not publish research about us or publish inaccurate or unfavorable research about us, our business or our market, or if they change their recommendations regarding our common stock adversely, the trading price or trading volume of our common stock could decline.

The trading market for our common stock will be influenced in part by the research and reports that securities or industry analysts may publish about us, our business, our market, or our competitors. If one or more of these analysts initiate research with an unfavorable rating or downgrade our common stock, provide a more favorable recommendation about our competitors or publish inaccurate or unfavorable research about our business, our common stock price would likely decline. If any analyst who may cover us were to cease coverage of us or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause the trading price or trading volume of our common stock to decline.

Shares of our common stock will be subordinate to any senior preferred stock we may issue and to any future indebtedness.

Shares of our common stock will rank junior to any shares of our senior preferred stock or shares of our senior preferred stock that we may issue in the future and to any future indebtedness we may incur, as well as to all creditor claims and other non-equity claims against us and our assets available to satisfy claims on us, including claims in a bankruptcy or similar proceeding.

Furthermore, unlike indebtedness, where principal and interest customarily are payable on specified due dates, in the case of our common stock, (i) dividends are payable only when and if declared by our board of directors or a duly authorized committee of our board of directors, and (ii) as a corporation, we are restricted to making dividend payments and redemption payments out of legally available assets. We have never paid a dividend on our common stock and have no current intention to pay dividends in the future. Furthermore, our common stock places no restrictions on our business or operations or on our ability to incur indebtedness or engage in any transactions, subject only to the voting rights available to our stockholders generally.

USE OF PROCEEDS

We estimate that we will receive net proceeds from this offering of approximately $328.7 million (or approximately $378.0 million if the underwriters' option to purchase up to 617,647 additional shares of common stock is exercised in full), based on the public offering price of $85.00 per share of common stock and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds of the offering to continue to advance our programs in Gastroenterology, Rheumatology, and Dermatology, including to fund preclinical studies, clinical trials, manufacturing, and Phase 3 readiness, as well as a new program to advance SPY072 into late-stage development for HS. We also intend to use a portion of the net proceeds to further develop and support our general infrastructure. Finally, we may use a portion of the net proceeds to in-license, acquire, or invest in additional businesses, technologies, products, or assets, and to fund the development of such new acquired or in-licensed products and technologies. Any remaining proceeds will be used for other ongoing research and development, working capital and other general corporate purposes.

Based on our current business plans, we believe that the net proceeds from this offering, together with our existing current cash, cash equivalents and short-term investments, will be sufficient to fund our planned operations into the second half of 2029. Our expected use of proceeds from this offering represents our current intentions based on our present plans and business condition. As of the date of this prospectus supplement, we cannot predict with certainty all of the particular uses for the proceeds to be received upon the completion of this offering or the amounts that we will actually spend on the uses set forth above. The amount and timing of our actual expenditures will depend on numerous factors, including the pace and results of our research and development efforts, the timing and success of clinical trials, the timing and costs associated with the manufacture and supply of product candidates, the timing of regulatory submissions and any unforeseen cash needs. As a result, our management will have broad discretion in the application of the net proceeds, and investors will be relying on the judgment of our management regarding the application of the net proceeds of this offering. For additional information regarding our potential capital requirements, including factors that could cause actual costs to vary from the estimates set forth above, see "Risk Factors."

Pending the use of the proceeds to us from this offering, we intend to invest these proceeds in interest-bearing, investment-grade securities, certificates of deposit, money market funds or government securities.

DILUTION

Dilution represents the difference between the amount per share of common stock paid by purchasers in this offering and the pro forma as-adjusted net tangible book value per share of our common stock immediately after this offering. The data in this section are derived from our balance sheet as of June 30, 2026. Net tangible book value per share of common stock is equal to our total tangible assets less the amount of our total liabilities, divided by the sum of the number of shares of common stock outstanding as of June 30, 2026, excluding shares of common stock underlying outstanding options, unvested restricted stock units and warrants. Our net tangible book value as of June 30, 2026, was approximately $1.1 billion, or $12.50 per share of common stock. For purposes of this "Dilution" section, except as otherwise noted, all subsequent share and per share information assumes the conversion of all outstanding shares of our Series A Preferred Stock into shares of common stock without regard to any beneficial ownership limitations, except where expressly noted otherwise. Assuming such conversion, our pro forma net tangible book value per share as of June 30, 2026 was $10.81 per share of common stock.

We present dilution on a pro forma as-adjusted basis to give effect to (i) the assumed conversion of all outstanding shares of our preferred stock as described above and (ii) our receipt of the estimated net proceeds from the sale of shares of our common stock in this offering, based on the public offering price of $85.00 per share of common stock and after deducting the commissions and estimated offering expenses payable by us. On a pro forma as-adjusted basis, our net tangible book value as of June 30, 2026, would have been approximately $1.4 billion, or $13.49 per share of common stock. This represents an immediate increase in net tangible book value to existing stockholders of $2.68 per share of common stock and immediate dilution in net tangible book value to investors participating in this offering of $71.51 per share of common stock. The following table illustrates this dilution per share of common stock:

Public offering price per share of common stock		$ 85.00
Net tangible book value per share of common stock as of June 30, 2026 (excluding the assumed conversion of preferred stock)	$ 12.50	
Pro forma net tangible book value per share as of June 30, 2026, giving effect to the conversion of preferred stock without regard to any beneficial ownership limitations	10.81	
Increase in pro forma net tangible book value per share of common stock attributable to investors participating in this offering	2.68	
Pro forma as-adjusted net tangible book value per share of common stock immediately after this offering		13.49
Dilution per share of common stock to investors participating in this offering		$ 71.51

If the underwriters fully exercise their option to purchase additional shares of common stock, the pro forma as-adjusted net tangible book value after this offering would increase by approximately $0.38 per share of common stock, and there would be an immediate dilution of approximately $71.13 per share of common stock to investors participating in this offering.

Except as noted above, the foregoing excludes, in each case as of June 30, 2026:

- 12,660,773 shares of common stock issuable upon the exercise of outstanding stock options having a weighted-average exercise price of $19.76 per share;
- 197,032 shares of common stock issuable upon the vesting of restricted stock units outstanding;
- 8,207,770 shares of common stock reserved for issuance pursuant to future equity awards under the 2016 Plan, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2016 Plan;
- 500,884 shares of common stock reserved for issuance pursuant to future equity awards under the 2018 Plan, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2018 Plan;

- 952,808 shares of common stock reserved for future issuance under the 2016 ESPP, as well as any future increases in the number of shares of our common stock reserved for future issuance under the 2016 ESPP; and
- 1,532,591 shares of common stock issuable upon the exercise of outstanding warrants having an exercise price of $22.49 per share.

As of June 30, 2026, 346,045 shares of Series A Preferred Stock were issued and outstanding, convertible into 13,841,800 shares of common stock as of such date. After June 30, 2026, 527,502 shares of common stock have been sold pursuant to the Sales Agreement through the date of this prospectus supplement. On September 22, 2026, 1,160,620 shares of common stock were issued in connection with the cashless net exercise of 1,532,591 outstanding warrants.

Furthermore, we may choose to raise additional capital through the sale of equity or convertible debt securities due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. New investors may experience further dilution if any of our outstanding options or warrants are exercised, new options are issued and exercised under our equity incentive plans or we issue additional shares of common stock, other equity securities or convertible debt securities in the future.

CERTAIN MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS

The following discussion is a summary of certain material U.S. federal income tax considerations applicable to the ownership and disposition of our common stock, which we refer to collectively as our securities. This summary is based upon U.S. federal income tax law as of the date of this prospectus supplement, which is subject to change or differing interpretations, possibly with retroactive effect.

This summary does not discuss all potential tax considerations that may be important to particular investors in light of their individual circumstances, including, without limitation:

- banks, insurance companies or other financial institutions;
- tax-exempt entities or governmental organizations;
- brokers, traders or dealers in securities or currencies;
- persons that own, or are deemed to own, more than five percent of our capital stock;
- persons required for U.S. federal income tax purposes to conform the timing of income accruals to their financial statements under Section 451(b) of the Code;
- U.S. expatriates and certain former citizens or long-term residents of the United States;
- persons who hold our securities as a position in a hedging transaction, “straddle,” “conversion transaction” or other risk reduction transaction;
- persons that have elected the mark-to-market method of tax accounting;
- partnerships or other entities or arrangements treated as pass-through entities for U.S. federal income tax purposes (or investors in any such entities);
- persons deemed to sell our securities under the constructive sale provisions of the Internal Revenue Code of 1986, as amended (the “Code”);
- regulated investment companies or real estate investment trusts;
- pension plans or funds, or an entity that is wholly owned by a pension plan or fund;
- controlled foreign corporations;
- passive foreign investment companies; or
- persons that acquire our securities as compensation for services.

In addition, this summary does not discuss other U.S. federal tax consequences (*e.g.*, estate or gift tax), any state, local, or non-U.S. tax considerations or the Medicare tax or alternative minimum tax. In addition, this summary is limited to investors that will hold our securities as “capital assets” (generally, property held for investment) under the Code. No assurance can be given that the Internal Revenue Service (“IRS”) would not assert, or that a court would not sustain, a position contrary to any part of the discussion of the tax consequences set forth below.

For purposes of this summary, a “U.S. Holder” is a beneficial holder of securities that, for U.S. federal income tax purposes, is:

1. an individual who is a citizen or resident of the United States;
2. a corporation or other entity treated as a corporation for U.S. federal income tax purposes created in, or organized under the law of, the United States, any state thereof, or the District of Columbia;

3. an estate the income of which is includible in gross income for U.S. federal income tax purposes regardless of its source; or

4. a trust (A) the administration of which is subject to the primary supervision of a U.S. court and which has one or more "United States persons" (within the meaning of the Code) who have the authority to control all substantial decisions of the trust or (B) that has in effect a valid election under applicable Treasury regulations to be treated as a United States person.

A "non-U.S. Holder" is a beneficial holder of securities that is neither a U.S. Holder nor a partnership or other entity or arrangement treated as a pass-through entity for U.S. federal income tax purposes.

The tax treatment of a partner in a partnership (or other entity or arrangement taxable as a partnership for U.S. federal income tax purposes) that holds our securities generally will depend on the status of the partner and the activities of the partnership. Partnerships holding our securities and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences applicable to them.

THIS DISCUSSION OF U.S. FEDERAL INCOME TAX CONSIDERATIONS IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT TAX ADVICE. PROSPECTIVE HOLDERS SHOULD CONSULT THEIR TAX ADVISORS CONCERNING THE U.S. FEDERAL INCOME TAX CONSEQUENCES TO THEM OF OWNING AND DISPOSING OF OUR SECURITIES, AS WELL AS THE APPLICATION OF ANY STATE, LOCAL AND NON-U.S. INCOME, ESTATE AND OTHER TAX CONSIDERATIONS.

U.S. Holders

Distributions

In the event that we make a distribution of cash or other property (other than certain pro rata distributions of our stock) in respect of our securities, such distribution will be treated as a dividend to the extent paid out of our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Distributions in excess of current and accumulated earnings and profits will be treated as a non-taxable return of capital to the extent of the U.S. Holder's basis in its securities and, to the extent the amount of the distribution exceeds a U.S. Holder's adjusted tax basis in such securities, the excess will be treated as gain from the disposition of such securities (the tax treatment of which is discussed below under "-Sale, Exchange or Other Taxable Disposition of Our Securities").

Dividends we pay to a U.S. Holder that is a corporation generally will qualify for the dividends received deduction if the requirements relating to the requisite holding period are satisfied. With certain exceptions, and provided certain holding period requirements are met, dividends we pay to a non-corporate U.S. Holder generally will constitute "qualified dividends" that currently are subject to tax at preferential long-term capital gains rates.

Sale, Exchange or Other Taxable Disposition of Our Securities

Upon a sale, taxable exchange or other taxable disposition of our securities, a U.S. Holder will generally recognize taxable gain or loss in an amount equal to the difference between (1) the amount realized upon such sale, exchange or taxable disposition and (2) the U.S. Holder's tax basis in the security. Such gain or loss will generally be treated as long-term capital gain or loss if the security is held by the U.S. Holder for more than one year at the time of such sale, exchange or disposition. Long-term capital gains recognized by certain non-corporate U.S. holders generally are taxed at preferential rates. The deductibility of capital losses is subject to certain limitations.

Information Reporting and Backup Withholding

In general, information reporting requirements may apply to dividends paid to a U.S. Holder and to the proceeds of the sale, exchange or other taxable disposition of our securities, unless the U.S. Holder is an exempt recipient. Backup withholding may apply to such payments if the U.S. Holder fails to provide a taxpayer identification number, typically on an IRS Form W-9, or a certification of exempt status or has been notified by the IRS that it is subject to backup withholding (and such notification has not been withdrawn).

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules will be allowed as a refund or a credit against a U.S. Holder's U.S. federal income tax liability provided the required information is timely furnished to the IRS.

Non-U.S. Holders

Distributions

Any distributions treated as dividends for U.S. federal income tax purposes we pay to a non-U.S. Holder with respect to shares of our securities will generally be subject to withholding tax at a 30% rate (or such lower rate specified by an applicable income tax treaty). To obtain the benefit of a reduced rate under an applicable income tax treaty, a non-U.S. Holder must certify as to its non-U.S. status, and to such right under the applicable income tax treaty on a properly completed IRS Form W-8BEN or IRS Form W-8BEN-E. If, however, a non-U.S. Holder provides an IRS Form W-8ECI, certifying that the dividend is effectively connected with the non-U.S. Holder's conduct of a trade or business within the United States, the dividend will not be subject to withholding. Instead, such dividends are subject to U.S. federal income tax at regular rates applicable to U.S. persons generally and, for corporate holders, may also be subject to a 30% "branch profits tax." Non-U.S. Holder may be eligible for a lower rate of "branch profits taxes" under an applicable U.S. income tax treaty.

Sale, Exchange or Other Taxable Disposition of Our Securities

Subject to the discussions below regarding FATCA and backup withholding, a non-U.S. Holder will generally not be subject to U.S. federal income or withholding tax in respect of gain recognized on a sale, exchange or other taxable disposition of our securities unless:

- the gain is effectively connected with the conduct of a trade or business by the non-U.S. Holder within the United States (and, if an applicable tax treaty so requires, is attributable to a U.S. permanent establishment or fixed base maintained by the non-U.S. Holder);
- the non-U.S. Holder is an individual who is present in the United States for 183 days or more in the taxable year of disposition and certain other conditions are met; or
- we are or have been a "United States real property holding corporation" for U.S. federal income tax purposes during a specified period and certain other requirements are met. We do not expect to be a "United States real property holding corporation" for U.S. federal income tax purposes, but there can be no assurance in that regard.

Gain described in the first bullet point above will be subject to tax at the regular rates applicable to U.S. persons generally. Any gains described in the first bullet point above of a non-U.S. Holder that is a corporation may also be subject to an additional "branch profits tax" at a 30% rate (or lower applicable treaty rate). Gain described in the second bullet point above will generally be subject to a flat 30% U.S. federal income tax, which gain may be offset by certain U.S. source capital losses (even though a Non-U.S. holder is not considered a resident of the United States), provided timely filed U.S. federal income tax returns have been filed with respect to such losses. If the third bullet point above applies to a non-U.S. Holder, gain recognized by such holder on the sale, exchange or other taxable disposition of our securities will be subject to tax at the regular rates applicable to U.S. persons generally, and certain withholding requirements may apply. Non-U.S. Holders are urged to consult their tax advisors regarding the application of these rules, including possible eligibility for benefits under income tax treaties.

Foreign Account Tax Compliance Act

Under the Foreign Account Tax Compliance Act ("FATCA"), withholding at a rate of 30% will generally be required on dividends in respect of our securities held by or through certain foreign financial institutions (including investment funds), unless such institution (i) enters into an agreement with the U.S. Department of the Treasury to report, on an annual basis, information with respect to shares in, and accounts maintained by, the institution to the extent such shares or accounts are held by certain U.S. persons and by certain non-U.S. entities that are wholly or partially owned by U.S. persons and to withhold on certain payments, (ii) complies with the terms of an

intergovernmental agreement between the United States and an applicable foreign country, or (iii) otherwise qualifies for an exemption. Accordingly, the entity through which our securities are held will affect the determination of whether such withholding is required. Similarly, dividends in respect of shares of our securities held by an investor that is a non-financial non-U.S. entity that does not qualify under certain exemptions will be subject to withholding at a rate of 30%, unless such entity either (i) certifies that such entity does not have any "substantial United States owners" or (ii) provides certain information regarding the entity's "substantial United States owners," which we or the applicable withholding agent will in turn provide to the Secretary of the Treasury. An intergovernmental agreement between the United States and an applicable foreign country, or future Treasury regulations or other guidance, may modify these requirements. We will not pay any additional amounts to investors in respect of any amounts withheld. Withholding under FATCA may also apply to payments of gross proceeds from a sale or other disposition of our securities. However, under proposed Treasury regulations, withholding on gross proceeds is not required. Although such regulations are not final, applicable withholding agents may rely on the proposed regulations until final regulations are issued. If withholding under FATCA is required on any payment in respect of our securities, non-U.S. investors not otherwise subject to withholding (or that otherwise would be entitled to a reduced rate of withholding) may be required to seek a refund or credit from the IRS. Non-U.S. investors are encouraged to consult their tax advisors regarding the possible implications of FATCA on their investment in our securities.

Information Reporting and Backup Withholding

Information returns will be filed with the IRS in connection with payments of dividends and the proceeds from certain sales, exchanges or other taxable dispositions of our securities. Copies of the information returns reporting such dividends and withholding may also be made available to the tax authorities in the country in which the respective non-U.S. Holder resides under the provisions of an applicable income tax treaty. A non-U.S. Holder may have to comply with certification procedures, such as delivering an IRS Form W-8BEN, IRS Form W-8BEN-E, or IRS Form W-8ECI, in addition to other requirements, to establish that it is not a "United States person" in order to avoid certain information reporting and backup withholding requirements. The certification procedures required to claim a reduced rate of withholding under a treaty generally will satisfy the certification requirements necessary to avoid backup withholding.

In addition, proceeds of the sale, exchange or other taxable disposition of our common stock within the United States or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting if the applicable withholding agent receives a certification that the holder is not a "United States person" in accordance with the procedures above and satisfies the other requirements, or the holder otherwise establishes an exemption. Proceeds of such a sale, exchange or disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker generally will not be subject to backup withholding or information reporting.

Backup withholding is not an additional tax. The amount of any backup withholding from a payment to a non-U.S. Holder will be allowed as a credit against such holder's U.S. federal income tax liability and may entitle such holder to a refund, provided that the required information is timely furnished to the IRS.

All non-U.S. Holders should consult their tax advisors regarding the application of information reporting and backup withholding to them.

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated October 5, 2026, among us and Jefferies LLC, TD Securities (USA) LLC, Leerink Partners LLC and Stifel, Nicolaus & Company, Incorporated, as the representatives of the underwriters named below, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below.

Underwriters	Number Of Shares Of Common Stock
Jefferies LLC	1,317,648
TD Securities (USA) LLC	988,236
Leerink Partners LLC	988,236
Stifel, Nicolaus & Company, Incorporated	576,470
LifeSci Capital, LLC	247,058
Total	4,117,648

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent, such as the receipt by the underwriters of officers' certificates, legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act and to contribute payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in our common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for our common stock, that you will be able to sell any of our common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the securities, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares of common stock and other conditions contained in the underwriting agreement such as the receipt by the underwriters of officer's certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriters have advised us that they do not intend to confirm sales to any account over which they exercise discretionary authority.

Commissions and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers, which may include the underwriters, at that price, less a concession not in excess of $3.06 per share. After the offering, the public offering price, concession and reallowance to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds to us, before expenses, in connection with this offering. Such amounts are

shown assuming both no exercise and full exercise by the underwriters of their option to purchase additional shares of common stock.

	Per Share Of Common Stock	Total	
		Without Option To Purchase Additional Shares	With Option To Purchase Additional Shares
Public offering price	$ 85.00	$ 350,000,080.00	$ 402,500,075.00
Underwriting discounts and commissions	$ 5.10	$ 21,000,004.80	$ 24,150,004.50
Proceeds to us, before expenses	$ 79.90	$ 329,000,075.20	$ 378,350,070.50

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions, referred to above, will be approximately $350,000. We have also agreed to reimburse the underwriters up to $15,000 for expenses incurred in connection with determining this offering's compliance with the rules of the Financial Industry Regulatory Authority, Inc. ("FINRA"). These reimbursed expenses are deemed underwriting compensation for this offering. The underwriters have also agreed to reimburse us for certain of our expenses incurred in connection with this offering.

Listing

Our common stock is traded on the Nasdaq Global Select Market under the symbol "SYRE."

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase, from time to time, in whole or in part, up to an aggregate of shares of common stock from us at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares of common stock proportionate to that underwriter's initial purchase commitment as indicated in the table above.

No Sales of Similar Securities

We and our executive officers and directors have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer to sell, pledge, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of any shares of our common stock beneficially owned (as such term is used in Rule 13d-3 of the Exchange Act) or any other securities so owned that are convertible into or exercisable or exchangeable for our common stock; or

- dispose of any shares of common stock, options to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially.

This restriction terminates after the close of trading of the common stock on and including the 60th day after the date of this prospectus supplement. The representatives may, in their sole discretion, and at any time or from time to time before the termination of the 60-day period, release all or any portion of the securities subject to lock-up agreements.

With respect to the Company, this restriction does not apply to (A) the transactions contemplated by this offering, (B) issuance and sale by the Company of common stock pursuant to the Sales Agreement, provided that no sales be made under the Sales Agreement until the earlier of (x) the exercise in full by the underwriters of their option to purchase common stock pursuant to the underwriting agreement and (y) the 30th day following the date of

this prospectus supplement, and (C) the issuance by the Company of common stock or options to purchase common stock, or the issuance of common stock upon exercise of options, pursuant to stock options, stock bonuses or other stock plans or arrangements, provided that each holder of such common stock or options who is a director or officer of the Company agrees in writing with the underwriters not to sell, offer, dispose of or otherwise transfer any such common stock or options during the 60-day lock-up period without the prior written consent of the representatives.

With respect to our directors and officers, subject to certain conditions, this restriction does not apply to (A) the establishment of new trading plans pursuant to Rule 10b5-1 under the Exchange Act, (B) sales or transfers of securities made pursuant to a trading plan pursuant to Rule 10b5-1 under the Exchange Act that has been entered into prior to the date of the lock-up agreement, (C) the exercise of options to purchase shares of common stock granted under stock incentive plans or stock purchase plans of the Company, (D) the transfer of securities to the Company or sold in connection with a vesting event of the Company's securities or upon the exercise of options to purchase the Company's securities, on a "cashless" or "net exercise" basis or to cover tax withholding obligations in connection with such vesting or exercise, (E) the transfer or disposition of securities occurring by operation of law, (F) the transfer of securities pursuant to a bona fide third party tender offer, merger, consolidation or other similar transaction, (G) transfers by bona fide gift, (H) transfers by will or intestate succession, (I) transfers to a trust whose beneficiaries consist exclusively of one or more of the undersigned and/or a family member, (J) transfers to any corporation, partnership, limited liability company, investment fund or other entity controlled or managed, or under common control or management or a family member, or (K) transfers as distributions to partners, members or stockholders of the locked up party.

There are no existing agreements between the underwriters and any of our stockholders who will execute a lock-up agreement that provide consent to the sale of shares of common stock prior to the expiration of the lock-up period.

Stabilization

The underwriters have advised us that they, pursuant to Regulation M under the Exchange Act, and certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of our common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either "covered" short sales or "naked" short sales.

"Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

"Naked" short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of our common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of our common stock. A syndicate covering transaction is the bid for or the purchase of shares of our common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in

connection with the offering if shares of common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or on web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus supplement and the accompanying prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied on by investors.

Other Activities and Relationships

The underwriters and certain of their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory services, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their respective affiliates have performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses. For example, TD Securities (USA) LLC is the sales agent under the Sales Agreement. Under the Sales Agreement, we may offer and sell, from time to time, shares of our common stock through TD Securities (USA) LLC through an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Disclaimers about Non-U.S. Jurisdictions

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant State"), no securities have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the securities which have been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant

State, all in accordance with the Prospectus Regulation, except that the securities may be offered to the public in that Relevant State at any time:

(a) to any legal entity which is a "qualified investor" as defined under Article 2 of the Prospectus Regulation;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the Prospectus Regulation), subject to obtaining the prior consent of representatives for any such offer; or

(c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of securities shall require us or any of the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression "offer to the public" in relation to the securities in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase or subscribe for any securities, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129.

Notice to Prospective Investors in the United Kingdom

No securities have been offered or will be offered pursuant to this offering to the public in the United Kingdom except that the securities may be offered to the public in the United Kingdom at any time:

(a) where (i) the offer is conditional on the admission of the securities to trading on the London Stock Exchange plc's main market (in reliance on the exception in paragraph 6(a) of Schedule 1 of the POATR) or (ii) the securities being offered are at the time of the offer already admitted to trading on London Stock Exchange plc's main market (in reliance on the exception in paragraph 6(b) of Schedule 1 of the POATR);

(b) to any qualified investor as defined in paragraph 15 of Schedule 1 of the POATR;

(c) to fewer than 150 persons (other than qualified investors as defined in paragraph 15 of Schedule 1 of the POATR), subject to obtaining the prior consent of the underwriters for any such offer; or

(d) in any other circumstances falling within Part 1 of Schedule 1 of the POATR.

For the purposes of this provision, the expression an "offer to the public" in relation to the securities in the United Kingdom means the communication to any person which presents sufficient information on: (a) the securities to be offered; and (b) the terms on which they are to be offered, to enable an investor to decide to buy or subscribe for the securities and the expression "POATR" means the Public Offers and Admissions to Trading Regulations 2024.

Notice to Prospective Investors in Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than: (i) to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or (ii) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong (the "SFO") and any rules made under that Ordinance; or in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong (the "CO") or which do not constitute an offer or invitation to the public for the purpose of the CO or the SFO. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), that is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities that are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the SFO and any rules made under that Ordinance.

This prospectus supplement and the accompanying prospectus have not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus supplement and the accompanying prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus supplement and accompanying prospectus and that he is not acquiring, and has not been offered, any securities in circumstances that contravene any such restrictions.

Notice to Prospective Investors in Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended, the "FIEL") and the underwriters will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (the term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Notice to Prospective Investors in Singapore

This prospectus supplement and the accompanying prospectus have not been and will not be lodged or registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and the accompanying prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities offered hereby may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than: (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"); (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA; or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person that is:

- a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)), the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares of common stock pursuant to an offer made under Section 275 of the SFA except:
    - to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
    - where no consideration is or will be given for the transfer;
    - where the transfer is by operation of law;
    - as specified in Section 276(7) of the SFA; or
    - as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Notice to Prospective Investors in Canada

(A) Resale Restrictions

The distribution of securities in Canada is being made only in the provinces of Ontario, Quebec, Alberta, British Columbia, Manitoba, New Brunswick and Nova Scotia on a private placement basis exempt from the requirement that we prepare and file a prospectus with the securities regulatory authorities in each province where trades of these securities are made. Any resale of the securities in Canada must be made under applicable securities laws which may vary depending on the relevant jurisdiction, and which may require resales to be made under available statutory exemptions or under a discretionary exemption granted by the applicable Canadian securities regulatory authority. Purchasers are advised to seek legal advice prior to any resale of the securities.

(B) Representations of Canadian Purchasers

By purchasing securities in Canada and accepting delivery of a purchase confirmation, a purchaser is representing to us and the dealer from whom the purchase confirmation is received that:

- the purchaser is entitled under applicable provincial securities laws to purchase the securities without the benefit of a prospectus qualified under those securities laws as it is an "accredited investor" as defined under National Instrument 45-106 - Prospectus Exemptions or Section 73.3(1) of the Securities Act (Ontario), as applicable,
- the purchaser is a "permitted client" as defined in National Instrument 31-103-Registration Requirements, Exemptions and Ongoing Registrant Obligations,
- where required by law, the purchaser is purchasing as principal and not as agent, and
- the purchaser has reviewed the text above under Resale Restrictions.

(C) Conflicts of Interest

Canadian purchasers are hereby notified that certain of the underwriters are relying on the exemption set out in section 3A.3 or 3A.4, if applicable, of National Instrument 33-105 - *Underwriting Conflicts* from having to provide certain conflict of interest disclosure in this document.

(D) Statutory Rights of Action

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if the offering memorandum (including any amendment thereto) such as this document contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser of these securities in Canada should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

(E) Enforcement of Legal Rights

All of our directors and officers as well as the experts named herein may be located outside of Canada and, as a result, it may not be possible for Canadian purchasers to effect service of process within Canada upon us or those persons. All or a substantial portion of our assets and the assets of those persons may be located outside of Canada and, as a result, it may not be possible to satisfy a judgment against us or those persons in Canada or to enforce a judgment obtained in Canadian courts against us or those persons outside of Canada.

(F) Taxation and Eligibility for Investment

Canadian purchasers of securities should consult their own legal and tax advisors with respect to the tax consequences of an investment in the securities in their particular circumstances and about the eligibility of the securities for investment by the purchaser under relevant Canadian legislation.

Notice to Prospective Investors in Australia

This prospectus supplement and the accompanying prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia (the "Corporations Act"), has not been lodged with the Australian Securities and Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus supplement and the accompanying prospectus in Australia, you confirm and warrant that you are either:

- a "sophisticated investor" under Section 708(8)(a) or (b) of the Corporations Act;
- a "sophisticated investor" under Section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the Company that complies with the requirements of Section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
- a person associated with the Company under Section 708(12) of the Corporations Act; or
- a "professional investor" under Section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act, any offer made to you under this prospectus supplement and the accompanying prospectus is void and incapable of acceptance.

Further, you warrant and agree that you will not offer any of the securities issued to you pursuant to this prospectus supplement and the accompanying prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under Section 708 of the Corporations Act.

Notice to Prospective Investors in Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968 (the "Israeli Securities Law"), and has not been filed with or approved by the Israel Securities Authority. In Israel, this prospectus supplement and the accompanying prospectus are being distributed only to, and is directed only at, and any offer of the securities offered hereby is directed only at: (i) a limited number of persons in accordance with the Israeli Securities Law; and (ii) investors listed in the first addendum to the Israeli Securities Law, as it may be amended from time to time (the "Addendum"), consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and "qualified individuals," each as defined in the Addendum, collectively referred to as qualified investors (in each case, purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors are required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of the Addendum and agree to it.

Notice to Prospective Investors in Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange ("SIX") or on any other stock exchange or regulated trading facility in Switzerland. This prospectus supplement and the accompanying prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus supplement and the accompanying prospectus, nor any other offering or marketing material relating to the securities or the offering, may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus supplement and the accompanying prospectus, nor any other offering or marketing material relating to the offering, the Company or the securities offered hereby, have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus supplement and the accompanying prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market

Supervisory Authority FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (the "CISA"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities offered hereby.

EXPERTS

The consolidated financial statements of Spyre Therapeutics, Inc. as of December 31, 2025 and for the year then ended, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2025 have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

The financial statements as of December 31, 2024 and for each of the two years in the period ended December 31, 2024 incorporated in this prospectus supplement by reference to the Annual Report on Form 10-K for the year ended December 31, 2025 have been so incorporated 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.

LEGAL MATTERS

The validity of the common stock being offered in this prospectus supplement will be passed on by Ropes & Gray LLP, Boston, Massachusetts. Paul Hastings LLP, New York, New York, is representing the underwriters in connection with this offering.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the informational requirements of the Exchange Act, and in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. The SEC maintains an Internet website that contains reports, proxy statements and other information about registrants, like us, that file electronically with the SEC. The address of that site is *www.sec.gov*. Statements contained in this prospectus supplement as to the contents of any contract or other document are not necessarily complete, and in each instance, we refer you to the copy of the contract or document filed as an exhibit to the registration statement, each such statement being qualified in all respects by such reference. We also maintain a website at *www.spyre.com*. We have included our website address for the information of prospective investors and do not intend it to be an active link to our website. Information contained on our website does not constitute a part of this prospectus supplement (or any document incorporated by reference herein or therein).

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to those publicly available documents. The information incorporated by reference is an important part of this prospectus supplement, and information that we file after the date hereof with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below (in each case, other than portions of documents not deemed to be filed):

- Annual Report on Form 10-K for the year ended December 31, 2025, filed with the SEC on February 19, 2026 (and any portions of our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 10, 2026, that are incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2025); and
- Quarterly Reports on Form 10-Q for the quarters ended March 31, 2026 and June 30, 2026, filed with the SEC on May 5, 2026 and August 4, 2026; and
- Current Reports on Form 8-K filed with the SEC on April 13, 2026, April 13, 2026, April 16, 2026, May 29, 2026, June 1, 2026, June 15, 2026, August 25, 2026 and September 8, 2026; and
- the description of our common stock contained in our registration statement on Form 8-A, filed with the SEC on March 28, 2016, including any amendments or reports filed for the purpose of updating such description.

Because we are incorporating by reference future filings with the SEC, this prospectus supplement is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement or in any document previously incorporated by reference have been modified or superseded.

This prospectus supplement incorporates by reference the documents listed above and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of the initial registration statement and the effectiveness of the registration statement and following the effectiveness of the registration statement until the offering of the securities under the registration statement is terminated or completed, except that we are not incorporating by reference any information furnished (and not filed) with the SEC, including any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K (unless expressly provided to the contrary).

You may request a copy of these filings (other than exhibits to such documents unless such exhibits are specifically incorporated by reference herein), at no cost, by contacting us, either orally or in writing, at the following:

Spyre Therapeutics, Inc.
221 Crescent Street
Building 23, Suite 105
Waltham, Massachusetts 02453
(617) 651-5940

Information about us is also available at our website at *http://www.spyre.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 supplement and is not incorporated by reference into this prospectus supplement. We have authorized no one to provide you with any information that differs from that contained in this prospectus supplement. Accordingly, we take no responsibility for any other information that others may give you. You should not assume that the information in this prospectus supplement is accurate as of any date other than the date of the front cover of this prospectus supplement.

PROSPECTUS

COMMON STOCK
PREFERRED STOCK
DEBT SECURITIES
WARRANTS
UNITS

From time to time, we may issue, in one or more series or classes, an indeterminate number of shares of our common stock, preferred stock, debt securities, warrants and/or units, at prices and on terms that we will determine at the time of the offering.

This prospectus provides you with a general description of the securities we may offer. Each time we offer securities, we will provide specific terms of the securities offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. We may not sell any securities under this prospectus without delivery of the applicable prospectus supplement. If information in any prospectus supplement is inconsistent with the information in this prospectus, then the information in that prospectus supplement will apply and will supersede the information in this prospectus.

You should read this prospectus, the applicable prospectus supplement and any related free writing prospectus carefully, as well as any documents incorporated by reference, before you invest in any of the securities being offered.

Our shares of common stock are listed on the Nasdaq Global Select Market under the symbol “SYRE.” The last reported sale price of our common stock on the Nasdaq Global Select Market on June 25, 2026 was $88.67 per share. We recommend that you obtain current market quotations for our common stock prior to making an investment decision.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading “**Risk Factors**” contained in this prospectus beginning on page 5 and any applicable prospectus supplement, and under similar headings in the other documents that are incorporated by reference into this prospectus.

Neither the Securities and Exchange Commission 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.

Prospectus dated June 26, 2026

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ABOUT THIS PROSPECTUS

This prospectus is a part of an automatic shelf registration statement on Form S-3ASR that we filed with the Securities and Exchange Commission (the "SEC" or the "Commission") as a "well-known seasoned issuer," as defined in Rule 405 under the Securities Act of 1933, as amended (the "Securities Act"), utilizing a "shelf" registration process. Under this shelf registration process, we may sell any combination of the securities described in this prospectus in one or more offerings. This prospectus provides you with a general description of the securities we may offer.

Each time we sell securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus. You should carefully read both this prospectus and any prospectus supplement together with additional information under the headings "Where You Can Find More Information" and "Incorporation of Certain Information by Reference."

We have not authorized anyone to provide you with any information other than that contained or incorporated by reference in this prospectus and any applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. This prospectus, any applicable supplement to this prospectus or any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus, any applicable supplement to this prospectus or any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus, any applicable prospectus supplement or any related free writing prospectus is delivered, or securities are sold, on a later date.

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 taken as a whole.

"Spyre" and all product candidate names are our common law trademarks. This prospectus contains additional trade names, trademarks and service marks of other companies, which are the property of their respective owners. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies. Solely for convenience, trademarks and trade names referred to in this prospectus may appear without the ® or ™ 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 signed a license agreement for, 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 and May 14, 2024, by and among us, Paragon Therapeutics, Inc. and Parapyre Holding LLC.

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."

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CAUTIONARY NOTE CONCERNING FORWARD-LOOKING STATEMENTS

This prospectus contains "forward-looking statements" within the meaning of Section 27A of 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 contained in this prospectus, other than statements of historical fact, including, without limitation, statements regarding any future payouts under our contingent value rights issued in connection with the acquisition of Spyre Therapeutics, Inc. ("Pre-Merger Spyre") (the "Asset Acquisition"); our future results of operations and financial position; our business strategy, including our ability to elevate the standard in immunology by delivering more complete disease control, greater durability, and a simpler treatment experience for patients and to develop best-in-class therapeutics for inflammatory bowel disease ("IBD"), rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondyloarthritis (axSpA) and other immune-mediated diseases that meaningfully improve both efficacy and convenience compared to today's standard of care and our ability to develop first-in-class therapeutics for rheumatic diseases ("RD"); our plans to expand the development of our product candidates, including SPY002, to indications beyond IBD and RD; our ability to achieve the expected benefits or opportunities with respect to our product candidates, including their potential commercialization; the potential consistency of the SPY001, SPY002, SPY072 and SPY003 Phase 1 trial and Phase 2 trial final data readouts with previously disclosed data for our programs; expectations regarding the drug delivery of our product candidates, including in the form of a subcutaneous injection; the planned dosing regimen for SPY001, SPY002, SPY072 and SPY003, and combinations thereof, including the potential for a Q3M-Q6M dosing profile and the potential for such dosing profile to be the leading product profile in IBD and RD; our non-clinical and clinical development activities, including our plans for and timing of cohort initiation and data readouts for the ongoing SKYWAY Phase 2 basket trial and SKYLINE Phase 2 platform trial, enrollment of clinical trials, and the inclusion of each rational combination in Part B of the SKYLINE Phase 2 platform trial and the number of data readouts expected to be delivered in 2026 and 2027; estimated market sizes and potential growth opportunities; the potential efficacy, tolerability, convenience, commercial viability and safety profile of our product candidates, including in combinations; the potential therapeutic benefits and economic value of our product candidates as monotherapies or in combinations and their extended half-life; our ability to achieve the expected benefits or opportunities and related timing with respect to the Asset Acquisition; the expected impact of macroeconomic conditions, including inflation, increasing interest rates and volatile market conditions, and current or potential bank failures, as well as global events, including the ongoing military conflict between the United States and Iran and Ukraine and Russia, the conflicts in the Middle East, and geopolitical tensions between the United States and other countries, including China, on our operations, and the implementation of changes in law, tariffs, sanctions, export or import controls, and other government measures that could impact our business operations, including restricting international trade by the United States, China or other countries, are forward-looking statements. 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 include the risks set forth under the heading "Risk Factors" in this prospectus and in the documents incorporated by reference in this prospectus and the applicable prospectus supplement. 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. This prospectus and registration statement also contain or incorporate by reference estimates, projections, and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained such industry, business, market, and other data from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources.

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.

THE COMPANY

We are a clinical-stage biotechnology company committed to developing next-generation therapies that elevate the standard in immunology by delivering more complete disease control, greater durability, and a simpler treatment experience for patients. Our pipeline includes investigational extended half-life antibodies targeting α4β7, TL1A, and IL-23 in development as monotherapies and pair-wise combinations.

For more information about our business, please see our most recent Annual Report on Form 10-K, as supplemented and updated by subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K that we have filed or will file with the SEC, and in other documents that are incorporated by reference into this prospectus.

Corporate Information

We were formed as a Limited Liability Company ("LLC") in Delaware on December 16, 2013 under the name Aeglea BioTherapeutics Holdings, LLC and were converted from a Delaware LLC to a Delaware corporation on March 10, 2015. On June 22, 2023, we completed the acquisition of Pre-Merger Spyre, and on November 27, 2023, we completed our corporate rebranding, changing our name to Spyre Therapeutics, Inc.

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. Our website is *www.spyre.com*. The information on, or that can be accessed through, our website is not part of this prospectus and is not incorporated by reference herein. We have included our website address in this prospectus solely as an inactive textual reference.

RISK FACTORS

Investing in our securities involves risks. You should carefully consider the risks, uncertainties and other factors described in our most recent Annual Report on Form 10-K, as supplemented and updated by subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K that we have filed or will file with the SEC, and in other documents that are incorporated by reference into this prospectus, as well as the risk factors and other information contained in or incorporated by reference into any accompanying prospectus supplement, before investing in any of our securities. Our business, financial condition, results of operations, cash flows or prospects could be materially and adversely affected by any of these risks. The risks and uncertainties described in the documents incorporated by reference herein are not the only risks and uncertainties that you may face.

For more information about our SEC filings, please see “Where You Can Find More Information” and “Incorporation of Certain Information by Reference.”

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. Unless otherwise specified in a prospectus supplement accompanying this prospectus, the net proceeds from the sale by us of the securities to which this prospectus relates will be used to continue to advance our programs in IBD and RD, including to fund preclinical studies, clinical trials and manufacturing in support of our antibody programs. We also intend to use a portion of the net proceeds to further develop and support our general infrastructure. Finally, we may use a portion of the net proceeds to in-license, acquire, or invest in additional businesses, technologies, products, or assets, and to fund the development of such new in-licensed or acquired technologies and products. Any remaining proceeds will be used for other ongoing research and development, working capital and other general corporate purposes.

Our expected use of proceeds from the sale of the securities offered hereby represents our current intentions based on our present plans and business condition. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the proceeds to be received from the sale of the securities offered hereby or the amounts that we will actually spend on the uses set forth above.

Pending the use of the net proceeds, we may invest the proceeds in interest-bearing, investment-grade securities, certificates of deposit, money market funds or government securities. When we offer and sell the securities to which this prospectus relates, the prospectus supplement related to such offering will set forth our intended use of the proceeds, if any, received from the sale of such securities.

SECURITIES WE MAY OFFER

This prospectus contains summary descriptions of the securities we may offer from time to time. These summary descriptions are not meant to be complete descriptions of each security. The particular terms of any security will be described in the applicable prospectus supplement.

DESCRIPTION OF SECURITIES

Capital Stock

The following is a summary of the material terms of our capital stock, as well as other material terms of our second amended and restated certificate of incorporation (as amended from time to time, our "Certificate of Incorporation") and our amended and restated bylaws (as amended from time to time, our "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 our Bylaws. For more information on how you can obtain copies of our Certificate of Incorporation and our Bylaws, see the heading "Where You Can Find More Information."

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, of which 1,086,341 shares have been designated as Series A Non-Voting Convertible Preferred Stock, $0.0001 par value per share ("Series A Preferred Stock"), and 271,625 shares have been designated as Series B Non-Voting Convertible Preferred Stock, $0.0001 par value per share ("Series B Preferred Stock").

As of June 24, 2026, there were 87,936,477 shares of our common stock, 346,045 shares of Series A Preferred Stock and no 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

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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.

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 Delaware General Corporation Law (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 that 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 that 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.

- Series A Preferred Stock veto right. Pursuant to our Certificate of Designation of Preferences, Rights and Limitations of Series A Non-Voting Convertible Preferred Stock (the "Series A Certificate of Designation"), we may not, without the affirmative vote of the holders of a majority of the then outstanding shares of our Series A Preferred Stock, while at least 30% of the originally issued Series A Preferred Stock remains issued and outstanding, consummate any Fundamental Transaction (as defined in the Series A Certificate of Designation) or any merger, consolidation, stock sale 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.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock and preferred stock is Equiniti 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."

Debt Securities

The paragraphs below describe the general terms and provisions of the debt securities we may issue. When we offer to sell a particular series of debt securities, we will describe the specific terms of the securities in a supplement to this prospectus, including any additional covenants or changes to existing covenants relating to such series. The prospectus supplement also will indicate whether the general terms and provisions described in this prospectus apply to a particular series of debt securities. You should read the actual indenture if you do not fully understand a term or the way we use it in this prospectus.

If we issue debt securities at a discount from their principal amount, then, for purposes of calculating the aggregate initial offering price of the offered debt securities issued under this prospectus, we will include only the initial offering price of the debt securities and not the principal amount of the debt securities.

We have summarized below the material provisions of the indenture, or indicated which material provisions will be described in the related prospectus supplement. The prospectus supplement relating to any particular debt securities offered will describe the specific terms of the debt securities, which may be in addition to or different from the general terms summarized in this prospectus. We have included the form of the indenture as an exhibit to our registration statement of which this prospectus is a part, and it is incorporated into this prospectus by reference. Because the summary in this prospectus and in any prospectus supplement does not contain all of the information

that you may find useful, you should read the documents relating to the debt securities that are described in this prospectus or in any applicable prospectus supplement. Please read "Where You Can Find More Information" in this prospectus to find out how you can obtain a copy of those documents. References below to an "indenture" are references to the indenture, as supplemented, under which a particular series of debt securities is issued. As used under this heading, the term "debt securities" includes the debt securities being offered by this prospectus and all other debt securities issued by us under the indenture.

General

The indenture:

- does not limit the amount of debt securities that we may issue;
- allows us to issue debt securities in one or more series;
- does not require us to issue all of the debt securities of a series at the same time; and
- allows us to reopen a series to issue additional debt securities without the consent of the holders of the debt securities of such series.

The prospectus supplement for each offering of debt securities will provide the following terms, where applicable:

- the title of the debt securities and whether they are senior, senior subordinated or subordinated debt securities;
- the aggregate principal amount of the debt securities being offered and any limit on their aggregate principal amount, and, if the series is to be issued at a discount from its face amount, the method of computing the accretion of such discount;
- the price at which the debt securities will be issued, expressed as a percentage of the principal and, if other than the full principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof or, if applicable, the portion of the principal amount of such debt securities that is convertible into common stock or preferred stock or the method by which any such portion shall be determined;
- if convertible, the terms on which such debt securities are convertible, including the initial conversion price or rate or the method of calculation, how and when the conversion price or exchange ratio may be adjusted, whether conversion or exchange is mandatory, at the option of the holder or at our option, the conversion or exchange period, and any other provision in relation thereto, and any applicable limitations on the ownership or transferability of common stock or preferred stock received on conversion;
- the date or dates, or the method for determining the date or dates, on which the principal of the debt securities will be payable;
- the fixed or variable interest rate or rates of the debt securities, or the method by which the interest rate or rates is determined;
- the date or dates, or the method for determining the date or dates, from which interest will accrue;
- the dates on which interest will be payable;
- the record dates for interest payment dates, or the method by which we will determine those dates;
- the persons to whom interest will be payable;
- the basis upon which interest will be calculated if other than that of a 360-day year of twelve 30-day months;

- any collateral securing the performance of our obligations under the debt securities;
- the place or places where the principal of, premium, if any, and interest on, the debt securities will be payable;
- where the debt securities may be surrendered for registration of transfer or conversion or exchange;
- where notices or demands to or upon us in respect of the debt securities and the applicable indenture may be served;
- any provisions regarding our right to redeem or purchase debt securities or the right of holders to require us to redeem or purchase debt securities;
- any right or obligation we have to redeem, repay or purchase the debt securities pursuant to any sinking fund or analogous provision;
- the currency or currencies (including any composite currency) in which the debt securities are denominated and payable if other than United States dollars, and the currency or currencies (including any composite currency) in which principal, premium, if any, and interest, if any, will be payable, and if such payments may be made in a currency other than that in which the debt securities are denominated, the manner for determining such payments, including the time and manner of determining the exchange rate between the currency in which such securities are denominated and the currency in which such securities or any of them may be paid, and any additions to, modifications of or deletions from the terms of the debt securities to provide for or to facilitate the issuance of debt securities denominated or payable in a currency other than U.S. dollars;
- whether the amount of payments of principal of, premium, if any, or interest on, the debt securities may be determined according to an index, formula or other method and how such amounts will be determined;
- whether the debt securities will be in registered form, bearer form or both, and the terms of these forms;
- whether the debt securities will be issued in whole or in part in the form of a global security and, if applicable, the identity of the depositary for such global security;
- any provision for electronic issuance of the debt securities or issuance of the debt securities in uncertificated form;
- whether and upon what terms the debt securities of such series may be defeased or discharged, if different from the provisions set forth in the indenture for the series to which the supplemental indenture or authorizing resolution relates;
- any provisions granting special rights to holders of securities upon the occurrence of such events as specified in the applicable prospectus supplement;
- any deletions from, modifications of, or additions to our events of default or covenants or other provisions set forth in the indenture for the series to which the supplemental indenture or authorizing resolution relates; and
- any other material terms of the debt securities, which may be different from the terms set forth in this prospectus.

We may issue debt securities at a discount below their principal amount and provide for less than the entire principal amount thereof to be payable upon declaration of acceleration of the maturity of the debt securities. We refer to any such debt securities throughout this prospectus as “original issue discount securities.” The applicable prospectus supplement will describe the United States federal income tax consequences and other relevant considerations applicable to original issue discount securities.

Neither the DGCL nor our governing instruments define the term “substantially all” as it relates to the sale of assets. Additionally, Delaware cases interpreting the term “substantially all” rely upon the facts and circumstances of each particular case. Consequently, to determine whether a sale of “substantially all” of our assets has occurred, a holder of debt securities must review the financial and other information that we have disclosed to the public.

The applicable prospectus supplement will also describe any material covenants to which a series of debt securities will be subject and the applicability of those covenants to any of our subsidiaries to be restricted thereby, which are referred to herein as “restricted subsidiaries.” The applicable prospectus supplement will also describe provisions for restricted subsidiaries to cease to be restricted by those covenants.

Events of Default

Unless the applicable prospectus supplement states otherwise, when we refer to “events of default” as defined in the indentures with respect to any series of debt securities, we mean:

- our failure to pay interest on any debt security of such series when the same becomes due and payable and the continuance of any such failure for a period of 30 days;
- our failure to pay the principal or premium of any debt security of such series when the same becomes due and payable at maturity, upon acceleration, redemption or otherwise;
- our failure or the failure of any restricted subsidiary to comply with any of its agreements or covenants in, or provisions of, the debt securities of such series or the indenture (as they relate thereto) and such failure continues for a period of 60 days after our receipt of notice of the default from the trustee or from the holders of at least 25 percent in aggregate principal amount of the then outstanding debt securities of that series (except in the case of a default with respect to the provisions of the indenture regarding the consolidation, merger, sale, lease, conveyance or other disposition of all or substantially all of the assets of us (or any other provision specified in the applicable supplemental indenture or authorizing resolution), which will constitute an event of default with notice but without passage of time); or
- certain events of bankruptcy, insolvency or reorganization occur with respect to us or any restricted subsidiary of ours that is a significant subsidiary (as defined in the indenture).

If an event of default occurs and is continuing with respect to debt securities of any series outstanding, then the trustee or the holders of 25% or more in principal amount of the outstanding debt securities of that series will have the right to declare the principal amount of all the debt securities of that series to be due and payable immediately. However, the holders of at least a majority in principal amount of outstanding debt securities of such series may rescind and annul such declaration and its consequences, except an acceleration due to nonpayment of principal or interest on such series, if the rescission would not conflict with any judgment or decree and if all existing events of default with respect to such series have been cured or waived.

The indenture also provides that the holders of at least a majority in principal amount of the outstanding debt securities of any series, by notice to the trustee, may, on behalf of all holders, waive any existing default and its consequences with respect to such series of debt securities, other than any event of default in payment of principal or interest.

The indenture will require the trustee to give notice to the holders of debt securities within 90 days after the trustee obtains knowledge of a default that has occurred and is continuing. However, the trustee may withhold notice to the holders of any series of debt securities of any default, except a default in payment of principal or interest, if any, with respect to such series of debt securities, if the trustee considers it in the interest of the holders of such series of debt securities to do so.

The holders of a majority of the outstanding principal amount of the debt securities of any series will have the right to direct the time, method and place of conducting any proceedings for any remedy available to the trustee with respect to such series, subject to limitations specified in the indenture.

Amendment, Supplement and Waiver

Without notice to or the consent of any holder, we and the trustee may amend or supplement the indenture or the debt securities of a series:

- to cure any ambiguity, omission, defect or inconsistency;
- to comply with the provisions of the indenture regarding the consolidation, merger, sale, lease, conveyance or other disposition of all or substantially all of our assets;
- to provide that specific provisions of the indenture shall not apply to a series of debt securities not previously issued or to make a change to specific provisions of the indenture that only applies to any series of debt securities not previously issued or to additional debt securities of a series not previously issued;
- to create a series and establish its terms;
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to release a guarantor in respect of any series which, in accordance with the terms of the indenture applicable to such series, ceases to be liable in respect of its guarantee;
- to add a guarantor subsidiary in respect of any series of debt securities;
- to secure any series of debt securities;
- to add to our covenants for the benefit of the holders or surrender any right or power conferred upon us;
- to appoint a successor trustee with respect to the securities;
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act of 1939, as amended (the "Trust Indenture Act");
- to make any change that does not adversely affect the rights of holders; or
- to conform the provisions of the indenture to the final offering document in respect of any series of debt securities.

The indenture will provide that we and the trustee may amend or supplement any provision of the debt securities of a series or of the indenture relating to such series with the written consent of the holders of at least a majority in principal amount of the outstanding debt securities of such series. However, without the consent of each holder of a debt security the terms of which are directly amended, supplemented or waived, an amendment, supplement or waiver may not:

- reduce the amount of debt securities of such series whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest, including defaulted interest;
- reduce the principal of or extend the fixed maturity of any debt security or alter the provisions with respect to redemptions or mandatory offers to repurchase debt securities of a series in a manner adverse to holders;
- make any change that adversely affects any right of a holder to convert or exchange any debt security into or for shares of our common stock or other securities, cash or other property in accordance with the terms of such security;
- modify the ranking or priority of the debt securities of the relevant series;
- release any guarantor of any series from any of its obligations under its guarantee or the indenture otherwise than in accordance with the terms of the indenture;

- make any change to any provision of the indenture relating to the waiver of existing defaults, the rights of holders to receive payment of principal and interest on the debt securities, or to the provisions regarding amending or supplementing the indenture or the debt securities of a particular series with the written consent of the holders of such series, except to increase the percentage required for modification or waiver or to provide for consent of each affected holder of debt securities of such series;
- waive a continuing default or event of default in the payment of principal of or interest on the debt securities; or
- make any debt security payable at a place or in money other than that stated in the debt security, or impair the right of any holder of a debt security to bring suit as permitted by the indenture.

The holders of a majority in aggregate principal amount of the outstanding debt securities of such series may, on behalf of all holders of debt securities of that series, waive any existing default under, or compliance with, any provision of the debt securities of a particular series or of the indenture relating to a particular series of debt securities, other than any event of default in payment of interest or principal.

Defeasance

The indenture will permit us to terminate all our respective obligations under the indenture as they relate to any particular series of debt securities, other than the obligation to pay interest, if any, on and the principal of the debt securities of such series and certain other obligations, at any time by:

- depositing in trust with the trustee, under an irrevocable trust agreement, money or government obligations in an amount sufficient to pay principal of and interest, if any, on the debt securities of such series to their maturity or redemption; and
- complying with other conditions, including delivery to the trustee of an opinion of counsel to the effect that holders will not recognize income, gain or loss for federal income tax purposes as a result of our exercise of such right and will be subject to federal income tax on the same amount and in the same manner and at the same times as would have been the case otherwise.

The indenture will also permit us to terminate all of our respective obligations under the indenture as they relate to any particular series of debt securities, including the obligations to pay interest, if any, on and the principal of the debt securities of such series and certain other obligations, at any time by:

- depositing in trust with the trustee, under an irrevocable trust agreement, money or government obligations in an amount sufficient to pay principal and interest, if any, on the debt securities of such series to their maturity or redemption; and
- complying with other conditions, including delivery to the trustee of an opinion of counsel to the effect that (A) we have received from, or there has been published by, the Internal Revenue Service a ruling, or (B) since the date such series of debt securities were originally issued, there has been a change in the applicable federal income tax law, in either case to the effect that, and based thereon such opinion of counsel shall state that, holders will not recognize income, gain or loss for federal income tax purposes as a result of our exercise of such right and will be subject to federal income tax on the same amount and in the same manner and at the same times as would have been the case otherwise.

In addition, the indenture will permit us to terminate substantially all our respective obligations under the indenture as they relate to a particular series of debt securities by depositing with the trustee money or government obligations sufficient to pay all principal and interest on such series at its maturity or redemption date if the debt securities of such series will become due and payable at maturity within one year or are to be called for redemption within one year of the deposit.

Transfer and Exchange

A holder will be able to transfer or exchange debt securities only in accordance with the indenture. The registrar may require a holder, among other things, to furnish appropriate endorsements and transfer documents, and to pay any taxes and fees required by law or permitted by the indenture.

Concerning the Trustee

The indenture will contain limitations on the rights of the trustee, should it become our creditor, to obtain payment of claims in specified cases or to realize on property received in respect of any such claim as security or otherwise. The indenture will permit the trustee to engage in other transactions; however, if it acquires any conflicting interest, it must eliminate such conflict or resign.

The indenture will provide that in case an event of default occurs and is not cured, the trustee will be required, in the exercise of its power, to use the degree of care of a prudent person in similar circumstances in the conduct of such person's own affairs. The trustee shall be under no obligation to exercise any of the rights or powers vested in it by the indenture at the request or direction of any of the holders pursuant to the indenture, unless such holders shall have offered to the trustee security or indemnity satisfactory to the trustee against the costs, expenses and liabilities that might be incurred by it in compliance with such request or direction.

No Recourse Against Others

The indenture will provide that there is no recourse under any obligation, covenant or agreement in the applicable indenture or with respect to any debt security against any of our or our successor's past, present or future stockholders, employees, officers or directors.

Governing Law

The laws of the State of New York will govern the indenture and the debt securities.

Warrants

We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series, from time to time. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from those securities.

If we issue warrants, they will be evidenced by warrant agreements or warrant certificates issued under one or more warrant agreements, which are contracts between us and an agent for the holders of the warrants. We urge you to read the prospectus supplement related to any series of warrants we may offer, as well as the complete warrant agreement and warrant certificate that contain the terms of the warrants. If we issue warrants, forms of warrant agreements and warrant certificates relating to warrants for the purchase of common stock, preferred stock and debt securities will be incorporated by reference into the registration statement of which this prospectus is a part from reports we would subsequently file with the SEC.

Units

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the

registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

- the title of the series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- a discussion of certain United States federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

We may also sell equity securities covered by this registration statement in an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act. Such offering may be made into an existing trading market for such securities in transactions at other than a fixed price, either:

- on or through the facilities of the Nasdaq Global Select Market or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale; and/or
- to or through a market maker otherwise than on the Nasdaq Global Select Market or such other securities exchanges or quotation or trading services.

Such at the market offerings, if any, may be conducted by underwriters acting as principal or agent.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of any underwriters, dealers or agents, if any;
- the purchase price of the securities and the proceeds we will receive from the sale;
- any options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;
- any public offering price;
- any discounts or concessions allowed or re-allowed or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement. Any public offering price and any discounts or concessions allowed or re-allowed or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities, and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to offerings pursuant to this prospectus, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we offer, other than our shares of common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. These transactions may be effected on any exchange or over-the-counter market or otherwise.

Any underwriters who are qualified market makers on the Nasdaq Global Select Market may engage in passive market making transactions in the securities on the Nasdaq Global Select Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker’s bid, however, the passive market maker’s bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

LEGAL MATTERS

Certain legal matters, including the legality of the securities offered, will be passed upon for us by Ropes & Gray LLP, Boston, Massachusetts. 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 consolidated financial statements of Spyre Therapeutics, Inc. as of December 31, 2025 and for the year then ended, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2025 have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

The financial statements as of December 31, 2024 and for each of the two years in the period ended December 31, 2024 incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2025 have been so incorporated 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.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the SEC, and we have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the securities offered by this prospectus. This prospectus, which forms part of the registration statement, does not contain all of the information included in the registration statement, including its exhibits and schedules. For further information about us and the securities described in this prospectus, you should refer to the registration statement, its exhibits and schedules and our reports, proxies, information statements and other information filed with the SEC.

Our filings are available to the public on the Internet, through a database maintained by the SEC at *www.sec.gov*. We also maintain a website at *www.spyre.com*. We have included our website address for the information of prospective investors and do not intend it to be an active link to our website. Information contained on our website does not constitute a part of this prospectus or any applicable prospectus supplement (or any document incorporated by reference herein or therein).

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to those publicly available documents. The information incorporated by reference is an important part of this prospectus, and information that we file after the date hereof with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below (in each case, other than portions of documents not deemed to be filed):

- Annual Report on Form 10-K for the year ended December 31, 2025, filed with the SEC on February 19, 2026 (and any portions of our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 10, 2026, that are incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2025);
- Quarterly Report on Form 10-Q for the quarter ended March 31, 2026, filed with the SEC on May 5, 2026;
- Current Reports on Form 8-K, filed with the SEC on April 13, 2026, April 13, 2026, April 16, 2026, May 29, 2026, June 1, 2026, and June 15, 2026; and
- the description of our common stock contained in our registration statement on Form 8-A, filed with the SEC on March 28, 2016, including any amendments or reports filed for the purpose of updating such description.

Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated, and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded.

This prospectus incorporates by reference the documents listed above and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of the initial registration statement and the effectiveness of the registration statement and following the effectiveness of the registration statement until the offering of the securities under the registration statement is terminated or completed, except that we are not incorporating by reference any information furnished (and not filed) with the SEC, including any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K (unless expressly provided to the contrary).

You may request a copy of these filings (other than exhibits to such documents unless such exhibits are specifically incorporated by reference herein), at no cost, by contacting us, either orally or in writing, at the following:

Spyre Therapeutics, Inc.
221 Crescent Street
Building 23, Suite 105
Waltham, Massachusetts 02453
(617) 651-5940

Information about us is also available at our website at *http://www.spyre.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 authorized no one to provide you with any information that differs from that contained in this prospectus. Accordingly, we take no responsibility for any other information that others may give you. You should not assume that the information in this prospectus is accurate as of any date other than the date of the front cover of this prospectus.

4,117,648 Shares

Common Stock

Joint Book-Running Managers

Jefferies **TD Cowen** **Leerink Partners** **Stifel**

Passive Bookrunner

LifeSci Capital

October 5, 2026