UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2025

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from_____ to

Commission file number 001-37722

SPYRE THERAPEUTICS, INC.

(Exact name of Registrant as specified in its charter)

Delaware	**46-4312787**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
221 Crescent Street Building 23, Suite 105 Waltham, MA	**02453**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, including area code: (617) 651-5940

Securities registered pursuant to Section 12(b) of the Exchange Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 Par Value Per Share	SYRE	The Nasdaq Stock Market LLC (Nasdaq Global Select Market)

Securities registered pursuant to Section 12(g) of the Exchange Act: None

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Exchange Act. Yes ☐ No ☒

Indicate by check mark whether the Registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). Yes ☒ No ☐

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

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

If an emerging growth company, indicate by check mark if the Registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the Registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the Registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the Registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant on June 30, 2025 (the last business day of the Registrant's second fiscal quarter), based upon the closing price of $14.97 of the Registrant's common stock as reported on The Nasdaq Global Select Market, was approximately $1.1 billion.

Indicate the number of shares outstanding of each of the Registrant's classes of common stock, as of the latest practicable date.

Class	Outstanding at February 12, 2026
Common stock, $0.0001 par value per share	78,540,164 shares

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement ("Proxy Statement") relating to the 2026 Annual Meeting of Stockholders will be filed with the Commission within 120 days after the end of the Registrant's 2025 fiscal year and is incorporated by reference into Part III of this Report.

TABLE OF CONTENTS

		Page
PART I		
Item 1.	Business	1
Item 1A.	Risk Factors	42
Item 1B.	Unresolved Staff Comments	90
Item 1C.	Cybersecurity	90
Item 2.	Properties	91
Item 3.	Legal Proceedings	91
Item 4.	Mine Safety Disclosures	91
PART II		
Item 5.	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	92
Item 6.	[Reserved]	93
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	94
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	107
Item 8.	Financial Statements and Supplementary Data	109
Item 9.	Changes in and Disagreements with Accountants on Accounting and Financial Disclosure	161
Item 9A.	Controls and Procedures	161
Item 9B.	Other Information	162
Item 9C.	Disclosure Regarding Foreign Jurisdictions that Prevent Inspections	162
PART III		
Item 10.	Directors, Executive Officers and Corporate Governance	163
Item 11.	Executive Compensation	163
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	163
Item 13.	Certain Relationships and Related Transactions, and Director Independence	163
Item 14.	Principal Accountant Fees and Services	163
PART IV		
Item 15.	Exhibits and Financial Statement Schedules	164
Item 16.	Form 10-K Summary	167
SIGNATURES		168

NOTE ABOUT FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and Section 27A of the Securities Act of 1933, as amended, or the Securities Act. All statements contained in this Annual Report other than statements of historical fact, including statements regarding any future payouts under our contingent value rights ("CVRs") issued in connection with the Asset Acquisition (as defined herein); our ability to achieve the expected benefits or opportunities and related timing with respect to our acquisition of the assets 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 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; the potential consistency of the SPY001, SPY002, SPY072 and SPY003 Phase 1 trial final data readouts with previously disclosed data for our programs; the planned induction and maintenance dosing regimen for SPY001 and our other product candidates, including the potential for a Q3M-Q6M dosing profile; the potential for increased or accelerated efficacy; potential alignment with regulatory authorities and anticipated regulatory submissions; expected timing for regulatory feedback; the length of time that we believe our existing cash resources will fund operations; estimated market sizes and potential growth opportunities; expected competitors and competing products; our nonclinical and clinical development activities, including clinical trial designs, submission of investigational new drug ("IND") applications and biologics license applications ("BLA"), as well as foreign equivalents, 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, the inclusion of each rational combination in Part B of the SKYLINE-UC Phase 2 platform trial and the number of data readouts expected to be delivered in 2026 and 2027, and related regulatory feedback; 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 provide anticipated readouts ahead of any disclosed bispecific approaches against our targets; expectations regarding our intellectual property portfolio, including our current and future patents and patent applications; use of net proceeds from our public offerings; the expected impact of macroeconomic conditions, including inflation, increasing interest rates and volatile market conditions, current or potential bank failures, as well as global events, including the ongoing military conflict in Ukraine, conflict between Israel and various other parties, recent events in Venezuela, geopolitical tensions between the United States and other countries, including China, on our operations, and the implementation of tariffs, sanctions, export or import controls, and other measures that restrict international trade by the United States, China or other governments; and the receipt and timing of potential regulatory designations, approvals and commercialization of product candidates, 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, including those described in Item 1A, “Risk Factors” included in this Annual Report. 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. In light of these risks, uncertainties, and assumptions, the forward-looking events and circumstances discussed in this Annual Report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. We undertake no obligation to update publicly any forward-looking

statements for any reason after the date of this report to conform these statements to actual results or to changes in our expectations, except as required by law. You should read this Annual Report with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

Unless the context indicates otherwise, as used in this Annual Report, the terms “Spyre,” "Aeglea BioTherapeutics, Inc.," "Aeglea," “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 Annual Report 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.

All references to “our product candidates,” “our programs” and “our pipeline” in this Annual Report 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. (“Paragon”) and Parapyre Holding LLC (“Parapyre”) (the “Paragon Agreement”).

Please be advised that on September 8, 2023, we effected a reverse stock split of our common stock at a ratio of 1-for-25 (the “Reverse Split”). Except as indicated otherwise, all share numbers related to our common stock disclosed in this Annual Report 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.”

PART I

ITEM 1. BUSINESS

Company Overview

Spyre Therapeutics, Inc. (NASDAQ: SYRE) is a clinical-stage biotechnology company pioneering long-acting antibodies and antibody combinations to redefine the standard of care for inflammatory bowel disease (“IBD”) and rheumatic diseases. Spyre’s pipeline includes extended half-life antibodies targeting α4β7, TL1A, and IL-23 in development as monotherapies and pair-wise combinations.

Our Strategy

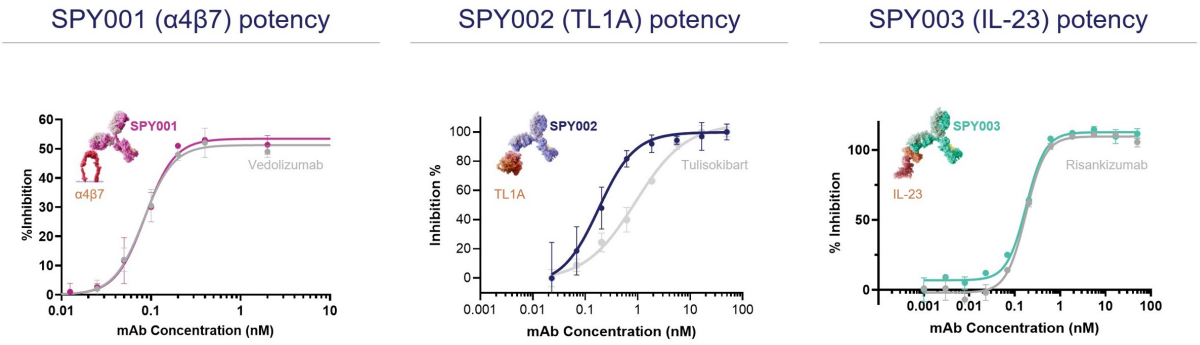
Our goal is to develop next-generation therapeutics to redefine the standard of care for the treatment of IBD and other immune-mediated diseases, relying on three strategic pillars:

- Advancing a portfolio of next-generation monotherapies - novel antibody candidates engineered for optimized potency, selectivity, and pharmacokinetics ("PK") against validated IBD targets
- Evaluating paradigm-changing IBD combinations - fixed-dose-combinations of our engineered investigational antibodies designed to enable superior efficacy, safety, and convenience
- Expansion of our anti-TL1A program into additional indications - pipeline-in-a-product potential in diseases with first-in-class and best-in-class opportunity, starting with rheumatoid arthritis ("RA"), psoriatic arthritis ("PsA"), and axial spondyloarthritis ("axSpA")

Next-generation monotherapies

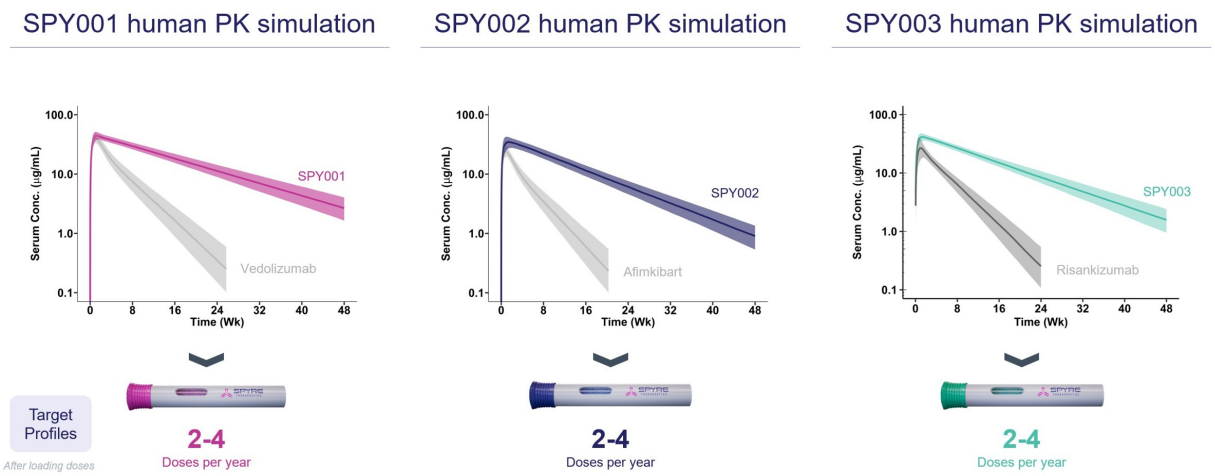
Our next-generation monotherapy antibody candidates targeting α4β7, TL1A, and IL-23 are engineered to match or exceed the potency of comparator first generation molecules (Figure 1), maintain selectivity, incorporate Fc domain modifications called YTE substitutions in order to increase pharmacokinetic half-life (Figure 2), and are formulated as high-concentration, citrate-free formulations. Combined, these attributes have the potential to enable quarterly or twice annual subcutaneous ("SC") maintenance dosing, and have upside potential to increase or accelerate efficacy via increasing PK exposures, based on published exposure-response or dose-response relationships for each mechanism in IBD.

Figure 1. Potency of SPY001, SPY002, and SPY003 compared to first-generation in-class molecules



Source: Data on file. Potency refers to in vitro potency: SPY001 assay reports inhibition of cells expressing a4b7 binding to MAdCAM-1. SPY002 assay reports inhibition of TL1A-induced apoptosis in TF-1 cells. SPY003 assay reports inhibition of cellular STAT3 signaling. Vedolizumab, tulisokibart, and risankizumab are synthesized comparator antibodies.

Figure 2. Increased pharmacokinetic half-life of SPY001, SPY002, and SPY003 compared to first-generation in-class molecules

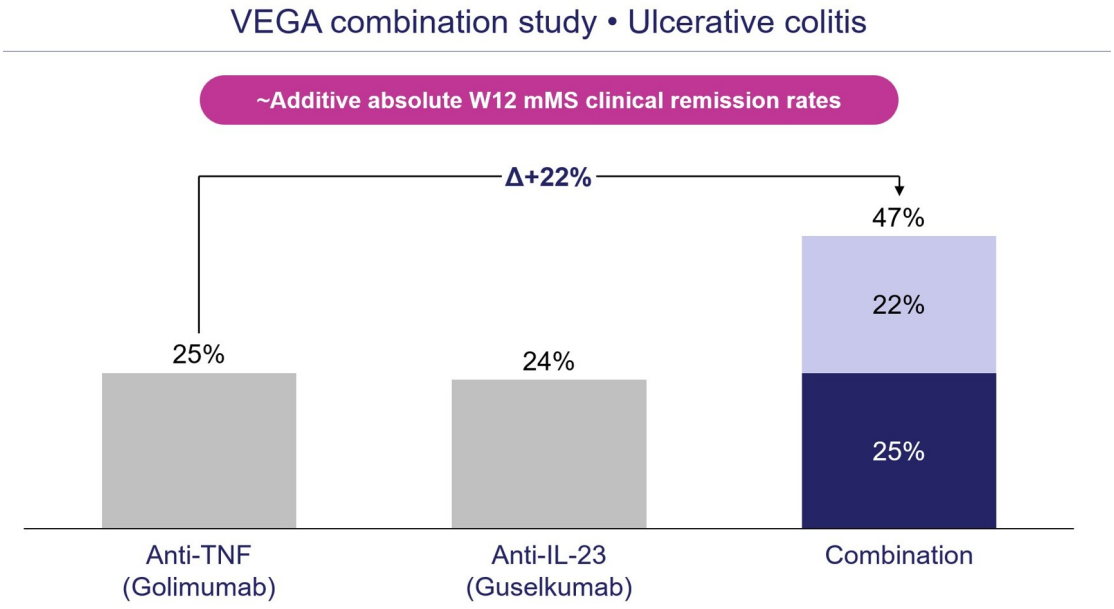


SPY001 PK simulation based on PK data as of 03/19/2025 cutoff; SPY002 PK simulation based on PK data from 5/31/2025 cutoff; SPY003 PK simulation based on PK data from 9/15/2025 cutoff. Vedolizumab, Afimkibart, and Risankizumab simulations based on published data (Rosario, M, et. al. (2015); Danese, Silvio, et al. (2024); Thakre, Neha et. al. (2024)); no head-to-head clinical trials have been conducted. Concept image of drug delivery device shown for illustrative purposes only.

Paradigm-changing IBD combinations

Each of our next-generation monotherapy antibody candidates was selected for its attractive risk-benefit profile in preclinical development and targets distinct pathways involved in the pathogenesis of IBD, with the goal of developing pairwise combination therapies. The benefits of co-administration of two targeted therapies in IBD were previously demonstrated by a third-party clinical trial where combination treatment with an anti-TNF antibody and an anti-IL-23 antibody resulted in approximately additive efficacy (47% clinical remission for the combination vs. 25% and 24% for each of the monotherapy agents, Figure 3). Spyre's portfolio of investigational combination therapies has unique potential to deliver products with superior efficacy, safety, and convenience compared to the other combination products in clinical development in IBD.

Figure 3. Third-party demonstration of combination therapy in IBD



Source: Feagan, B. G. et al. Lancet Gastroenterol. Hepatol. 8, 307–320 (2023). mMS=modified mayo score

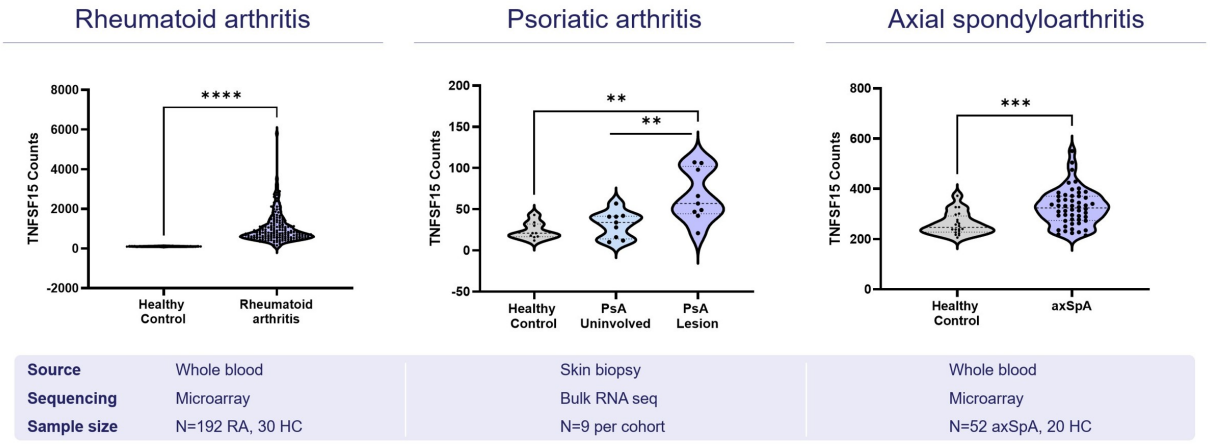
Anti-TL1A indication expansion

TL1A has been implicated in a wide range of human diseases beyond IBD based on genetic, translational, and/or preclinical data, including diseases within but not limited to: rheumatic diseases such as RA, PsA, and axSpA, as well as systemic sclerosis-interstitial lung disease, asthma, pulmonary sarcoidosis, psoriasis, hidradentis suppurativa, and atopic dermatitis. Among these diseases, multiple publications support anti-TL1A as a potential treatment option for rheumatic disease, with further validation from in-house in vivo experiments:

- TL1A is elevated in RA, PsA, and axSpA patients relative to healthy controls and increases with disease duration and severity (Figure 4)
- TL1A administration exacerbates arthritis in murine models of arthritis and administration of anti-TL1A antibodies reduces arthritis
- TL1A blockade using Spyre's anti-TL1A antibodies matched or exceeded the efficacy of anti-TNF treatment in a collagen induced rat model of arthritis
- Robust anti-TL1A activity further replicated in mouse models of arthritis and match the efficacy of anti-TNF (Figure 5)
- Additionally, anti-TL1A treatment led to comparable improvements in psoriatic skin lesions in mouse IMQ model as anti-IL-23 and anti-TNF (Figure 6)

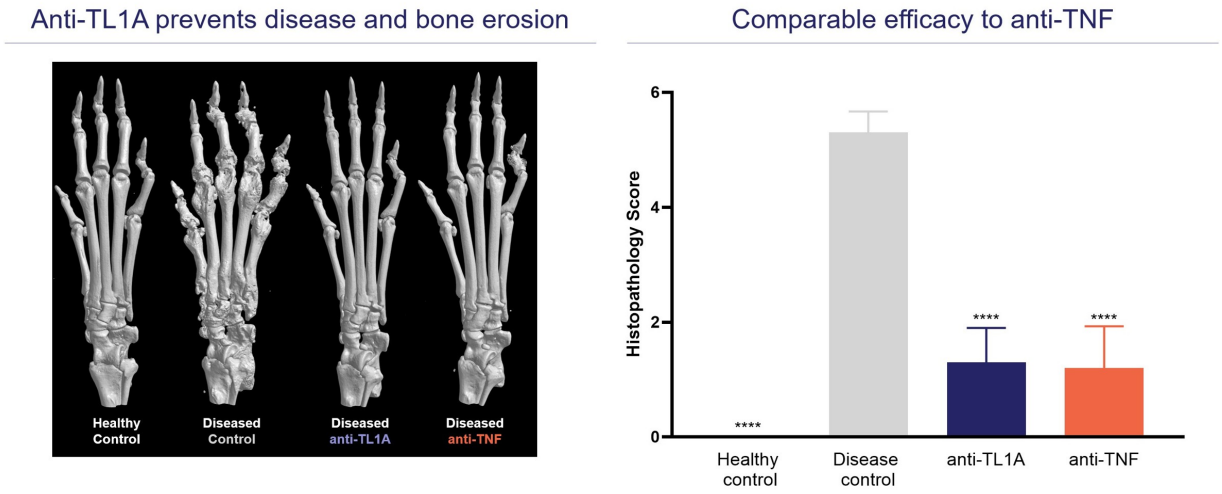
If successful in development and in obtaining regulatory approval, SPY072's projected quarterly to twice-annual subcutaneous dosing in a single autoinjector has the potential to be the first-in-class and best-in-class anti-TL1A for these rheumatic diseases and represents an attractive opportunity to meaningfully expand the value of our portfolio.

Figure 4. Upregulation of TL1A in RA, PsA, and axSpA relative to healthy controls



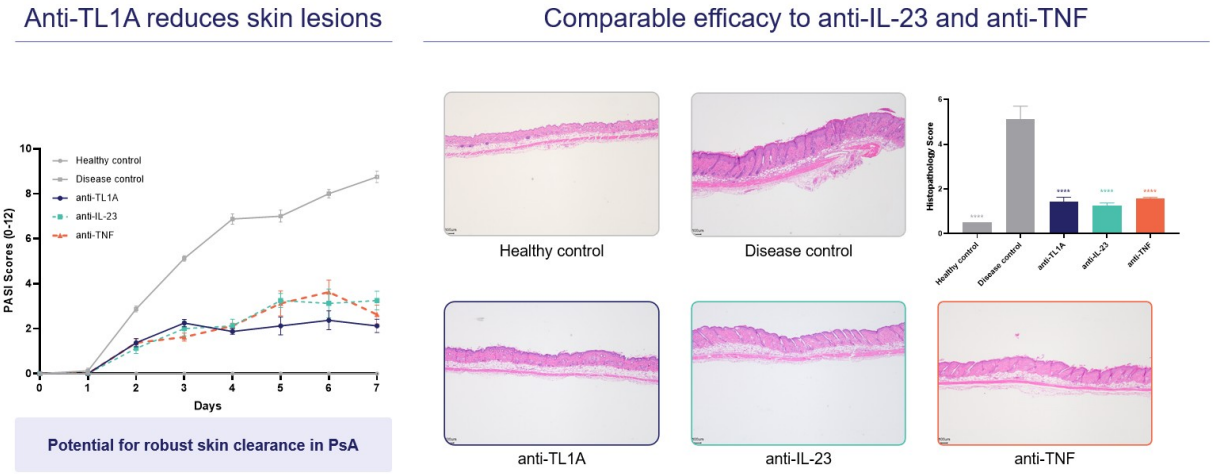
*Spyre analysis of RA-MAP, Li, Sifang, et al. BMC Musculoskeletal Disorders 25.1 (2024), and Johnsson, Hanna, et al. Arthritis Research & Therapy. ** P≤0.01, *** P ≤0.001, **** P ≤0.0001. Unpaired tailed t-test used for RA and axSpA analysis, One-way ANOVA used in PsA. RA=rheumatoid arthritis; PsA=psoriatic arthritis; axSpA=axial spondyloarthritis; HC=healthy controls.*

Figure 5. TL1A blockade matched or exceeded the efficacy of anti-TNF in rodent models of arthritis



*Source: Data on file. **** P ≤0.0001*

Figure 6. Anti-TL1A treatment improved IMQ-induced psoriatic skin lesions in mice with comparable efficacy to anti-IL-23 and anti-TNF



*Source: Data on file. **** P ≤0.0001*

Inflammatory Bowel Disease

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

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

experience steady growth, driven by rising disease prevalence, increasing diagnosis rates, and evolving treatment paradigms.

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

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

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

Rheumatoid Arthritis

RA is a chronic inflammatory autoimmune condition that primarily affects the joints. It is characterized by pain, stiffness and swelling of one or more joints and can progress from mild swelling of the joints in early stages to severe deformations of the feet, ankles, and hands in late/severe stages. RA is thought to arise from an aberrant immune response to modified proteins in mucosal tissue and the synovium, driven by genetic risk factors and environmental stressors. RA affects more than 1.5 million individuals in the U.S., with stable-to-increasing incidence of ~40 per 100,000 individuals. Despite several advanced treatment options, a significant number of people living with RA continue to suffer from active disease. Today's treatments are associated with many challenges, including low rates of remission, loss of response, and a high frequency of injections that may lead to poor compliance.

Psoriatic Arthritis

PsA is a chronic inflammatory autoimmune condition that typically affects both the joints and skin. It is characterized by pain, stiffness, and swelling of one or more joints and can progress from mild swelling of the joints in early stages to severe deformations of the joints in late/severe stages. Other characteristics can include psoriasis (PsO; scaly patches on the skin and/or nail discoloration and pitting), dactylitis (swollen fingers and toes), and spondylitis (painful inflammation in the spine). PsA is thought to arise from genetic and environmental triggers, though the pathogenesis is multifactorial and not well understood. PsA affects approximately 0.8 million individuals in the U.S., with estimates suggesting that up to 15% of PsO patients may have undiagnosed PsA. Despite several advanced treatment options, a significant number of people living with PsA continue to suffer from active disease. Today's treatments are associated with many challenges, including inability to adequately address both joint and skin symptoms, loss of response, and a high frequency of injections that may lead to poor compliance.

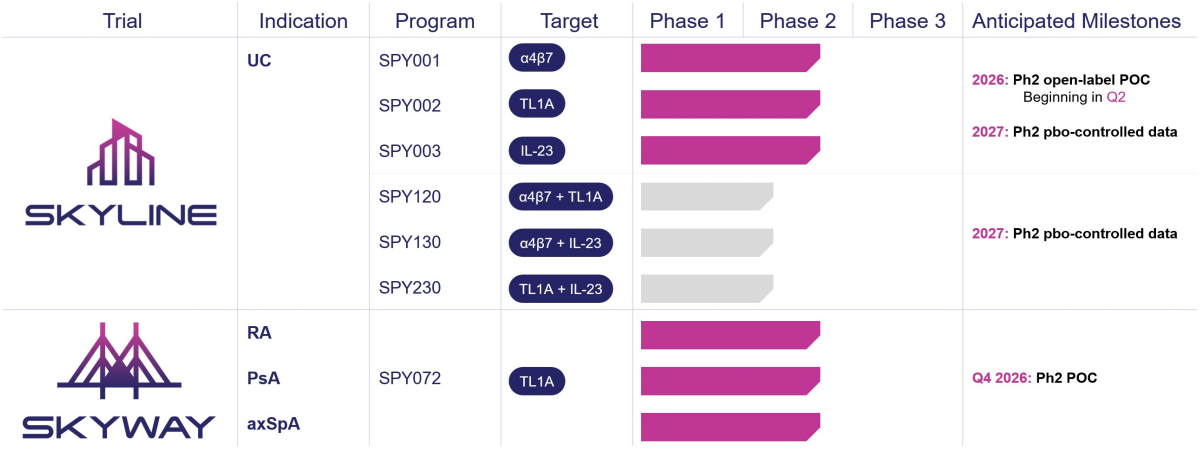
Axial Spondyloarthritis

AxSpA is a chronic inflammatory autoimmune condition that primarily affects the axial skeleton (spine), with radiographic and non-radiographic subtypes. It is characterized by persistent back pain, stiffness, fatigue, joint stiffness, and frequent occurrence of extra-articular manifestations, such as anterior uveitis, IBD, and psoriasis. AxSpA is thought to arise when biomechanical stress, genetics, environmental triggers, and other factors lead to overactivation of the immune system in the spine. AxSpA affects an estimated 3 million individuals in the U.S., though only approximately 1 million of those are diagnosed. Despite some advanced treatment options, a significant number of people living with axSpA continue to suffer from active disease. Today's treatments are associated with many challenges, including incomplete / loss of response, lack of MOAs to cycle through, and a high frequency of injections that may lead to poor compliance.

Our Portfolio

We are advancing a pipeline of monoclonal antibodies ("mAbs") for the treatment of IBD and other immune-mediated diseases. The following table (Figure 7) summarizes our pipeline and development strategy, including our SKYLINE Phase 2 platform trial evaluating SPY001, SPY002, SPY003, and pairwise combinations thereof in patients with moderately to severely active UC and our SKYWAY basket trial evaluating SPY072 in three rheumatic diseases: RA, PsA, and axSpA:

Figure 7. Spyre portfolio



SKYLINE Phase 2 Platform Trial in UC

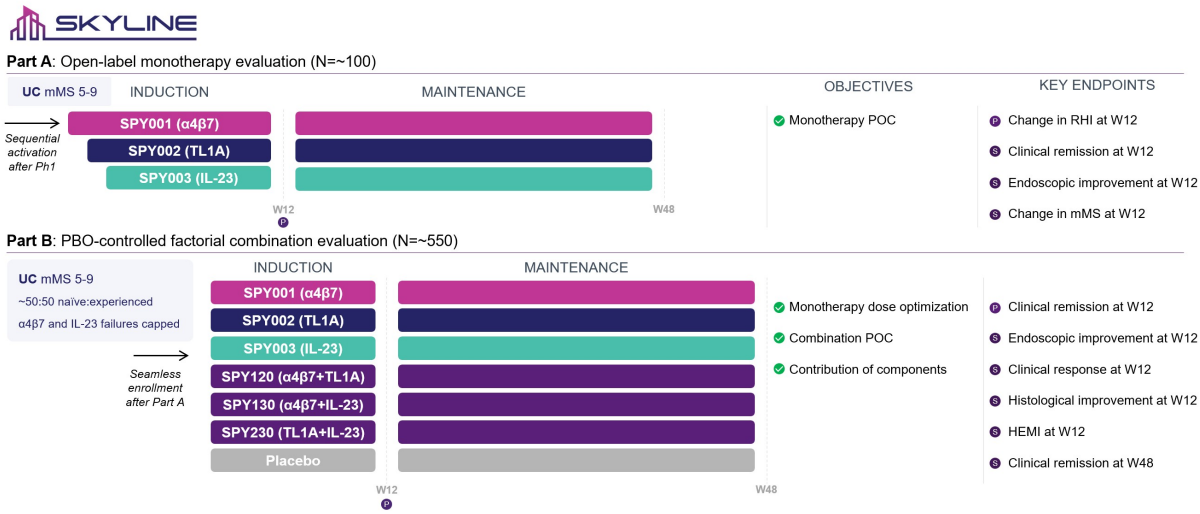
In May 2025, we initiated our SKYLINE Phase 2 platform trial evaluating SPY001, SPY002, SPY003, as well as pairwise combinations thereof (six investigational agents in total), in patients with moderately to severely active UC (Figure 8). The trial consists of two parts:

- **Part A:** Open-label assessment of the safety and preliminary efficacy of a single dose level of each investigational monotherapy, with induction data expected to begin reading out in Q2 2026.

- **Part B:** Randomized and placebo-controlled assessment of the safety and efficacy of monotherapies and combinations, designed to provide dose-ranging data on monotherapies, proof-of-concept and contribution of components for combinations, with induction data expected in 2027.

SKYLINE is currently enrolling subjects into Part A of the trial, with Part B expected to begin enrolling after all Part A arms complete enrollment.

Figure 8. SKYLINE trial design



mMS=modified mayo score; RHI=Robarts Histopathology Index; HEMI=Histo-Endoscopic Mucosal Improvement; P=primary endpoint; S=secondary endpoint. Initiation of each cohort subject to regulatory clearance.

SKYWAY Phase 2 Basket Trial in Rheumatic Diseases (RA, PsA, axSpA)

In September 2025, we initiated our SKYWAY Phase 2 randomized and placebo-controlled basket trial of SPY072 in patients with moderately to severely active RA, PsA, or axSpA (Figure 9). The trial consists of three sub-studies:

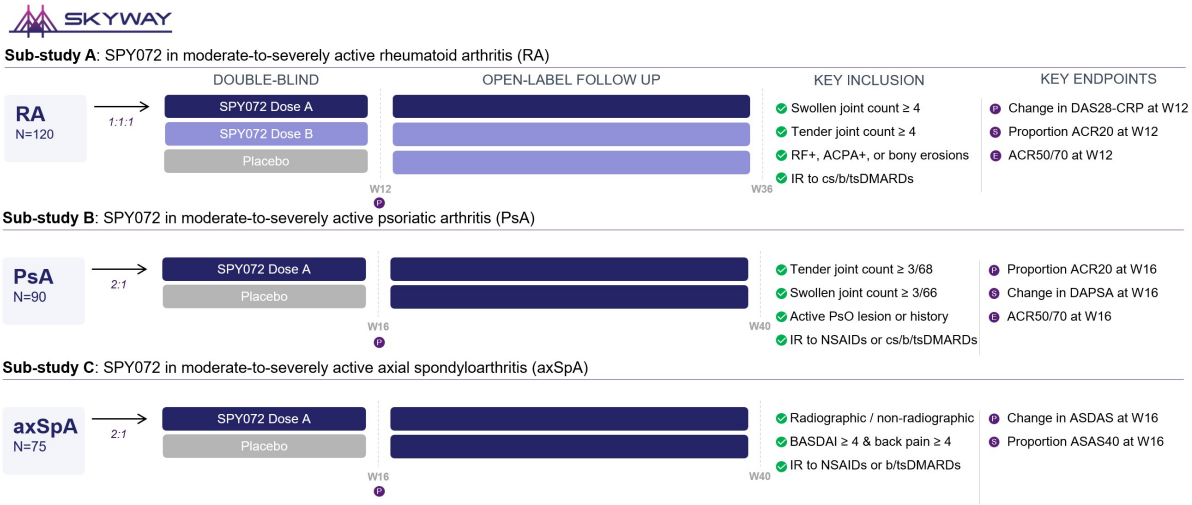
- **RA sub-study:** Double-blind, placebo-controlled safety and efficacy study of two dose levels of SPY072 at Week 12 with open-label follow-up through Week 36.

- **PsA sub-study:** Double-blind, placebo-controlled safety and efficacy study of a single dose level of SPY072 at Week 16 with open-label follow-up through Week 40.

- **axSpA sub-study:** Double-blind, placebo-controlled safety and efficacy study of a single dose level of SPY072 at Week 16 with open-label follow-up through Week 40.

Topline proof-of-concept data for all three indications are expected in Q4 2026.

Figure 9. SKYWAY trial design



RF=rheumatoid factor; ACPA= Anti-citrullinated protein antibodies; cs/b/tsDMARD=conventional synthetic, biologic, or targeted synthetic disease modifying antirheumatic drugs; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; P=primary endpoint; S=secondary endpoint; E=exploratory endpoint. IR=inadequate response

SPY001 – anti-α4β7 mAb

SPY001 is a highly potent, highly selective, and humanized monoclonal immunoglobulin G1 investigational antibody designed to bind selectively to the α4β7 integrin being developed for the treatment of IBD (UC and CD). The α4β7 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 α4β7 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 α4β7 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.

SPY001 demonstrates similar potency and selectivity as synthesized vedolizumab in preclinical *in vitro* models including surface plasmon residence and cellular adhesion assays. We initiated a first-in-human ("FIH") Phase 1 trial for SPY001 in June 2024. The SPY001 Phase 1 trial was a double blind, placebo-controlled trial in healthy volunteers consisting of a single-ascending dose ("SAD") component and a multi-ascending dose ("MAD") component. The trial enrolled 56 healthy adult participants into five SAD cohorts and two MAD cohorts

in the main portion of the trial. The primary endpoint was safety, with PK and anti-drug antibodies ("ADA") serving as secondary endpoints. Additional cohorts were added to the trial to evaluate PK in healthy volunteers of various ethnicities to facilitate subsequent global clinical trials.

Interim results were initially presented in November 2024, with additional data presented in May 2025 with up to eight months of follow up. To date, SPY001 has demonstrated a favorable safety profile across all dose groups, a meaningfully differentiated PK profile supporting potential quarterly or twice annual maintenance dosing, and rapid, complete saturation of α4β7 receptors beyond six months with a single dose of 600mg. Based on these results, SPY001 was advanced into the SKYLINE Phase 2 platform clinical trial.

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.

TL1A is a protein that plays a role in regulating the immune system and is elevated in gut tissue of individuals with IBD and serum or synovial tissue of individuals with RA, PsA, and axSpA. 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 IBD and rheumatic disease patients, potentially reducing disease activity.

SPY002 and SPY072 bind and inhibit TL1A with subnanomolar potency in preclinical cellular assays. We initiated FIH Phase 1 trials for SPY002 and SPY072 in the fourth quarter of 2024. The Phase 1 trials were each double blind, placebo-controlled evaluations in healthy volunteers, consisting of five SAD cohorts. Each trial enrolled 40 healthy adult participants across the five SAD cohorts in the main portion of the trial. The primary endpoint is safety, with PK and ADAs serving as secondary endpoints, and PD markers as exploratory endpoints. Phase 1 trial enrollment is complete.

Phase 1 data were presented in June 2025 and October 2025, with up to 24-weeks of follow up. To date, SPY002 and SPY072 have demonstrated favorable safety profiles, meaningfully differentiated PK profiles supporting potential quarterly or twice annual maintenance dosing, and complete suppression of free TL1A through up to 20-24 weeks at single 100mg doses. Based on these results, SPY002 has advanced to the SKYLINE Phase 2 platform trial and SPY072 has advanced to the SKYWAY Phase 2 basket trial.

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 ("NHPs").

We initiated a FIH trial in March 2025. The SPY003 Phase 1 trial is a double blind, placebo-controlled trial in healthy volunteers trial that enrolled 59 healthy adult participants into five SAD cohorts, one multiple dose (MD) cohort, and one Chinese ethnobridging cohort. The primary endpoint is safety, with PK and ADAs serving as secondary endpoints. Phase 1 trial enrollment is now complete.

Interim Phase 1 data were disclosed in November 2025, and additional data were presented in February 2026 with up to 20 weeks of follow-up, demonstrating that SPY003 exhibited a favorable safety profile

and a meaningfully differentiated PK profile supporting quarterly or twice annual maintenance dosing. Based on these results, SPY003 was advanced to the SKYLINE Phase 2 platform trial.

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.

These preclinical data, in addition to our positive interim Phase 1 results for SPY001 and SPY002, support the advancement of SPY120 into Part B of the SKYLINE Phase 2 platform trial.

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.

These preclinical data, in addition to our positive interim Phase 1 results for SPY001 and SPY003, support SPY130 being advanced in Part B of the SKYLINE Phase 2 platform trial.

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.

These preclinical data, in addition to our positive interim Phase 1 results for SPY002 and SPY003, support SPY230 being advanced in Part B of the SKYLINE Phase 2 platform trial.

Employees and Human Capital Resources

As of December 31, 2025, we had 102 employees, all of whom were employed full time. We also engage temporary employees and consultants to augment our existing workforce. None of our employees are represented by a labor union or covered under a collective bargaining agreement. We consider our relationship with our employees to be good.

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

Commercial

Should any of our product candidates be approved for commercialization, we intend to develop a plan to commercialize them in the United States and other key markets, through internal infrastructure and/or external partnerships in a manner that will enable us to realize the full commercial value of our product candidates. In January 2026 we hired our first Chief Commercial Officer, but given our stage of development, we have not yet established a robust commercial organization or distribution capabilities.

Manufacturing and Supply

We do not currently own or operate facilities for product manufacturing, testing, storage, and distribution. All of our nonclinical and clinical drug supply development, manufacturing, storage, distribution and testing are outsourced to third-party manufacturers and facilities. Our manufacturing strategy enables us to more efficiently direct financial resources to the research, development and commercialization of programs rather than diverting resources to internally develop and maintain manufacturing facilities. As our programs advance through development, we expect to enter into longer-term commercial supply agreements with key suppliers and manufacturers to fulfill and secure our supply needs.

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

On December 18, 2025, President Trump signed the Fiscal Year 2026 National Defense Authorization Act, which includes the BIOSECURE Act. The BIOSECURE Act prohibits federal departments and agencies from contracting with or providing loans or grants to any entity where the biotechnology equipment or services of a designated "biotechnology company of concern" ("BCOC") would be used in the performance of that contract, grant, or loan. Generally, a BCOC is a biotechnology company that is subject to the jurisdiction, direction, control, or operates on behalf of a foreign adversary's government and poses a risk to the national security of the U.S. BCOCs include entities listed on the Department of Defense Section 1260H list of "Chinese military companies" and additional entities to be designated through an interagency process led by the Office of Management and Budget ("OMB"). OMB has not yet identified any BCOCs. We are in the process of creating manufacturing capabilities with third parties outside of China, including within the United States, and have taken several measures to strengthen our supply chain in the event that our manufacturers are impacted. Among other things, we intend to establish domestic inventory of key materials and are accelerating our clinical resupply campaigns to ensure we have a sufficient stockpile of drug substance. We will also continue to closely monitor geopolitical risk and implement additional mitigations and supply chain redundancies, as needed. See the risk factors entitled “We may be negatively impacted by changes in law or other policy, including healthcare reform initiatives,” and “We currently rely, and plan to rely in the future, on third parties to conduct and support our preclinical studies and clinical trials. If these third parties do not properly and successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our product candidates.”

Biologics Master Services Agreement

In April 2023, Paragon and WuXi Biologics entered into the WuXi Biologics MSA, which was subsequently novated to us by Paragon on September 19, 2023 pursuant to the Novation Agreement. The WuXi Biologics MSA was subsequently amended and restated in October 2024. The WuXi Biologics MSA governs certain development activities and Good Manufacturing Practice ("GMP") manufacturing and testing for the SPY001, SPY002, and SPY003 programs, as well as potential future programs, on a work order basis. Under the WuXi Biologics MSA, we are obligated to pay WuXi Biologics a service fee and all non-cancellable obligations in the amount specified in each work order associated with the agreement for the provision of services.

The WuXi Biologics MSA terminates on the later of (i) October 14, 2029 or (ii) the completion of services under all work orders executed by the parties prior to October 14, 2029, unless terminated earlier. The term of each work order terminates upon completion of the services under such work order, unless terminated earlier. We can terminate the WuXi Biologics MSA or any work order at any time upon 30 days' prior written notice and immediately upon written notice if WuXi Biologics fails to obtain or maintain required material governmental licenses or approvals. We can also terminate the WuXi Biologics MSA, or any work order, in the event that any law is enacted that has, or could be reasonably expected to have, a material adverse effect on us or any of our products that is the subject of the WuXi Biologics MSA, in each case, as a result of WuXi Biologics providing services under the WuXi Biologics MSA or us being a party to the WuXi Biologics MSA. Either party may terminate a work order (i) at any time upon six months' prior notice with reasonable cause, provided however that if WuXi Biologics terminates a work order in such manner, no termination or cancellation fees shall be paid by us and (ii) immediately for cause upon (a) the other party's material breach that remains uncured for 30 days after notice of such breach, (b) the other party's bankruptcy or (c) a force majeure event that prevents performance for a period of at least 90 days.

Cell Line License Agreement

In April 2023, Paragon and WuXi Biologics entered into the Cell Line License Agreement, which was subsequently novated to us by Paragon pursuant to the Novation Agreement. The Cell Line License Agreement was subsequently amended and restated in October 2024. Under the Cell Line License Agreement, we received a non-exclusive, worldwide, sublicensable license to certain of WuXi Biologics's know-how, cell line, biological materials (the "WuXi Biologics Licensed Technology") and media and feeds to make, have made, use, sell and import certain therapeutic products produced through the use of the cell line licensed by WuXi Biologics under the Cell Line License Agreement (the "WuXi Biologics Licensed Products"). Specifically, the WuXi Biologics Licensed Technology is used in certain manufacturing activities in support of the SPY001, SPY002, and SPY003 programs.

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

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

Intellectual Property

Overview

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

Patent Rights Relating to Our Anti-α4β7 Program

As of January 31, 2026, we exclusively license or owned four patent families directed to antibodies that target integrin receptor α4β7, including SPY001, pharmaceutical formulations and compositions, and methods of using those antibodies. The first patent family is directed to compositions of matter including SPY001, method of treatment and dosing regimen and includes 2 U.S granted patents and patent applications filed in the U.S. and in foreign jurisdictions including Europe, Japan, and China. We would expect these patents upon issuance to expire in 2044, absent any applicable patent term extensions. The second patent family is directed to methods of using SPY001 and includes an international (PCT) patent application. If the PCT patent application is pursued in the U.S. or any foreign jurisdictions and matures into one or more issued patents, we would expect those patents to expire in 2045, absent any applicable patent term extensions. The third patent family is directed to pharmaceutical formulations containing SPY001 and includes a PCT patent application. If the PCT patent application is pursued in the U.S. or any foreign jurisdictions and matures into one or more issued patents, we would expect those patents to expire in 2045, absent any applicable patent term extensions. The fourth patent family is directed to other α4β7 antibody compositions and includes a U.S. patent application and a PCT patent application. If the PCT patent application is pursued in any foreign jurisdictions and matures into one or more issued patents, and if the US patent application matures into a U.S. patent, we would expect those patents upon issuance to expire in 2044, absent any applicable patent term extensions.

Patent Rights Relating to Our Anti-TI1A Program

As of January 31, 2026, we exclusively license or own ten patent families directed to antibodies that target TL1A, including SPY002 and SPY072, and methods of using those antibodies. The first patent family is directed to SPY002 and SPY072 compositions of matter and includes 2 U.S. granted patents, and a PCT patent application. If the PCT application is pursued in any foreign jurisdictions and matures into one or more issued patents, we would expect those patents upon issuance to expire in 2044, absent any applicable patent term extensions. The second patent family is directed to composition comprising other anti-TL1A antibody compositions and includes applications filed in the U.S., Europe, Japan, and China. If Spyre pursues the U.S. or any foreign jurisdictions and it matures into one or more issued patents, we would expect those patents upon issuance to expire in 2044, absent any applicable patent term extensions. The next six patent families are directed to methods of using SPY002 and SPY072 and includes six PCT patent applications. If these PCT patent applications are pursued in the U.S. and any foreign jurisdictions and mature into one or more issued patents, we would expect those patents upon issuance to expire in 2046, absent any applicable patent term extensions. The remaining two patent families are directed to SPY002 and SPY072 compositions and as of January 31, 2026, each family includes two provisional patent applications. If these provisional applications are pursued non-provisionally and mature into one or more issued patents, we would expect those patents upon issuance to expire in 2046, absent any applicable patent term extensions.

Patent Rights Relating to Our Anti-IL-23 Program

As of January 31, 2026, we exclusively license or own two patent families directed to antibodies that target IL-23, including SPY003, and methods of using those antibodies and formulations thereof. The first patent family is directed to compositions of matter including SPY003 and includes a U.S. patent application and a PCT patent application. If the PCT patent application is pursued in any foreign jurisdictions and matures into an issued patent or the Argentina or Taiwan applications are pursued and mature into one or more issued patents, we would expect those patents upon issuance to expire in 2045, absent any applicable patent term extensions. The second patent family is directed to pharmaceutical formulations and compositions including SPY003 and as of January 31, 2026, includes one provisional application. If the provisional application is pursued non-provisionally and matures into one or more issued patents, we would expect those patents upon issuance to expire in 2046, absent any applicable patent term extensions.

Patent Rights Relating to Our Combination Programs

As of January 31, 2026, we own four patent families directed to combinations of SPY001, SPY002, and SPY003. The first patent family is directed to methods of treatment with a combination of SPY001 and SPY002 (SPY120) and includes a PCT patent application. If the PCT application is pursued in the U.S. or any foreign jurisdictions and matures into one or more issued patents, we would expect those patents upon issuance to expire in 2045, absent any applicable patent term extensions. The second patent family is directed to methods

of treatment with a combination of SPY001 and SPY003 (SPY130) and includes, as of January 31, 2026, one provisional application. If this provisional application is pursued non-provisionally and matures into one or more issued patents, we would expect those patents upon issuance to expire in 2046, absent any applicable patent term extensions. The remaining two patent families are directed to methods of treatment with a combination of SPY002 and SPY072 and SPY003 (SPY230) and as of January 31, 2026, each family includes two provisional patent applications. If these provisional applications are pursued non-provisionally and mature into one or more issued patents, we would expect those patents upon issuance to expire in 2046, absent any applicable patent term extensions.

Other IP Rights

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

Trademark Rights Relating to the Spyre Therapeutics Name and Logo

As of January 31, 2026, we own trademark registrations for the Spyre name and name plus logo for research and development services of new pharmaceutical products in Australia, China, Europe, and the UK.

Paragon Agreement

In May 2023, Pre-Merger Spyre entered into the Paragon Agreement with Paragon and Parapyre. Pursuant to the Paragon Agreement, we received the option to license the intellectual property rights related to four research programs (collectively, the "Option") from Paragon in accordance with a license agreement to be entered into following each exercise of the Option.

On July 12, 2023, December 14, 2023 and June 5, 2024, we exercised our Option available under the Paragon Agreement with respect to the SPY001, SPY002 and SPY003 research programs, respectively. In May 2024, we signed license agreements with Paragon for rights to royalty-bearing, world-wide, exclusive licenses to develop, manufacture, commercialize or otherwise exploit certain antibodies and products targeting α4β7 integrin (SPY001 program) (the "SPY001 License Agreement") and TL1A (SPY002 program) (the "SPY002 License Agreement") and, in October 2024, we signed a license agreement for rights to a royalty-bearing, world-wide, exclusive license to develop, manufacture, commercialize or otherwise exploit certain antibodies and products targeting IL-23 (SPY003 program) (the "SPY003 License Agreement" and, together with the SPY001 License Agreement and the SPY002 License Agreement, the "License Agreements") in the field of IBD. The SPY003 License Agreement was subsequently amended and restated in February 2025 to, among other things, clarify each party's rights and obligations with respect to license exclusivity and patent prosecution and correct certain clerical errors. The Option with respect to one additional program remains unexercised under the Paragon Agreement.

Under the terms of each License Agreement, we are obligated to pay Paragon up to $22.0 million upon the achievement of specific development, regulatory and clinical milestones for the first product under each agreement, respectively, that achieves such specified milestones, including a milestone payment of $5 million upon the first dosing of a human patient in a Phase 3 trial. With respect to the SPY002 License Agreement only, on a product by product basis, we are obligated to pay sublicensing fees of up to approximately $20 million upon the achievement of mostly commercial milestones. Subject to the execution of the Option with respect to the remaining research program, we expect to be obligated to make similar payments upon and following the execution of a license agreement with respect to such research program.

Competition

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

We are aware of several companies with product candidates in development for the treatment of patients with IBD, including Merck's tulisokibart, Roche/Roivant's afimkibart, and Sanofi/Teva's duvakitug TL1A antibodies; additional IL-23/IL-23Rs including icotrokinra (Johnson & Johnson) and picankibart (Innovent); oral anti-integrin agents including Lilly's MORF-057, and Gilead's GS-1427; PDE4 inhibitor PALI-2108 (Palisade Bio); multispecifics including PF-07261271 targeting TL1A and IL-12/23 (Pfizer and Roche), SOR102 targeting TNF and IL-23 (Sorriso), HXN-1002 targeting α4β7 and TL1A (Sanofi/Earendil), HXN-1003 targeting TL1A and IL-23 (Sanofi/Earendil), SIM0709 targeting TL1A and IL-23 (Simcere and Boehringer Ingelheim) and XmAb412 targeting TL1A and IL-23 (Xencor).

If approved for the treatment of patients with moderate-to-severe RA, SPY072 would compete with TNF antibodies including Humira (AbbVie), Cimzia (UCB), Enbrel (Amgen), Remicade (Johnson & Johnson), and Simponi (Johnson & Johnson); T-cell activation inhibitor Orencia (Bristol Myers Squibb); IL-6R antibodies Actemra (Roche) and Kevzara (Sanofi); CD20 antibody Rituxan (Roche); IL-1R antibody Kineret (Sobi); and JAK inhibitors including Xeljanz (Pfizer), Rinvoq (AbbVie), and Olumiant (Lilly). Our products would also compete with biosimilars or generics, either currently approved or in development, to many of these products.

We are aware of several companies with product candidates in development for the treatment of patients with RA, including Merck's tulisokibart and Roche/Roivant's afimkibart TL1A antibodies; Anaptys' rosnilimab, Johnson and Johnson's JNJ-4703, and Gilead's GS-0151 PD-1 agonists; RIPK1 inhibitors including Lilly's ocadusertib; additional TNF inhibitors including Zenas' ZB002 half-life extended antibody and Sanofi's oral small molecule balinatunfib; BTLA agonist GS-0272 (Gilead); Treg cell therapy SBT-77-7101 (Sonoma Biotherapeutics); MC1/3 agonist resomelagon/AP1189 (Synact Pharma); bispecific fusion proteins including plamotamab/XmAb-13676 (Xencor); and IL-1α/β inhibitors including a lutikizumab and ravagalimab combination (AbbVie).

If approved for the treatment of patients with moderate-to-severe PsA, SPY072 would compete with TNF antibodies including Humira (AbbVie), Cimzia (UCB), Enbrel (Amgen), Remicade (Johnson & Johnson), and Simponi (Johnson & Johnson); T-cell activation inhibitor Orencia (Bristol Myers Squibb); IL-17 antibodies Cosentyx (Novartis), Taltz (Lilly), and Bimzelx (UCB); CD20 antibody Rituxan (Roche); IL-12/23 antibody Stelara (Johnson & Johnson); IL-23 antibodies Skyrizi (AbbVie) and Tremfya (Johnson & Johnson); PDE4 antibody Otezla (Amgen); and JAK inhibitors including Xeljanz (Pfizer) and Rinvoq (AbbVie). Our products would also compete with biosimilars or generics, either currently approved or in development, to many of these products.

We are aware of several companies with product candidates in development for the treatment of patients with PsA, including TYK2 inhibitor Sotyktu (Bristol Myers Squibb); IL-23 antibodies including icotrokinra (Johnson & Johnson) and tildrakizumab (Sun Pharma); IL-17A/F nanobody sonelokimab (MoonLake); and multiple combination trials including a Tremfya (IL-23) and Simponi (TNF) combination (Johnson & Johnson), a lutikizumab (IL-1α/β) and Skyrizi (IL-23) combination (AbbVie), and a Taltz (IL-17) and Zepbound (GIP/GLP-1 receptor agonist) combination (Lilly).

If approved for the treatment of patients with moderate-to-severe axSpA, SPY072 would compete with TNF antibodies including Humira (AbbVie), Cimzia (UCB), Enbrel (Amgen), Remicade (Johnson & Johnson), and Simponi (Johnson & Johnson); IL-17 antibodies Cosentyx (Novartis), Taltz (Lilly), and Bimzelx (UCB); and JAK inhibitors including Xeljanz (Pfizer) and Rinvoq (AbbVie). Our products would also compete with biosimilars or generics, either currently approved or in development, to many of these products.

We are aware of several companies with product candidates in development for the treatment of patients with axSpA, including TL1A inhibitor tulisokibart (Merck); IL-17A inhibitor gumokimab (Akesobio) and IL-17A/F nanobody sonelokimab (MoonLake); and PDE4 inhibtior mufemilast (Hemay).

Government Regulation

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of biologics such as those we are developing. We, along with our third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. Generally, before a new therapeutic product can be marketed, considerable data demonstrating a biological product candidate's quality, safety, purity and potency, or a small molecule drug candidate's quality, safety and efficacy, must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority. For biological product candidates, potency is similar to efficacy and is interpreted to mean the specific ability or capacity of the product, as indicated by appropriate laboratory tests or by adequately controlled clinical data obtained through the administration of the product in the manner intended, to effect a given result.

Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post-marketing may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications from the sponsor, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on our company and our products or product candidates.

United States Biologics Regulation

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

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

- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMPs, and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with GCP; and
- FDA review and approval of a BLA to permit commercial marketing of the product for particular indications for use in the United States.

Preclinical and Clinical Development

Once a therapeutic product candidate is identified for development, it must undergo preclinical studies before commencing any testing in humans. Preclinical studies include laboratory evaluations of product chemistry, formulation and stability, as well as studies to evaluate the candidate's potential for efficacy and toxicity in animals. The conduct of preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including current GLPs.

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

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

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

Human clinical trials are typically conducted in three sequential phases that may overlap.

- Phase 1. The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2. The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to

identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- Phase 3. The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

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

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

BLA Submission and Review

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

In addition, under the Pediatric Research Equity Act ("PREA"), a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless a different timeline has been previously agreed upon by the FDA, through approval of a pediatric study plan, described below. The Food and Drug Administration Safety and Innovation Act requires that a sponsor who is planning to submit a marketing application for a biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial pediatric study plan ("PSP") within sixty days after an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. Once a BLA has been accepted for filing, the FDA's goal is to review standard applications within ten months after the FDA accepts the application for filing, or, if the application qualifies for priority review, six months after the FDA accepts the application for

filing. In both standard and priority reviews, the review process may also be extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may convene an advisory committee to provide clinical insight on application review questions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

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

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

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

Expedited Development and Review Programs

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

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

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

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

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

Combination Therapy

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

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

encouraged sponsors to engage in early and regular consultation with the relevant review division at the agency throughout the development process for its proposed combination.

Regulation of Combination Products

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

Post-Approval Requirements

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

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

or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

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

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and consistent with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label uses of their products. Additionally, promotional materials for approved biologic products must be submitted to the FDA in conjunction with their first use.

Biosimilars and Reference Product Exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the "ACA"), includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), which created an abbreviated approval pathway for biological products that are highly similar, or "biosimilar," to or interchangeable with an FDA-approved reference biological product. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

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

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. Additionally, many states have passed laws concerning the ability of pharmacies to substitute biosimilar and interchangeable products for the reference product.

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

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

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

Patent Term Extension

In the United States, after a BLA is approved, owners of relevant drug patents may apply for up to a five-year patent extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory process. The allowable patent term extension is typically calculated as one-half the time between, the latter of the effective date of an IND and issue date of the patent for which extension is sought, and the submission date of a BLA, plus the time between BLA submission date and the BLA approval date up to a maximum of five years. The time can be shortened if the FDA determines that the applicant did not pursue licensure with due diligence. The total patent term after the extension may not exceed 14 years from the date of product licensure. Only one patent applicable to a licensed biological product is eligible for extension and only those claims covering the product, a method for using it, or a method for manufacturing it may be extended and the application for the extension must be submitted prior to the expiration of the patent in question. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Some, but not all, foreign jurisdictions possess patent term extension or other additional patent exclusivity mechanisms that may be more or less stringent and comprehensive than those of the United States.

Other Healthcare Laws and Compliance Requirements

Biopharmaceutical manufacturers, particularly manufacturers of marketed products, are subject to wide-ranging healthcare regulation and enforcement by federal, state and local government authorities in the U.S. as well as by foreign jurisdictions. Biopharmaceutical manufacturers must comply with various federal, state and local laws targeting fraud and abuse in the healthcare industry, including anti-kickback and false claims laws.

The federal Anti-Kickback Statute generally prohibits, among other things, a pharmaceutical manufacturer from directly or indirectly soliciting, offering, receiving, or paying any remuneration in cash or in kind where one purpose is either to induce the referral of an individual for, or the purchase or prescription of, a particular drug that is payable by a federal health care program, including Medicare or Medicaid. A person or entity does not need to have actual knowledge of the statute or a specific intent to violate the statute. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, but protection is available only if all requirements are met. Our practices, such as paying

physicians for consulting services, may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. A claim arising from a violation of the federal Anti-Kickback Statute also constitutes a false or fraudulent claim for purposes of the FCA. Other federal and state anti-kickback statutes exist. For example, another healthcare anti-kickback statute prohibits certain payments related to referrals of patients to certain providers (such as clinical laboratories) and applies to services reimbursed by private health plans as well as government health care programs.

Federal and state false claims laws, such as the federal civil False Claims Act (“FCA”), generally prohibit anyone from knowingly and willfully, among other activities, presenting, or causing to be presented for payment to third party payors (including Medicare and Medicaid) claims for drugs or services that are false or fraudulent. Pharmaceutical and other healthcare companies have been prosecuted under these laws for engaging in a variety of different types of conduct that “caused” the submission of false claims to federal healthcare programs. Such laws are not always limited to activities involving government programs or payors. For example, a federal healthcare fraud statute prohibits the knowing and willful execution, or attempt to execute, a scheme to defraud a health care benefit program, including private health plans, or obtain, through false or fraudulent pretenses, money or property owned by, or under the custody or control of, such a health care benefit program. Laws and regulations have also been enacted by the federal government and various states to regulate the sales and marketing practices of pharmaceutical manufacturers. The laws and regulations generally limit financial interactions between manufacturers and health care providers; require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government; and/or require disclosure to the government and/or public of financial interactions (so-called “sunshine laws” and "sunshine reporting"). State and local laws may also require disclosure of pharmaceutical pricing information and marketing expenditures or licensure of sales representatives. Manufacturers must also submit information to the FDA on the identity and quantity of drug samples requested and distributed by a manufacturer during each year.

Biopharmaceutical manufacturers are also subject to federal pricing and price reporting laws. Such laws require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products. The laws may also require biopharmaceutical manufacturers to offer products at discounted prices to specific government programs or specific purchasers as a condition for participation in certain government health benefit programs. Federal consumer protection and unfair competition laws broadly regulate our marketplace activities and activities that potentially harm consumers.

The distribution of biological products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage, and security requirements intended to prevent the unauthorized sale of such products.

Sanctions for the violation of healthcare laws vary by law but may be significant and compliance is challenging. For example, violations of fraud and abuse laws may be punishable by criminal or civil sanctions, including fines and civil monetary penalties, and/or exclusion from federal health care programs (including Medicare and Medicaid). The scope of the federal and the various analogous state anti-kickback, false claims, and similar fraud and abuse laws vary, but is generally broad. Many of the fraud and abuse laws and regulations contain ambiguous requirements or require administrative guidance for implementation. Federal and state authorities are paying increased attention to enforcement of these laws within the pharmaceutical industry, and private individuals have been active in alleging violations of the laws and bringing suits on behalf of the government under the FCA as evidenced by numerous significant settlements. Violations of international fraud and abuse laws could result in similar penalties, including exclusion from participation in health programs outside the U.S.

Given the scope, complexity and lack of clarity in healthcare laws and their implementation, our activities could be subject to scrutiny and the imposition of penalties under the laws. If we were subject to allegations concerning, or were convicted of violating, these laws, our business could be harmed.

Data Privacy and Cybersecurity Requirements (U.S.)

We are subject to numerous and evolving U.S. federal and state laws and regulations governing the collection, use, disclosure, transfer, and security of personal information, including health-related information, any of which may impose operational constraints, create compliance complexity, and increase enforcement and litigation exposure. Applicable federal and state frameworks include HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH"), and its implementing regulations (including the Privacy, Security, Breach Notification, and Enforcement Rules), state health information privacy laws, state data breach notification laws, a growing number of state comprehensive consumer privacy laws, as well as other consumer protection laws and regulations that could apply to our operations or the operations of our partners. In addition, sector- and data-specific laws—such as those addressing marketing communications, data security, and the sale/transfer of certain bulk sensitive data—may apply to aspects of our operations or the operations of our partners. In addition to statutory regimes, we are also subject to evolving state tort and other common law restrictions that may govern privacy and data security practices, including potential duties and liability under theories such as negligence, invasion of privacy, breach of confidence, and implied contract. Courts and enforcement authorities continue to apply and test these doctrines in the data privacy and cybersecurity context, which can expand obligations and remedies and increase litigation exposure and compliance costs

Certain of our activities may be subject to HIPAA, which imposes standards for the privacy of protected health information ("PHI"), the security of electronic PHI, breach notification to individuals and regulators, and enforcement. HIPAA applies directly to "covered entities" (health care providers, health plans, and health care clearinghouses), as well as their "business associates" and their covered subcontractors that perform certain services that involve using, disclosing, creating, receiving, maintaining, or transmitting individually identifiable PHI for or on behalf of such covered entities.

Requirements imposed by HIPAA on covered entities and business associates include: (i) entering into agreements that require business associates and their covered subcontracts to protect PHI provided by the covered entity against improper use or disclosure; (ii) complying with HIPAA privacy standards that limit the use and disclosure of information about a patient's past, present, or future physical or mental health or condition, or the patient's receipt of health care, where the information identifies, or could reasonably be used to identify, the individual; (iii) implementing administrative, physical, and technical safeguards to ensure the confidentiality, integrity, and availability of electronic PHI and to protect against reasonably anticipated threats, hazards, or impermissible uses or disclosures; and (iv) reporting of breaches of unsecured PHI to affected individuals and, where applicable, regulators. Entities found to be in violation of HIPAA may be subject to significant civil, criminal, and administrative fines and penalties, and may be required to enter into resolution agreements and corrective action plan with the U.S. Department of Health and Human Services ("HHS") to resolve allegations of non-compliance. A covered entity or business associate can also be liable for civil money penalties for violations based on an act or omission of its agents, including downstream business associates. HITECH increased the civil and criminal penalties applicable to covered entities and business associates and authorized state attorneys general to bring civil actions in federal court to enforce HIPAA and seek damages, injunctive relief, and attorneys' fees and costs. To the extent we submit electronic healthcare claims and payment transactions that do not comply with HIPAA's electronic data transmission standards, payments to us may be delayed or denied.

Several states have enacted or are implementing health-data-specific statutes outside HIPAA—such as laws in Washington and Nevada—that broadly regulate the collection, use, and disclosure of "consumer health data," including certain research, analytics, website, and marketing activities. These laws may impose consent, notice, contract, and data security obligations, create limitations on sharing with third parties and processors, and provide private rights of action or enhanced enforcement, which could affect aspects of our operations that are not subject to HIPAA. Even where HIPAA and state health information privacy laws do not apply, the FTC and state attorneys general have asserted that violations of consumer privacy or failures to implement appropriate data security measures may constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act and state consumer protection laws.

In addition, the amended CCPA and approximately 19 other comprehensive state privacy laws, together with their implementing regulations, establish individual rights regarding personal information, impose notice, purpose-limitation, data minimization, and security obligations, and require specific contracts with service

providers and other third parties. Some of these laws also require honoring opt-out signals for targeted advertising or certain profiling, restrict processing of "sensitive" personal information, and mandate assessments for higher-risk processing activities. Scope and exemptions vary by state: for example, the CCPA applies to personal information of consumers, business representatives, and employees, includes additional protections for "sensitive personal information," and generally excludes PHI subject to HIPAA; other states may exempt entities regulated by HIPAA or data processed in the context of clinical trials, or neither, which complicates compliance and increases legal risk and costs. We are also subject to state data breach notification statutes, like the New York SHIELD Act, that require notification to affected individuals and, in some cases, regulators and consumer reporting agencies following certain security incidents.

In connection with clinical research, we also handle personal information subject to privacy and/or confidentiality obligations in informed consent documents and clinical trial agreements, as well as ethical and regulatory standards governing human subjects research. Depending on the trial and role of the parties involved, our activities may be subject to oversight by institutional review boards, and we may rely on de-identification, coding, or limited data sets, along with contractual restrictions, to manage privacy and data sharing in research contexts.

We also depend on a network of service providers and partners-including clinical sites, contract research organizations, laboratories, data hosting providers, and other vendors-to support our operations. As a result, we implement contractual and technical controls, diligence, and monitoring of third parties that create, receive, maintain, or transmit personal information on our behalf, and, where data is accessed from or transferred to locations outside the United States, we apply or rely on third parties to implement cross-border transfer mechanisms and safeguards as required by applicable law.

In addition, the U.S. Department of Justice ("DOJ") has promulgated rules restricting the sale, transfer, or access to certain categories of bulk sensitive personal data, including health data, genetic information, and other categories deemed to present heightened risks if aggregated and transferred in large volumes. The DOJ Bulk Data Rule is designed to prevent the misuse of bulk data by foreign adversaries and to mitigate national security risks associated with the transfer of sensitive information. We are actively evaluating the applicability of these requirements to our operations and monitoring regulatory developments in this area. Should the rule apply to any aspect of our business, we may be required to implement additional due diligence, risk assessment, notification, and recordkeeping measures, particularly with respect to cross-border data transfers and transactions involving bulk sensitive data. Noncompliance may result in civil or criminal penalties, and ongoing evaluation of our obligations under the DOJ Bulk Data Rule remains a component of our broader data governance and compliance program.

Our use of artificial intelligence ("AI") and machine learning technologies in research, analytics, and business operations is subject to a rapidly evolving legal and regulatory landscape. Federal and state authorities are increasingly focused on the responsible use of AI, including requirements for transparency, accountability, and the mitigation of algorithmic bias and discrimination. Several states have enacted or are considering laws that regulate the use of AI in processing personal information, mandate impact assessments for high-risk AI applications, and require disclosures regarding automated decision-making. We may be required to implement measures to assess and address potential biases in AI models, ensure explainability and fairness, and provide individuals with rights regarding automated processing of their data. In addition, federal agencies such as the FDA have issued guidance on the use of AI in medical device development and clinical research, which may impact our operations. As regulatory expectations continue to develop, we may need to update our policies, procedures, and technical controls to ensure compliance with applicable AI-related requirements. The requirements of these laws and regulations continue to develop, and new laws, amendments, or interpretive guidance may require us to modify our data handling practices, implement additional controls, or incur increased compliance costs. Noncompliance or perceived noncompliance could result in regulatory investigations and enforcement actions, private litigation, fines and penalties, or orders requiring changes to our business practices.

Coverage and Reimbursement

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

healthcare programs, such as Medicare and Medicaid, and private payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates, if and when approved, will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government healthcare programs, private health insurers and other organizations.

Within the U.S., no uniform policy for coverage and reimbursement exists in the United States, and coverage and reimbursement for drug products can differ significantly from payor to payor. One third-party payor's decision to cover a particular drug product does not ensure that other payors will also provide coverage for the drug product. Factors payors consider in determining coverage include whether the product is:

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

Even if products are covered, third party payors may seek to control utilization of the products through various mechanisms (e.g., requiring a prescriber to obtain prior authorization from a health plan before the product will be covered by the health plan or establishing patient copays and deductibles that encourage use of other products over our products). Coverage of a product by a third-party payor does not mean that reimbursement will be adequate. Third party reimbursement may not be sufficient to enable us to maintain price levels high enough to realize an appropriate return on our investment in product development. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or requested by private payors in exchange for coverage or by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold. Our ability to commercialize our product candidates successfully may be adversely affected by discounts or rebates that we are required to provide in order to ensure coverage of our products and compete in the marketplace.

Significant uncertainty exists as to the coverage and reimbursement status of new drug products. There may be considerable delays in obtaining reimbursement for newly-approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA. Third-party payors may also seek, with respect to an approved product, additional clinical evidence, including comparative effectiveness evidence, that goes beyond the data required to obtain marketing approval in order to demonstrate clinical benefits and value relative to other therapies before covering new products. If so, we may be required to conduct additional pharmacoeconomic studies beyond what is required for marketing approval.

Third-party payors are increasingly challenging the prices charged for pharmaceutical or biological products and related services, examining the medical necessity and reviewing the cost effectiveness of such products and services. For products administered under the supervision of a physician, inadequate reimbursement for the product itself or the treatment or procedure in which the product is used may adversely impact physician utilization. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product that receives approval. Decreases in third-party reimbursement for any product or a decision by a third-party not to cover a product could reduce physician usage and patient demand for the product.

We cannot be sure that adequate coverage and reimbursement will be available, or remain available, for any drug that we commercialize. Coverage and reimbursement may impact the demand for, or the price of, our products and any product candidate for which we obtain marketing approval and limits on coverage and reimbursement may adversely affect our ability to successfully commercialize any product candidate for which we obtain marketing approval.

Finally, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, drug pricing in the European Union is primarily a national competence, with each member state setting its own prices and reimbursement rules according to national budgets and health systems. The national rules and policies should comply with EU transparency laws to ensure that national pricing and reimbursement decisions for medicines are transparent, non-discriminatory, and timely, thereby facilitating the free movement of

pharmaceuticals within the European Union. To obtain reimbursement and pricing approval, countries may require the completion of clinical trials to establish relative clinical effectiveness to guide cost effectiveness assessment of a new treatment method to currently available therapies before it can be adopted for use in the respective national health systems. A member state may approve a specific price for the medicinal product or implement a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country with price controls or reimbursement limitations for pharmaceutical products will grant favorable reimbursement and pricing terms for any of our product candidates. Historically, products launched in the European Union do not follow price structures of the U.S. and are generally subject to lower prices.

Healthcare Reform

The United States and some foreign jurisdictions are considering or have enacted a number of reform proposals to change the healthcare system. There is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access.

For example, in March 2010, the U.S. Congress enacted the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act (the "ACA") which substantially changed the way healthcare is delivered as well as financed by both governmental and private insurers in the United States. The ACA expanded health care coverage through the Medicaid expansion and subsidization of private health insurance, implemented the "individual mandate" for health insurance coverage (by imposing a tax penalty on individuals who did not obtain insurance), and changed the coverage and reimbursement of drug products under government healthcare programs. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future.

In the U.S., in recent years, the pharmaceutical industry has been a particular focus of healthcare reform efforts and has been significantly affected by major legislative, administrative and executive initiatives. For example, the Inflation Reduction Act of 2022 (IRA) included a number of changes intended to address rising prescription drug prices in Medicare Parts B and D. These changes included caps on Medicare Part D out-of-pocket costs, Medicare Part B and Part D drug price inflation rebates, a new Medicare Part D manufacturer discount drug program (replacing the previous coverage gap discount program) and a drug price negotiation program for certain high-spend Medicare Part B and D drugs. The IRA has had and will likely continue to have a significant impact on the pharmaceutical industry. Beyond the IRA, changes to Medicaid effective in 2024 eliminated the Medicaid rebate cap. Additionally, changes to certain Medicare price reporting requirements for drugs beginning in 2026 will likely increase the administrative and compliance burden for manufacturers.

Recently, drug pricing and payment has been subject to a number of reform initiatives. For example, President Trump issued an Executive Order in April 2025 with multiple directives aimed at lowering drug prices, including refining the Medicare drug price negotiation program established by the IRA; accelerating competition for high-cost prescription drugs by accelerating approval of generics and biosimilars and facilitating the process for re-classifying prescription drugs as over-the-counter drugs; and increasing drug importation. In May 2025, President Trump issued another Executive Order that directed government agencies and officials to identify most-favored nation pricing targets for prescription drugs (and looked to pharmaceutical manufacturers to make significant progress towards delivering target prices to patients); prevent foreign countries from disproportionately shifting the cost of global pharmaceutical research and development to the United States; and facilitate direct-to-consumer purchasing programs for pharmaceutical manufacturers to sell their products to patients at the most-favored-nation price. In the wake of the Executive Orders and related executive initiatives, a number of pharmaceutical manufacturers have announced direct-to-consumer offerings with discounted prices and/or reached agreement with the federal government regarding pricing for drugs, including prices for Medicaid drugs and newly launched products. A website sponsored by the federal government that is anticipated to offer pharmaceutical direct-to-consumer channels has also been announced. Federal agencies are developing new drug pricing pilot programs, such as a voluntary Medicaid initiative which would authorize the federal government to negotiate Medicaid supplemental rebates with participating manufacturers on behalf of state Medicaid programs, in exchange for standardized coverage criteria for participating manufacturer drugs, and the proposed Medicare Part B and Part D pilot models that, if finalized as proposed, would replace existing inflation-based Medicare rebates with rebates determined on the basis of international prices, for drugs and

patients subject to the model. Many of these reform initiatives would require additional legal and/or administrative action to implement and may be subject to legal challenge.

Other federal healthcare reform efforts or actions may affect access to healthcare coverage or the funding of health care benefits, although the full impact of such efforts or actions cannot be predicted. For example, the Congressional Budget Office has estimated that Medicaid provisions in the 2025 budget reconciliation legislation, including restrictions in eligibility and funding for Medicaid, as well as changes to the healthcare marketplace such as the elimination of certain subsidies, will increase the number of uninsured.

At the state level, individual states are increasingly implementing initiatives designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and measures to encourage importation from other countries and bulk purchasing. For example, certain states have formed Prescription Drug Affordability Boards that assert authority to set reimbursement rates and/or drug pricing in the state. States are also increasingly expanding or changing Medicaid supplemental rebate programs to secure additional rebates from manufacturers in exchange for drug coverage and to limit coverage of certain drugs for certain Medicaid patients or to all Medicaid patients. These and other future state-level reform activities could negatively affect Medicaid coverage and reimbursement for our products.

Other recent government actions also may affect prices or payments for prescription drugs. For example, the Trump Administration's recently announced tariff on branded or patented drugs may adversely impact our ability to realize an adequate return on the sale of drug products (if approved) that are imported from abroad or manufactured using products or materials imported from abroad. The timeline for implementation of this tariff has not yet been finalized. As another example, the Budget Control Act of 2011, as amended, resulted in the imposition of reductions in Medicare (but not Medicaid) payments to providers in 2013 and will remain in effect into 2032 unless additional Congressional action is taken. Any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs that may be implemented and/or any significant taxes or fees that may be imposed on us could have an adverse impact on our results of operations.

Reform efforts have been and may continue to be subject to scrutiny and legal challenge, which increases uncertainty. For example, the IRA drug price negotiation program has been challenged in litigation filed by various pharmaceutical manufacturers and industry groups.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state measures designed to, among other things, reduce the cost of prescription drugs, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, in May 2019, CMS adopted a final rule allowing Medicare Advantage Plans the option to use step therapy for Part B drugs, permitting Medicare Part D plans to apply certain utilization controls to new starts of five of the six protected class drugs, and requiring the Explanation of Benefits for Part D beneficiaries to disclose drug price increases and lower cost therapeutic alternatives, which went into effect on January 1, 2021.

The nature and extent of future healthcare reforms cannot be predicted. There is uncertainty regarding the nature or impact of any drug pricing or broader healthcare or other reform implemented at the federal or state level and the extent to which such action may be subject to litigation or other challenges. Ongoing efforts to contain or reduced costs of healthcare and/or impose price controls may adversely affect the demand for our product candidates, if approved, and our ability to achieve or maintain profitability.

In the EU, similar political, economic and regulatory developments may affect our, or our collaborators', ability to profitably commercialize our current or any future products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The EU is undergoing a revision of its general pharmaceutical legislation, commonly known as the 'Pharma Package' to help ensure, among others, fair access to safe, effective and affordable medicines across the EU. It also seeks to improve the competitiveness of the pharmaceutical industry by reducing regulatory burdens and strengthening supply

chain security to prevent and manage shortages. The legislative process for the EU Pharma Package began with the European Commission's proposal in April 2023, followed by the development of positions by the European Parliament and the Council. This culminated in Trilogue negotiations, with a political agreement reached in December 2025. The agreed text now awaits formal adoption by both the Parliament and Council, after which it will be published in the Official Journal of the EU. The new Directive and Regulation will then enter into force following a transition period of 18 to 36 months, ultimately modernizing EU pharmaceutical law to better support innovation, access, and supply. In addition, the European Commission proposed in December 2025 the Biotech Act which seeks to strengthen the competitiveness of the biotechnology sector and facilitate the development and timely market entry of biotechnology innovations, while ensuring high standards for the protection of human health. In international markets, reimbursement and healthcare payment systems vary significantly from country to country, and many countries have instituted price ceilings on specific products and therapies. Our future products, if any, might not be considered clinically appropriate or justified for a specific indication, or cost-effective by third-party payors as reimbursement decisions typically require robust scientific evidence of effectiveness or national health systems and demonstration of therapeutic value to advance patient care. An adequate level of reimbursement might not be available for such products and third-party payors' reimbursement policies or national health systems might adversely affect our, or our collaborators' ability to sell any future products profitably.

Other Government Regulation Outside of the United States

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

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

The requirements and process governing the conduct of clinical trials, including requirements to conduct additional clinical trials, product licensing, safety reporting, post-authorization requirements, marketing and promotion, interactions with healthcare professionals, pricing and reimbursement may vary widely from country to country. No action can be taken to market any product in a country until an appropriate marketing approval has been granted by the regulatory authorities in that country. The current approval process varies from country to country, and the time spent in gaining approval may vary from that required for FDA approval. In certain countries, the sales price of a product must also be agreed or approved by payors or the respective national health systems before commercial launch. The pricing review period typically commences following marketing approval. Although a product may receive marketing approval from a regulatory authority, the price agreed upon during the review process may not be commercially sustainable to justify a commercial launch in those countries.

Regulation in the European Union

European Data and Security Laws

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

processors, and the security and confidentiality of the personal data. EU Member States may also impose additional requirements in relation to health, genetic and biometric data through their national legislation.

As mentioned above, we depend on a network of service providers and partners-including clinical sites, contract research organizations, laboratories, data hosting providers, and other vendors-to support our operations and may share personal data with these organizations. As a result, we implement contractual and technical controls, diligence, and monitoring of third parties that create, receive, maintain, or transmit personal data on our behalf, and we apply cross-border transfer mechanisms and safeguards as required by applicable law. We also may rely on pseudonymization or anonymization, coding or limited data sets, along with contractual restrictions (including entering into data processing agreements as required under the GDPR) to manage privacy and data sharing in these contexts.

In addition, the GDPR imposes specific restrictions on the transfer of personal data to countries outside of the European Economic Area ("EEA") that are not considered by the European Commission ("EC") to provide an adequate level of data protection. Appropriate safeguards are required to enable such transfers. Among the appropriate safeguards that can be used, the data exporter may use the standard contractual clauses ("SCCs"). When relying on SCCs, data exporters are also required to conduct a transfer risk assessment to verify if anything in the law and/or practices of the third country may impinge on the effectiveness of the SCCs in the context of the transfer at stake and, if so, to identify and adopt supplementary measures that are necessary to bring the level of protection of the data transferred to the EU standard of essential equivalence. Where no supplementary measure is suitable, the data exporter should avoid, suspend or terminate the transfer. With regard to the transfer of data from the EEA to the United States, on July 10, 2023, the EC adopted its adequacy decision for the EU-US Data Privacy Framework. On the basis of the new adequacy decision, personal data can flow from the EEA to U.S. companies participating in the framework. With regard to the transfer of data from the EU to the United Kingdom (UK), personal data may freely flow from the EEA to the UK since the EC deemed the UK to have an adequate data protection level, and these adequacy decisions were extended in December 2025, and are now valid until December 27, 2031.

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

Furthermore, there are specific requirements relating to processing health data from clinical trials, including those related to public disclosure obligations provided in the EU Clinical Trials Regulation No. 536/2014 (“CTR”), European Medicines Agency ("EMA") data transparency initiatives and voluntary commitments by industry. Failure to comply with these obligations could lead to considerable risks of government enforcement actions and significant penalties against us, harm to our reputation, and adversely impact our business performance and operating efficiency.

Additionally, following the UK’s withdrawal from the EU and the EEA, companies also have to comply with the UK’s data protection laws (including the UK GDPR (as defined in section 3(10) (as supplemented by section 205(4)) of the Data Protection Act 2018 (the “DPA 2018”)), the DPA 2018, and related data protection laws in the UK). On June 19, 2025, the UK’s Data (Use and Access) Act (“DUAA”) took effect, which introduces certain relatively minor amendments to the data protection regime in the UK, and therefore creates slight divergences between the EU and UK data protection regimes. Separate from the fines that can be imposed by the GDPR, the UK regime has the ability to fine up to the greater of £17.5 million or 4% of global turnover.

Companies are subject to specific data sharing and transfer rules under the UK regime which broadly mirror the GDPR rules. We therefore also apply or rely on third parties to implement data sharing and cross-border transfer mechanisms and safeguards, as set out above, in these contexts. On February 2, 2022, the UK Secretary of State laid before the UK Parliament the international data transfer agreement (“IDTA”) and the international data transfer addendum to the EC’s standard contractual clauses for international data transfers (Addendum) and a document setting out transitional provisions. The IDTA and Addendum came into force on

March 21, 2022 and replaced the old SCCs for the purposes of the UK regime. Regarding transfers from the UK to the EEA, personal data may flow freely since the EEA is deemed to have an adequate data protection level for purposes of the UK regime.

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

The EU Directive 2002/58/EC (as amended by Directive 2009/136/EC) ("ePrivacy Directive") also imposes obligations on organizations operating in the EU. The ePrivacy Directive is transposed into law in each EU member state and in the UK, so local transposition and enforcement can vary. It contains a prohibition on accessing information on an individual's device, such as through the use of cookies and other similar technologies, without informed consent, as well as rules on direct marketing. On November 19, 2025, the EC published the Digital Omnibus Package ("Omnibus Proposals"), aimed at simplifying the EU's digital regulatory framework. The Omnibus Proposals would streamline the rules governing cookies and tracking technologies, potentially removing the requirement to obtain explicit consent for certain categories of cookies. If adopted, these changes could ease compliance obligations around the use of cookies and tracking tools in the EU. In the UK, the ePrivacy Directive was transposed into UK law as the Privacy and Electronic Communications (EC Directive) Regulations 2023 ("PECR") which imposes equivalent requirements on UK operations. The UK's DUAA made certain limited amendments to PECR, most notably bringing its enforcement powers in line with the UK GDPR, so that monetary penalties under PECR can now reach the greater of £17.5 million or 4% of an organization's total worldwide annual turnover.

The EU has also recently implemented a number of cybersecurity laws, some of which are applicable to the healthcare industry. For example, the Network and Information Security Directive (Directive (EU) 2022/2555) applies to organizations operating in the EU in the healthcare sector and imposes stringent cybersecurity obligations on in-scope organizations, including in relation to supply chain management and incident reporting.

Drug and Biologic Development Process

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

The EU Clinical Trials Regulation, which replaced the Clinical Trials Directive and has been in force since 2022, aims to harmonize and streamline clinical trial processes across Member States through a centralized application system, the Clinical Trials Information System (CTIS), enabling sponsors to submit a single application for approval. One national regulatory authority, designated as the reporting Member State, leads the validation and evaluation of applications in consultation with other concerned Member States. Applications may be amended and resubmitted if rejected, and approved trials may commence in all relevant Member States, although individual states retain the right to "opt out" in limited circumstances. The Regulation also simplifies safety reporting rules, introduces enhanced transparency requirements such as mandatory submission of trial results summaries to the EU Database. Since January 31, 2023, all initial clinical trial applications must be submitted through CTIS which now serves as the single entry point for clinical trial-related information and data. By January 31, 2025, all ongoing trials approved under the former Clinical Trials Directive must transition to CTIS and comply with the CTR. On July 19, 2023, the EC published guidance for this transition, clarifying that previously assessed documentation will not be reassessed, EU-endorsed templates do not require updates, and site suitability forms are only needed for new trial sites.

Under the CTR, clinical trials must comply with national laws, regulations, and the applicable GCP and GLP standards, and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use ("ICH") guidelines on Good Clinical Practice, as well as the ethical principles outlined in the Declaration of Helsinki.

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

Drug Marketing Authorization

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

Centralized Authorization Procedure

The centralized procedure provides for the grant of a single MA that is issued by the EC following the scientific assessment of the application by the EMA that is valid for all EU Member States as well as in the three additional EEA Member States (Norway, Iceland and Liechtenstein). The centralized procedure is compulsory for specific medicinal products, including for medicines developed by means of certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (gene therapy, somatic cell therapy, or tissue engineered medicines) and medicinal products with a new active substance indicated for the treatment of certain diseases (HIV/AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases). For medicinal products containing a new active substance for indications that do not fall within the mandatory centralized procedure, they are eligible for centralized assessment if they constitute significant therapeutic, scientific or technical innovations or for which the grant of a MA through the centralized procedure would be in the interest of public health at EU level.

Under the centralized procedure, the Committee for Medicinal Products for Human Use ("CHMP") at the EMA is responsible for the initial assessment of an MAA. The CHMP also oversees the scientific assessment of various post-authorization and maintenance activities, including the assessment of variations or extensions to an existing MA. The standard timeframe for the evaluation of an MAA by the EMA's CHMP is 210 days from receipt of a valid MAA, excluding clock-stops for the applicant to provide additional written or oral information in response to the CHMP's list of questions. As a result, the overall process typically takes a year or more, unless the application is eligible for an accelerated assessment. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. Upon request, the CHMP may reduce the time frame to 150 days if the applicant provides sufficient justification for an accelerated assessment. The CHMP will provide a positive opinion regarding the application only if it meets the required standards for quality, safety and efficacy. This opinion is then transmitted to the EC, which has the ultimate authority for granting MA, ordinarily within 67 days after receipt of the CHMP opinion.

Decentralized Authorization Procedure

The decentralized procedure permits companies to file identical MAAs for a medicinal product not falling within the mandatory centralized procedure to the competent authorities in various EU Member States simultaneously if such medicinal product has not received marketing approval in any EU Member State. In this procedure, the reference member state is appointed to lead the scientific review for agreement with the competent authorities of the other EU Member States concerned by the procedure, the concerned member states. A member state may refuse to accept the assessment provided by the reference member state on

grounds of a potential serious risk to public health that is defined as a situation where there is a significant probability that a serious hazard resulting from a human medicinal product in the context of its proposed use will affect public health.

Risk Management Plan

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

MA Validity Period

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

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

The UK applies a rule, consistent with directly applicable EU law, requiring that nationally approved medicinal products must be placed on the market within three years from the date the marketing authorization is granted. When the Medicines and Healthcare products Regulatory Agency (MHRA) becomes aware that the three-year period is approaching expiry, it will notify the marketing authorization holder in advance that the authorization will cease to be valid if the product is not marketed within the required timeframe. The MHRA provides notification to the marketing authorization holder in both scenarios referenced previously: first, where a product has held a marketing authorization for three years but has not been placed on the market at all; and second, where a product was previously marketed but has subsequently not been placed on the market for a consecutive period of three years. This process ensures compliance with regulatory requirements and maintains the integrity of the national medicines supply.

Following the UK's exit from the EU, the three-year "sunset clause" for centrally authorized products in the UK was effectively reset from the date of conversion (January 1, 2021). This means that any product not placed on the market in Great Britain by early 2024 risked losing its validity unless the appropriate notification was made. The Medicines and Healthcare products Regulatory Agency (MHRA) is responsible for managing this process for UK marketing authorizations (PLGB MAs), requiring marketing authorization holders to provide updates on the marketing status of their products. The Windsor Framework agreement establishes that, effective from January 1, 2025, the Medicines and Healthcare products Regulatory Agency (MHRA) will serve as the sole regulatory authority for approving medicines for the entire UK market, encompassing both Northern Ireland and Great Britain. This change replaces the previous system, where Northern Ireland followed EU rules and Great Britain was regulated independently by the MHRA. Under the new arrangements, a unified UK-wide authorization process will apply, ensuring that medicines in Northern Ireland are regulated by the MHRA in the same manner as in Great Britain. The primary focus of the Windsor Framework is to streamline regulatory procedures, eliminate the need for separate authorizations, and guarantee equal and timely access to medicines throughout the UK.

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

three year period will start running from the last date the drug was placed on the UK market before the end of the Brexit Transition Period. We do not have approved products that fall within the Brexit Transition Period.

Advanced Therapy Medicinal Products

In the EU, medicinal products, including advanced therapy medicinal products ("ATMPs") are subject to extensive pre- and post-market regulation by regulatory authorities at both the EU and national levels. ATMPs comprise gene therapy products, somatic cell therapy products and tissue engineered products, which are genes, cells or tissues that have undergone substantial manipulation and that are administered to human beings in order to cure, diagnose or prevent diseases or regenerate, repair or replace a human tissue. Pursuant to Regulation (EC) No 1394/2007, the Committee for Advanced Therapies ("CAT") is responsible in conjunction with the CHMP for the evaluation of ATMPs. The CHMP and CAT are also responsible for providing guidelines on ATMPs. These guidelines provide additional guidance on the factors that the EMA will consider in relation to the development and evaluation of ATMPs and include, among other things, the preclinical studies required to characterize ATMPs. Although such guidelines are not legally binding, compliance with them is often necessary to gain and maintain approval for product candidates.

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

Exceptional Circumstances and Conditional Approval

Similar to accelerated approval regulations in the United States, EU pharmaceutical law provides two regulatory pathways to facilitate early patient access to medicines when comprehensive clinical data are not yet available: conditional marketing authorization ("CMA") and marketing authorization under exceptional circumstances ("MAUEC"). Conditional marketing authorization is granted for medicines that address unmet medical needs, such as those for serious or rare diseases, where the immediate availability of the product offers significant benefit despite incomplete data. Under this pathway, the applicant is required to submit additional clinical data within a specified timeframe to confirm the benefit-risk profile of the medicine. The authorization is valid for one year and may be renewed annually until sufficient data are provided to support full authorization. Marketing authorization under exceptional circumstances applies when it is not feasible to obtain comprehensive data, typically due to the rarity of the condition, limitations in scientific knowledge, or ethical constraints that make further studies impossible or inappropriate. Instead of expecting future comprehensive data, this pathway relies on ongoing obligations such as enhanced safety monitoring and risk management plans. The authorization remains valid as long as these obligations are satisfied. The key difference between these pathways is that CMA anticipates the eventual completion of the data package, whereas MAUEC recognizes that full data cannot reasonably be obtained and instead relies on alternative measures to manage risk. Both pathways require a positive benefit-risk assessment, address unmet medical needs, and ensure that the immediate benefit to patients outweighs the risks, but they differ in their expectations for future data collection and regulatory oversight.

Data and Marketing Exclusivity

Under EU pharmaceutical law, reference medicinal products are granted 8 years of data exclusivity, during which generic and biosimilar manufacturers cannot rely on the originator's non-clinical and clinical data for regulatory approval. This is followed by 2 years of marketing exclusivity, preventing generics and biosimilars from entering the market for a total of 10 years. If, within the first 8 years, the reference product is approved for a new indication that provides significant clinical benefit, the exclusivity period may be extended to 11 years. These rules ensure that generics and biosimilars cannot seek approval or enter the market until the exclusivity periods have expired, balancing incentives for innovation with future market competition.

A reference medicinal product for data and marketing exclusivity typically contains a new active substance and requires a full dossier, including pharmaceutical, non-clinical, and clinical trial data, for approval. The European Medicines Agency (EMA), based on the scientific assessment and opinion of its Committee for Medicinal Products for Human Use (CHMP), determines whether a product contains a new active substance.

Data and marketing exclusivity do not prevent other companies from generating their own data through independent development to demonstrate the safety, quality, and efficacy of their own products.

Recent reforms introduced through the EU Pharma Package and the proposed Biotech Act bring significant changes, including streamlined authorization procedures, enhanced measures for access and affordability, stricter management of medicine shortages, strengthened post-market surveillance, and new requirements addressing environmental and ethical considerations. These initiatives are designed to modernize and harmonize medicines regulation, facilitate patient access to innovative therapies, and provide robust oversight of emerging technologies across the EU.

The legislative process for the EU Pharma Package began with the European Commission's proposal in April 2023, followed by the development of positions by the European Parliament and the Council. This culminated in Trilogue negotiations, with a political agreement reached in December 2025. The agreed text now awaits formal adoption by both the Parliament and Council, after which it will be published in the Official Journal of the EU. The new Directive and Regulation will then enter into force following a transition period of 18 to 36 months, ultimately modernizing EU pharmaceutical law to better support innovation, access, and supply. Under the agreed EU Pharma Package, companies launching new medicines will benefit from eight years of data protection and one year of market exclusivity, with a possible additional year for innovative products meeting specific criteria.

Pediatric Development

In the EU, an approved PIP is required to be obtained by the company prior to any application for marketing authorization of a medicinal product based on a full dossier of pharmaceutical, non-clinical, and clinical data that has not yet been approved in the EU. This requirement also applies to authorized products protected by a supplementary protection certificate (SPC) or a patent eligible for an SPC, when seeking authorization for new indications, pharmaceutical forms, or routes of administration.

A PIP is a research and development program designed to ensure that adequate data are generated to determine the conditions under which a medicinal product may be authorized for use in the pediatric population. Companies developing new medicinal products must submit a PIP, along with a request for agreement, to the European Medicines Agency (EMA). The EMA's Pediatric Committee (PDCO) evaluates the PIP and provides an opinion, upon which the EMA issues a binding decision.

Companies are required to conduct pediatric clinical trials in accordance with the agreed PIP and within the specified timelines. The resulting pediatric study data must accompany the application for authorization for it to be validated and approved by the EMA. However, a PIP may include a deferral of the initiation or completion of some or all studies, based on scientific, technical, or public health grounds—for example, if it is appropriate to conduct adult studies first or if pediatric studies will take longer to complete. A waiver from the PIP requirement may be granted if the product or product class is likely to be ineffective or is likely to be to be unsafe in the pediatric population, if the disease or condition occurs only in adults, or if the product does not offer significant therapeutic benefit over existing pediatric treatments.

Unless a waiver or deferral has been granted, the MAA must include the results of all pediatric clinical trials and all information collected in compliance with the approved PIP. If a deferral is granted, the pediatric studies may be completed at a later date. A "PIP Compliance Check" is conducted during the validation period of an MAA to confirm that pediatric product development is being conducted in accordance with the approved PIP at that time.

Medicinal products granted marketing authorization based on pediatric clinical trials conducted in accordance with an approved PIP are eligible for a six-month extension of the SPC (if in effect at the time of approval), or, for orphan medicinal products, a two-year extension of orphan market exclusivity, regardless of whether the pediatric data result in approval of a pediatric indication. For applications resulting in the authorization of a new pediatric indication, a one-year extension of data and marketing exclusivity may be granted. However, the regulatory framework prohibits double awards of these exclusivity rights for the same product.

In the UK, the MHRA has established a closely aligned process, frequently accepting agreed EU PIPs and decisions to streamline UK submissions. However, the MHRA maintains UK-specific requirements, such as the need for a UK PIP for new medicines. Following the Windsor Framework, MHRA is responsible for regulatory control of medicines (including pediatric medicines) for the entire UK market (England, Scotland, Wales, and Northern Ireland).

Orphan Designation and Exclusivity

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

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

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

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

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

PRIME Designation

The EMA has established the Priority Medicines ("PRIME") scheme, an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIME scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme if compelling non-clinical data in a relevant model provide early evidence of promising activity or proof of principle. Additionally, first-in-human studies should demonstrate adequate exposure to achieve the desired pharmacotherapeutic effects and tolerability. Products accepted onto the PRIME scheme benefit from, among others, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and potentially accelerated MAA assessment once a dossier has been submitted. Importantly, once a candidate medicine has been selected for the PRIME scheme, a dedicated contact point and rapporteur from the CHMP or CAT are appointed facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting with the CHMP/CAT rapporteur initiates these relationships and includes a team of multidisciplinary experts to provide guidance on the overall development plan and regulatory strategy. PRIME eligibility does not change the standards for product approval, and there is no assurance that any such designation or eligibility will result in expedited review or approval.

Post-Approval Regulation

Similar to the United States, both MA holders and manufacturers of medicinal products in the EU are subject to comprehensive regulatory oversight by the EMA, the EC and/or the competent regulatory authorities of the EU Member States. The regulatory oversight covers every stage of the authorization process, from initial grant of an approval to ongoing monitoring of compliance with EU cGMPs, manufacturing authorizations, pharmacovigilance rules and requirements governing advertising, promotion, sale, and distribution, recordkeeping, importing and exporting of medicinal products.

These regulatory requirements are designed to ensure that the safety, quality, and efficacy standards of medicinal products are consistently maintained throughout their lifecycle. Failure by us or by any of our third-party partners, including suppliers, manufacturers and distributors to comply with EU laws and the related national laws of individual EU Member States governing the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of MA[, statutory health insurance], bribery and anti-corruption or other applicable regulatory requirements may result in administrative, civil or criminal sanctions. These include delays or refusal to authorize the conduct of clinical trials or to grant MA, product withdrawals and recalls, product seizures, withdrawal or suspension of authorizations, restrictions on regulated activities such as production, distribution, manufacturing or clinical trials, operating restrictions, financial penalties.

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

These pharmacovigilance rules require holders of MAs the obligation to develop a system capable of collecting, collating, assessing and reporting post-authorization data to monitor the ongoing risks and benefits of marketed medicinal products as well as the requirement to conduct additional clinical studies or post-authorization safety or efficacy studies to address uncertainties about the benefit-risk balance, or to measure the effectiveness of risk-management measures. Such post-authorization measures may be time-consuming and expensive and could impact our profitability. MA holders must establish and maintain a pharmacovigilance system designed to monitor the safety of authorized medicinal products and detect any change to their risk-benefit balance and appoint an individual qualified person for pharmacovigilance, who is responsible for the oversight of that system. Key obligations include expedited reporting of unexpected serious adverse reactions and submission of Periodic Safety Update Reports ("PSURs") in relation to medicinal products for which they hold MAs. The EMA reviews PSURs for medicinal products authorized through the centralized procedure. If the EMA, based on the scientific assessment conducted by its advisory committees, determines that the risk-benefit profile of a product has changed, it may issue an opinion recommending suspension, withdrawal, or variation of the existing MA. The scientific opinion must be ratified by the EC in a legally binding decision. If the MA holder fails to meet the obligations set out in the EC's decision, the validity of the MA may be compromised. For

centrally authorized products, non-compliance with pharmacovigilance requirements can result in regulatory sanctions, including financial penalties imposed by the EC.

The manufacturing process for pharmaceutical products in the EU is highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC (repealed by Directive 2017/1572 on January 31, 2022), Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice ("GMP"). These requirements include compliance with EU cGMP standards when manufacturing pharmaceutical products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU. Amendments or replacements of at least Directive 2001/83/EC and Regulation (EC) No 726/2004 are part of the reform proposal for European pharmaceutical legislation under the EU Pharma Package, as deta. Similarly, the distribution of pharmaceutical products into and within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU Member States. The manufacturer or importer must have a qualified person who is responsible for certifying that each batch of product has been manufactured in accordance with GMP and the terms of a marketing authorization or clinical trial authorization, before releasing the product for commercial distribution in the EU or for use in a clinical trial. Manufacturing facilities are subject to periodic inspections by the competent authorities for compliance with cGMPs.

Advertising and Promotion Regulations

The advertising and promotion of our products is also subject to EU laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other national legislation of individual EU Member States may apply to the advertising and promotion of medicinal products and may differ from one country to another. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics (SmPC) as approved by the competent regulatory authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the MA granted for the medicinal product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. All advertising and promotional activities for the product must be consistent with the approved SmPC and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription-only medicines is also prohibited in the EU. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on its promotional activities with healthcare professionals.

EU regulation advertising and promotion of medicinal products is retained ed in the UK following Brexit as directly applicable EU law, by virtue of the EU (Withdrawal) Act the Human Medicines Regulations 2012 and The Human Medicines (Amendment etc.) (EU Exit) Regulations 2019.

Anti-Corruption Legislation

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

Payments made to physicians in certain EU Member States also must be publicly disclosed. Moreover, agreements with physicians must often be the subject of prior notification and approval by the physician's employer, his/her regulatory professional organization, and/or the competent authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes, or professional codes of

conduct, applicable in the individual EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

In the UK, the pharmaceutical sector is recognized as being particularly vulnerable to corrupt practices. The UK Bribery Act 2010 impacts pharmaceutical promotion through its interaction with the self-regulatory Code of Practice of the Association of the British Pharmaceutical Industry (ABPI). The Serious Fraud Office (SFO) and Prescription Medicines Code of Practice Authority (PMCPA) work together to prevent bribes disguised as promotional activities, such as excessive hospitality offered to healthcare professionals for prescription medicines. The ABPI Code, enforced by the PMCPA, serves as the primary self-regulatory safeguard, establishing strict rules on inducements and requiring transparency to prevent violations of both anti-bribery laws and industry codes, especially in relation to prescribing decisions. Due to the Bribery Act 2010's far-reaching territorial application, the potential penalized act does not have to occur in the UK to become within its scope. If the act or omission does not take place in the UK, but the person's act or omission would constitute an offense if carried out there and the person has a close connection with the UK, an offense will still have been committed.

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

Regulations in the UK and Other Markets

The UK formally left the EU on January 31, 2020 and EU laws now only apply to the UK in respect of Northern Ireland as laid out in the Protocol on Ireland and Northern Ireland and as amended by the Windsor Framework sets out a long-term set of arrangements for the supply of medicines into Northern Ireland. The EU and the UK agreed on a trade and cooperation agreement ("TCA"), which includes provisions affecting the life sciences sector (including on customs and tariffs). There are some specific provisions concerning pharmaceuticals, including the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP issued documents. The TCA does not, however, contain wholesale mutual recognition of UK and EU pharmaceutical regulations and product standards.

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

To be used or sold in the UK, a drug must have a valid MA granted through the national application process. National applications are governed by the Human Medicines Regulations (SI 2012/1916). Applications are made electronically through the Medicines and Healthcare products Regulatory Agency ("MHRA") Submissions Portal. The MHRA operates fixed submission and assessment timetables for innovative medicines applications to facilitate consultation with its statutory advisory committee, the Commission on Human Medicines (CHM). The MHRA assessment procedure for a marketing authorization application (MAA) involves an initial evaluation, including orphan designation if applicable, and consultation with expert advisory groups as needed. By Day 90, applicants receive a consolidated request for information (RFI), which pauses the review clock until a complete response is submitted electronically. Responses are assessed by Day 150, with further RFIs issued for minor issues or a CHM letter for major objections. Each subsequent RFI requires a complete response within three months, and the clock is restarted upon submission. Applicants may make written or oral representations to the CHM if major objections remain. Final compliance checks are conducted once all issues are resolved, and the MHRA issues a grant or refusal letter specifying any conditions and the MA expiry date. The entire assessment process is designed to be completed within 210 calendar days, excluding any procedural clock-stops for additional information representations. Orphan drug designation is determined at the time of granting the MA.

In addition, the MHRA 150-day accelerated review is a specialized, fast-track national MA procedure designed for innovative medicines, new active substances, and biosimilars, aiming for a decision in 150 "clock-on" days rather than the standard 210. It requires high-quality applications, typically involving one round of questions and a 60-day cool-down period for responses.

On August 30, 2023, the MHRA published detailed guidance on its recently announced new International Recognition Procedure (“IRP”) for MAAs. The IRP applies from January 1, 2024 and replaces existing EU decision reliance procedure to apply for authorizations from seven international regulators (e.g. Health Canada, Swissmedic, FDA and EMA, among others). The IRP allows the MHRA to take into account the assessment and decision-making of the "Reference Regulators” to perform a targeted assessment of IRP applications but retain the authority to reject applications if the evidence provided is considered insufficiently robust. There exist two recognition timetables for new IRP MAAs: IRP Route A (60 days) and IRP Route B (110 days), both starting from validation. Eligibility is determined via an applicant-completed form six weeks before submission. Recognition A applies to applications with Reference Regulator approval within the past two years, with no clock-stop, but may revert to Recognition B if major objections arise. IRP Route B covers Reference Regulatory approvals within the past ten years (or exceptionally older) and applies if specific criteria, such as conditional approvals, manufacturing changes, or UK-specific requirements, are met. IRP Route B allows for consultation with the CHM and aligns with CHM dates for new active substances. Applications not eligible for either timetable may be submitted as full national applications if MHRA requirements are met. IRP can be used for post-authorization measures including line extensions, variations, and renewal applications.

There will be no pre-MA orphan designation. Instead, the MHRA will review applications for orphan designation in parallel to the corresponding MA application. The criteria are essentially the same as the EU rules, but have been tailored for the market, i.e., the prevalence of the condition in UK, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period or market exclusivity will be set from the date of first approval of the product in Great Britain.

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

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

Additional Regulation

In addition to the foregoing, local, state and federal laws, including in the United States and Israel, regarding such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous or biohazardous substances, we could be liable for damages, environmental remediation, and/or governmental fines. We believe that we are in material compliance with applicable environmental laws and occupational health and safety laws that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations. We may incur significant costs to comply with such laws and regulations now or in the future.

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. Pursuant to an Agreement and Plan of Merger, dated June 22, 2023, by and among us, Aspen Merger Sub I, Inc., a Delaware corporation and a wholly owned subsidiary of the Company, Sequoia Merger Sub II, LLC, a Delaware limited liability company and one of our wholly owned subsidiaries, and Pre-Merger Spyre, we acquired Pre-Merger Spyre (the "Asset Acquisition") and on November 27, 2023, we

completed our corporate rebranding, changing our name to Spyre Therapeutics, Inc. Through the Asset Acquisition, we received the option to license the intellectual property rights related to four research programs pursuant to the Paragon Agreement, and subsequently executed license agreements for our α4β7, TL1A, and IL-23 programs.

Our common stock currently trades on The Nasdaq Global Select Market under the ticker symbol "SYRE." Our principal executive offices are located at 221 Crescent Street, Building 23, Suite 105, Waltham, MA 02453 and our telephone number is (617) 651-5940. Our website is www.spyre.com. The information on, or that can be accessed through, our website is not part of this Annual Report on Form 10-K and is not incorporated by reference herein. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference.

Available Information

We file Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other information with the U.S. Securities and Exchange Commission ("SEC"). Our filings with the SEC are available free of charge on the SEC's website at *www.sec.gov* and on our website, spyre.com, under the "Investors & Media" tab as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

Item 1A. Risk Factors

The following summarizes the principal factors that make an investment in the Company speculative or risky, all of which are more fully described in the Risk Factors section below. This summary should be read in conjunction with the Risk Factors section and should not be relied upon as an exhaustive summary of the material risks facing our business. The occurrence of any of these risks, could harm our business, financial condition, results of operations and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this Annual Report on Form 10-K and those we may make from time to time. You should consider all of the risk factors described in our public filings when evaluating our business.

Risk Factor Summary

Risks Related to Our Financial Condition and Capital Requirements

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

Risks Related to Discovery, Development and Commercialization

- Our programs are in clinical and preclinical stages of development and may fail or suffer delays or may be more costly than anticipated for various reasons, including but not limited to delays or failures in achieving alignment with regulatory authorities on interpretation of data and its sufficiency to support safety and efficacy of our product candidates, participant recruitment or other clinical trial or supply challenges.
- We are substantially dependent on the success of the SPY001, SPY002, SPY072 and SPY003 programs, alone or in combination, and may fail to achieve our development goals in the time frames we expect.
- Any drug delivery device used may have its own regulatory development, supply, and other risks.
- We may not be successful in building a pipeline of product candidates with commercial value.
- Our studies and trials may be insufficient to support regulatory approval of any product candidates.
- We may not be successful in discovering, developing and commercializing our intra-portfolio investigational drug combinations to achieve superior outcomes relative to the use of other therapies.
- Preliminary or “topline” data from our clinical trials may change as more data becomes available.
- Our current or future clinical trials may reveal significant adverse events or undesirable side effects.
- We may fail to capitalize on more profitable or potentially successful product candidates.
- Our products may not achieve regulatory approval, market acceptance or commercial success.
- Our programs may compete with each other and they face third-party program competition.
- Regulatory authorities may not accept data from clinical trials we conduct at sites outside the United States or other jurisdiction.

Risks Related to Government Regulation

- We may not be able to achieve our timelines or obtain timely regulatory approvals of product candidates.
- We may not be able to meet requirements for chemistry, manufacturing and control of our programs.
- Our product candidates may face competition sooner than anticipated based on rules and regulations that may apply or government decisions with respect to our intellectual property.
- Even if we receive regulatory approval, we will be subject to extensive ongoing regulatory obligations.
- We may be negatively impacted by healthcare legislative reform measures and other changes in law.
- Our potential revenue may be adversely affected due to unfavorable regulations, laws and/or policies.
- We may face criminal liability or other consequences if we violate U.S. and foreign trade regulations.
- Any accelerated review designations we may pursue may not hasten development or regulatory review.
- We may be negatively impacted by disruptions at the FDA and other government agencies, including as a result of a government shutdown.

Risks Related to Our Intellectual Property

- We may fail in obtaining, maintaining and protecting our patents and other proprietary rights.

- We may be subject to patent infringement claims or may need to file such claims.
- We may be subject to claims of wrongful hiring of employees or wrongful use of confidential information.
- Our patents and our ability to protect our products may be impaired by changes to patent laws.
- Our patent protection could be reduced or eliminated for non-compliance with legal requirements.
- We may fail to identify or interpret relevant third-party patents.
- We may become subject to claims challenging the inventorship or ownership of our intellectual property.
- Patent terms may be inadequate to protect our competitive position of our programs.
- Our technology licensed from various third parties may be subject to retained rights or may be affected by failure to comply with obligations in license agreements or other disruptions to business relationships with licensors resulting in loss of license rights that are important to our business.
- We have limited foreign intellectual property rights and may not be able to protect our intellectual property and proprietary rights throughout the world.
- The intellectual property landscape around engineered antibodies is highly dynamic, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and may prevent, delay or otherwise interfere with our product discovery and development efforts.

Risks Related to Our Reliance on Third Parties

- We may fail to maintain collaborations and licensing arrangements with third parties that we rely on.
- Third parties we rely on for nonclinical studies and clinical trials may fail to satisfy contractual duties.
- We may be unable to use third-party manufacturing sites, our third-party manufacturers may encounter difficulties in production or we may need to switch or create third-party manufacturer redundancies.

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

- We may experience difficulties in managing the growth of our organization.
- We may fail to attract or retain highly qualified personnel.
- Our ability to operate in foreign markets is subject to regulatory burdens, risks and uncertainties.
- Our estimates of market opportunity may be inaccurate and our business may not grow at similar rates.
- Our employees or third parties may engage in misconduct or other improper activities.
- We may be impacted by information security incidents, cybersecurity or data breaches or other improper access to our data that could have a negative impact on our business or reputation.
- Our expanding use of AI exposes us to operational, regulatory, legal, and ethical risks that could adversely affect our business, reputation, financial condition, and results of operations.
- Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.
- We may fail to comply with privacy, data security, safety and other regulations despite compliance efforts.
- We may be subject to adverse legislative or regulatory tax changes.
- We may fail to realize the benefits of our business or product acquisitions or our strategic alliances.

Risks Related to Our Common Stock

- The market price of our common stock has historically been volatile and may drop in the future.
- Our certificate of incorporation, Delaware law and certain contracts include anti-takeover provisions.
- We do not anticipate paying any dividends in the foreseeable future.
- Future sales and issuances of equity/debt may dilute stockholders and/or result in a drop in our stock price.
- Our principal stockholders own a significant percentage of our stock.

General Risk Factors

- Our product liability insurance may be insufficient to cover costly and damaging liability claims.
- Litigation costs and the outcome of litigation could have a material adverse effect on our business.
- We continue to incur significant costs for compliance with public company laws and regulations.
- Our failure to maintain proper and effective internal controls may adversely affect our ability to report our financial condition and results of operations in a timely and accurate manner, decrease investor confidence in us, and reduce the value of our common stock. For example, in the fourth quarter of 2024, we identified a material weakness in our internal control over financial reporting which resulted in restatements of our previously-issued financial statements to amend certain net loss per share disclosures.
- Our business could be adversely affected by macroeconomic conditions, including geopolitical unrest.

Risks Related to Our Financial Condition and Capital Requirements

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

As of December 31, 2025, we had $756.5 million of cash, cash equivalents, and marketable securities. We will need to raise additional capital to continue to fund our operations in the future. If we are unable to raise additional capital when needed, we will not be able to continue as a going concern.

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

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

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

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

Any of these events could have a material adverse effect on our business, operating results and prospects. Even if successful in raising new capital, we could be limited in the amount of capital we raise due to investor demand restrictions placed on the amount of capital we raise or other reasons.

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

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

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

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

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

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

We are a biopharmaceutical company with a limited operating history. Since inception, we have incurred significant operating losses. For the years ended December 31, 2025, 2024 and 2023, we reported a net loss of $155.2 million, $208.0 million and $338.8 million, respectively. As of December 31, 2025, we had an

accumulated deficit of $1.1 billion. We will need to raise substantial additional capital to continue to fund our operations in the future.

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

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

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

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

- continue the nonclinical and clinical development of our product candidates;
- continue efforts to discover and develop new product candidates;
- continue the manufacturing of our product candidates or increase volumes manufactured by third parties;
- advance our product candidates into larger, more expensive clinical trials;
- initiate additional nonclinical studies or clinical trials for our product candidates;
- seek regulatory and marketing approvals and reimbursement for our product candidates;
- establish a sales, marketing, and distribution infrastructure to commercialize any products for which we may obtain marketing approval and market for ourselves;
- seek to identify, assess, acquire, and/or develop other product candidates;
- make milestone, royalty, or other payments under third-party license agreements;
- seek to maintain, protect, and expand our intellectual property portfolio;
- seek to attract and retain skilled personnel; and

- experience any delays or encounter issues with the development and potential for regulatory approval of our clinical and product candidates such as safety issues, manufacturing delays, clinical trial accrual delays, longer follow-up for ongoing or planned studies or trials, additional major studies or trials, or supportive trials necessary to support marketing approval.

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

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

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

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

To the extent that we raise additional capital through the sale of equity, including pursuant to any sales under convertible debt or other securities convertible into equity, the ownership interest of our stockholders will be diluted, and the terms of these new securities may include liquidation or other preferences that adversely affect the rights of our stockholders. For instance, in December 2023, we sold an aggregate of 6,000,000 shares of our common stock and 150,000 shares of our Series B Preferred Stock pursuant to a private placement to certain investors for gross proceeds of approximately $180 million, in March 2024, we sold an aggregate of 121,625 shares of our Series B Preferred Stock pursuant to a private placement to certain investors for gross proceeds of approximately $180 million and in October 2025, we sold 17,094,594 shares of our common stock in an underwritten public offering for gross proceeds of approximately $316 million. Subject to certain beneficial ownership limitations set by each holder of Series B Preferred Stock, each share of Series B Preferred Stock is convertible into an aggregate of 40 shares of our common stock. Following stockholder approval of the Series B Conversion Proposal, 254,958 shares of Series B Preferred Stock automatically converted to 10,198,320 shares of common stock; 16,667 shares of Series B Preferred Stock did not automatically convert due to beneficial ownership limitations and remain outstanding as of December 31, 2025.

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

Risks Related to Discovery, Development and Commercialization

We face competition from entities that have developed or may develop programs for the diseases and/or mechanisms of action targeted by our product candidates.

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

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

Furthermore, adverse events or disappointing results in clinical trials of third parties, including our competitors developing product candidates that target similar mechanisms of action and/or in the same indications as our product candidates, could reduce expectations regarding the potential success or perceived benefits of any of our programs, increase regulatory scrutiny of our product candidates, decrease confidence of current or potential trial participants and clinical trial collaborators in our investigational programs and/or have a negative impact on collaborations or demand for any product we may develop. These events also could result in the suspension, discontinuation, or clinical hold of or modification to our clinical trials. If public perception is influenced by claims that the use of therapies with shared or similar characteristics as ours is unsafe, ineffective or otherwise fails to meet expectations, our product candidates may not be accepted or favored by the general public, the medical community or the investment community and potential clinical trial subjects may be discouraged from enrolling in our clinical trials or may discontinue their participation in our clinical trials. Negative developments could result in reduced probability of success of clinical trials involving our product candidates, challenges enrolling clinical trial participants, greater governmental regulation, stricter labeling requirements, decreased market potential and potential regulatory delays in the testing or approvals of our product candidates.

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

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

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

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

- regulators, such as the U.S. Food and Drug Administration ("FDA"), or ethics committees (“ECs”)/institutional review boards (“IRBs”) may not authorize us or our investigators to commence a clinical trial, conduct a clinical trial at a prospective trial site or as otherwise planned;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations (“CROs”), the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites, and any CRO personnel changes could lead to operational delays or complications;
- clinical trial sites may deviate from trial protocol or drop out of a clinical trial;
- clinical trials of any product candidates may fail to demonstrate safety or efficacy, produce negative or inconclusive results, or may otherwise fail to improve on the existing standard of care, and we may decide, or regulators may require us, to conduct additional nonclinical studies or clinical trials, or we may decide to abandon product development programs;
- the number of participants required for clinical trials of any product candidates may be larger than we anticipate and enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our CROs or other third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- We may fail to adhere to clinical trial protocols or fail to perform in accordance with the FDA’s or any other regulatory authority’s good clinical practice (“GCP”) requirements or applicable regulatory guidelines in other countries or our clinical trial protocols may require changes;
- we may elect to, or regulators and/or ECs/IRBs may require that we or our investigators materially modify, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants in our trials are being exposed to unacceptable health risks;
- we may select clinical endpoints that require prolonged periods of observation or analyses of resulting data;
- we may experience delays if we or our CMOs are required to make changes to manufacturing processes or us to make any necessary changes to such manufacturing process;
- we may experience delays in identifying, recruiting and training suitable clinical investigators and their study teams;
- the cost of clinical trials of any of our programs may be greater than we anticipate;
- the quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be inadequate to initiate or complete a given clinical trial;

- we may be unable to manufacture sufficient quantities of our product candidates for use in clinical trials;
- reports from clinical testing of other therapies may raise safety or efficacy concerns about our programs;
- the FDA or other regulatory authorities may not agree with our interpretation of the results of clinical trials or non-clinical studies or our clinical trial designs and plans;
- we may fail to establish an appropriate safety profile for a product candidate based on clinical or nonclinical data for such product candidates as well as data emerging from other therapies in the same class as our product candidates; and
- the FDA or other regulatory authorities may require us to submit additional data such as long-term toxicology studies, additional clinical data or additional manufacturing data or impose other requirements before permitting us to initiate clinical trials or approving marketing/commercial sales.

Commencing clinical trials in the United States and in other countries is subject to acceptance by the FDA and other regulatory authorities of an investigational new drug ("IND") application or similar application and finalizing the trial design based on discussions with the FDA or other regulatory authority. In the event that the FDA or other regulatory authority requires us to complete additional nonclinical studies or clinical trials or we are required to satisfy other regulatory authority requests prior to commencing future planned clinical trials, the start of such planned clinical trials may be delayed or such planned clinical trials may be commenced in a modified manner. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any future clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional nonclinical studies or clinical trials, delay the enrollment of our clinical trials or impose stricter approval conditions than we currently expect. Additionally, if the results of our nonclinical studies or clinical trials are not positive or are only modestly positive or if there are safety concerns, we may be required to repeat or conduct additional clinical trials or nonclinical studies for our product candidates beyond those that we currently expect. Even if we conduct such additional nonclinical studies or clinical trials or otherwise modify our planned clinical trials, the FDA or other regulatory authorities could determine that the data from our nonclinical studies or clinical trials are insufficient to support the safety and efficacy of our product candidates. There are equivalent processes and risks applicable to clinical trial applications in other countries outside of the United States, which may require us to complete additional nonclinical studies or clinical trials, delay the enrollment of our clinical trials or otherwise modify our planned clinical trials or impose stricter approval conditions than we currently expect. Most product candidates that commence clinical trials are never approved as products, and our current or future clinical trials ultimately may fail to support the approval of our current or any future product candidates.

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

We are substantially dependent on the success of our SPY001, SPY002, SPY072 and SPY003 programs, alone or in combination, and our current and planned clinical trials of such programs may not be successful.

Our future success is substantially dependent on our ability to timely obtain marketing approval for, and then successfully commercialize, our SPY001, SPY002, SPY072 and SPY003 programs, alone or in combination. We are investing a majority of our efforts and financial resources into the research and development of these programs. We initiated a a Phase 2 platform trial of SPY001, SPY002 and SPY003, including combinations, for IBD in the United States and certain other countries beginning with SPY001 in May 2025. We are currently enrolling subjects into Part A of the Phase 2 UC platform trial and plan to initiate enrollment into Part B, which includes combination arms, in our Phase 2 UC platform trial after Part A completes enrollment, with each arm subject to regulatory feedback and approval. We also initiated a Phase 2 basket trial of SPY072 for RD, including RA, PsA and axSpA, in the United States and Europe in September 2025 and December 2025, respectively, with initiation expected in certain other countries subject to regulatory feedback

and approval. The FDA and/or other regulatory authorities may not agree with our clinical trial designs for our SKYWAY Phase 2 basket trial or with our proposed timing for enrollment or trial design of the combination arms of our SKYLINE Phase 2 platform trial. Alignment with regulatory authorities on issues that arise before clinical trials commence, during clinical trials or after our clinical trials are completed could result in additional capital expenditures or delays in development that could have a material adverse impact on our business. The success of our programs is dependent on observing longer half-lives of our product candidates in humans and comparable or better safety and efficacy profiles than other mAbs currently marketed or in development. We believe these longer half-lives have the potential to result in more favorable dosing schedules for our product candidates, assuming they successfully complete clinical development and obtain marketing approval. To the extent we do not observe these extended half-lives with favorable safety and efficacy profiles when we dose patients with our product candidates, it would significantly and adversely affect the clinical and commercial potential of our product candidates.

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

The success of our product candidates will depend on a variety of factors. We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any current or future collaborator. Accordingly, we cannot assure you that we will ever be able to generate revenue through the sale of these product candidates, even if approved. If we are not successful in commercializing SPY001, SPY002, SPY072 or SPY003, alone or in combination, or are significantly delayed in doing so, our business will be materially harmed.

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

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

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

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

regulatory clearance of the devices. Even if approval is obtained for our products, we may also be dependent on those third-party companies continuing to maintain such approvals or clearances, if required, for their drug delivery devices once they have been received. Failure of third-party companies to supply the devices, to successfully complete studies on the devices in a timely manner, or to obtain or maintain required approvals or clearances of the devices could result in increased development costs, delays in or failure to obtain regulatory approval and delays in product candidates reaching the market or in gaining approval or clearance for expanded labels for new indications.

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

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

We may ultimately discover that our investigational products developed with half-life extension technologies do not possess certain properties required for therapeutic effectiveness and could lead to adverse effects. We currently have only interim Phase 1 clinical data in healthy volunteers and nonclinical data regarding the increased half-life and drug clearance properties of our programs and the anticipated half-life extension and/or drug clearance properties of each of our product candidates may not be seen in participants in our clinical trials. In addition, programs using half-life extension technologies may demonstrate different chemical and pharmacological properties in participants than they do in laboratory studies. This technology and any programs resulting therefrom may not demonstrate the same chemical and pharmacological properties in humans and may interact with human biological systems in unforeseen, ineffective or harmful ways.

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

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

Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidate in humans. Our clinical trials may not be conducted as planned or completed on schedule, if at all, and failure can occur at any time during the preclinical study or clinical trial process. For example, we depend on the availability of NHPs to conduct certain preclinical studies that we are required to complete prior to submitting an IND or foreign equivalent and initiating clinical development. There is no guarantee that we will always be able to source NHPs for our drug development activities on our preferred timelines. The cost of obtaining NHPs for our future preclinical development activities could increase significantly if short or long term shortages occur in their availability. If we are unable to source NHPs on our

preferred timelines, it could result in delays to our development timelines. Similarly, we may experience difficulty in conducting our clinical trials as planned if we are unable to enroll a sufficient number of participants in any such trial as a result of variables outside of our control. See the risk factor titled "If we encounter difficulties enrolling participants in our current and future clinical trials, our clinical development activities could be delayed or otherwise adversely affected."

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

We cannot be sure that the FDA, or comparable foreign regulatory authority, as applicable, will agree with our clinical development plans. If the FDA and/or comparable foreign regulatory authority requires us to materially modify our proposed trial designs, conduct additional trials or enroll additional participants, our development timelines may be delayed. We cannot be sure that submission of an IND, clinical trial application or similar application will result in the FDA or comparable foreign regulatory authorities, as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could cause regulatory authorities to suspend or terminate them.

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

A key element of our strategy is the development of intra-portfolio investigational drug combinations. If we are not successful in discovering, developing and commercializing investigational products that take advantage of different mechanisms of action to achieve superior outcomes relative to the use of monotherapies or other combinations, our ability to achieve our strategic objectives would likely be impaired.

A key element of our strategy is to build a broad portfolio of investigational products that will allow for the development of intra-portfolio combinations. We believe that by developing or licensing these investigational products, we can control the combinations we pursue and, if and when approved, maximize the commercial potential of these combinations. However, these combinations have not been tested before and may fail to achieve superior outcomes relative to the use of single agents or other combinations, may exacerbate adverse events associated with one of the investigational products when used as monotherapy, may yield new adverse events not observed with either of the monotherapies, or may fail to demonstrate sufficient safety or efficacy in clinical trials to enable us to complete those clinical trials or obtain marketing approval for the combinations. In addition, demonstrating that our combinations are superior to our single agents is likely necessary for marketing authorization of the combinations. However, comparing active treatments may be difficult to do in a controlled manner in our clinical trials, and we may be unable to interpret the results of comparisons between our combinations and single agents in a manner that satisfies regulatory requirements.

Even if we are successful in developing combinations, competition from other investigational products in the same class which are either already approved or further along in development than ours may prevent us from realizing the commercial potential of our combinations and prevent us from achieving our strategic objectives.

Development of combination therapies may present more or different challenges than development of monotherapies.

We plan to pursue development of our investigational products in combination with one or more additional products or investigational products. The development of combination therapies may be more complex than the development of monotherapies and generally requires that sponsors demonstrate the contribution of each investigational product to the claimed effect and the safety and efficacy of the combination as a whole. Regulatory authority requirements for the development of combination therapies may make the design and conduct of clinical trials more complex and/or burdensome, requiring more clinical trial participants and additional time and cost to complete than we plan or anticipate. We also may not be able to meet the FDA's or comparable foreign regulatory authority's current or future approval standards required for combination therapies or combination products, if we decided to administer or package combinations as a single drug product. For example, under the "combination rule", the FDA may not file or approve a fixed-dose combination product unless each component of a proposed drug product is shown to make a contribution to the claimed effects and the dosage of each component (amount, frequency, duration) is safe and effective for the intended population. To satisfy these requirements, the FDA typically requires a clinical factorial trial, designed to assess the effects attributable to each drug in the combination product. This is particularly true when the ingredients are directed at the same sign or symptom of the disease or condition. The FDA has accepted a variety of approaches to satisfy the combination rule, but the FDA has stated that factorial studies may be unethical (e.g., omitting a drug known to improve survival) or impractical (there may be too many components to conduct a factorial trial, meaning the trial cannot be conducted). The FDA has also stated that it may be possible to use other types of clinical and nonclinical data and mechanistic information available to demonstrate the contributions of the individual active ingredients to the effect of the combination. In addition, combination products may require dose selection for each agent in the combination, which may require more and/or larger groups of participants than single agents. Our clinical trial and research efforts may not satisfy regulators' expectations of adequate exploration of dose ranging required for drug approval. Moreover, the applicable requirements for approval of combinations may differ from country to country.

In the event that one of our investigational products were to fail to demonstrate sufficient safety and efficacy data or establish its contribution to the claimed effects of combinations or if we are unable to meet the FDA's or comparable foreign regulatory authority's current or future approval standards required for combination therapies or combination products in a timely manner, we would need to identify and research alternative monotherapy or combination treatments, run additional trials to produce supportive data or modify existing clinical trial plans. In the event we are unable to do so or are unable to do so on commercially reasonable terms or we are unable to continue development of one or more of investigational products, our business and prospects would be materially harmed.

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

We may experience difficulties in participant enrollment in our current and future clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of participants who remain in the trial until its conclusion. The enrollment of participants will depend on many factors, including:

- the prevalence and severity of the disease under investigation;
- the participant eligibility and the inclusion and exclusion criteria defined in the protocol;
- the incidence and prevalence of target trial populations under clinical investigation;
- the proximity of participants to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;

- clinicians' and participants' perceptions as to the potential advantages of the drug candidate(s) being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- our ability to obtain and maintain participant consents;
- our ability to monitor participants adequately during and after treatment;
- the risk that participants enrolled in clinical trials will drop out of the trials before completion or fail to attend scheduled trial visits; and
- factors we may not be able to control, including the impacts of public health crises, which may limit the availability of participants, investigators or their staff, or clinical sites.

In addition, our clinical trials will compete with other clinical trials with product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of participants available to us, because some participants who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of participants who are available for our clinical trials at such clinical trial sites. Additionally, the number of participants required for clinical trials of our programs may be larger than we anticipate. Even if we are able to enroll a sufficient number of participants for our current or future clinical trials, we may have difficulty maintaining participants in our clinical trials. Our inability to enroll or maintain a sufficient number of participants would result in significant delays in completing clinical trials or receipt of marketing approvals, increased development costs or our cessation of one or more clinical trials altogether.

Additionally, our ability to successfully initiate, enroll, and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including, without limitation: difficulty in establishing or managing relationships with CROs and physicians; different standards for the conduct of clinical trials; different standard-of-care for patients with a particular disease; difficulty in locating qualified local consultants, physicians and partners; and potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

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

From time to time, we may publicly disclose preliminary or topline data from our nonclinical studies and clinical trials, which are based on a preliminary analysis of then-available data. The results and related findings and conclusions are subject to change following a more comprehensive review or taking into account additional data that becomes available. In reviewing preliminary or topline data, we also make assumptions, estimations, calculations and conclusions as part of our analyses that may change once a complete data set is available. As a result, the preliminary or topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated or subsequently made subject to audit and verification procedures. Any preliminary or topline data should be viewed with caution until the final data are available.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular product candidate, the approvability or commercialization of the particular product candidate and our company in general. In addition, the information we choose to publicly disclose regarding a particular nonclinical study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the preliminary, topline or interim data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

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

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

Our product candidates have mechanisms of action in common with other approved drugs that have been associated with certain adverse reactions in patients. For example, nasopharyngitis, headache, arthralgia, nausea, pyrexia, upper respiratory tract infection, fatigue, cough, bronchitis, influenza, back pain, rash, pruritus, sinusitis, oropharyngeal pain, and pain in extremities are the most common adverse reactions noted with ENTYVIO®, which is in the same drug class as SPY001 and is approved for the treatment of moderately to severely active UC in adults and of moderately to severely active CD in adults. In addition, mAbs targeting TL1A such as our product candidates SPY002 and SPY072 in clinical trials are associated with patient adverse reactions that most commonly include headache, nausea, nasopharyngitis, urinary tract infection, SARS-CoV-2 infection, fever, fatigue, arthralgia, and back pain. Finally, for SKYRIZI®, which is in the same drug class as SPY003 and is approved for the treatment of moderately to severely active UC in adults and of moderately to severely active CD in adults, the most common adverse reactions are upper respiratory infections, headache, arthralgia, injection site reactions, abdominal pain, anemia, pyrexia, back pain, arthropathy, and urinary tract infection in patients with CD and arthralgia, pyrexia, injection site reactions, and rash in patients with UC. Participants in our clinical trials for SPY001, SPY002, SPY072 and SPY003, or combinations thereof, may experience similar or additional adverse reactions such as infections (including rare infections such as tuberculosis or JC virus reactivation, which could lead to multifocal leukoencephalopathy), infusion-related reactions, other hypersensitivity reactions (including injection site reactions and delayed hypersensitivity reactions), and hepatotoxicity, as has been observed with other biologics, including those with similar mechanisms of action.

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

If any of the foregoing events occur or if one or more of our research programs prove to be unsafe, our entire pipeline could be affected, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Because we have limited financial and managerial resources, we focus our research and development efforts on certain selected programs. For example, we are initially focused on our SPY001, SPY002 and SPY003 programs, including combinations thereof, and our SPY072 program. As a result, we may forgo or delay pursuit of opportunities with other programs that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

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

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

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

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

We have multiple product candidates, alone and in combination, in development for the same indication, IBD, and are developing one product candidate (SPY072) for RD. We may in the future develop our programs for other I&I indications. Each such program targets a single or multiple mechanisms of action that could provide differentiation from standard of care or each other. However, developing multiple programs for a single indication may negatively impact our business if the programs compete with each other. For example, if multiple programs are conducting clinical trials at the same time, they could compete for the enrollment of participants. In addition, if multiple product candidates are approved for the same indication, they may compete for market share, which could limit our future revenue.

We are conducting and may conduct future clinical trials for our programs at sites in the United States and various other jurisdictions, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We are conducting and may conduct future clinical trials in the United States and various other countries. The acceptance of trial data from clinical trials conducted outside the United States or other jurisdiction by the FDA or comparable foreign regulatory authority may be subject to conditions imposed by such regulatory authority or may not be accepted at all. For example, in cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the applicable clinical trial data on the basis of foreign data alone unless, among other conditions, (i) the clinical trial is well-designed and conducted and performed by qualified investigators in accordance with ethical principles, (ii) the trial population adequately represents the U.S. population, and (iii) the data is applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. Many foreign regulatory authorities have similar approval requirements. In addition, clinical trials are subject to the applicable local laws of the jurisdictions where the trials are conducted and acceptance of the data by the FDA or any comparable foreign regulatory authority may depend on its determination that the trials also complied with all applicable local laws and regulations. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would likely result in the need for additional trials, which would be costly and time-consuming and would delay or permanently halt our development of the applicable product candidates. Even if the FDA or any comparable foreign regulatory authority accepted such data, it could require us to modify our ongoing or planned clinical trials to receive clearance to initiate such trials in the applicable jurisdiction or to continue such trials once initiated.

Further, conducting international clinical trials presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled participants in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs that could restrict or limit our ability to conduct our clinical trials, the administrative burdens of conducting clinical trials under multiple sets of foreign regulations, foreign exchange fluctuations, as well as political and economic risks relevant to foreign countries. For additional disclosures regarding political and economic risks involved with international clinical trials, see the risk factor titled “Our business could be adversely affected by economic downturns, inflation, increases in interest rates, natural disasters, public health crises, political crises, U.S. elections, international or geopolitical events, such as the conflict between Russia and Ukraine, recent events in Venezuela, and conflicts in the Middle East, the implementation of measures that restrict international trade or other macroeconomic conditions, which could have a material and adverse effect on our results of operations and financial condition.”

Risks Related to Government Regulation

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

The process of obtaining regulatory approvals, both in the United States and abroad, is unpredictable, expensive and typically takes many years following commencement of clinical trials, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. We cannot commercialize product candidates in the United States without first obtaining regulatory approval from the FDA. Similarly, we cannot commercialize product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of our product candidates, including SPY001, SPY002, SPY072 and SPY003, alone or in combination, we must demonstrate through lengthy, complex and expensive nonclinical studies and clinical trials that our product candidates are both safe and effective for each targeted indication. Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Further, our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining

marketing approval. The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional nonclinical, clinical or other data. Our product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including: the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials; we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication; the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval; serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates; we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks; the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical trials; the data collected from clinical trials of our product candidates may not be acceptable or sufficient to support the submission of a BLA or other submission or to obtain regulatory approval in the United States or elsewhere, and we may be required to conduct additional clinical trials; the FDA or the applicable foreign regulatory authority may disagree regarding the formulation, labeling and/or the specifications of our product candidates; the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval. In addition, the FDA and comparable foreign regulatory authorities may undergo leadership changes, change their policies, issue additional regulations or revise existing regulations, or take other actions, which may impact our clinical development plans or prevent or delay approval of our programs under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals and increase the costs of compliance.

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

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

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

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

Manufacturing biologics is highly susceptible to losses due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. The impact to drug supply may be compounded by the long lead times needed to manufacture additional drug product due to plant capacity

limitations or other potential restrictions at our CMOs. In some cases, even minor deviations from normal manufacturing processes may result in reduced production yields, lot failures, product defects, product liability claims, or other supply disruptions. If issues arise at our third-party manufacturers' facilities, such facilities may need to be closed for an extended period of time to investigate and remedy the issues, which could delay clinical trials and adversely affect our business. Problems in third-party manufacturing process or facilities could restrict our ability to ensure sufficient clinical material for our clinical trials or delay or prevent us from obtaining marketing approval.

Scaling up a biologic manufacturing process can be a difficult task and is associated with additional risks, including cost overruns, process scale-up, process reproducibility, stability issues, compliance with current good manufacturing practices ("cGMPs"), lot consistency and timely availability of sufficient quantity of raw materials. Even if we obtain regulatory approval for any of our product candidates, manufacturers may not be able to manufacture the approved product to specifications acceptable to the FDA or other comparable foreign regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product or to meet potential future demand. If our third-party manufacturers are unable, or decide not, to adequately validate or scale-up the manufacturing process at our current manufacturers' facilities, we will need to transfer to another manufacturer and complete the manufacturing validation process, which can be lengthy. If our manufacturers are unable to produce sufficient quantities of drug substance and/or drug product for clinical trials or for commercialization we will need to identify and negotiate with other CMOs an agreement for clinical and/or commercial supply and it is not certain we will be able to come to agreement timely or on terms acceptable to us, which would likely jeopardize our ability to provide any product candidates to trial subjects in clinical trials and products to patients, if approved.

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

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

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

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

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

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

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

***We may be negatively impacted by changes in law or other policy, including healthcare reform initiatives*.**

Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay development of or regulatory approval of our product candidates and/or increase our manufacturing costs, general operating costs or other costs. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we fail to adequately prepare for the impacts of or are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, our product candidates may be delayed in obtaining regulatory approval or may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability. In addition, the impact of legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the current presidential administration on us and the pharmaceutical industry as a whole is unclear. These government actions could cause delays in our business plans, increase the cost of execution of our business plans or otherwise have a material adverse effect on our business. For example, the federal government recently announced tariffs on goods imported from China and other countries, which have been followed by threatened or enacted counter-measures by certain countries. These measures could impact the cost of manufacturing our product candidates for our ongoing and planned clinical trials and may increase other costs such as import and export costs across different jurisdictions, costs of drug product and clinical trial supplies, and other costs of running our trials and executing on our business plans, which could negatively impact our financial position. We may seek alternative or additional sources for our drug substance or drug product for our clinical trials, clinical trial sites, or service providers, which could negatively impact our expected costs, timelines and business plan. Additionally, the BIOSECURE Act enacted as part of the FY 2026 National Defense Authorization Act has the potential to severely restrict our ability to purchase services or products from, or otherwise collaborate with, certain Chinese "biotechnology companies of concern" without losing the ability to contract with, or otherwise receive funding from, the U.S. government. If any of our CMOs are identified as a BCOC, we could be required to switch or move development of our product candidates from one CMO to another, and as a result we may incur additional development costs or delays in manufacturing product for clinical trials or commercialization. In the U.S., in recent years, the pharmaceutical industry has been a particular focus of healthcare reform efforts and has been significantly affected by major legislative, administrative and executive initiatives addressing drug pricing and payment, access to healthcare or funding of healthcare as well as more general actions affecting federal budgets and tariffs. See the section titled "Business – Government Regulation – Healthcare Reform" in this Annual Report for a more detailed description of healthcare reform measures that may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates.

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

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. In the U.S., these laws include, but are not limited to the following, some of which are likely to apply only if or when we obtain marketing approval for a product candidate:

- federal false claims, false statements, and civil monetary penalties laws prohibiting, among other things, any person from knowingly presenting, or causing to be presented, a false claim for payment of government funds or knowingly making, or causing to be made, a false statement to get a false claim paid;
- the federal anti-kickback law, which prohibits, among other things, persons from offering, soliciting, receiving, or providing remuneration, directly or indirectly, to induce either the referral of an individual for, or the purchasing or ordering of, a good or service for which payment may be made under federal healthcare programs such as Medicare and Medicaid;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which, in addition to privacy protections applicable to healthcare providers and other entities, prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- the FDCA, which among other things, strictly regulates drug marketing, prohibits manufacturers from marketing products prior to approval or for off-label use and regulates the distribution of samples;
- federal laws that require pharmaceutical manufacturers to calculate, report and certify certain complex product prices and other data to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs, which data may be used in the calculation of reimbursement and/or discounts on approved products;
- the federal Open Payments (or federal "sunshine" law), which requires pharmaceutical and medical device companies to monitor and report certain financial interactions with certain healthcare providers to the Center for Medicare & Medicaid Services within the U.S. Department of Health and Human Services for re-disclosure to the public, as well as ownership and investment interests held by physicians and their immediate family members;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- analogous state laws and regulations, including state anti-kickback and false claims laws, consumer protection and unfair competition laws and laws governing privacy, security and breaches of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- state laws that require pharmaceutical companies to comply with specific compliance standards, restrict financial interactions between pharmaceutical companies and healthcare providers, report drug product pricing information, financial interactions with health care providers, or marketing expenditures and/or require the registration of pharmaceutical sales representatives.

The distribution of biopharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

See the section titled "Business – Government Regulation – Other Healthcare Laws and Compliance Requirements" in this Annual Report for a more detailed description of certain laws that may affect our ability to operate.

Ensuring compliance is time-consuming and costly. If and when one of our product candidates is approved, our compliance efforts will need to expand and evolve to address newly applicable laws. Given the breadth of the laws and regulations, limited guidance for certain laws and regulations and evolving government interpretations of the laws and regulations, governmental authorities may possibly conclude that our business practices are non-compliant. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects.

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

We intend to seek approval to market our product candidates in both the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. Our ability to successfully commercialize any product candidates that we may develop will depend in significant part on the extent to which reimbursement for these product candidates and related treatments will be available from government health administration authorities, government health benefit programs, private health insurers, such as managed care plans, and other organizations. Government authorities and other third-party payors decide which medications they will pay for and establish reimbursement levels. Government authorities and other third-party payors have attempted to control costs by restricting coverage, controlling utilization and limiting the amount of reimbursement for particular medications. Third party payors may take action to encourage use of other products perceived to be clinically superior or more cost effective which may limit demand for our products. Our ability to commercialize our product candidates successfully may also be adversely affected by discounts or rebates that we are required to provide in order to ensure coverage of our products and compete in the marketplace. Additionally, if any of our product candidates is approved and we are found to have improperly promoted off-label uses of those product candidates, we may become subject to significant liability, which would materially adversely affect our business and financial condition. See the sections titled "Business – Government Regulation – Coverage and Reimbursement" and "Business – Government Regulation – Regulation in the European Union" in this Annual Report for a more detailed description of the government regulations and third-party payor practices that may affect our ability to commercialize our product candidates.

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

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

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

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

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

We may seek a breakthrough therapy, fast track, or other designation for appropriate product candidates. Designations such as these are within the discretion of the FDA, or other comparable foreign regulatory authorities. The receipt of a designation for a product candidate may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify under one of FDA's designation programs, the FDA may later decide that the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Additionally, changes in the leadership of the FDA and other actions taken by the presidential administration, including mass layoffs within the federal government, may impose constraints on the FDA's ability to engage in activities in the normal course and may result in reductions to the FDA's budget, employees and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to take advantage of the benefits for the Fast Track Designation and progress development of our programs or obtain regulatory approval for our programs. See the section titled "Business – Government Regulation – United States Biologics Regulation – Expedited Development and Review Programs" in this Annual Report for a more detailed description of the process for seeking expedited designations such as fast track or breakthrough therapy designations.

Disruptions at the FDA and other government agencies, including as a result of the government shutdown, could negatively affect the review of our regulatory submissions, which could negatively impact our business.

The ability of the FDA to review and approve regulatory submissions can be affected by a variety of factors, including the government shutdown as well as statutory, regulatory and policy changes, inadequate government budget funding levels or a reduction in the FDA's workforce and its ability to hire and retain key personnel, disruptions caused by government shutdowns and public health crises. There have been mass layoffs of federal employees since the start of the current presidential administration in January 2025, the full impact of which is unclear at this time. Such disruptions could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. In addition, the presidential administration has made and is expected to continue to make significant changes in the leadership of the FDA and other U.S. federal regulatory agencies and changes to U.S. federal government policy that have led to, in some cases, legal challenges and uncertainty around the funding, functioning and policy priorities of the U.S. federal regulatory agencies, including the FDA.

We are unable to predict the extent to which the presidential administration may impose or seek to impose leadership or policy changes at the FDA or changes to rules and policies impacting our business and operations. It is unclear how these executive actions or other potential actions by the federal government will impact the FDA or other regulatory authorities that oversee our business. Government proposals to reduce or eliminate budgetary deficits may include reduced allocations to the FDA and other related government agencies. These budgetary pressures may reduce the FDA's ability to perform its responsibilities, which could result in delays in our clinical trial timelines. If a significant reduction in the FDA's workforce occurs, the FDA's budget is significantly reduced or a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions or take other actions critical to the development or manufacturing of our product candidates, which could have a material adverse effect on our business.

Additionally, the U.S. Supreme Court's June 2024 decision in *Loper Bright Enterprises v. Raimondo* overturned the longstanding Chevron doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The *Loper* decision could result in additional legal challenges to regulations and guidance issued by federal agencies, including FDA and the Center for Medicare & Medicaid Services, on which we rely. Any such legal challenges, if successful, could have a material impact on our business. Additionally, the *Loper* decision may result in increased regulatory uncertainty, inconsistent judicial interpretations, and other impacts to the agency rulemaking process, any of which could adversely impact our business and operations. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action or as a result of legal challenges, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, our business could be materially harmed.

Risks Related to Our Intellectual Property

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Geopolitical instability in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of patent applications and the maintenance, enforcement or defense of issued patents. For example, the United States and foreign government actions related to Russia's invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees that have citizenship or nationality in, are registered in, or have predominately primary place of business or profit-making activities in the United States and other countries that Russia has deemed unfriendly without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected. In addition, a European Unified Patent Court ("UPC") entered into force on June 1, 2023. The UPC is a common patent court that hears patent infringement and revocation proceedings effective for member states of the EU. This could enable third parties to seek revocation of a European patent in a single proceeding at the UPC rather than through multiple proceedings in each of the jurisdictions in which the European patent is validated. Given that we own or license certain European patents or applications for our current pipeline, any such revocation and loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and products. Moreover, the controlling laws and regulations of the UPC will develop over time, and may adversely affect our ability to enforce or defend the validity of any European patents we may obtain. We may decide to opt out from the UPC any future European patent applications that we may file and any patents we may obtain. If certain formalities and requirements are not met, however, such European patents and patent applications could be challenged for non-compliance and brought under the jurisdiction of the UPC. We cannot

be certain that future European patents and patent applications will avoid falling under the jurisdiction of the UPC, if we decide to opt out of the UPC, or that we will have the ability to opt out of the UPC in the future.

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

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

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

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

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

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

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

paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

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

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

Our technology licensed from various third parties may be subject to retained rights or may be affected by our failure to comply with obligations under license agreements or other disruptions to business relationships with licensors resulting in loss of license rights that are important to our business.

Our current or future licensors may retain certain rights under the relevant agreements with us, including the right to use the underlying technology for noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. It is difficult to monitor whether our licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse. In addition, under our license agreements, we may be generally responsible for bringing any actions against third parties for infringing on the patents we have licensed. Certain of our license agreements may also require us to meet development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products. In spite of our efforts, our licensors might conclude that we have materially breached our obligations under such license agreements and might therefore terminate the license agreements, thereby removing or limiting our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may seek regulatory approval of, and to market, products identical to ours or we may be required to cease our development and commercialization of one or more product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and growth prospects. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights to third parties under our collaborative development relationships;
- our diligence obligations under the license agreement with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates and what activities satisfy those diligence obligations;

- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or broaden what we believe to be the scope of the licensor's rights to our intellectual property and technology, or increase what we believe to be our financial or other obligations under the relevant agreement, any of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. It is also possible that a third party could be granted limited licenses to some of the same technology, in certain circumstances. Any such events could result in the loss of our ability to develop and commercialize one or more product candidates or we could lose other significant rights, any of which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

We have limited foreign intellectual property rights and may not be able to protect our intellectual property and proprietary rights throughout the world.

We have limited intellectual property rights outside of the United States. Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of foreign countries do not protect intellectual property rights to the same extent as the federal and state laws of the United States. In addition, intellectual property license agreements we enter into may not always include worldwide rights. Consequently, we may not be able to prevent third parties from using our intellectual property in all countries outside the United States, or from selling or importing products made using our intellectual property in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is difficult or impractical. These products may compete with our product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology and pharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our patents and intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Moreover, the initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have invoked compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

The intellectual property landscape around engineered antibodies is highly dynamic, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating

their intellectual property rights, the outcome of which would be uncertain and may prevent, delay or otherwise interfere with our product discovery and development efforts.

Due to the intense research and development that is taking place in the field of engineered antibodies, including by us and our competitors, the intellectual property landscape is evolving and in flux, and it may remain uncertain for the coming years. There may be significant intellectual property related litigation and proceedings relating to our owned and in-licensed, and other third party, intellectual property and proprietary rights in the future.

Our commercial success depends upon our ability and the ability of our collaborators and licensors to develop, manufacture, market, and sell any product candidates that we may develop and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights as well as administrative proceedings for challenging patents, including interference, derivation, inter partes review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be subject to and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates we may develop, including interference proceedings, post-grant review, inter partes review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the EPO. Numerous U.S. and foreign issued patents and pending patent applications that are owned by third parties exist in the fields in which we are developing our product candidates and they may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit.

As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of therapies, products or their methods of use or manufacture. We are aware of certain third-party patent applications that, if issued, may be construed to cover some of our product candidates. There may also be third-party patents of which we are currently unaware with claims to technologies, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents.

Because of the large number of patents issued and patent applications filed in our field, third parties may allege they have patent rights encompassing our product candidates, technologies or methods. Third parties may assert that we are employing their proprietary technology without authorization and may file patent infringement claims or lawsuit against us, and if we are found to infringe such third-party patents, we may be required to pay damages, cease commercialization of the infringing technology, or obtain a license from such third parties, which may not be available on commercially reasonable terms or at all.

Our ability to commercialize our product candidates in the United States and abroad may be adversely affected if we cannot obtain a license on commercially reasonable terms to relevant third-party patents that cover our product candidates. Even if we believe third-party intellectual property claims are without merit, there can be no assurance that a court would find in our favor on questions of infringement, validity, enforceability, or priority. A court of competent jurisdiction could hold that these third-party patents are valid, enforceable, and infringed, which could materially and adversely affect our ability to commercialize any product candidates we may develop and any other product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there can be no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If we are found to infringe a third party's intellectual property rights, and we are unsuccessful in demonstrating that such patents are invalid or unenforceable, we could be required to obtain a license from such third party to continue developing, manufacturing, and marketing impacted product candidates we may develop and our technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, we may be unable to commercialize certain product candidates or such commercialization efforts may be significantly delayed, which could in turn significantly harm our business. We also could be forced, including by court order,

to cease developing, manufacturing, and commercializing the infringing technology or product candidates. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations, and prospects.

Defense of third-party claims of infringement of misappropriation, or violation of intellectual property rights involves substantial litigation expense and would be a substantial diversion of management and employee time and resources from our business. Some third parties may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, financial condition, results of operations and prospects. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Any of the foregoing events could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Our Reliance on Third Parties

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

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

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

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

We may face significant competition in attracting appropriate collaborators, and more established companies may also be pursuing strategies to license or acquire third-party intellectual property rights that we consider attractive. These companies may have a competitive advantage over us due to their size, financial resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Whether we reach a definitive agreement for a collaboration will depend upon, among other things, our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Collaborations are complex and time-consuming to negotiate,

document and execute. In addition, consolidation among large pharmaceutical and biotechnology companies has reduced the number of potential future collaborators. We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market.

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

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

Any third parties conducting our nonclinical studies and clinical trials will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot control whether they devote sufficient time and resources to our programs. These third parties may be involved in mergers, acquisitions or similar transactions and may have relationships with other commercial entities, including our competitors, for whom they may also be conducting nonclinical studies, clinical trials or other product development activities, which could negatively affect their performance on our behalf and the timing thereof and could lead to products that compete directly or indirectly with our current or future product candidates. If any of our relationships with these third parties, including CMOs and CROs, are terminated, we may not be able to enter into arrangements with alternative CMOs, CROs or other third parties or to do so on commercially reasonable terms. Switching or adding additional CMOs or CROs involves additional cost and requires company resources. In addition, there is a natural transition period when a new CMO or CRO begins work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CMOs and CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

If these CMOs, CROs or other third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure (including by clinical sites or investigators) to adhere to our nonclinical and clinical protocols or regulatory requirements or for other reasons, our nonclinical studies and clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially and our ability to generate revenues could be delayed significantly.

In addition, we currently rely on foreign CROs and CMOs, including WuXi Biologics, and will likely continue to rely on foreign CROs and CMOs in the future. We or the foreign CROs or CMOs we work with may be subject to U.S. legislation, including the BIOSECURE Act included as part of the FY 2026 National Defense Authorization Act, sanctions, trade restrictions and other foreign regulatory requirements which could increase the cost or reduce the supply of material available to us, delay the procurement or supply of such material or have an adverse effect on our ability to secure significant commitments from governments to purchase our potential therapies or disrupt our supply chain. For example, in April 2025, the United States government imposed significant tariffs on imports from China and other countries and may impose more restrictions on goods, including biologically derived substances, manufactured in or imported from China or impose other restrictions on companies' ability to work with Chinese biotechnology companies. We are in the process of creating manufacturing capabilities with third parties outside of China, including within the United States, and have taken several measures to strengthen our supply chain in the event that our manufacturers are impacted; however, to the extent the aforementioned restrictions or future tariffs are applicable to the material we import from China and other countries or if we are not able to secure supply of our product candidates as a result of applicable legislation, our business and financial condition could be adversely affected despite our mitigation efforts.

Further, the biopharmaceutical industry in China is strictly regulated by the Chinese government. Changes to Chinese regulations or government policies affecting biopharmaceutical companies are unpredictable and may have a material adverse effect on our collaborators in China which could have an adverse effect on our business, financial condition, results of operations and prospects. Evolving changes in China's public health, economic, political, and social conditions and the uncertainty around China's relationship with other governments, such as the United States and the UK, could also negatively impact our ability to manufacture our product candidates for our ongoing or planned clinical trials or have an adverse effect on our ability to secure government funding, which could adversely affect our financial condition and cause us to delay our clinical development programs.

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

We do not currently own any facility that may be used as our clinical or commercial manufacturing and processing facility and must currently rely on CMOs to manufacture our product candidates. We have not yet caused our product candidates to be manufactured on a commercial scale and may not be able to do so for any of our programs, if approved. We currently have a sole source relationship for our supply of the SPY001, SPY002 and SPY003 programs. If there should be any disruption in such supply arrangement, including any adverse events affecting our suppliers, it could have a negative effect on the clinical development of our programs and other operations while we work to identify and qualify alternate supply sources. We may not control the manufacturing process of, and may be completely dependent on, our contract manufacturing partners for compliance with cGMP requirements and any other regulatory requirements of the FDA or comparable foreign regulatory authorities for the manufacture of our product candidates. Beyond periodic audits, we have limited control over the ability of our CMOs to maintain adequate quality control, quality assurance and other qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any approval in the future, we may need to find alternative manufacturing facilities, which would require the incurrence of significant additional costs and delays, and materially adversely affect our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Similarly, our failure, or the failure of our CMOs, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations.

Moreover, our CMOs may experience manufacturing difficulties due to resource constraints, supply chain issues, proposed or actual legislative changes or requirements, or as a result of labor disputes or unstable political environments, including tariffs and restrictions imposed by the United States or other foreign governments on goods required for the operation of their business. If any CMOs on which we will rely fail to

manufacture quantities of our product candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a cost that allows us to achieve profitability, our business, financial condition and prospects could be materially and adversely affected. In addition, our CMOs and other third parties are responsible for transporting temperature-controlled materials that can be inadvertently degraded during transport due to several factors, rendering certain batches unsuitable for trial use for failure to meet, among others, our integrity and purity specifications. We and any of our CMOs may also face product seizure or detention or refusal to permit the import or export of products or increased costs as a result of tariffs on imports imposed by the United States or other foreign governments. Our business could be materially adversely affected by business disruptions to our third-party providers that could materially adversely affect our anticipated timelines, potential future revenue and financial condition and increase our costs and expenses. Each of these risks could delay or prevent the completion of our nonclinical studies and clinical trials or the approval of any of our product candidates by the FDA, resulting in higher costs or adversely impact commercialization of our product candidates. See the section titled "Business – Manufacturing and Supply" in this Annual Report a more detailed description of our manufacturing plans and assumptions and the factors that may affect the success of our programs.

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

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

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

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

We are a clinical stage biotechnology company with a limited operating history, and, as of December 31, 2025, we had 102 employees. We have been and will continue to be highly dependent on the research and development, clinical and business development expertise of our executive officers, as well as the other principal members of our management, scientific and clinical team. Any such officers and other principal members may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees.

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

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

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

Our future growth may depend, in part, on our ability to develop and commercialize our product candidates in foreign markets for which we may rely on collaboration with third parties. Recent and ongoing changes in the United States trade policy with foreign countries, including the continued uncertainty surrounding U.S. tariffs and retaliatory measures by foreign governments may disrupt the global supply chain for biopharmaceutical products. Any direct tariffs, if imposed on pharmaceutical products, may result in increased costs for raw materials and contract manufacturing services, reduced ability to source critical CMOs, and a delay in our development timelines.

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

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

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

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

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

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

Our internal information technology systems, as well as those of any of our CROs, manufacturers, other contractors or consultants, third-party service providers, and potential future collaborators, are subject to the risk of failure, security breaches, data privacy incidents, or other unauthorized or improper

access to, use of, or destruction of proprietary, confidential, employee, or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand, and material disruption to our business.

To achieve our business objectives, we depend on our own internal IT systems and networks, as well as those of third parties and their vendors. These systems are used to process and store sensitive data—including confidential research, business plans, financial information, intellectual property, trade secrets and various personal data that may be legally protected. They also play a critical role in maintaining the continuity of our supply chain and operations, and are integral to many of the products provided to customers.

Although we have implemented security measures designed to protect our information systems and the data they store, the size and complexity of these systems—and the increasing volume of information maintained on our internal IT systems and those of our third-party CROs, other contractors (including clinical trial sites), service providers, supply chain partners, and consultants—make them potentially vulnerable to a range of risks. These risks include breakdowns or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners and/or other third parties, or from cyber-attacks by malicious third parties. Such incidents could compromise our system infrastructure or lead to the loss, destruction, alteration or dissemination of, or damage to, our data. The evolving use of AI by malicious actors is expected to further intensify cybersecurity threats. For example, AI can be leveraged to develop adaptive malware, generate highly convincing phishing or impersonation attacks (such as deepfakes), or automate the discovery and exploitation of software vulnerabilities, thereby increasing the likelihood and sophistication of future attacks.

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

To the extent that any disruption or security breach were to result in loss, destruction, unavailability, alteration or dissemination of, or damage to, our data or applications, or for it to be believed or reported that any of these occurred, we could incur liability and reputational damage and the development and commercialization of our product candidates could be delayed. Even prompt detection and response may not fully mitigate impacts, and remediation efforts could divert management attention and increase costs. The use of AI by attackers may also contribute to faster, more coordinated attacks that evade traditional detection methods, placing additional pressure on our security infrastructure and incident response capabilities. Further, our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption in, or failure or security breach of, our systems or third-party systems where information important to our business operations or commercial development is stored.

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

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

security incidents. Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences. For further discussion of our evolving privacy and data security compliance obligations, see “Business - Government Regulation - Data Privacy and Cybersecurity Requirements (U.S.)” and “Regulation in the European Union - European Data and Security Laws.”

We rely on third-party service providers and technologies to operate critical business systems to process sensitive information in a variety of contexts. Certain third-party platforms or vendors may incorporate AI-driven automation or analytics into their offerings, which may expose us to new categories of risk, such as data being repurposed for AI training, unexplainable outputs generated by machine learning models, or unintended reliance on automated decision-making systems that lack transparency or auditability. Our ability to monitor these third parties’ information security practices is limited, and these third parties may not have adequate information security measures in place. If our third-party service providers experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties’ infrastructure in our supply chain or our third-party partners’ supply chains have not been compromised.

Internally, we are also evaluating and, in some cases, implementing AI-enabled technologies to support business operations, data analysis, and other workflow efficiencies. Although these tools offer potential benefits, they also present new and evolving risks, including exposure to biased outputs, regulatory uncertainty around AI governance, and the possibility that sensitive data could inadvertently be incorporated into AI model training datasets or disclosed through model inference. As global laws and guidance surrounding AI systems continue to evolve, noncompliance could result in restrictions on our use of AI, reputational consequences, or enforcement activity.

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

Our contracts may not always include limitations of liability, and even when such provisions are present, there can be no assurance that they will be adequate to protect us from liabilities, damages, or claims arising from our data privacy and security obligations. We can also not guarantee that our cybersecurity insurance coverage will be sufficient to protect us from or mitigate liabilities arising out of our privacy and security practices or that such coverage will continue to be available on commercially reasonable terms or at all. Moreover, even robust cybersecurity and privacy controls under frameworks such as the National Institute of Standards and Technology ("NIST") cannot eliminate all risk, and we have identified cybersecurity risks that, if realized, are reasonably likely to materially affect us.

Our expanding use of AI exposes us to operational, regulatory, legal, and ethical risks that could adversely affect our business, reputation, financial condition, and results of operations.

We increasingly develop, procure, and deploy AI and machine learning (ML) tools across our operations. While these tools may create efficiencies, they also introduce material risks related to data quality and bias, transparency and explainability, validation and lifecycle management, cybersecurity, intellectual property, privacy, discrimination, liability, and third-party dependencies. Errors or bias in AI outputs, inadequate monitoring, or insufficient documentation could impair clinical development, pharmacovigilance, manufacturing quality, or commercial activities, resulting in delays, higher costs, product or batch actions, or reputational harm.

The emergence of AI and other technologies may exacerbate other risks, including those related to regulation, litigation, compliance issues, ethical concerns, confidentiality, and data privacy or security. For example, regulatory uncertainty related to AI or other emerging technologies may require significant resources

to adjust business practices to comply with developing laws. Several governmental authorities have already proposed or enacted laws and other guidance governing AI.

For example, in the United States, the FDA has outlined a risk based credibility framework for AI used to support drug and biologics development, signaling expectations for context of use validation, lifecycle maintenance, traceability, and explainability, and continues to oversee AI/ML enabled medical devices; these expectations could increase development costs and elongate review. These and other developing obligations may prevent or make it harder for us to conduct or enhance our business using AI, or lead to regulatory fines, penalties, or other liability. Further, use of AI technologies could lead to unintended consequences, such as data leakage, healthcare fraud and abuse, cybersecurity incidents, intellectual property infringement, or unintended biases. Our AI use must also comply with privacy regimes, including the UK GDPR and EU GDPR (e.g., restrictions on automated decision making and profiling, and stringent transparency and data subject rights). Divergent and evolving requirements across jurisdictions may require region specific controls, duplicated validation, or delayed deployments; failure to comply could lead to investigations, fines, injunctions, adverse regulatory outcomes, litigation, loss of market access, or reputational damage.

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

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an ownership change, the corporation's ability to use its pre-change net operating loss carryforwards ("NOLs"), and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. For these purposes, an ownership change generally occurs where the aggregate stock ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation's stock increases its ownership by more than 50 percentage points over its lowest ownership percentage over a 3-year period. Upon certain events since our conversion from a Delaware limited liability company to a Delaware corporation in 2015, it is possible that we may have triggered an "ownership change" limitation. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership (some of which are outside of our control). As a result, if we earn net taxable income, our ability to use our pre-change NOLs and other pre-change tax attributes to offset U.S. federal taxable income or taxes may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

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

We, and the third parties upon whom we rely, are or may become subject to numerous domestic and foreign laws, regulations, and standards governing privacy, data protection, and information security, as well as contractual and ethical obligations, many of which overlap or conflict and are subject to changing interpretations. As noted, these include the HIPAA/HITECH framework for protected health information in certain contexts; the amended CCPA and approximately 19 other comprehensive state privacy laws and their implementing regulations; state health data laws; federal and state consumer protection laws; data breach notification statutes; and the DOJ Bulk Data Rule. Outside the United States, we are subject to the GDPR, the DPA 2018, DUAA, CTR, the ePrivacy Directive, among others. These regimes impose obligations such as purpose limitation, data minimization, security safeguards, vendor contracting, impact/risk assessments, transparency and individual rights, breach notification, and restrictions on automated decision-making and profiling. New and proposed laws increasingly emphasize data localization and restrictions on cross-border transfers, and regulators have signaled heightened enforcement. Failure or perceived failure by us or our third parties to comply with any of these requirements could result in investigations, enforcement actions, litigation (including class claims), fines and penalties, remedial orders, restrictions on processing, reputational harm, increased compliance and operational costs, and other adverse consequences that could materially and negatively affect our business, financial condition and results of operations. See the section titled "Business – Government Regulation – Data Privacy and Cybersecurity Requirements (U.S.)" and related international data protection disclosures" in this Annual Report for a more detailed description of the laws that may affect our ability to operate.

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

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

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

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our stockholders or us. We assess the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where we have operations to determine the potential effect on our business and any assumptions we have made about our future taxable income. We cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on our business if they were to be enacted. For example, the United States enacted the Inflation Reduction Act of 2022, which implements, among other changes, a 1% excise tax on certain stock buybacks. In addition, beginning in 2022, the Tax Cuts and Jobs Act eliminated the previously available option to deduct research and development expenditures and requires taxpayers to amortize them generally over five years for research activities conducted in the United States and over 15 years for research activities conducted outside the United States. On July 4, 2025, the U.S. Congress enacted the One Big Beautiful Bill Act, which includes a provision restoring the immediate deductibility of domestic research and development expenditures. The impact of this newly enacted law on our tax position will depend on how the provision is implemented and interpreted by the Internal Revenue Service and other regulatory authorities. In addition, we have no assurance as to whether, when and how this provision may be subject to further amendment or repeal. Such changes, among others, may adversely affect our effective tax rate, results of operation and general business condition.

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

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

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

Our cash held in non-interest-bearing and interest-bearing accounts exceeds the Federal Deposit Insurance Corporation ("FDIC") insurance limits. If such banking institutions were to fail, we could lose all or a portion of those amounts held in excess of such insurance limitations. However, the FDIC may not make all account holders whole in the event of future bank failures. In addition, even if account holders are ultimately made whole with respect to a future bank failure, account holders' access to their accounts and assets held in their accounts may be substantially delayed. Any material loss that we may experience in the future or inability

for a material time period to access our cash and cash equivalents could have an adverse effect on our ability to pay our operational expenses or make other payments, which could adversely affect our business.

Risks Related to Our Common Stock

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

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

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

- period-to-period fluctuations in our financial results.

Moreover, the capital markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of our common stock. For example, escalating trade tensions, elevated interest rates and regulatory uncertainty have caused significant market volatility in recent months, and particularly in the biotechnology and biopharmaceutical industries. If the market price of our common stock does not exceed the price at which a stockholder purchases its shares, such stockholder may not realize any return on its investment in us and may lose some or all of its investment.

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

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

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

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

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

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

acquiring any interest in any shares of our capital stock shall be deemed to have notice of and to have consented to this provision of our Certificate of Incorporation and Bylaws.

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

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

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

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

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

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

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

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

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

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

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

General Risk Factors

We may become exposed to costly and damaging liability claims, either when testing our programs in the clinic or at the commercial stage, and our product liability insurance may not cover all damages from such claims.

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of pharmaceutical products. While we currently have no products that have been approved for commercial sale, the use of our product candidates in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims may be made by participants or patients that use the product candidate or product, healthcare providers, pharmaceutical companies, or others selling such products. Any claims against us, regardless of their merit, could be difficult and costly to defend and could materially and adversely affect the market for our products or any prospects for commercialization of our products. Although we currently maintain adequate product liability insurance for our product candidates, it is possible that our liabilities could exceed our insurance coverage or that in the future we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Litigation costs and the outcome of litigation could have a material adverse effect on our business.

From time to time, we may be subject to litigation claims through the ordinary course of our business operations regarding, but not limited to, securities litigation, employment matters, security of patient and employee personal information, contractual relations with collaborators and licensors and intellectual property rights. Litigation to defend ourselves against claims by third parties, or to enforce any rights that we may have against third parties, could result in substantial costs and diversion of our resources, causing a material adverse effect on our business, financial condition, results of operations or cash flows.

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

As a public company, and particularly after December 31, 2024, when we ceased to be a “smaller reporting company” and “non-accelerated filer,” and became a “large accelerated filer,” we have and will continue to incur significant legal, accounting and other expenses associated with public company reporting requirements, including costs associated with corporate governance requirements, such as requirements under the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, as well as rules implemented by the SEC and Nasdaq. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact (in ways we cannot currently anticipate) the manner in which we operate our business. In addition, changing laws, regulations, and standards relating to corporate governance and public disclosure, including those related to climate change and other environmental, social and governance focused disclosures, are creating uncertainty for public companies, increasing legal and financial compliance costs, and making some activities more time-consuming. These rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. These rules and regulations may also make it difficult and expensive for us to obtain directors’ and officers’ liability insurance. Our management and other personnel will continue to devote a substantial amount of time to these compliance initiatives, and we will continue to incur increased legal and financial compliance costs. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors or as our executive officers, which may adversely affect investor confidence and

could cause our business or stock price to suffer. In addition, the increased costs may require us to reduce costs in other areas of our business or increase the prices of our product candidates, once commercialized. Moreover, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

We are no longer a "smaller reporting company" within the meaning of the Securities Act and as a result we are or will be subject to certain enhanced disclosure requirements which will require us to incur significant expenses and expend time and resources.

We are no longer a "smaller reporting company," as of January 1, 2025 and, as a result, we are required to comply with various disclosure and compliance requirements that did not previously apply, such as the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act, the requirement that we hold a nonbinding advisory vote on executive compensation and obtain stockholder approval of any golden parachute payments not previously approved, the requirement to provide full and more detailed executive compensation disclosure and the reduction in the amount of time for filing our periodic and annual reports. Compliance with these additional requirements increases our legal and financial compliance costs and causes management and other personnel to divert attention from operational and other business matters to these additional public company reporting requirements. In addition, if we are not able to comply with changing requirements in a timely manner, the market price of our stock could decline and we could be subject to delisting proceedings by the stock exchange on which our common shares are listed, or sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

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

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

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock may be negatively affected. For example, in the fourth quarter of 2024, we identified a material weakness in our internal control over financial reporting which resulted in restatements of our previously-issued financial statements to amend certain net loss per share disclosures.

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, and the rules and regulations of Nasdaq. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. In addition to our management's report on the effectiveness of our internal controls over financial reporting, our independent registered public accounting firm is required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing, and possible remediation. We must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our annual report filing for that year, as required by Section 404 of the Sarbanes-Oxley Act.

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

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim consolidated financial statements will not be prevented or detected on a timely basis. As described in our Annual Report for the year ended December 31, 2024, we identified a material weakness in our internal control over financial reporting in connection with our net earnings (loss) per share disclosures, which resulted in the restatement of our consolidated financial statements as of and for the year ended December 31, 2023, as well as the quarterly condensed consolidated financial information for the interim periods ended March 31, 2024, June 30, 2024, and September 30, 2024. We have implemented measures designed to improve our disclosure controls and procedures and internal control over financial reporting to address the underlying causes of this material weakness, including enhancing the design of controls relevant to the preparation and presentation of financial reporting matters related to net earnings (loss) per share calculations and disclosures to ensure that economic substance beyond the legal form of our capital structure is considered when preparing disclosures related to net earnings (loss) per share.

In addition, our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected. In addition, we may encounter problems or delays in completing the implementation of any requested improvements and receiving a favorable attestation in connection with the attestation provided by our independent registered public accounting firm.

As a public company, we incur significant legal, accounting, insurance, and other expenses, and our management and other personnel have and will need to continue to devote a substantial amount of time to compliance initiatives resulting from operating as a public company. We may experience difficulty in meeting these reporting requirements in a timely manner for each period.

Our business could be adversely affected by economic downturns, inflation, increases in interest rates, natural disasters, public health crises, political crises, U.S. elections, international or geopolitical events, such as the conflict between Russia and Ukraine, recent events in Venezuela, and conflicts in the Middle East, the implementation of measures that restrict international trade or other macroeconomic conditions, which could have a material and adverse effect on our results of operations and financial condition.

The global economy, including credit and financial markets, has experienced extreme volatility and disruptions, including, among other things, diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, supply chain shortages, increases in inflation rates, higher interest rates, and uncertainty about economic stability. Adverse macroeconomic conditions, including inflation, slower growth or recession, new or increased tariffs and other barriers to trade, especially in light of recent comments and executive orders made by the Trump administration, changes to fiscal and monetary policy or government budget dynamics (particularly in the pharmaceutical and biotechnology areas), tighter credit, higher interest rates, volatility in financial markets, high unemployment, labor availability constraints, currency fluctuations and other challenges in the global economy have in the past adversely affected, and may in the future adversely affect, us and our business partners and suppliers. The United States has previously announced tariffs on imports from most countries, including significant tariffs on imports from Canada, Mexico and China. Historically, tariffs have led to increased trade and political tensions. In response to tariffs, other countries have implemented retaliatory tariffs on U.S. goods. Political tensions as a result of trade policies could reduce trade volume, investment, technological exchange and other economic activities between major international economies, resulting in a material adverse effect on global economic conditions and the stability of global financial markets. There is substantial uncertainty about the duration of existing tariffs and whether additional tariffs may be imposed, modified or suspended. The Federal Reserve has raised interest rates multiple times in response to concerns about inflation and it may raise them again. Higher interest rates, coupled with reduced

government spending and volatility in financial markets, may increase economic uncertainty and affect consumer spending. Similarly, geopolitical uncertainties, international conflicts and government actions, including the ongoing military conflicts between Russia and Ukraine, recent events in Venezuela, and conflicts in the Middle East involving Israel and various other parties, including Iran, Hamas and Hezbollah, as well as other conflicts in the region, rising tensions with China and the implementation of tariffs, sanctions, export or import controls, and other measures that restrict international trade by the United States, China or other governments, have created extreme volatility in the global capital markets and may have further global economic consequences, including disruptions of the global supply chain. Any such volatility and disruptions may adversely affect our business or the third parties on whom we rely. If the equity and credit markets deteriorate, including as a result of political unrest or war, it may make any necessary debt or equity financing more costly, more dilutive, or more difficult to obtain in a timely manner or on favorable terms, if at all. Increased inflation rates can adversely affect us by increasing our costs, including labor and employee benefit costs.

We may in the future experience disruptions as a result of such macroeconomic conditions, including delays or difficulties in initiating or expanding clinical trials and manufacturing or shipping sufficient quantities of materials. Any one or a combination of these events could have a material and adverse effect on our results of operations and financial condition. For example, our business may be generally exposed to the impact of political or civil unrest or military action. While we do not have any employees or offices in Ukraine, Venezuela, Russia or countries in the Middle East, including Israel, we do have third-party partners with locations in Europe, South America and the Middle East, which may be affected by the ongoing conflicts affecting such countries. In addition, we are pursuing sites for our Phase 2 platform trial in Israel and Ukraine. These sites may be materially impacted by the increasing military conflicts in Europe and the Middle East, could result in difficulties enrolling and retaining participants and/or delivering drug samples in such areas on schedule and cause delay in our clinical trials and/or increase trial costs. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic or political climate and financial market conditions could adversely impact our business.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 1C. CYBERSECURITY

In the ordinary course of business, we collect, use, store, and transmit digitally confidential, sensitive, proprietary, personal, and health-related information. The secure maintenance of this information and our information technology systems is important to our operations and business strategy. To this end, we have implemented processes using the cybersecurity risk framework published by the NIST designed to assess, identify, and manage risks from potential unauthorized occurrences on or through our information technology systems that may result in adverse effects on the confidentiality, integrity, and availability of these systems and the data residing therein. These processes are managed and monitored by a dedicated information technology team, which is led by our Vice President, Information Technology ("IT"), and include mechanisms, controls, technologies, systems, and other processes designed to prevent or mitigate data loss, theft, misuse, or other security incidents or vulnerabilities affecting the data and maintain a stable information technology environment. Our cybersecurity risk management processes also incorporate the use of automated and data-driven tools provided by third-party vendors to support threat detection, monitoring, and incident response, and are designed to address evolving cybersecurity threats, including those that may be enabled by artificial intelligence. Specific measures include regular penetration and vulnerability testing, data recovery testing, security audits, and ongoing risk assessments. We conduct due diligence on and audits of key technology vendors, contract research organizations (CROs), and other third-party contractors and suppliers. Additionally, we conduct employee training that covers identifying threats (phishing, social engineering), secure practices (strong passwords, multi-factor authentication, safe internet use, data handling), and incident response (reporting procedures), turning employees into the first line of defense through regular, engaging education on topics like malware, remote work security, physical security, cloud security, mobile devices, and social media risks. We also regularly consult with outside advisors and experts. Their assistance helps us assess, identify, and manage cybersecurity risks, anticipate future threats and trends, and understand their potential impact on our risk environment.

Our Vice President, IT, who reports directly to our Chief Financial Officer, has over 26 years of experience managing information technology and cybersecurity matters and is certified as a Certified Information Systems Security Professional. Together with other members of our senior leadership team, our Vice President, IT is responsible for assessing and managing cybersecurity risks. We consider cybersecurity, along with other significant risks that we face, within our overall enterprise risk management framework. In the last fiscal year, we have not identified risks from known cybersecurity threats, including as a result of any prior cybersecurity incidents, that have materially affected us, but we face certain ongoing cybersecurity risks that, if realized, are reasonably likely to materially affect us. Additional information on cybersecurity risks we face is discussed in Part I, Item 1A, "Risk Factors".

The Board of Directors, as a whole and at the committee level, has oversight for the most significant risks facing us and for our processes to identify, prioritize, assess, manage, and mitigate those risks. The Audit Committee, which is comprised solely of independent directors, has been designated by our Board to oversee cybersecurity risks. The Audit Committee receives regular updates on cybersecurity and information technology matters and related risk exposures from our Vice President, IT, as well as other members of the senior leadership team. The Board also receives updates from management and the Audit Committee on cybersecurity risks on at least an annual basis.

ITEM 2. PROPERTIES

We do not maintain physical corporate offices. Our employees work remotely. We believe these arrangements support our current needs. We maintain a mailing address at 221 Crescent St., Building 23, Suite 105, Waltham, MA 02453. As we expand, we believe that suitable additional alternative spaces will be available in the future on commercially reasonable terms, if required.

ITEM 3. LEGAL PROCEEDINGS

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

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information and Holders

Our common stock is traded on The Nasdaq Stock Market LLC under the symbol "SYRE."

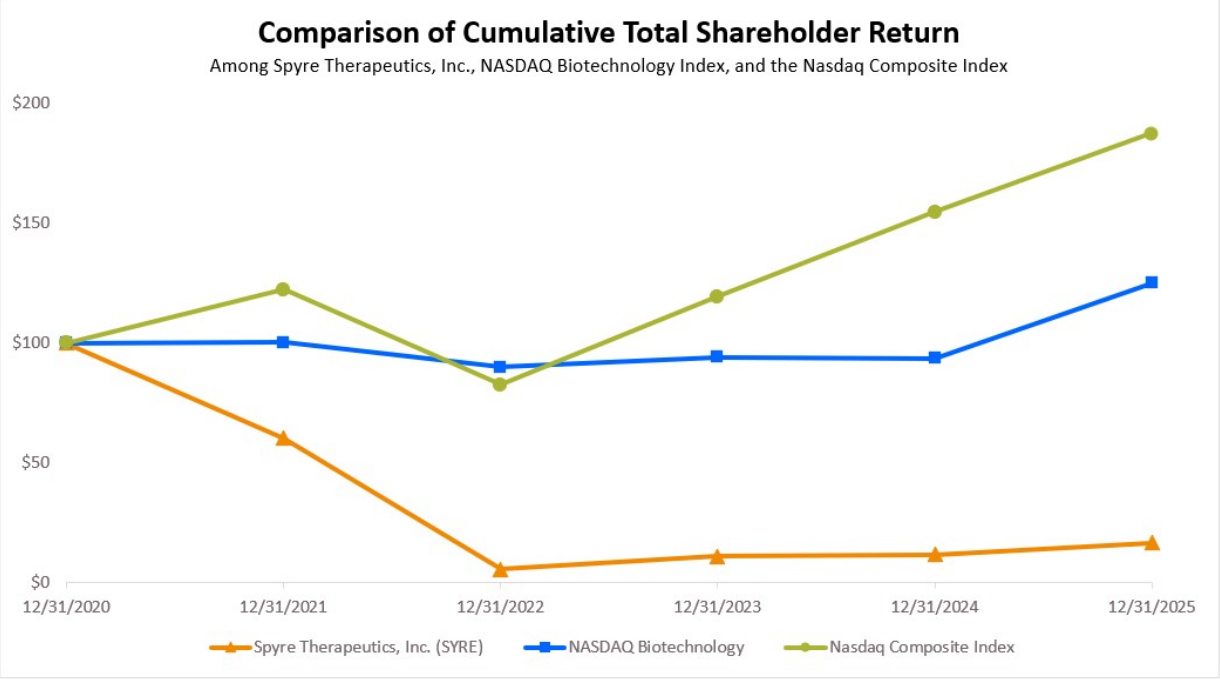
As of February 12, 2026, there were approximately 24 stockholders of record of our common stock based on information provided by our transfer agent. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Stock Price Performance Graph

This graph shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

The following stock performance graph compares our total stock return with the total return for (i) the Nasdaq Composite Index and the (ii) the Nasdaq Biotechnology Index for the period from December 31, 2020 through December 31, 2025. The figures represented below assume an investment of $100 in our common stock at the closing price of $196.75 on December 31, 2020 and in the Nasdaq Composite Index and the Nasdaq Biotechnology Index on December 31, 2020 and the reinvestment of dividends into shares of common stock. The comparisons in the table are required by the SEC and are not intended to forecast or be indicative of possible future performance of our common stock.

During 2023, the Company completed a reverse merger, which brought in an entirely new pipeline of product candidates targeting IBD, and refreshed the Board and executive team to lead development of this new pipeline and sunset legacy asset development. Additionally, the Company has since expanded its pipeline into RD. The graph below includes pre-reverse merger stock performance, which is not relevant to Spyre's current stock performance.



Company/Index	2020	2021	2022	2023	2024	2025
Spyre Therapeutics, Inc. (SYRE)	$ 100.00	$ 60.36	$ 5.72	$ 10.94	$ 11.83	$ 16.65
NASDAQ Biotechnology	$ 100.00	$ 100.02	$ 89.90	$ 94.03	$ 93.49	$ 124.75
Nasdaq Composite Index	$ 100.00	$ 122.18	$ 82.43	$ 119.22	$ 154.48	$ 187.14

Dividends

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future.

Recent Sales of Unregistered Securities

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

ITEM 6. [RESERVED]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes appearing in this Annual Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. As used in this report, unless the context suggests otherwise, "we", "us", "our", "the Company," "Aeglea BioTherapeutics, Inc." or "Spyre" refers to Spyre Therapeutics, Inc. and its consolidated subsidiaries taken as a whole.

Acquisition of Pre-Merger Spyre

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

Through the Asset Acquisition, we received the option to license certain intellectual property rights related to four research programs (collectively, the "Option"). On July 12, 2023, we exercised the Option with respect to one of these research programs to be granted an exclusive license to all of Paragon's rights, title and interest in and to intellectual property rights, including inventions, patents, sequence information and results, under SPY001, our α4β7 integrin program, to develop and commercialize antibodies and products worldwide in all therapeutics disorders. On December 14, 2023, we exercised the Option under the Paragon Agreement to be granted an exclusive license to all of Paragon's rights, title and interest in and to intellectual property rights, including inventions, patents, sequence information and results, under SPY002, our TL1A program, to develop and commercialize antibodies and products worldwide in all therapeutics disorders. On June 5, 2024, we exercised the Option under the Paragon Agreement to be granted an exclusive license to all of Paragon's rights, title and interest in and to intellectual property rights, including inventions, patents, sequence information and results, under SPY003, our IL-23 program, to develop and commercialize antibodies and products worldwide solely in inflammatory bowel disease ("IBD") indications. The License Agreements pertaining to SPY001 and SPY002 between the Company and Paragon were executed in the second quarter of 2024, and the License Agreement pertaining to SPY003 was executed in October 2024 and subsequently amended and restated on February 24, 2025. Furthermore, as of the date of this Annual Report, the Option remains unexercised with respect to the intellectual property rights related to the last remaining research program under the Paragon Agreement. See discussion in Part I, Item 1 "Business - Intellectual Property" for further discussion of our intellectual property.

Overview

Following the Asset Acquisition, we have significantly reshaped the business into a clinical stage biotechnology company focused on developing next generation therapeutics for patients living with IBD, including ulcerative colitis ("UC") and Crohn's disease ("CD"), and other immune-mediated diseases. Our portfolio of novel and proprietary monoclonal antibody product candidates has the potential to address unmet needs in IBD and RD care by improving efficacy, safety, and/or dosing convenience relative to products currently available or product candidates in development. We have engineered our product candidates with the aim to bind potently and selectively to their target epitopes and to exhibit extended pharmacokinetic half-lives through modifications in the Fc domain, which modifications are designed to increase affinity to human FcRn and increase antibody recycling. We anticipate that half-life extension will enable less frequent administration as compared to marketed or development-stage mAbs that do not incorporate half-life extension modifications. In addition to the development of our product candidates as potential monotherapies, we plan to investigate combinations of our proprietary antibodies in nonclinical studies and clinical trials in order to evaluate whether combination therapy (co-administration or co-formulation of multiple monoclonal antibodies) can lead to greater

efficacy, as compared to monotherapies in IBD. We intend to deliver our product candidates through convenient, infrequently self-administered, subcutaneous maintenance injections, although the specific delivery mechanism or technology has not been selected given our early stage.

Business and Macroeconomic Conditions

The extent of the impact of macroeconomic events and conditions, including inflation, increasing interest rates, increasing financial market volatility and uncertainty, the impacts of geopolitical instabilities and government actions, including the ongoing military conflict in Ukraine, conflict between Israel and various other parties, recent events in Venezuela, geopolitical tensions between China and the United States, and the implementation of tariffs, sanctions, export or import controls, and other measures that restrict international trade by the United States, China or other governments, and their potential supply chain impact, and public health pandemics on our operational and financial performance will continue to depend on certain developments, including the impact on our clinical studies, employee or industry events, and effect on our suppliers and manufacturers, all of which are uncertain and cannot be predicted. Adverse effects of these large macroeconomic conditions have been prevalent in many of the areas where we, our clinical research organizations ("CROs"), suppliers or third-party business partners conduct business and as a result, we may experience disruptions in our operations. We have experienced and may in the future experience such disruption or delays due to these factors as well as delays due to labor shortages and supply chain disruptions in distribution of clinical trial materials, trial monitoring and data analysis that could materially adversely impact our business, results of operations and overall financial performance in future periods. As of the filing date of this Annual Report, the extent to which these macroeconomic events and conditions may impact our financial condition, results of operations or guidance is uncertain. The effect of these macroeconomic events and conditions may not be fully reflected in our results of operations and overall financial performance until future periods. See Part I, Item 1A “Risk Factors” for further discussion of the possible impact of these macroeconomic conditions on our business.

Components of Operating Results

Revenue

We have recognized license and development revenue from the Immedica Agreement (as defined below) related to our legacy product candidate pegzilarginase. On July 27, 2023, we announced that we entered into an agreement to sell the global rights to pegzilarginase to Immedica. The sale of pegzilarginase to Immedica superseded and terminated the Immedica Agreement.

We have not generated any revenue from commercial product sales. Our ability to generate product revenues in the future will depend on the successful development, regulatory approval, and commercialization of our product candidates.

Licensing and Sale of Pegzilarginase

In March 2021, we licensed to Immedica the rights to the commercialization of pegzilarginase in the European Economic Area, United Kingdom, Switzerland, Andorra, Monaco, San Marino, Vatican City, Turkey, Saudi Arabia, United Arab Emirates, Qatar, Kuwait, Bahrain, and Oman (the "Immedica Agreement"). The Immedica Agreement included a non-refundable upfront payment of $21.5 million from Immedica and up to $3.0 million of payments for development services provided to Immedica. Under the terms of the Immedica Agreement, we were eligible to receive additional regulatory and commercial milestone payments and were entitled to receive royalties in the mid-20% range on net sales of the product in countries included in the Immedica Agreement.

For the year ended December 31, 2023, we recognized revenue of $0.9 million under the Immedica Agreement. The total revenue generated during the year ended December 31, 2023 was attributable to the PEACE Phase 3 trial and PIP trials, drug supply, and royalties from an early access program in France.

On July 27, 2023, we announced that we entered into an agreement to sell the global rights to pegzilarginase to Immedica for $15.0 million in upfront cash proceeds and up to $100.0 million in contingent milestone payments. The sale of pegzilarginase to Immedica superseded and terminated the Immedica

Agreement. On July 27, 2023, the carrying value of the asset was zero as it was internally developed. Accordingly, we recognized a $16.4 million gain within Gain on sale of in-process research and development, which is comprised of $15.0 million in upfront cash proceeds and the reimbursement of $1.8 million in pre-paid manufacturing costs that was contingent upon a favorable opinion being received by the CHMP, net of transaction costs and the derecognition of pegzilarginase related nonfinancial assets and liabilities totaling $0.4 million.

The milestone payments are contingent on formal reimbursement decisions by national authorities in key European markets and pegzilarginase approval by the FDA, among other events. Subject to the terms of the contingent value rights agreement (the "CVR Agreement") we entered into with Equiniti Trust Company LLC (f/k/a American Stock Transfer & Trust Company LLC) as rights agent in connection with the Asset Acquisition, the upfront payment and contingent milestone payments actually received by us during the CVR term, net of expenses and adjustments, will be distributed to holders of our CVRs (as defined below) pursuant to the CVR Agreement.

During the twelve months ended December 31, 2025, the Company recognized a gain of $10.0 million within Gain on Sale of in-process research and development, for achieving certain reimbursement decision milestones during the period. As of December 31, 2025, $3.0 million remains outstanding and reflected in Prepaid expenses and other current assets. There was no similar gain during the twelve months ended December 31, 2024 nor similar receivable as of December 31, 2024.

Milestone payments, net of allowable expenses and adjustments, will be distributed to CVR holders pursuant to the CVR agreement resulting from the Asset Acquisition and will reduce the CVR liability.

Research and development expenses

Research and development expenses consist primarily of costs incurred for the discovery and development of our product candidates, historically including pegtarviliase and pegzilarginase, and now focused on our portfolio of product candidates for IBD and other immune-mediated diseases. We contract with external providers for nonclinical studies and clinical trials. Our research and development expenses include:

- costs from acquiring clinical trial materials and services performed for contracted services with contract manufacturing organizations, or CMOs;
- fees paid to clinical trial sites, CROs, CMOs, nonclinical research companies, and academic institutions;
- direct and pass through costs associated with research conducted under the Paragon Agreement; and
- employee and consultant-related expenses incurred, which include salaries, benefits, travel, and stock-based compensation.

Research and development costs are expensed as incurred. Advance payments for goods or services to be rendered in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

Research and development expenses have historically represented the largest component of our total operating expenses.

Our expenditures on current and future nonclinical and clinical development programs are subject to numerous uncertainties in timing and cost to completion. The duration, costs, and timing of nonclinical activities, clinical trials, and development of our product candidates will depend on a variety of factors, including:

- the scope, rate of progress, and expenses of our ongoing research activities as well as any additional nonclinical activities, clinical trials, and other research and development activities;
- future clinical trial results;
- uncertainties in clinical trial enrollment rates or drop-out or discontinuation rates of patients;
- changes in the competitive drug development environment;

- potential safety monitoring or other studies requested by regulatory agencies;
- significant and changing government regulation;
- the timing and receipt of regulatory approvals, if any; and
- macroeconomic events and conditions, including inflation, increasing interest rates, increasing financial market volatility and uncertainty, the impact of geopolitical instabilities and government actions, including ongoing military conflict in Ukraine, conflict in Israel and surrounding areas, recent events in Venezuela, geopolitical tensions between China and the United States, and the implementation of tariffs, sanctions, export or import controls, and other measures that restrict international trade by the United States, China or other governments, and its potential supply chain impact, and public health pandemics.

The process of conducting the necessary clinical research to obtain FDA and other regulatory approval is costly and time-consuming and the successful development of our product candidates is highly uncertain. The risks and uncertainties associated with our research and development projects are discussed more fully in Part I, Item 1A of this Annual Report titled “Risk Factors.” As a result of these risks and uncertainties, we are unable to determine with any degree of certainty the duration and completion costs of our research and development projects, or if, when, or to what extent we will generate revenues from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates.

General and administrative expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, legal, corporate development, information technology, and human resources functions. Other significant costs include legal fees relating to corporate matters and fees for insurance, accounting, consulting, facilities, and recruiting services.

We expect that our general and administrative expenses will increase in the future to support our continued research and development activities. These increases will likely include higher costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses. Additionally, we have incurred and expect to continue to incur increased costs associated with being a public company, including expenses related to services associated with maintaining compliance with Nasdaq listing rules and SEC requirements, insurance, and investor relations costs.

Restructuring

On April 12, 2023, based on the review of the inconclusive interim results from our Phase 1/2 clinical trial of pegtarviliase for the treatment of classical homocystinuria and other business considerations, we announced that we had initiated a process to explore strategic alternatives to maximize stockholder value and engaged an independent exclusive financial advisor to support this process. As a result, we implemented a restructuring plan that resulted in an approximate 83% reduction of our existing headcount by June 30, 2023.

All charges related to the restructuring activities were recognized during the year ended December 31, 2023. No further restructuring charges will be incurred under the restructuring plan.

Severance and Stock Compensation

We recognized restructuring expenses consisting of cash severance payments and other employee-related costs of $6.4 million during the year ended December 31, 2023. Cash payments for employee related restructuring charges of $1.1 million and $5.3 million were paid during December 31, 2024 and 2023, respectively. In addition, we recognized $1.0 million in non-cash stock-based compensation expense related to the accelerated vesting of stock-based awards for certain employees. We recorded these restructuring charges based on each employee’s role to the respective research and development and general and administrative operating expense categories on its consolidated statements of operations and comprehensive loss.

Sale of Assets

During the second quarter of 2023, we sold various lab equipment, consumables, and furniture and fixtures for total consideration of $0.5 million. After recording the disposal of all our property and equipment net of proceeds, we recorded a $0.7 million and $0.2 million loss on disposal of long-lived assets which is included in Research and development and General and administrative expenses, respectively.

Lease Right-of-use Asset and Leasehold Improvement Impairment

Effective June 30, 2023, we abandoned our leased office space in Austin, Texas. As a result, we recognized an impairment loss of $0.9 million related to the operating lease right-of-use asset and $1.7 million related to leasehold improvements. On August 7, 2023, we terminated our building lease in Austin, Texas. The negotiated termination agreement obligated us to pay the lessor a $2.0 million termination fee in exchange for releasing us of all further obligations under the lease. All charges related to the restructuring activities were recognized during the second quarter of 2023. No further restructuring charges will be incurred under the restructuring plan.

Interest income

Interest income consists of interest earned on our cash, cash equivalents, marketable securities, and restricted cash.

Income taxes

During the year ended December 31, 2024, we completed the merger of our nine U.S. subsidiaries (the "Former Subsidiaries") with and into our parent company, Spyre Therapeutics, Inc. In addition, we dissolved our subsidiaries in the United Kingdom and Ireland in 2026 and 2025, respectively, both of which had not had any operational activity since the closing of the Asset Acquisition. We filed a consolidated U.S. corporate federal income tax return for the 2024 tax year for us and our Former Subsidiaries.

Our income tax returns are subject to audit and adjustment by the taxing authorities. We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the financial statements and the tax bases of assets and liabilities. A valuation allowance is established against the deferred tax assets to reduce their carrying value to an amount that is more likely than not to be realized. The deferred tax assets and liabilities are classified as noncurrent along with the related valuation allowance. Due to our lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance.

We recognize benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on the technical merits, as the largest amount of benefits that is more likely than not to be realized upon the ultimate settlement. Our policy is to recognize interest and penalties related to the unrecognized tax benefits as a component of income tax expense.

Critical Accounting Policies and Estimates

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

Our critical accounting policies are those policies which require the most significant judgments and estimates in the preparation of our consolidated financial statements. The most significant estimates and assumptions that management considers in the preparation of our financial statements relate to accrued research and development costs; the valuation of consideration transferred in acquiring in-process research and development ("IPR&D"); the discount rate, probabilities of success, and timing of estimated cash flows in

the valuation of the CVR liability; inputs used in the Black-Scholes model for stock-based compensation expense; estimated future cash flows used in calculating the impairment of right-of-use lease assets; and estimated cost to complete performance obligations related to revenue recognition. The consideration transferred in acquiring IPR&D in connection with the acquisition of Pre-Merger Spyre was comprised of our common stock and shares of Series A Preferred Stock. To determine the fair value of the equity transferred, we considered the per share value of our PIPE financing that closed in June 2023 (the "June 2023 PIPE"), which was a financing involving a group of accredited investors.

We define our critical accounting policies as those accounting principles generally accepted in the United States that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations, as well as the specific manner in which we apply those principles. Our significant accounting policies are more fully described in Note 2 to our consolidated financial statements included elsewhere in this Annual Report.

Revenue recognition

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

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

We allocate the estimated transaction price to the identified performance obligations based on the relative estimated stand-alone selling price ("SSP") of each performance. SSP is based on the observable price of our goods and services, or when SSP is not directly observable, we estimate SSP based on factors such as forecasted revenues or costs, development timelines, discount rates, probabilities of technical and regulatory success, and considerations such as market conditions and entity-specific factors. We recognize revenue allocated to each performance obligation either at a point-in-time or over time in a manner that depicts the transfer of control of the promised goods and services to the customer. For performance obligations that are recognized over time, we estimate the measure of progress associated with the satisfaction of the performance obligation based on an input or output method, which may be based on factors such as costs incurred, labor hours expended, time elapsed, among other measures based on the nature of the performance obligation. The estimates made on an input or output method are subject to change and may result in material changes to revenue that could materially affect our results of operations. Please refer to Note 13, Strategic License Agreements, to the consolidated financial statements included elsewhere in this Annual Report.

Accrued research and development costs

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

We accrue for expenses resulting from obligations under the Paragon Agreement and agreements with CROs, CMOs, and other outside service providers for which payment flows do not match the periods over which materials or services are provided to us. We record accruals based on estimates of services received and efforts expended pursuant to agreements established with Paragon, CROs, CMOs, and other outside service providers. These estimates are typically based on contracted amounts applied to the proportion of work performed and determined through analysis with internal personnel and external service providers as to the progress or stage of completion of the services. We make significant judgments and estimates in determining the accrual balance in each reporting period. In the event advance payments are made to Paragon, a CRO, a CMO, or an outside service provider, the payments will be recorded as a prepaid asset which will be amortized as the contracted services are performed. As actual costs become known, we adjust our accruals. Inputs, such as the services performed, the number of patients enrolled, or the trial duration, may vary from our estimates, resulting in adjustments to research and development expense in future periods. Changes in these estimates that result in material changes to our accruals could materially affect our results of operations. However, there have been no material changes in estimates for the periods presented.

License Agreements Contingent Milestone Payments

The Company's license agreements include specific development, regulatory, and clinical milestone payments that are payable upon the resolution of a contingency, such as upon the selection of a development candidate, first dosing of a human patient in clinical trials or receipt of the Food and Drug Administration's ("FDA") approval of a Spyre drug. The achievement of these milestone payments involves many factors outside of the Company's control and therefore the associated likelihood can therefore not be considered probable until the related contingency is resolved. Based on the preceding, the Company accrues each milestone payment upon the achievement of the applicable milestone event.

Impairment of ROU Assets and Leasehold Improvements

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

Convertible Preferred Stock Issued through PIPE

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

Since the Series B Preferred Stock is no longer redeemable, the associated balances of the Series B Preferred Stock were reclassified from mezzanine equity to permanent equity during the second quarter of 2024.

Contingent Value Rights Liability

On July 3, 2023, we issued contingent value rights ("CVRs") to certain of our securityholders of record as of the close of business on that date (the "Legacy Stockholders"), but these were not issued to holders of shares of common stock or preferred stock issued to former stockholders of Pre-Merger Spyre or the investors (the "June 2023 Investors") in the June 2023 PIPE. Each CVR entitles the holder thereof to receive certain cash payments from proceeds received by the Company prior to the third anniversary of the CVR Agreement, if any, related to the disposition or monetization of certain legacy assets owned by us prior to the Asset Acquisition (the "Legacy Assets"). Certain contingent payments under the CVR Agreement qualify as derivatives under ASC 815, Derivatives and Hedging, and are recorded as a liability on the balance sheet as of December 31, 2025

and December 31, 2024. The CVR liability is considered a Level 3 instrument that is initially measured at its estimated fair value on the transaction date and subsequently remeasured at each reporting date with changes recorded in the consolidated statement of operations. The determination of the initial and subsequent fair value of the CVR liability requires significant judgment by management. Changes in any of the inputs not related to facts and circumstances existing as of the transaction date may result in a significant fair value adjustment, which can impact the results of operations in the period in which the adjustment is made. For example, changes in inputs related to the likelihood of regulatory approval increases or decreases as the regulatory approval process progresses and decisions or comments are issued by the applicable regulatory agencies.

Recently Issued Accounting Pronouncements

Information regarding recent accounting pronouncements is included in Item 8 of Part II, "Financial Statements and Supplementary Data", Note 2 in the "Notes to Consolidated Financial Statements" of this Annual Report.

Results of Operations

A discussion and analysis of our financial condition and results of operations for the year ended December 31, 2025 compared to the year ended December 31, 2024 and a discussion and analysis of our financial condition and results of operations for the year ended December 31, 2024 compared with the year ended December 31, 2023 is presented below.

Comparison of the Years Ended December 31, 2025 and 2024

The following table summarizes our results of operations for the years ended December 31, 2025 and 2024, together with the changes in those items in dollars and as a percentage:

	Year Ended December 31,		Dollar Change	% Change
	2025	2024		
	(in thousands)			
Operating expenses:				
Research and development	171,653	162,790	8,863	5%
General and administrative	47,909	45,776	2,133	5%
Gain on sale of in-process research and development asset	(10,000)	—	(10,000)	*
Total operating expenses	209,562	208,566	996	*
Loss from operations	(209,562)	(208,566)	996	*
Other income (expense):				
Interest income	24,885	21,312	3,573	*
Other income (expense), net	29,459	(20,713)	50,172	*
Total other income	54,344	599	53,745	*
Loss before income tax expense	(155,218)	(207,967)	(52,749)	*
Income tax benefit (expense)	15	(51)	66	*
Net loss	$ (155,203)	$ (208,018)	$ (52,815)	*

* Percentage not meaningful

Research and development expenses increased by $8.9 million, or 5%, to $171.7 million for the year ended December 31, 2025, from $162.8 million for the year ended December 31, 2024. The increase was primarily driven by increased clinical development activities and higher headcount partially offset by lower early-stage research and development.

	Year Ended December 31,		Dollar Change	% Change
	2025	2024		
	(in thousands)			
External research and development expenses:				
Preclinical	$ 16,016	$ 62,235	$ (46,219)	(74)%
IBD	98,290	64,919	33,371	51 %
Rheumatic diseases	16,552	—	16,552	*
Stock-based compensation [1]	—	14,459	(14,459)	(100)%
Legacy Aeglea assets	194	(906)	1,100	121 %
Total external research and development expense	131,052	140,707	(9,655)	(7)%
Internal research and development expenses:				
Compensation	22,893	11,728	11,165	95%
Stock-based compensation	16,270	9,112	7,158	79%
Other	1,438	1,243	195	16 %
Total internal research and development expenses	40,601	22,083	18,518	84 %
Total research and development expense	$ 171,653	$ 162,790	$ 8,863	5 %

[1] For the year ended December 31, 2024, $14.5 million was recognized as stock compensation expense related to the Parapyre Option Obligation. There was no similar expense for the year ended December 31, 2025.

External research and development expenses include costs associated with third parties contracted to conduct research and development activities on behalf of the Company, including through Paragon, CROs, CMOs, and third-party laboratories. For the year ended December 31, 2025 and 2024, external research and development costs accounted for $131.1 million and $140.7 million, respectively. Preclinical expenses decreased primarily due to a reduction in early-stage research and development activities given our pipeline's advancement coupled with lower intellectual property license and sub-licensing fees. IBD expenses increased primarily due to increases in clinical development costs related to ongoing or planned clinical trials. Rheumatic diseases costs increased due to increases in manufacturing, clinical development costs, and intellectual property licensing and sub-licensing fees. External stock-based compensation decreased due to our obligations ending under the Parapyre Option Obligation.

Internal research and development expenses include compensation and related costs associated with our research and development employees. For the year ended December 31, 2025 and 2024, internal research and development costs accounted for $40.6 million and $22.1 million, respectively. The increase was primarily driven by an increase in research and development headcount.

General and Administrative Expenses. General and administrative expenses increased by $2.1 million, or 5%, to $47.9 million for the year ended December 31, 2025, from $45.8 million for the year ended December 31, 2024. The increase was primarily attributable to an increase in compensation costs due to an increase in general and administrative headcount.

Gain on Sale of In-Process Research and Development Asset. During the year ended December 31, 2025, the Company recognized a gain of $10.0 million for an achieved milestone related to the 2023 sale of the global rights of the legacy Aeglea asset pegzilarginase to Immedica, driven by a favorable reimbursement decision for pegzilarginase in Europe. There was no similar gain or loss during the year ended December 31, 2024.

Interest Income. Interest income was $24.9 million and $21.3 million for the year ended December 31, 2025 and 2024, respectively. The increase was primarily due to higher investment balances.

Other income, net. Other income, net for the year ended December 31, 2025 increased by $50.2 million versus the year ended December 31, 2024 primarily driven by changes in the fair value of the CVR liability, which was primarily driven by changes in the likelihood of achievement of certain milestones and receipt of certain cash consideration within the CVR term, changes in estimated reimbursement rates compared to reimbursement target rates, changes in estimated cash flow dates, and an increase in risk-adjusted discount rates, partially offset by time value of money adjustments.

Comparison of the Years Ended December 31, 2024 and 2023

The following table summarizes our results of operations for the years ended December 31, 2024 and 2023, together with the changes in those items in dollars and as a percentage:

	Year Ended December 31,		Dollar Change	% Change
	2024	2023		
	(in thousands)			
Revenue:				
Development fee and royalty	—	886	(886)	(100%)
Total revenue	—	886	(886)	
Operating expenses:				
Research and development	162,790	89,504	73,286	82%
General and administrative	45,776	39,946	5,830	15%
Acquired in-process research and development	—	130,188	(130,188)	*
Gain on sale of in-process research and development asset	—	(16,449)	16,449	*
Total operating expenses	208,566	243,189	(34,623)	*
Loss from operations	(208,566)	(242,303)	(33,737)	*
Other income (expense):				
Interest income	21,312	6,147	15,165	*
Change in fair value of forward contract liability	—	(83,530)	83,530	*
Other expense, net	(20,713)	(19,130)	(1,583)	*
Total other income (expense)	599	(96,513)	97,112	*
Loss before income tax expense	(207,967)	(338,816)	(130,849)	*
Income tax (expense) benefit	(51)	26	(77)	*
Net loss	$ (208,018)	$ (338,790)	$ (130,772)	*

* Percentage not meaningful

Development Fee and Royalty Revenue. For the year ended December 31, 2024, we did not recognize any revenue in connection with the Immedica Agreement. For the year ended December 31, 2023, we recognized $0.9 million of development fee revenue in connection with the Immedica Agreement. The revenue generated during the year ended December 31, 2023, was attributable to the PEACE Phase 3 trial and drug supply and royalties from an early access program in France.

Research and development expenses increased by $73.3 million, or 82%, to $162.8 million for the year ended December 31, 2024, from $89.5 million for the year ended December 31, 2023. The increase was primarily driven by higher early-stage research and development and increased compensation costs partially offset by decrease in costs related to the Company's legacy rare disease pipeline.

	Year Ended December 31,		Dollar Change	% Change
	2024	2023		
	(in thousands)			
External research and development expenses:				
Preclinical	$ 62,235	$ 37,130	$ 25,105	68 %
IBD	64,919	6,017	58,902	979 %
Stock-based compensation [1]	14,459	11,328	3,131	28 %
Legacy Aeglea assets	(906)	18,187	(19,093)	(105)%
Total external research and development expense	140,707	72,662	68,045	94 %
			—	
Internal research and development expenses:			—	
Compensation	11,728	6,801	4,927	72%
Stock-based compensation	9,112	2,910	6,202	213%
Other	1,243	7,131	(5,888)	(83)%
Total internal research and development expenses	22,083	16,842	5,241	31 %
Total research and development expense	$ 162,790	$ 89,504	$ 73,286	82 %

[1] For the years ended December 31, 2024 and 2023, $14.5 million and $11.4 million was recognized as stock compensation expense related to the Parapyre Option Obligation, respectively.

External research and development expenses include costs associated with third parties contracted to conduct research and development activities on behalf of the Company, including through Paragon, CROs, CMOs, and third-party laboratories. For the year ended December 31, 2024 and 2023, external research and development costs accounted for $140.7 million and $72.7 million, respectively. The increase was primarily due to increased costs associated with our IBD pipeline candidates, including preclinical and manufacturing activities coupled with intellectual property license fees, and stock compensation expense related to the Parapyre Option Obligation, partially offset by decreased costs related to the Company's legacy rare disease pipeline.

Internal research and development expenses include compensation and related costs associated with our research and development employees, as well as costs associated with the Company's on-premises research laboratory. For the year ended December 31, 2024 and 2023, internal research and development costs accounted for $22.1 million and $16.8 million, respectively. The increase was primarily driven by an increase in research and development headcount, partially offset by a decrease in costs associated with our on-premises research laboratory that was decommissioned, including the elimination of related internal roles, in the first half of 2023.

General and Administrative Expenses. General and administrative expenses increased by $5.8 million, or 15%, to $45.8 million for the year ended December 31, 2024, from $39.9 million for the year ended December 31, 2023. The increase was primarily due to an increase in stock-based compensation expense, inclusive of acceleration expense related to legacy Aeglea officers and directors, partially offset by reduction in compensation costs primarily associated with lower legacy severance costs, and reduction in lease termination costs that were incurred in the prior year.

Acquired In-process Research and Development Expenses. Acquired IPR&D expenses were $130.2 million for the year ended December 31, 2023, as the acquisition of Pre-Merger Spyre was determined by management to be an asset acquisition, in accordance with U.S. GAAP as the product candidates were determined to have no alternative future use. There was no similar expense during the year ended December 31, 2024.

Gain on Sale of In-Process Research and Development Asset. Gain on sale of in-process research and development asset during the year ended December 31, 2023 was driven by the sale of pegzilarginase to Immedica. There was no similar gain or loss during the year ended December 31, 2024.

Interest Income. Interest income was $21.3 million and $6.1 million for the twelve months ended December 31, 2024 and 2023, respectively. The increase was primarily due to higher investment balances.

Change in Fair Value of Forward Contract Liability. Non-cash expenses associated with the change in fair value of the forward contract liability were $83.5 million for the year ended December 31, 2023. This expense was due to the change in fair value of the underlying Series A Preferred Stock between June 22, 2023 and the forward contract's settlement on July 7, 2023. There was no similar expense during the year ended December 31, 2024.

Other expense, net. Other expense, net for the year ended December 31, 2024 increased by $1.6 million versus the year ended December 31, 2023, primarily driven by changes in the fair value of the CVR liability.

Liquidity and Capital Resources

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

Since our inception and through December 31, 2025, we have funded our operations by raising an aggregate of approximately $1.6 billion of gross proceeds from the sale and issuance of convertible preferred stock and common stock, pre-funded warrants, the collection of grant proceeds, and the licensing of our product rights for commercialization of pegzilarginase in Europe and certain countries in the Middle East. As of December 31, 2025, we had an accumulated deficit of $1.1 billion.

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

Recent sources of liquidity

In June 2023, we sold 721,452 shares of convertible Series A preferred stock at $291.08 per share in a private placement offering for net proceeds of $197.3 million after deducting approximately $12.7 million of placement agent and other offering expenses.

In December 2023, we sold 6,000,000 shares of our common stock at an offering price of $15.00 and 150,000 shares of convertible Series B preferred stock at $600.00 per share for net proceeds of $169.1 million after deducting approximately $10.9 million of placement agent and other offering expenses.

In March 2024, we completed a private placement of 121,625 shares of Series B Preferred Stock at $1,480 per share resulting in net proceeds of approximately $168.9 million after deducting approximately $11.2 million of placement agent and other offering costs.

In November 2024, we sold 8,366,250 shares of our common stock in an underwritten public offering, inclusive of 1,091,250 shares pursuant to the full exercise of an over-allotment option, under our shelf

registration statement on Form S-3 at a price per share of $27.50, resulting in net proceeds of $215.9 million after deducting approximately $14.2 million of underwriting discounts and other offering costs.

During the year ended December 31, 2024, we sold an aggregate of 777,432 shares of common stock under an at-the-market offering program at an average price per share of $26.935 resulting in net proceeds of approximately $20.5 million after deducting approximately $0.4 million of sales agent commissions and other offering costs.

In October 2025, we sold 17,094,594 shares of our common stock in an underwritten public offering, inclusive of 2,229,729 shares pursuant to the full exercise of the underwriters' over-allotment option, under our shelf registration statement on Form S-3 at a price per share of $18.50, resulting in net proceeds of $296.4 million after deducting approximately $19.9 million of underwriting discounts and other offering costs.

During the three and twelve months ending December 31, 2025, we sold an aggregate of 445,668 shares of common stock under an at-the-market offering program at an average price per share of $33.772 resulting in net proceeds of $14.8 million, after deducting $0.3 million of sales agent commissions and other offering costs.

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

	Year Ended December 31,	
	2025	2024
Net cash and cash equivalents (used in) provided by:		
Operating activities	$ (169,252)	$ (157,410)
Investing activities	(143,475)	(353,285)
Financing activities	309,025	410,906
Effect of exchange rate on cash, cash equivalents, and restricted cash	—	(3)
Net decrease in cash and cash equivalents	$ (3,702)	$ (99,792)

Cash Used in Operating Activities

Cash used in operating activities for the year ended December 31, 2025 was $169.3 million and reflected a net loss of $155.2 million adjusted for a $10.0 million non-operating gain on sale of in-process research and development, a $29.8 million decrease in the fair value of the CVR liability, $8.1 million in net accretion of discount on marketable securities and a $5.9 million change in net operating assets and liabilities driven primarily by timing of payments to vendors, partially offset by share-based compensation expense of $37.6 million.

Cash used in operating activities for the year ended December 31, 2024 was $157.4 million and reflected a net loss of $208.0 million. Our net loss coupled with $11.4 million in net accretion of discount on marketable securities and a $4.5 million net change in operating assets and liabilities and was partially offset by non-cash expenses, including $44.8 million in stock-based compensation and $20.4 million change in fair value of CVR liability. The net change in operating assets and liabilities was primarily driven by timing of payments to vendors.

Cash (Used in) Provided by Investing Activities

Cash used in investing activities for the year ended December 31, 2025 was $143.5 million and primarily consisted of $522.2 million in purchases of marketable securities, $7.0 million in proceeds from the sale of in-process research & development asset partially offset by $371.7 million in maturities and sales of marketable securities.

Cash used in investing activities for the year ended December 31, 2024 was $353.3 million and primarily consisted of $599.3 million in purchases of marketable securities, partially offset by $246.0 million in maturities and sales of marketable securities.

Cash Provided by Financing Activities

Cash provided by financing activities for the year ended December 31, 2025 was $309.0 million, which primarily consisted of the net proceeds of $296.4 million and $14.8 million from the issuance common stock in the October 2025 follow-on offering and the December 2025 at-the-market offering program, respectively, $3.3 million proceeds from stock option exercises and sales of common stock under our Employee Stock Purchase Plan, partially offset by a $5.3 million payment to CVR holders.

Cash provided by financing activities for the year ended December 31, 2024 was $410.9 million, which primarily consisted of the net proceeds from the issuance of the Series B Preferred Stock in the March 2024 PIPE of $168.9 million, $215.9 million and $20.5 million in net proceeds from the issuance of common stock in connection with the November 2024 Offering and the at-the-market offering program, respectively, and $7.5 million from proceeds from stock option exercises and sales of common stock under our 2016 Employee Stock Purchase Plan and the exercise of pre-funded warrants partially offset by a $1.4 million payment to CVR holders.

Contractual Obligations and Other Commitments

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

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

Contingent contractual obligations

Through the Asset Acquisition, we received the Option to license certain intellectual property rights related to certain research programs. The exercise of the Option allows for us to enter into an exclusive license agreement with Paragon for the respective research program. Thus far we have exercised the Option and entered into license agreements with respect to SPY001, SPY002, SPY072 and SPY003. Under the terms of each License Agreement, we are obligated to pay Paragon up to $22.0 million based on specific development, regulatory and clinical milestones for the first product under each agreement. As of December 31, 2025, we have incurred a total of $18.0 million of milestone fees out of a total maximum of $66.0 million in potential milestone fees across all License Agreements. As of December 31, 2025, no milestone fees remain outstanding and payable. With respect to the SPY002 License Agreement only, on a product by product basis, we are obligated to pay sublicensing fees of up to approximately $20.0 million upon the achievement of mostly commercial milestones. As of December 31, 2025, we have incurred $2.6 million of sublicensing fees of which none is outstanding and payable.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

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

As of December 31, 2025, we held $756.5 million in cash, cash equivalents, marketable securities, and restricted cash, predominately all of which was denominated in U.S. dollars, and consisted primarily of investments in money market funds, commercial paper, U.S. government obligations, and corporate bonds.

We are also exposed to market risk related to changes in foreign currency exchange rates as a result of our entering into transactions denominated in currencies other than U.S. dollars. Due to the uncertain timing of expected payments in foreign currencies, we do not utilize any forward exchange contracts. All foreign transactions settle on the applicable spot exchange basis at the time such payments are made. For the year ended December 31, 2025, a majority of our expenditures were denominated in U.S. dollars. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

SPYRE THERAPEUTICS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

	Page
Audited Consolidated Financial Statements	
Report of Independent Registered Public Accounting Firm (ID 185 KPMG LLP)	110
Report of Independent Registered Public Accounting Firm (ID 238 Pricewaterhouse Coopers LLC)	112
Consolidated Balance Sheets	113
Consolidated Statements of Operations	114
Consolidated Statements of Comprehensive Loss	115
Consolidated Statements of Changes in Convertible Preferred Stock and Stockholders' Equity	116
Consolidated Statements of Cash Flows	118
Notes to Consolidated Financial Statements	120

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Spyre Therapeutics, Inc.:

Opinions on the Consolidated Financial Statements and Internal Control Over Financial Reporting

We have audited the accompanying consolidated balance sheet of Spyre Therapeutics, Inc. and subsidiaries (the Company) as of December 31, 2025, the related consolidated statements of operations, comprehensive loss, changes in convertible preferred stock and stockholders' equity, and cash flows for the year then ended, and the related notes (collectively, the consolidated financial statements). We also have audited the Company's internal control over financial reporting as of December 31, 2025, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2025, and the results of its operations and its cash flows for the year then ended, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2025 based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's consolidated financial statements and an opinion on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audit of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide

reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing separate opinions on the critical audit matter or on the accounts or disclosures to which it relates.

Evaluation of the fair value of the contingent value right liability

As described in Notes 1, 2, and 3 to the consolidated financial statements, in connection with the asset acquisition of Pre-Merger Spyre, a non-transferable contingent value right (CVR) was distributed to certain legacy stockholders of record as of the close of business on July 3, 2023. Holders of the CVR are entitled to receive certain cash payments from proceeds received by the Company prior to the third anniversary of the CVR Agreement, if any, related to the disposition or monetization of the Company's legacy assets during the one-year period following the closing of the Asset Acquisition. Management determined that certain contingent payments under the CVR Agreement qualified as derivatives and were recorded as a liability on the balance sheet. For derivative financial instruments accounted for as liabilities, the derivative instrument is initially recorded by management at its estimated fair value and is re-valued at each reporting date with changes recorded as other income (expense). The fair value of the CVR liability was determined using the probability weighted discounted cash flow method to estimate future cash flows associated with the sale of the legacy assets. As discussed in Note 3 to the consolidated financial statements, the CVR liability as of December 31, 2025 was $26.7 million.

We identified the evaluation of the fair value of the CVR liability as a critical audit matter. Subjective auditor judgment was required to evaluate certain key assumptions that are based on the outcome of uncertain future events, specifically the estimated probabilities of regulatory success and estimated cash flow dates assumptions.

The following are the primary procedures we performed to address this critical audit matter. We evaluated the design and tested the operating effectiveness of certain internal controls related to the Company's CVR liability valuation process, including controls over the estimated probabilities of regulatory success and estimated cash flow dates key assumptions utilized to determine the fair value of the CVR liability. We tested the completeness and accuracy of the underlying data for these key assumptions used in the probability weighted discounted cash flow method. We evaluated the reasonableness of these key assumptions by comparing them to relevant publicly available market and industry data and assessing probable outcomes, including likelihood of occurrence and impact on the fair value of the CVR liability.

/s/ KPMG LLP

We have served as the Company's auditor since 2025.

San Diego, California
February 19, 2026

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Spyre Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the consolidated balance sheet of Spyre Therapeutics, Inc. and its subsidiaries (the "Company") as of December 31, 2024, and the related consolidated statements of operations, of comprehensive loss, of changes in convertible preferred stock and stockholders' equity and cash flows for each of the two years in the period ended December 31, 2024, including the related notes as of and for each of the two years in the period ended December 31, 2024 (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2024 , and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2024 in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

Austin, Texas

February 27, 2025

We served as the Company's auditor from 2014 to 2025.

Spyre Therapeutics, Inc.
Consolidated Balance Sheets
(In thousands, except share and per share amounts)

	December 31,	
	2025	2024
ASSETS		
CURRENT ASSETS		
Cash and cash equivalents	$ 85,721	$ 89,423
Marketable securities	670,812	513,665
Prepaid expenses and other current assets	21,248	5,386
Total current assets	777,781	608,474
Other non-current assets	—	10
TOTAL ASSETS	$ 777,781	$ 608,484
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES		
Accounts payable	$ 8,904	$ 666
CVR liability	22,820	25,080
Accrued and other current liabilities	26,947	27,711
Related party accounts payable	14	603
Total current liabilities	58,685	54,060
Non-current CVR liability	3,860	36,620
TOTAL LIABILITIES	62,545	90,680
Commitments and Contingencies (Note 8, Note 9)		
CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY		
Series A non-voting convertible preferred stock, $0.0001 par value; 1,086,341 shares authorized and 346,045 shares issued and outstanding as of December 31, 2025 and December 31, 2024.	146,425	146,425
Series B non-voting convertible preferred stock, $0.0001 par value; 271,625 shares authorized and 16,667 shares issued and outstanding as of December 31, 2025 and December 31, 2024.	9,395	9,395
Preferred stock, $0.0001 par value; 8,642,034 shares authorized and no shares issued and outstanding as of December 31, 2025 and December 31, 2024.	—	—
Common stock, $0.0001 par value; 400,000,000 shares authorized as of December 31, 2025 and December 31, 2024; 78,189,811 shares and 60,257,023 shares issued and outstanding as of December 31, 2025 and December 31, 2024, respectively.	15	13
Additional paid-in capital	1,686,167	1,334,223
Accumulated other comprehensive income	869	180
Accumulated deficit	(1,127,635)	(972,432)
TOTAL CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY	715,236	517,804
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY	$ 777,781	$ 608,484

The accompanying notes are an integral part of these consolidated financial statements.

Spyre Therapeutics, Inc.
Consolidated Statements of Operations
(In thousands, except share and per share amounts)

	Year Ended December 31,		
	2025	**2024**	**2023**
Revenue:			
Development fee and royalty	—	—	886
Total revenue	—	—	886
Operating expenses:			
Research and development [1]	171,653	162,790	89,504
General and administrative [2]	47,909	45,776	39,946
Acquired in-process research and development	—	—	130,188
Gain on sale of in-process research and development asset	(10,000)	—	(16,449)
Total operating expenses	209,562	208,566	243,189
Loss from operations	(209,562)	(208,566)	(242,303)
Other income (expense):			
Interest income	24,885	21,312	6,147
Change in fair value of forward contract liability	—	—	(83,530)
Other income (expense), net	29,459	(20,713)	(19,130)
Total other income (expense)	54,344	599	(96,513)
Loss before income tax expense	(155,218)	(207,967)	(338,816)
Income tax benefit (expense)	15	(51)	26
Net loss	$ (155,203)	$ (208,018)	$ (338,790)
Net loss per share, basic and diluted, Series A Preferred Stock	$ (79.02)	$ (127.21)	$ (550.28)
Weighted-average Series A non-voting convertible preferred stock outstanding, basic and diluted	346,045	374,387	434,612
Net loss per share, basic and diluted, Series B Preferred Stock	$ (79.02)	$ (127.21)	$ (550.29)
Weighted-average Series B non-voting convertible preferred stock outstanding, basic and diluted	16,667	85,208	8,630
Net loss per share, basic and diluted, common	$ (1.98)	$ (3.18)	$ (13.76)
Weighted-average common shares outstanding, basic and diluted	64,056,442	47,027,638	6,897,065

[1] Includes $10.5 million, $40.1 million and $48.5 million in related party expenses for the years ended December 31, 2025, 2024 and 2023, respectively.

[2] Includes $1.0 million, $1.1 million and $0.1 million in related party expenses for the years ended December 31, 2025, 2024 and 2023, respectively.

The accompanying notes are an integral part of these consolidated financial statements.

Spyre Therapeutics, Inc.
Consolidated Statements of Comprehensive Loss
(In thousands)

	Year Ended December 31,		
	2025	2024	2023
Net loss	$ (155,203)	$ (208,018)	$ (338,790)
Other comprehensive income (loss):			
Foreign currency translation adjustment	(22)	4	37
Unrealized gain (loss) on marketable securities	711	(126)	313
Total comprehensive loss	$ (154,514)	$ (208,140)	$ (338,440)

The accompanying notes are an integral part of these consolidated financial statements.

Spyre Therapeutics, Inc.
Consolidated Statements of Changes in Convertible Preferred Stock and Stockholders' Equity
(In thousands)

	Series B Non-Voting Convertible Preferred Stock		Series A Non-Voting Convertible Preferred Stock		Series B Non-Voting Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
Balances—December 31, 2022	—	$ —	—	$ —	—	$ —	2,614	$ 6	$ 475,971	$ (48)	$ (425,624)	$ 50,305
Issuance of Series A non-voting convertible preferred stock in connection with private placement, net of financing costs	—	—	721	197,364	—	—	—	—	—	—	—	197,364
Issuance of Series A non-voting convertible preferred stock in connection with the asset acquisition of Spyre and settlement of related forward contract	—	—	365	189,741	—	—	—	—	—	—	—	189,741
Conversion of Series A non-voting convertible preferred stock into common stock	—	—	(649)	(202,178)	—	—	25,972	3	202,175	—	—	—
Issuance of Series B non-voting convertible preferred stock in connection with private placement, net of financing costs	150	84,555	—	—	—	—	—	—	—	—	—	—
Issuance of common stock in connection with private placement, net of financing costs	—	—	—	—	—	—	6,000	—	84,555	—	—	84,555
Issuance of common stock in connection with the asset acquisition of Spyre	—	—	—	—	—	—	518	1	3,767	—	—	3,768
Issuance of common stock in connection with exercise of pre-funded warrants	—	—	—	—	—	—	905	—	—	—	—	—
Issuance of common stock in connection with exercise of stock options and employee stock purchase plan	—	—	—	—	—	—	48	—	405	—	—	405
CVR distribution to common stockholders	—	—	—	—	—	—	—	—	(29,500)	—	—	(29,500)
Stock-based compensation expense	—	—	—	—	—	—	—	—	14,347	—	—	14,347
Issuance of Parapyre Option Obligation warrants	—	—	—	—	—	—	—	—	11,471	—	—	11,471
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	37	—	37
Unrealized gain on marketable securities	—	—	—	—	—	—	—	—	—	313	—	313
Net loss	—	—	—	—	—	—	—	—	—	—	(338,790)	$ (338,790)
Balances—December 31, 2023	150	$84,555	437	$184,927	—	$ —	36,057	$ 10	$ 763,191	$ 302	$ (764,414)	$ 184,016
Issuance of Series B non-voting convertible preferred stock in connection with private placement, net of financing costs	122	168,850	—	—	—	—	—	—	—	—	—	—
Stockholder approval of the issuance of common stock upon conversion of Series B convertible non-voting preferred stock	(272)	(253,405)	—	—	272	253,405	—	—	—	—	—	253,405
Conversion of Series B non-voting convertible preferred stock into common stock	—	—	—	—	(255)	(244,010)	10,198	1	244,009	—	—	—
Exchange of Series A non-voting convertible preferred stock for common stock	—	—	(91)	(38,502)	—	—	3,640	1	38,501	—	—	—
Issuance of common stock in connection with at-the-market offering program, net of financing costs	—	—	—	—	—	—	777	—	20,504	—	—	20,504

Issuance of common stock in connection with exercise of pre-funded warrants	—	—	—	—	—	—	250	—	1	—	—	1
Issuance of common stock in connection with follow-on offering, net of financing costs	—	—	—	—	—	—	8,366	1	215,673			215,674
Issuance of common stock in connection with exercise of stock options and employee stock purchase plan	—	—	—	—	—	—	931	—	7,511	—	—	7,511
Stock-based compensation expense	—	—	—	—	—	—	—	—	30,374	—	—	30,374
Issuance of Parapyre Option Obligation warrants	—	—	—	—	—	—	—	—	14,459	—	—	14,459
CVR distribution to common stockholders	—	—	—	—	—	—	38	—	—	—	—	—
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	4	—	4
Unrealized loss on marketable securities	—	—	—	—	—	—	—	—	—	(126)	—	(126)
Net loss	—	—	—	—	—	—	—	—	—	—	(208,018)	(208,018)
Balances—December 31, 2024	—	$ —	346	$146,425	17	$ 9,395	60,257	$ 13	$1,334,223	$ 180	$ (972,432)	$ 517,804
Issuance of common stock in connection with follow-on offering, net of financing costs	—	—	—	—	—	—	17,095	2	296,279			296,281
Issuance of common stock in connection with at-the-market offering program, net of financing costs	—	—	—	—	—	—	446	—	14,745	—	—	14,745
Issuance of common stock in connection with exercise of stock options and employee stock purchase plan	—	—	—	—	—	—	354	—	3,306	—	—	3,306
Stock-based compensation expense	—	—	—	—	—	—	—	—	37,614	—	—	37,614
Vesting of restricted stock units	—	—	—	—	—	—	38	—	—	—	—	—
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	(22)	—	(22)
Unrealized gain on marketable securities	—	—	—	—	—	—	—	—	—	711	—	711
Net loss	—	—	—	—	—	—	—	—	—	—	(155,203)	(155,203)
Balances—December 31, 2025	—	$ —	346	$146,425	17	$ 9,395	78,190	$ 15	$1,686,167	$ 869	$ (1,127,635)	$ 715,236

The accompanying notes are an integral part of these consolidated financial statements.

Spyre Therapeutics, Inc.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2025	2024	2023
CASH FLOWS FROM OPERATING ACTIVITIES			
Net loss	$ (155,203)	$ (208,018)	$ (338,790)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	—	—	744
Stock-based compensation	37,614	44,833	25,675
Acquired in-process research and development	—	—	130,188
Change in fair value of CVR liability	(29,769)	20,430	18,986
Change in fair value of forward contract liability	—	—	83,530
Gain on sale of in-process research and development asset	(10,000)	—	(16,449)
Lease ROU asset and leasehold improvement impairment loss	—	—	2,580
Loss on disposal of long-lived assets	—	—	915
Net (accretion of discount) amortization of premium on marketable securities	(8,090)	(11,404)	(2,318)
Interest proceeds from maturities of zero coupon debt securities	2,130	1,283	—
Amortization of operating lease assets	—	—	220
Other	—	—	15
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	(12,819)	(2,932)	3,245
Accounts payable	8,238	(230)	218
Deferred revenue	—	—	575
Development receivables	—	—	375
Operating lease liabilities	—	—	(2,326)
Accrued and other liabilities	(764)	14,609	(4,891)
Related party accounts payable	(589)	(15,981)	(2,402)
Net cash used in operating activities	(169,252)	(157,410)	(99,910)
CASH FLOWS FROM INVESTING ACTIVITIES			
Cash assumed from asset acquisition of Spyre	—	—	3,035
Proceeds from sale of in-process research & development asset	7,000	—	15,000
Proceeds from the sale of property plant and equipment	—	—	475
Purchases of marketable securities	(522,214)	(599,252)	(166,803)
Proceeds from maturities and sales of marketable securities	371,739	245,967	39,900
Net cash (used in) provided by investing activities	(143,475)	(353,285)	(108,393)
CASH FLOWS FROM FINANCING ACTIVITIES			
Proceeds from issuance of Series B non-voting convertible preferred stock in connection with private placement, net of placement and other offering costs	—	168,850	84,555
Proceeds from issuance of common stock in connection with at-the-market offering program, net of issuance costs	14,750	20,521	—
Proceeds from issuance of common stock in connection with follow-on offering, net of issuance costs	296,382	215,860	—
Payment of deferred offering costs in connection with shelf registration	(162)	(407)	—
Proceeds from issuance of Series A non-voting convertible preferred stock in connection with private placement, net of placement and other offering costs	—	—	197,364
Proceeds from issuance of common stock in connection with private placement, net of placement and other offering costs	—	—	84,555
Payment of contingent value rights liability	(5,251)	(1,430)	(5,786)
Proceeds from employee stock option exercises and employee stock plan purchases	3,306	7,511	405
Other financing cash flows	—	1	(16)
Net cash provided by financing activities	309,025	410,906	361,077
Effect of exchange rate on cash, cash equivalents, and restricted cash	—	(3)	25
NET (DECREASE) INCREASE IN CASH, CASH EQUIVALENTS, AND RESTRICTED CASH	(3,702)	(99,792)	152,799
CASH, CASH EQUIVALENTS, AND RESTRICTED CASH			
Beginning of period	89,423	189,215	36,416
End of period	$ 85,721	$ 89,423	$ 189,215

Supplemental Disclosure of Non-Cash Investing and Financing Information:			
Allocation of deferred offering costs against proceeds of issuance of common stock	$ 107	$ 204	$ —
Exchange of Series A non-voting convertible preferred stock for common stock	$ —	$ 38,502	$ —
Conversion of Series B non-voting convertible preferred stock into common stock	$ —	$ 244,010	$ —
Settlement of forward contract liability and issuance of Series A non-voting convertible preferred stock in connection with the asset acquisition of Spyre	$ —	$ —	$ 189,741
Conversion of Series A non-voting convertible preferred stock into common stock	$ —	$ —	$ 202,178
Reconciliation of Cash, Cash Equivalents, and Restricted Cash Reported in the Statement of Financial Position			
Cash and cash equivalents	85,721	89,423	$ 188,893
Restricted cash	$ —	$ —	$ 322
Total cash, cash equivalents, and restricted cash shown in the statement of cash flows	$ 85,721	$ 89,423	$ 189,215

The accompanying notes are an integral part of these consolidated financial statements.

1. The Company and Basis of Presentation

Spyre Therapeutics, Inc., formerly Aeglea BioTherapeutics, Inc., (“Spyre” or the “Company”) is a clinical stage biotechnology company focused on developing next generation therapeutics for patients living with inflammatory bowel disease and other immune-mediated diseases. The Company was formed as a Limited Liability Company ("LLC") in Delaware on December 16, 2013 under the name Aeglea BioTherapeutics Holdings, LLC and was converted from a Delaware LLC to a Delaware corporation on March 10, 2015. On November 27, 2023, the Company completed its corporate rebranding, changing the name of the Company to Spyre Therapeutics, Inc. The Company operates in one segment and has its principal offices in Waltham, Massachusetts.

On September 8, 2023, the Company effected a reverse stock split of its common stock at a ratio of 1-for-25 (the “Reverse Split”). Except as indicated otherwise, all share numbers related to the Company's common stock disclosed in these financial statements have been adjusted on a post-Reverse Split basis.

On April 12, 2023, based on the review of the inconclusive interim results from the Company's Phase 1/2 clinical trial of pegtarviliase for the treatment of Classical Homocystinuria and other business considerations, the Company announced that it had initiated a process to explore strategic alternatives to maximize stockholder value and engaged an independent exclusive financial advisor to support this process. As a result, in April 2023, the Company implemented a restructuring plan resulting in an approximate 83% reduction of the Company’s existing headcount.

On June 22, 2023, the Company acquired, in accordance with the terms of the Agreement and Plan of Merger (the "Acquisition Agreement"), the assets of Spyre Therapeutics, Inc. (“Pre-Merger Spyre”) as disclosed in Note 7 and 8, a privately held biotechnology company advancing a pipeline of antibody therapeutics with the potential to transform the treatment of inflammatory bowel disease through a research and development option agreement ("Paragon Agreement") with Paragon Therapeutics ("Paragon"). The asset acquisition was accomplished through a two-step reverse triangular merger whereby Aspen Merger Sub I, Inc., a Delaware corporation and a wholly owned subsidiary of the Company ("First Merger Sub"), merged with and into Pre-Merger Spyre, which existed at the time the Acquisition Agreement was entered into, became a wholly owned subsidiary of the Company in accordance with the terms of the Acquisition Agreement. Immediately following this merger, Pre-Merger Spyre merged with and into Sequoia Merger Sub II, LLC, a Delaware limited liability company and a wholly subsidiary of the Company (“Second Merger Sub”), in accordance with the terms of the Acquisition Agreement and Pre-Merger Spyre ceased to exist. Subsequently, Aeglea BioTherapeutics, Inc. was renamed Spyre Therapeutics, Inc. and is a different entity than Pre-Merger Spyre, which ceased to exist upon merging with Second Merger Sub. The transaction was structured as a stock-for-stock transaction pursuant to which all of Pre-Merger Spyre's outstanding equity interests were exchanged based on a fixed exchange ratio of 0.5494488 to 1 for consideration from the Company of 517,809 shares of common stock and 364,887 shares of Series A non-voting convertible preferred stock, par value of $0.0001 per share ("Series A Preferred Stock") (convertible on a 40 to 1 basis), in addition to the assumption of outstanding and unexercised stock options to purchase 2,734 shares of common stock from the Amended and Restated Spyre 2023 Equity Incentive Plan (the "Asset Acquisition"). The common stock and Series A Preferred Stock related to the Asset Acquisition were issued to the Pre-Merger Spyre stockholders on July 7, 2023. For additional information, see Note 7.

In connection with the Asset Acquisition, on June 26, 2023, the Company completed a private placement of shares of Series A Preferred Stock (the “June 2023 PIPE” and, together with the Asset Acquisition, the "June 2023 Transactions") to a group of investors (the “June 2023 Investors”). The Company sold an aggregate of 721,452 shares of Series A Preferred Stock (the “June 2023 PIPE Securities”) at $291.08 per share for net proceeds of $197.3 million after deducting approximately $12.7 million of placement agent and other offering expenses. For additional information, see Note 12.

In connection with the Asset Acquisition, a non-transferable contingent value right ("CVR") was distributed to stockholders of record of the Company as of the close of business on July 3, 2023 (the "Legacy Stockholders"), but was not distributed to the holders of shares of common stock or Series A Preferred Stock issued to the former stockholders of Pre-Merger Spyre or June 2023 Investors in the June 2023 Transactions.

Holders of the CVRs will be entitled to receive certain cash payments from proceeds received by the Company prior to the third anniversary of the CVR Agreement, if any, related to the disposition or monetization of its legacy assets during the one-year period following the closing of the Asset Acquisition. For additional information, see Note 3.

On November 21, 2023, the Company's stockholders approved the conversion of the Company's Series A non-voting convertible preferred stock to common stock. For additional information, see Note 12.

On December 11, 2023, the Company completed a private placement of shares of common stock and Series B non-voting convertible preferred stock, par value of $0.0001 per share ("Series B Preferred Stock") (convertible on a 40 to 1 basis) (collectively, the “December 2023 PIPE”) to a group of investors (the “December 2023 PIPE Investors”). The Company sold an aggregate of 6,000,000 shares of its common stock at an offering price of $15.00 per share and 150,000 shares of Series B Preferred Stock (the “December 2023 PIPE Securities”) at $600.00 per share for net proceeds of approximately $169.1 million after deducting approximately $10.9 million of placement agent and other offering expenses. For additional information, see Note 12.

On March 20, 2024, the Company completed a private placement of Series B Preferred Stock (convertible on a 40 to 1 basis) (the “March 2024 PIPE”) to a group of investors. The Company sold 121,625 shares of Series B Preferred Stock at $1,480 per share. The net proceeds from this offering were approximately $168.9 million after deducting placement and offering costs of $11.2 million.

On April 23, 2024, the Company entered into an exchange agreement with Fairmount Healthcare Fund II L.P. (the “Stockholder”), pursuant to which the Stockholder agreed to exchange an aggregate of 90,992 shares of Series A Preferred Stock, for an aggregate of 3,639,680 shares of the Company's common stock (the “April 2024 Exchange”). The common stock issued in connection with the April 2024 Exchange was issued without registration under the Securities Act of 1933, as amended (the “Securities Act”) in reliance on the exemption from registration contained in Section 3(a)(9) of the Securities Act. The April 2024 Exchange closed on April 25, 2024, with 346,045 shares of Series A Preferred Stock remaining outstanding following the April 2024 Exchange.

On May 14, 2024, the Company's stockholders approved the issuance of its common stock upon conversion of the Company's Series B Preferred Stock to common stock. A total of 254,958 shares of Series B Preferred Stock automatically converted to 10,198,320 shares of common stock; 16,667 shares of Series B Preferred Stock did not automatically convert and remained outstanding as of December 31, 2025.

On September 6, 2024, the Company filed a new shelf registration statement on Form S-3 that was declared effective by the SEC for the potential offering, issuance and sale by the Company of up to $500.0 million of its common stock, preferred stock, debt securities, warrants and/or units consisting of all or some of these securities. Concurrent with the filing of the shelf-registration statement, the Company entered into a sales agreement, dated September 6, 2024, with TD Securities (USA) LLC (“TD Cowen”) ("Sales Agreement"), as its sales agent, pursuant to which the Company may issue and sell shares of its common stock for an aggregate offering price of up to $200.0 million under an at-the-market (“ATM”) offering program included in the shelf registration. During the year ended December 31, 2024, the Company sold an aggregate of 777,432 shares of common stock under the ATM resulting in aggregate net proceeds of approximately $20.5 million after deducting commissions paid to TD Cowen as sales agent and other offering costs.

On November 18, 2024, the Company entered into an underwriting agreement (the "November 2024 Underwriting Agreement") with Jefferies LLC, Goldman Sachs & Co. LLC, Evercore Group L.L.C. and Guggenheim Securities, LLC as representatives of the several underwriters (collectively, the "November 2024 Underwriters"), pursuant to which the Company sold an aggregate of 8,366,250 shares of its common stock, inclusive of 1,091,250 shares pursuant to the full exercise of the November 2024 Underwriters' over-allotment option, at a public offering price per share of $27.50, resulting in net proceeds of approximately $215.9 million after deducting approximately $14.2 million of underwriting discounts and other offering costs (the "November 2024 Offering"). The November 2024 Offering closed on November 20, 2024 and the over-allotment option was exercised in full on November 26, 2024 and closed on November 29, 2024.

In February 2025, the Company filed a new shelf registration statement on Form S-3 (the "February 2025 Shelf Registration Statement") that was declared effective by the SEC for the potential offering, issuance and sale of up to $500.0 million of shares of common stock, preferred stock, debt securities, warrants and/or units consisting of all or some of these securities. Concurrent with the effectiveness of the February 2025 Shelf Registration Statement, the offering of unsold securities under a previous shelf registration statement on Form S-3 (File No. 333-281975), which was initially filed with the SEC on September 6, 2024 and became effective on September 18, 2024, was deemed terminated pursuant to Rule 415(a)(6) under the Securities Act. The February 2025 Shelf Registration Statement contains a sales agreement prospectus supplement covering the offering, issuance and sale by the Company of up to $179.1 million of shares of common stock that may be issued and sold under the Sales Agreement in connection with the ATM offering program. During the three and twelve months ended December 31, 2025, the Company sold an aggregate of 445,668 shares of common stock under the ATM offering program at an average price per share of $33.772 resulting in net proceeds of $14.8 million, after deducting sales agent commissions and other offering costs of $0.3 million. As of December 31, 2025, $164.1 million remained available for sale under the Sales Agreement. Subsequent to December 31, 2025 through February 12, 2026 the Company sold an aggregate of 296,396 shares of common stock under the ATM offering program at an average price per share of $33.566 resulting in net proceeds of $9.7 million after deducting sales agent commissions and other offering costs of $0.2 million.

On October 13, 2025, the Company entered into an underwriting agreement (the "October 2025 Underwriting Agreement") with Jefferies LLC, TD Securities (USA) LLC, Leerink Partners LLC and Stifel, Nicolaus & Company, Incorporated as representatives of the several underwriters (collectively, the "October 2025 Underwriters"), pursuant to which the Company sold an aggregate of 17,094,594 shares of its common stock, inclusive of 2,229,729 shares pursuant to the full exercise of the October 2025 Underwriters' over-allotment option, at a public offering price per share of $18.50, resulting in net proceeds of approximately $296.4 million after deducting approximately $19.9 million of underwriting discounts and other offering costs (the "October 2025 Offering"). The over-allotment option was exercised in full on October 14, 2025 and the transaction closed on October 15, 2025.

Liquidity

The Company is a clinical stage biotechnology company with a limited operating history, and due to its significant research and development expenditures, the Company has generated operating losses since its inception and has not generated any revenue from the commercial sale of any products. There can be no assurance that profitable operations will ever be achieved, and, if achieved, whether profitability can be sustained on a continuing basis.

Since its inception and through December 31, 2025, the Company has funded its operations by raising an aggregate of approximately $1.6 billion of gross proceeds from the sale and issuance of convertible preferred stock and common stock, pre-funded warrants, the collection of grant proceeds, and the licensing of its product rights for commercialization of pegzilarginase in Europe and certain countries in the Middle East. As of December 31, 2025, Spyre had an accumulated deficit of $1.1 billion, and cash, cash equivalents, and marketable securities of $756.5 million.

Based on current operating plans, the Company has sufficient resources to fund operations for at least one year from the issuance date of these financial statements with existing cash, cash equivalents, and marketable securities. The Company will need to secure additional financing in the future to fund additional research and development, and before a commercial drug can be produced, marketed and sold. If the Company is unable to obtain additional financing or generate license or product revenue, the lack of liquidity could have a material adverse effect on the Company.

Basis of Presentation

The consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States (“U.S. GAAP”) as defined by the Financial Accounting Standards Board (“FASB”) and include the accounts of the Company and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets, liabilities, and equity and the amount of revenues and expenses. Actual results could differ significantly from those estimates. The most significant estimates and assumptions that management considers in the preparation of the Company's financial statements relate to accrued research and development costs; the valuation of consideration transferred in acquiring in-process research & development ("IPR&D"); the discount rate, probabilities of success, and timing of estimated cash flows in the valuation of the CVR liability; inputs used in the Black-Scholes model for stock-based compensation expense; estimated future cash flows used in calculating the impairment of right-of-use lease assets; and estimated cost to complete performance obligations related to revenue recognition. The consideration transferred in acquiring IPR&D in connection with the acquisition of Pre-Merger Spyre was comprised of shares of the Company’s common stock and shares of Series A Preferred

Stock. To determine the fair value of the equity transferred, the Company considered the per share value of securities sold in the June 2023 PIPE, which was a financing event involving a group of accredited investors.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less from the date of purchase to be cash equivalents. Cash equivalents consist of money market funds and debt securities and are stated at fair value.

Marketable Securities

All investments have been classified as available-for-sale and are carried at estimated fair value as determined based upon quoted market prices or pricing models for similar securities. Management determines the appropriate classification of its investments in debt securities at the time of purchase. The Company may hold securities with stated maturities greater than one year until maturity. All available-for-sale securities are considered available to support current operations and are classified as current assets. The Company presents credit losses as an allowance rather than as a reduction in the amortized cost of the available-for-sale securities.

For available-for-sale debt securities in an unrealized loss position, the Company first assesses whether it intends to sell, or it is more likely than not that it will be required to sell the security before recovery of its amortized cost basis. If either of the criteria regarding intent or requirement to sell is met, the security's amortized cost basis is written down to fair value and recognized in other income (expense) in the results of operations. For available-for-sale debt securities that do not meet the aforementioned criteria, the Company evaluates whether the decline in fair value has resulted from credit losses or other factors. In making this assessment, management considers the extent to which fair value is less than amortized cost, any changes to the rating of the security by a rating agency, and adverse conditions specifically related to the security, among other factors. If this assessment indicates that a credit loss exists, an allowance is recorded for the difference between the present value of cash flows expected to be collected and the amortized cost basis of the security. Impairment losses attributable to credit loss factors are charged against the allowance when management believes an available-for-sale security is uncollectible or when either of the criteria regarding intent or requirement to sell is met.

Any unrealized losses from declines in fair value below the amortized cost basis as a result of non-credit loss factors is recognized as a component of accumulated other comprehensive (loss) income, along with unrealized gains. Realized gains and losses and declines in fair value, if any, on available-for-sale securities are included in other income (expense) in the results of operations. The cost of securities sold is based on the specific-identification method.

Restricted Cash

Restricted cash consisted of cash balances related to the Company's former operations in the United Kingdom for the period ended December 31, 2023. There were no restricted cash balances as of December 31, 2025 and 2024.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents, marketable securities, and restricted cash. The Company's investment policy limits investments to high credit quality securities issued by the U.S. government, U.S. government-sponsored agencies, highly rated banks, and corporate issuers, subject to certain concentration limits and restrictions on maturities. The financial instruments that potentially subject the Company to a concentration of credit risk consist principally of cash deposits. Accounts at each of the Company's two U.S. banking institutions are insured by the Federal Deposit Insurance Corporation ("FDIC") up to $250,000 per depositor. As of December 31, 2025 and 2024, balances at the Company's U.S. banking institutions exceeded the FDIC limits. The Company has not experienced any losses on its deposits of cash, cash equivalents, and restricted cash and its accounts are monitored by management to mitigate risk. The Company is exposed to credit risk in the

event of default by the financial institutions holding its cash, cash equivalents, and restricted cash, and bond issuers.

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation and amortization. Depreciation and amortization are computed using the straight-line method over the estimated useful lives of the assets. Repairs and maintenance that do not extend the life or improve an asset are expensed as incurred. Upon retirement or sale, the cost of disposed assets and their related accumulated depreciation and amortization are removed from the balance sheet. Any gain or loss is credited or charged to operations.

The useful lives of the property and equipment are as follows:

Laboratory equipment	5 years
Furniture and office equipment	5 years
Computer equipment	3 years
Software	3 years
Leasehold improvements	Shorter of remaining lease term or estimated useful life

The Company did not have any property, plant, and equipment assets as of December 31, 2025 and 2024.

Impairment of Long-Lived Assets

Long-lived assets are reviewed for indications of possible impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparison of the carrying amounts to the future undiscounted cash flows attributable to these assets. An impairment loss is recognized to the extent an asset group is not recoverable, and the carrying amount exceeds the fair value. The Company recognized a $2.6 million impairment loss for the year ended December 31, 2023 related to its leased office space in Austin, Texas (see Note 11 and Note 17 for additional information). There were no impairments of long-lived assets for the years ended December 31, 2025 and 2024.

Accrued Research and Development Costs

The Company records the costs associated with research nonclinical studies, clinical trials, and manufacturing development as incurred. These costs are a significant component of the Company’s research and development expenses, with a substantial portion of the Company’s on-going research and development activities conducted by third-party service providers, including contract research organizations ("CROs") and contract manufacturing organizations ("CMOs"), and the Company's related-party Paragon.

The Company accrues for expenses resulting from obligations under the Paragon Agreement and agreements with CROs, CMOs, and other outside service providers for which payment flows do not match the periods over which materials or services are provided to the Company. Accruals are recorded based on estimates of services received and efforts expended pursuant to agreements established with Paragon, CROs, CMOs, and other outside service providers. These estimates are typically based on contracted amounts applied to the proportion of work performed and determined through analysis with internal personnel and external service providers as to the progress or stage of completion of the services. The Company makes significant judgments and estimates in determining the accrual balance in each reporting period. In the event advance payments are made to Paragon, a CRO, CMO, or outside service provider, the payments will be recorded as a prepaid asset which will be amortized as the contracted services are performed. As actual costs become known, the Company adjusts its accruals. Inputs, such as the services performed, the number of patients enrolled, or the trial duration, may vary from the Company’s estimates, resulting in adjustments to research and development expense in future periods. Changes in these estimates that result in material changes to the Company’s accruals could materially affect the Company’s results of operations. Historically, the Company has not experienced any material deviations between accrued and actual research and development expenses.

License Agreements Contingent Milestone Payments

The Company's license agreements include specific development, regulatory, and clinical milestone payments that are payable upon the resolution of a contingency, such as upon the selection of a development candidate, first dosing of a human patient in clinical trials or receipt of the U.S. Food Drug and Administration's ("FDA") approval of a Spyre drug. The achievement of these milestone payments involves many factors outside of the Company's control and therefore the associated likelihood cannot be considered probable until the related contingency is resolved. Based on the preceding, the Company accrues each milestone payment upon the achievement of the applicable milestone event.

Leases

The Company determines if an arrangement is a lease at inception. Right-of-use ("ROU") assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. The classification of the Company's leases as operating or finance leases along with the initial measurement and recognition of the associated ROU assets and lease liabilities is performed at the lease commencement date. The measurement of lease liabilities is based on the present value of future lease payments over the lease term. As the Company's leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at the lease commencement date in determining the present value of future lease payments. To determine the incremental borrowing rate, the Company uses the lease-term appropriate current treasury bond rates adjusted for collateral and inflation risks combined with quoted bank financing rates. The ROU asset is based on the measurement of the lease liability and also includes any lease payments made prior to or on lease commencement and excludes lease incentives and initial direct costs incurred, as applicable. The lease terms may include options to extend or terminate the lease when it is reasonably certain the Company will exercise any such options. Rent expense for the Company's operating leases is recognized on a straight-line basis over the lease term. Amortization expense for the ROU asset associated with its finance leases is recognized on a straight-line basis over the term of the lease and interest expense associated with its finance leases is recognized on the balance of the lease liability using the effective interest method based on the estimated incremental borrowing rate.

As described in Note 11, the Company had lease agreements with lease and non-lease components prior to its restructuring. As allowed under Topic 842, the Company elected to not separate lease and non-lease components for any leases involving real estate and office equipment classes of assets and, as a result, accounted for the lease and non-lease components as a single lease component. The Company also elected to not apply the recognition requirement of Topic 842 to leases with a term of 12 months or less for all classes of assets. As of December 31, 2025 and 2024, the Company had no operating or finance lease obligations.

Fair Value of Financial Instruments

The Company uses fair value measurements to record fair value adjustments to certain financial and non-financial assets and liabilities and to determine fair value disclosures. The accounting standards define fair value, establish a framework for measuring fair value, and require disclosures about fair value measurements. Fair value is defined as the price that would be received from selling an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. When determining the fair value measurements for assets and liabilities required to be recorded at fair value, the principal or most advantageous market in which the Company would transact are considered along with assumptions that market participants would use when pricing the asset or liability, such as inherent risk, transfer restrictions, and risk of nonperformance.

The accounting standard for fair value establishes a fair value hierarchy based on three levels of inputs, the first two of which are considered observable and the last unobservable, that requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. A financial instrument's categorization within the fair value hierarchy is based upon the lowest level of input that is significant to the fair value measurement.

The three levels of inputs that may be used to measure fair value are as follows:

Level 1: Observable inputs, such as quoted prices in active markets for identical assets or liabilities.

Level 2: Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3: Valuations based on unobservable inputs to the valuation methodology and including data about assumptions that market participants would use in pricing the asset or liability based on the best information available under the circumstances.

Financial instruments carried at fair value include cash equivalents and marketable securities. The carrying amounts of accounts payable and accrued liabilities approximate fair value due to their relatively short maturities.

Revenue Recognition

Under ASC Topic 606, "Revenue from Contracts with Customers" ("Topic 606"), an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation.

The Company assesses its license arrangements within the scope of Topic 606 in accordance with this framework as follows:

License revenue

The Company assesses whether the goods or services promised within each contract are distinct to identify those that are performance obligations. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. In assessing whether a promised good or service is distinct, and therefore a performance obligation, the Company considers factors such as the research, stage of development of the licensed product, manufacturing and commercialization capabilities of the customer and the availability of the associated expertise in the general marketplace. The Company also considers the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, the Company is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, they are considered performance obligations.

The transaction price is determined and allocated to the identified performance obligations in proportion to their stand-alone selling prices ("SSP") on a relative SSP basis. SSP is based on observable prices of the performance obligations or, when such prices are not observable, are estimated. The estimation of SSP may include factors such as forecasted revenues or costs, development timelines, discount rates, probabilities of technical and regulatory success, and considerations such as market conditions and entity-specific factors. In certain circumstances, the Company may apply the residual method to determine the SSP of a good or service if the SSP is considered highly variable or uncertain. The Company validates the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, the Company estimates the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services

to a customer. The Company determines the amount of variable consideration by using the expected value method or the most likely amount method. The Company includes the amount of estimated variable consideration in the transaction price to the extent that it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development, regulatory or commercial milestone payments, the Company evaluates whether the milestones are considered likely of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant cumulative revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are generally not considered likely of being achieved until those approvals are received.

In determining the transaction price, the Company adjusts consideration for the effects of the time value of money if the timing of payments provides the Company with a significant benefit of financing. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensee and the transfer of the promised goods or services to the licensees will be one year or less. For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and if the license is deemed to be the predominant item to which the royalties relate, the Company recognizes royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied.

The Company recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time, recognition is based on the use of an output or input method.

The Company's contracts may be modified for changes in the customer's requirements. If contract modifications are for additional goods and services that are distinct from the existing contract, the modification will be accounted for as either a separate contract or a termination of the existing contract, depending on whether the additional goods or services reflects the SSP.

If the additional goods or services in a contract modification are not distinct from the existing contract, they are accounted for as if they were part of the original contract. The effect of the contract modification on the transaction price and the measure of progress for the performance obligation to which it relates is recognized as an adjustment to revenue on a cumulative catch-up basis. The cumulative catch-up adjustment is calculated using an updated measure of progress applied to the sum of (1) the remaining consideration allocated to the partially satisfied performance obligation and (2) the revenue already recognized on that performance obligation. The revenue recognized for fully satisfied goods or services and distinct from the remaining performance obligations is not altered by the modification.

Collaborative arrangements

The Company analyzes its license arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and therefore within the scope of ASC Topic 808, Collaborative Arrangements ("Topic 808"). This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For arrangements within the scope of Topic 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of Topic 808 and which elements of the collaboration are more reflective of a vendor-customer relationship and therefore within the scope of Topic 606. For elements of collaboration arrangements that are accounted for pursuant to Topic 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election. For those elements of the arrangement that are accounted for pursuant to Topic 606, the Company applies the five-step model described above.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development costs include, but are not limited to, salaries, benefits, travel, stock-based compensation, consulting costs, contract research service costs, laboratory supplies and facilities, contract manufacturing costs, and costs paid to other third parties that conduct research and development activities on the Company's behalf. Amounts incurred in connection with license agreements are also included in research and development expense.

Advance payments for goods or services to be rendered in the future for use in research and development activities are recorded as a prepaid asset and expensed as the related goods are delivered or the services are performed.

Stock-Based Compensation

The Company recognizes the cost of stock-based awards granted to employees and non-employees based on the estimated grant-date fair values of the awards. The fair values of stock options are estimated on the date of grant using the Black-Scholes option pricing model. The fair values of restricted stock units ("RSUs") are based on the fair value of the Company's common stock on the date of the grant. The value of the award is recognized as compensation expense on a straight-line basis over the requisite service period. Forfeitures are recognized when they occur, which may result in the reversal of compensation costs in subsequent periods as the forfeitures arise. Compensation expense for employee and non-employee share-based payment awards with performance conditions is recognized when the performance condition is deemed probable.

Convertible Preferred Stock Issued through PIPE

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

Since the Series B Preferred Stock is no longer redeemable, the associated balances of the Series B Preferred Stock were reclassified from mezzanine equity to permanent equity during the second quarter of 2024.

Contingent Milestone Proceeds

The Company recognizes contingent milestone proceeds associated from the sale of in-process research and development assets in earnings once the achievement of the milestone becomes probable and payment to the Company is contractually required.

Acquisitions

The Company evaluates acquisitions of assets and other similar transactions to assess whether or not the transaction should be accounted for as a business combination or asset acquisition by first applying a screen test to determine whether substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar identifiable assets. If so, the transaction is accounted for as an asset acquisition. If not, further determination is required as to whether or not the Company has acquired inputs and processes that have the ability to create outputs, which would meet the definition of a business. Significant judgment is required in the application of the test to determine whether an acquisition is a business combination or an acquisition of assets.

Acquisitions meeting the definition of business combinations are accounted for using the acquisition method of accounting, which requires that the purchase price be allocated to the net assets acquired at their

respective fair values. In a business combination, any excess of the purchase price over the estimated fair values of the net assets acquired is recorded as goodwill.

The Company measures and recognizes asset acquisitions that are not deemed to be business combinations based on the cost to acquire the assets, which includes pre-acquisition direct costs recorded in accrued professional and consulting fees. Goodwill is not recognized in asset acquisitions. When a transaction accounted for as an asset acquisition includes an IPR&D asset, the IPR&D asset is only capitalized if it has an alternative future use other than in a particular research and development project. Otherwise, the cost allocated to acquire an IPR&D asset with no alternative future use is charged to expense at the acquisition date.

Contingent Value Rights

The Company evaluates its contracts to determine if those contracts qualify as derivatives under ASC 815, Derivatives and Hedging ("ASC 815"). For derivative financial instruments that are accounted for as liabilities, the derivative instrument is initially recorded at its fair value and is then re-valued at each reporting date. Any changes in fair value are recorded as other income or expense for each reporting period. Derivative instrument liabilities are classified in the balance sheet as current or non-current based on whether or not net-cash settlement of the derivative instrument is probable within the next 12 months from the balance sheet date. The Company determined that certain contingent payments under the CVR Agreement qualified as derivatives under ASC 815, and as such, were recorded as a liability on the balance sheet. This value is then remeasured for future expected payout as well as the increase in fair value due to the time value of money. These gains or losses, if any, are recognized in the consolidated statements of operations and comprehensive loss within Other (expense) income, net.

The Company applies a scenario-based method and weighs them based on the possible achievement of certain milestones. The milestone payments are contingent on formal reimbursement decisions by national authorities in key European markets and pegzilarginase approval by the FDA, among other events. This fair value measurement is based on significant inputs not observable in the market and thus represents a Level 3 measurement as defined in ASC 820, Fair Value Measurement. The key assumptions used include the discount rate, probability of regulatory success, reimbursement rates from certain government agencies and estimated cash flow dates. The estimated value of the CVR consideration is based upon available information and certain assumptions which the Company's management believes are reasonable under the circumstances. The ultimate payout under the CVRs may differ materially from the assumptions used in determining the fair value of the CVR consideration.

Income Taxes

The Company uses the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the financial statements and the tax bases of assets and liabilities. Additionally, any changes in income tax laws are immediately recognized in the year of enactment.

A valuation allowance is established against the deferred tax assets to reduce their carrying value to an amount that is more likely than not to be realized. The deferred tax assets and liabilities are classified as noncurrent along with the related valuation allowance. Due to a lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance.

The Company recognizes benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on the technical merits, as the largest amount of benefits that is more likely than not to be realized upon the ultimate settlement. The Company's policy is to recognize interest and penalties related to the unrecognized tax benefits as a component of income tax expense, if applicable. As of December 31, 2025 and 2024, the Company had no unrecognized tax benefits and there were no interest or penalties incurred by the Company in the years ended December 31, 2025, 2024, or 2023.

Comprehensive Loss

Comprehensive loss is the change in stockholders' equity from transactions and other events and circumstances other than those resulting from investments by stockholders and distributions to stockholders. The Company's other comprehensive income (loss) is currently comprised of changes in unrealized losses and gains on available-for-sale securities and foreign currency translation adjustments reflecting the cumulative effect of changes in exchange rates between the foreign entity's functional currency and the reporting currency.

Recently Adopted Accounting Pronouncements

In December 2023, the FASB issued ASU No. 2023-09, Income Taxes (Topic 740) - Improvements to Income Tax Disclosures, to require enhanced income tax disclosures to provide information to assess how an entity's operations and related tax risks, tax planning, and operational opportunities affect its tax rate and prospects for future cash flows. The amendments in this update provide that a business entity disclose (1) a tabular income tax rate reconciliation, using both percentages and amounts, (2) separate disclosure of any individual reconciling items that are equal to or greater than 5% of the amount computed by multiplying the income (loss) from continuing operations before income taxes by the applicable statutory income tax rate, and disaggregation of certain items that are significant and (3) amount of income taxes paid (net of refunds received) disaggregated by federal, state and foreign jurisdictions, including separate disclosure of any individual jurisdictions greater than 5% of total income taxes paid. These amendments are effective for the Company for annual periods in beginning in 2025, applied prospectively, with early adoption and retrospective application permitted. The Company applied the amendments prospectively for the year ended December 31, 2025, and the impact of the adoption of the amendments in this update was not material to the Company's consolidated financial position and results of operations since the amendments require only enhancement of existing income tax disclosures in the footnotes to the Company's consolidated financial statements. See Note 18, Income Taxes.

Not Yet Adopted Accounting Pronouncements

In November 2024, the FASB issued ASU 2024-03, Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses to improve disclosures about public business entities' expenses and to provide more detailed information around the types of expenses included in commonly presented expense captions. ASU 2024-03 is effective for fiscal years beginning after December 15, 2026, and interim periods for fiscal years beginning after December 15, 2027, and can be applied on a prospective basis or on a retrospective basis to all periods presented. Early adoption is permitted. This ASU will have no impact on the Company's consolidated financial condition or results of operations. The Company is currently evaluating the impact of adopting ASU 2024-03 on its disclosures.

In December 2025, the FASB issued ASU No. 2025-11, Interim Reporting (Topic 270): Narrow-Scope Improvements. The ASU clarifies interim disclosure requirements and the applicability of Topic 270. The objective of the amendments is to provide further clarity about the current interim disclosure requirements. The ASU is effective for interim reporting periods within annual reporting periods beginning after December 15, 2027. Adoption of this ASU can be applied either a prospective or a retrospective approach. Early adoption is permitted. The Company is currently evaluating the impact of adopting ASU 2024-03 on its disclosures.

In December 2025, the FASB issued ASU No. 2025-12, Codification Improvements. The update represents changes to the Codification that clarify, correct errors in or make other improvements to a variety of topics that are intended to make it easier to understand and apply. Generally, the amendments in this Update are not intended to result in significant changes for most entities. The ASU is effective for interim reporting periods within annual reporting periods beginning after December 15, 2026. The adoption method of this ASU may vary, on an issue-by-issue basis. Early adoption is permitted. The Company is currently evaluating the impact of adopting ASU 2024-03 on its disclosures.

3. Fair Value Measurements

The Company measures and reports certain financial instruments as assets and liabilities at fair value on a recurring basis. The following tables set forth the fair value of the Company's financial assets and liabilities at fair value on a recurring basis based on the three-tier fair value hierarchy (in thousands):

	December 31, 2025			
	Level 1	Level 2	Level 3	Total
Financial Assets				
Money market funds	$ 74,004	$ —	$ —	$ 74,004
U.S. government treasury securities	266,064	—	—	266,064
U.S. government agency securities	—	119,590	—	119,590
Commercial paper	—	194,355	—	194,355
Corporate bonds	—	100,790	—	100,790
Total financial assets	$ 340,068	$ 414,735	$ —	$ 754,803
Liabilities:				
CVR liability	$ —	$ —	$ 26,680	$ 26,680
Total liabilities	$ —	$ —	$ 26,680	$ 26,680

	December 31, 2024			
	Level 1	Level 2	Level 3	Total
Financial Assets				
Money market funds	$ 65,902	$ —	$ —	$ 65,902
U.S. government treasury securities	227,244	—	—	227,244
U.S. government agency securities	—	86,681	—	86,681
Commercial paper	—	165,130	—	165,130
Corporate bonds	—	56,448	—	56,448
Total financial assets	$ 293,146	$ 308,259	$ —	$ 601,405
Liabilities:				
CVR liability	$ —	$ —	$ 61,700	$ 61,700
Total liabilities	$ —	$ —	$ 61,700	$ 61,700

The Company measures the fair value of money market funds and U.S. government treasury securities on quoted prices in active markets for identical asset or liabilities. The Level 2 assets include U.S. government agency securities, commercial paper and corporate bonds, and are valued based on quoted prices for similar assets in active markets and inputs other than quoted prices that are derived from observable market data.

The Company evaluates transfers in and out of Level 3 at the end of each reporting period. There were no transfers in or out of Level 3 during the periods presented.

As of December 31, 2025 and 2024, the Company had $26.7 million and $61.7 million, respectively, of financial liabilities outstanding measured at fair value.

Forward Contract Liability

In connection with the Asset Acquisition, the Company entered into a contract for the issuance of 364,887 shares of Series A Preferred Stock as part of the consideration transferred. This forward contract was classified as a liability because the underlying preferred shares were contingently redeemable. Further, the

forward contract liability was considered a Level 2 liability based on observable market data for substantially the full term of the liability and was initially measured at its estimated fair value on the transaction date based on the underlying price per share on an as-converted basis of the June 2023 PIPE Securities issued in the June 2023 PIPE. Subsequent remeasurement of the fair value of the forward contract liability through its settlement date was based on the market price of the Company's common stock, which represents the redemption value of the Series A Preferred Stock.

The fair value of the forward contract at the transaction date, June 22, 2023, was $106.2 million. The liability was settled with the issuance of the Series A Preferred Stock on July 7, 2023 for $189.7 million. For the year ended December 31, 2023, $83.5 million was recorded as Other income (expense) in the consolidated statements of operations in connection with the change in fair value of the forward contract liability. There was no similar expense for the year ended December 31, 2025 and 2024.

The following table presents changes in the forward contract liability for the periods presented (in millions):

	Forward Contract Liability
Beginning balance as of June 22, 2023	$ 106.2
Change in fair value	83.5
Issuance of Series A Preferred Stock on July 7, 2023	(189.7)
Ending balance as of December 31, 2023	$ —

CVR Liability

In connection with the Asset Acquisition, a non-transferable contingent value right was distributed to the Legacy Stockholders, but was not distributed to holders of shares of the Company's common stock or Series A Preferred Stock issued to the June 2023 Investors or former stockholders of Pre-Merger Spyre in connection with the June 2023 Transactions. Holders of the CVRs will be entitled to receive certain cash payments from proceeds received by the Company prior to the third anniversary of the CVR Agreement, if any, related to the disposition or monetization of the Company’s legacy assets during the one-year period following the closing of the Asset Acquisition.

The fair value of the CVR liability was determined using the probability weighted discounted cash flow method to estimate future cash flows associated with the sale of the legacy assets. Analogous to a dividend being declared/approved in one period and paid out in another, the liability was recorded at the date of approval, June 22, 2023, as a common stock dividend, returning capital to the Legacy Stockholders. Changes in fair value of the liability will be recognized as a component of Other income (expense) in the consolidated statement of operations and comprehensive loss in each reporting period. The liability value is based on significant inputs not observable in the market such as estimated cash flows, estimated probabilities of regulatory success, and discount rates, which represent a Level 3 measurement within the fair value hierarchy. The significant inputs used to estimate the fair value of the CVR liability were as follows:

	December 31, 2025
Estimated cash flow dates	05/15/26 - 08/15/29
Estimated probability of success	0% - 72%
Estimated reimbursement rate compared to reimbursement target	45% - 55%
Risk-adjusted discount rates	9.85% - 9.97%

The change in fair value between December 31, 2024 and December 31, 2025 was a $29.8 million decrease, primarily driven by changes in the likelihood of achievement of certain milestones and receipt of certain cash consideration within the CVR term, changes in estimated reimbursement rates compared to reimbursement target rates, changes in estimated cash flow dates, and an increase in risk-adjusted discount rates, partially offset by time value of money adjustments.

The following table presents changes in the CVR liability for the periods presented (in thousands):

	CVR Liability
Beginning balance as of December 31, 2024	$ 61,700
Changes in the fair value of the CVR liability	(29,769)
Payments	(5,251)
Ending Balance as of December 31, 2025	$ 26,680

4. Cash Equivalents and Marketable Securities

The following tables summarize the estimated fair value of the Company's cash equivalents and marketable securities and the gross unrealized gains and losses (in thousands):

	December 31, 2025			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Cash equivalents:				
Money market funds	$ 74,004	$ —	$ —	$ 74,004
Commercial paper	9,987	—	—	9,987
Total cash equivalents	$ 83,991	$ —	$ —	$ 83,991
Marketable securities:				
Commercial paper	$ 184,423	$ 25	$ (80)	$ 184,368
Corporate bonds	100,753	60	(23)	100,790
U.S. government treasury securities	265,316	748	—	266,064
U.S. government agency securities	119,450	153	(13)	119,590
Total marketable securities	$ 669,942	$ 986	$ (116)	$ 670,812

	December 31, 2024			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Cash equivalents:				
Money market funds	$ 65,902	$ —	$ —	$ 65,902
Commercial paper	21,832	6	—	21,838
U.S. government treasury securities	—	—	—	—
Total cash equivalents	$ 87,734	$ 6	$ —	$ 87,740
Marketable securities:				
Commercial paper	$ 143,265	$ 104	$ (77)	$ 143,292
Corporate bonds	56,471	25	(48)	56,448
U.S. government treasury securities	227,155	385	(296)	227,244
U.S. government agency securities	86,616	137	(72)	86,681
Total marketable securities	$ 513,507	$ 651	$ (493)	$ 513,665

The following table summarizes the available-for-sale securities in an unrealized loss position for which an allowance for credit losses has not been recorded as of December 31, 2025 and 2024, aggregated by major security type and length of time in a continuous unrealized loss position:

	December 31, 2025					
	Less Than 12 Months		12 Months or Longer		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
Commercial paper	$ 99,837	$ (80)	$ —	$ —	$ 99,837	$ (80)
Corporate bonds	58,296	(23)	—	—	58,296	(23)
U.S. government agency securities	22,828	(13)	—	—	22,828	(13)
Total marketable securities	$ 180,961	$ (116)	$ —	$ —	$ 180,961	$ (116)

	December 31, 2024					
	Less Than 12 Months		12 Months or Longer		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
Commercial paper	$ 67,200	$ (77)	$ —	$ —	$ 67,200	$ (77)
Corporate bonds	42,916	(48)	—	—	42,916	(48)
U.S. government treasury securities	126,588	(296)	—	—	126,588	(296)
U.S. government agency securities	12,560	(72)	—	—	12,560	(72)
Total marketable securities	$ 249,264	$ (493)	$ —	$ —	$ 249,264	$ (493)

The Company evaluated its securities for credit losses and considered the decline in market value to be primarily attributable to current economic and market conditions and not to a credit loss or other factors. Additionally, the Company does not intend to sell the securities in an unrealized loss position and does not expect they will be required to sell the securities before recovery of the unamortized cost basis. As of December 31, 2025 and 2024, an allowance for credit losses had not been recognized. Given the Company's intent and ability to hold such securities until recovery, and the lack of significant change in credit risk of these investments, the Company does not consider these marketable securities to be impaired as of December 31, 2025 and 2024.

There were $0.7 million and $0.3 million net unrealized gains on marketable securities for the years ended December 31, 2025 and 2023, respectively, and $0.1 million net unrealized losses for the year ended December 31, 2024. There were no realized gains on marketable securities for the years ended December 31, 2025, 2024 and 2023.

Interest on marketable securities is included in interest income. Accrued interest receivable on available-for-sale debt securities totaled $4.5 million and $3.4 million as of December 31, 2025 and 2024, respectively, and is excluded from the estimate of credit losses.

The following table summarizes the contractual maturities of the Company's marketable securities at estimated fair value (in thousands):

	December 31,	
	2025	2024
Due in one year or less	$ 440,895	$ 338,442
Due in 1 - 2 years	229,917	175,223
Total marketable securities	$ 670,812	$ 513,665

The Company may sell investments at any time for use in current operations even if they have not yet reached maturity. As a result, the Company classifies marketable securities, including securities with maturities beyond twelve months, as current assets.

5. Property and Equipment, Net

The Company did not have any property, plant, and equipment assets as of December 31, 2025 and 2024.

Depreciation and amortization expense for the years ended December 31, 2023 was $0.7 million. There was no depreciation and amortization expense for the year ended December 31, 2025 and 2024. All of the Company's long-lived assets were located in the United States.

Sale of Assets

On April 12, 2023, based on the review of the inconclusive interim results from the Company's Phase 1/2 clinical trial of pegtarviliase for the treatment of classical homocystinuria and other business considerations, the Company announced that it had initiated a process to explore strategic alternatives to maximize stockholder value and engaged an independent exclusive financial advisor to support this process. As a result, the Company implemented a restructuring plan resulting in an approximate 83% reduction of the Company's existing headcount by June 30, 2023.

During the second quarter of 2023, the Company sold various lab equipment, consumables, and furniture and fixtures for total consideration of $0.5 million. After recording the disposal of all the Company's property and equipment net of proceeds, the Company recorded a $0.7 million and $0.2 million loss on disposal of long-lived assets which is included in Research and development and General and administrative expenses, respectively.

6. Accrued and Other Current Liabilities

Accrued and other current liabilities consist of the following (in thousands):

	December 31,	
	2025	2024
Accrued compensation	$ 7,940	$ 5,688
Accrued contracted research and development costs	17,424	20,861
Accrued professional and consulting fees	1,404	661
Other	179	501
Total accrued and other current liabilities	$ 26,947	$ 27,711

7. Asset Acquisition

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

With respect to the Asset Acquisition, the Company determined that Aeglea was the acquirer for accounting purposes under ASC 805. The primary factors considered were a) the relative voting rights in the combined entity not resulting in a change of control, b) legacy members of the Company's Board of Directors maintained control of the Board of Directors, and c) the only change in the composition of senior management

was the appointment of a new Chief Operating Officer. Next, the Company considered whether the Asset Acquisition should be defined as a business under ASC 805. ASC 805-10-55-5A through 55-5C describe a screen test to determine whether an acquired set of assets and activities is not a business. We determined that substantially all (greater than 90%) of the fair value of the assets acquired were concentrated in a single asset, Spyre's Option to license intellectual property rights related to SPY001, SPY002, SPY003 and an additional research program pursuant to the Paragon Agreement. Accordingly, the Company treated the Asset Acquisition as an asset acquisition for accounting purposes. Even if the transaction would have failed the screen test, Pre-Merger Spyre lacked the financial resources to have inputs, processes, and outputs to constitute a business under ASC 805.

The Company completed the Asset Acquisition of Pre-Merger Spyre, in accordance with the terms of the Acquisition Agreement. Under the terms of the Acquisition Agreement, the Company issued 517,809 shares of common stock and 364,887 shares of Series A Preferred Stock to former Pre-Merger Spyre security holders. In addition, outstanding and unexercised stock options to purchase 2,734 shares of common stock were assumed from the Amended and Restated Spyre 2023 Equity Incentive Plan.

At the acquisition date, the Company recorded forward contracts to represent the obligation to issue shares of the Company's common stock and shares of Series A Preferred Stock. The forward contract related to the common stock was recorded as Additional paid-in capital as the instrument is indexed to the Company's common stock. The forward contract related to the Series A Preferred Stock was recorded as a liability, as the underlying stock has a cash redemption feature. On July 7, 2023, both the shares of common stock and Series A Preferred Stock were issued and the forward contract liability associated with the Series A Preferred Stock was settled accordingly.

The Company concluded that the arrangement meets the definition of an asset acquisition rather than a business combination, as substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset, the Option to exclusively license IPR&D. The Company determined that the Option to license IPR&D was a single asset as the Company's strategy relies on developing the entire portfolio of individual treatments to create combination treatments that simultaneously address different mechanisms of irritable bowel disease with a single treatment. The Company also determined that the pipeline candidates within the portfolio are similar in nature and risk profile. In addition, the Company did not obtain any substantive processes, assembled workforce, or employees capable of producing outputs in connection with the Asset Acquisition.

The Company determined that the cost to acquire the asset was $113.2 million which was recorded as acquired IPR&D. The fair value of the consideration issued consisted of the 364,887 shares of Series A Preferred Stock (14,595,480 shares of common stock on an as-converted basis) and 517,809 shares of common stock, valued at $291.08 per share and $7.277 per share, respectively.

The Asset Acquisition costs are shown on the following table (in millions):

	June 22, 2023
Consideration transferred in Series A Preferred Stock and common stock	$ 110.0
Transaction costs incurred by the Company	3.2
Total cost to acquire asset	$ 113.2

The allocation of the purchase price to net assets acquired is as a follows:

	June 22, 2023
Acquired in-process research and development	$ 130.2
Cash acquired	3.0
Assumed liabilities	(20.0)
Total cost to acquire asset	$ 113.2

8. Paragon Agreement

In May 2023, Pre-Merger Spyre entered into the original Paragon Agreement with Paragon and Parapyre Holding LLC ("Parapyre"), which was subsequently amended and restated on September 29, 2023 and May 14, 2024. Pursuant to the Paragon Agreement, the Option provided for the right to acquire the intellectual property rights related to four research programs from Paragon in accordance with a license agreement to be entered into following each exercise of the Option. Under the Paragon Agreement, the terms of such license agreement would be consistent with the economics and other terms set out in the Paragon Agreement and, in the event of failure to reach an agreement on the definitive terms, the matter would be resolved via arbitration. In consideration for the Option granted under the Paragon Agreement, Pre-Merger Spyre was obligated to pay Paragon an upfront cash amount of $3.0 million in research initiation fees. In addition, Pre-Merger Spyre was obligated to compensate Paragon on a quarterly basis for its services performed under each research program based on the actual costs incurred with mark-up costs pursuant to the terms of the Paragon Agreement. As of the date of the Asset Acquisition, Pre-Merger Spyre had incurred total expenses of $19.0 million under the Paragon Agreement since inception, which included the $3.0 million research initiation fee and $16.0 million of historical reimbursable expenses owed to Paragon. As of June 22, 2023, $19.0 million was unpaid and was assumed by the Company through the Asset Acquisition. Furthermore, the Paragon Agreement provided for an annual equity grant of options to purchase 1% of the then outstanding shares of Spyre's common stock, on a fully diluted basis, on the last business day of each calendar year, during the term of the Paragon Agreement, at the fair market value determined by the board of directors of Spyre (the "Parapyre Option Obligation").

As a result of the Asset Acquisition, the Company assumed the rights and obligations of Pre-Merger Spyre under the Paragon Agreement, including the Parapyre Option Obligation. Pursuant to the Paragon Agreement, on a research program-by-research program basis following the finalization of the research plan for each respective research program, the Company is required to pay Paragon a nonrefundable fee in cash of $0.8 million.

In September 2023, the Company amended the Paragon Agreement to amend and restate certain terms of the option grant pertaining to the Parapyre Option Obligation, including but not limited to (i) defining that the annual equity grant of warrants is based on the outstanding shares of the Company's common stock on a fully-diluted basis, (ii) establishing the grant date as the last business day of 2023 and 2024, and (iii) defining the term of the warrants granted as ten years.

In May 2024, the Company, Paragon and Parapyre entered into a second amended and restated antibody discovery and option agreement that amends and restates that certain amended and restated antibody discovery and option agreement, dated September 29, 2023, by and between Paragon, Parapyre and Spyre Therapeutics, LLC, in order to, among other things, (i) replace the Company's subsidiary with the Company as a party to the agreement and (ii) amend certain terms related to the SPY003 research program, including without limitation, (a) establishing an SPY003 antibody selection process pursuant to which the Company and Paragon shall alternate in turn to select a project antibody to be included and excluded, respectively, from the Company's rights under its option to license certain intellectual property rights related to SPY003 from Paragon until all project antibodies under the SPY003 research program have been selected; (b) reducing the development costs invoiced to the Company for the SPY003 research program incurred from and after April 1, 2024 through completion of the SPY003 antibody selection process by 50%; (c) requiring Paragon to reimburse the Company for 50% of the development costs for the SPY003 research program incurred prior to April 1, 2024; provided, that Paragon receives rights to at least one SPY003 project antibody following completion of the SPY003 antibody selection process; (d) obligating the Company to exercise its option to license the intellectual property rights to SPY003 project antibodies and technology following the completion of the SPY003 antibody selection process; and (e) establishing a license agreement term sheet for the SPY003 research program with substantially similar milestone payment terms and royalty payment terms as the SPY001 License Agreement. See Note 9 for disclosures related to the License Agreements entered into with Paragon.

9. Licensing Agreements

On July 12, 2023, December 14, 2023, and June 5, 2024, the Company exercised the Option available under the Paragon Agreement with respect to the SPY001, SPY002, and SPY003 research programs, respectively.

On May 14, 2024, the Company and Paragon entered into (i) a license agreement (the “SPY001 License Agreement”), pursuant to which Paragon granted the Company a royalty-bearing, world-wide, exclusive license to develop, manufacture, commercialize or otherwise exploit certain antibodies and products targeting α4ß7 integrin and (ii) a license agreement (the “SPY002 License Agreement”), pursuant to which Paragon granted the Company a royalty-bearing, world-wide, exclusive license to develop, manufacture, commercialize or otherwise exploit certain antibodies and products targeting TL1A, respectively.

On October 11, 2024, the Company and Paragon entered into a license agreement (the "SPY003 License Agreement" and, together with the SPY001 License Agreement and the SPY002 License Agreement, the "License Agreements"), pursuant to which Paragon granted the Company a royalty-bearing, world-wide, exclusive license to develop, manufacture, commercialize or otherwise exploit certain antibodies and products targeting IL-23 in the field of IBD.

On February 24, 2025, the SPY003 License Agreement was amended and restated to, among other things, clarify each party's rights and obligations with respect to license exclusivity and patent prosecution and correct certain clerical errors.

Under the terms of each License Agreement, the Company is obligated to pay Paragon up to $22.0 million based on specific development, regulatory and clinical milestones for the first product under each agreement, respectively, that achieves such specified milestones, including a milestone payment of $3.0 million upon the first dosing of a human patient in a Phase 2 trial. In addition, the following summarizes other key terms of each License Agreement:

- Paragon will provide the Company with an exclusive license (such license, with respect to the SPY003 License Agreement only, being limited to the field of IBD) to its patents covering the related antibody, the method of use and its method of manufacture.
- Paragon will not conduct any new campaigns that generate anti-α4ß7 or anti-TL1A monospecific antibodies in any field or anti-IL-23 monospecific antibodies in the field of IBD, in each case for at least 5 years.
- The Company will pay Paragon a low single-digit percentage royalty for single antibody products and a mid single-digit percentage royalty for products containing more than one antibody from Paragon.
- There is a royalty step-down of 1/3rd if there is no Paragon patent in effect during the royalty term.
- The royalty term ends on the later of (i) the last-to-expire licensed patent or Company patent directed to the manufacture, use or sale of a licensed antibody in the country at issue or (ii) 12 years from the date of first sale of a Company product.
- Agreement may be terminated on 60 days’ notice by the Company; on material breach without cure; and to the extent permitted by law, on a party’s insolvency or bankruptcy.
- With respect to the SPY002 License Agreement only, on a product by product basis, the Company will pay sublicensing fees of up to approximately $20.0 million upon the achievement of mostly commercial milestones.

The Company recognizes the expense associated with each milestone when the achievement of the milestone is deemed probable. During the years ended December 31, 2025 and 2024, the Company recognized expense of $8.5 million and $9.5 million, respectively, related to Paragon license milestone payments recorded within Research and development expenses in the accompanying condensed statement of operations. There was no such expense for the year ended December 31, 2023.

For the years ended December 31, 2025 and 2024, the Company made cash milestone payments to Paragon totaling $8.5 million and $9.5 million. There were no such payments for the year ended December 31, 2023. As of December 31, 2025 and 2024, there were no Paragon license milestone payments outstanding and payable to Paragon.

Additionally, the Company recognized $1.9 million and $0.7 million related to sublicensing fees and which was recorded as Research and development expenses in the accompanying statement of operations for the year ended December 31, 2025 and 2024, respectively. There was no such expense for the year ended December 31, 2023. For the year ended December 31, 2025 and 2024, the Company made sublicensing fees payments to Paragon totaling $2.4 million and $0.2 million. There were no such payments for the year ended December 31, 2023.

As of December 31, 2025 and 2024, nil and $0.5 million in sublicensing fees were outstanding and payable to Paragon, respectively.

10. Related Party Transactions

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

The following is the summary of expenses related to the Paragon Agreement and License Agreements, which are ultimately settled in cash (in millions) and recorded within Research and development in the consolidated statement of operations for the periods presented:

	Year Ended December 31,		
	2025	2024	2023
Reimbursable costs under the Paragon Agreement	$ 0.1	$ 15.3	$ 37.1
License Agreements milestone and sublicensing fees	10.4	10.2	—
Total related party expense (excludes stock comp)	$ 10.5	$ 25.5	$ 37.1

The following is the summary of Related party accounts payable and other current liabilities (in millions):

	December 31,	
	2025	2024
Reimbursable costs under the Paragon Agreement	$ —	$ 0.1
License Agreements development milestone liability (see Note 9)	—	0.5
Total related party accounts payable	$ —	$ 0.6

Paragon Agreement

In connection with the Asset Acquisition, the Company assumed the rights and obligations of Pre-Merger Spyre under the Paragon Agreement. Under the Paragon Agreement, Spyre is obligated to compensate Paragon for its services performed under each research program based on the actual costs incurred with mark-up costs pursuant to the terms of the Paragon Agreement. As of the date of the Asset Acquisition, Pre-Merger Spyre had incurred total expenses of $19.0 million under the Paragon Agreement since inception, which included the $3.0 million research initiation fee and $16.0 million of reimbursable expenses under the Paragon Agreement for historical costs owed to Paragon. As of the acquisition date, $19.0 million was unpaid and was

assumed by the Company through the Asset Acquisition. The Paragon Agreement was amended and restated on September 29, 2023 and May 14, 2024. Please refer to Note 8 for additional information on the Paragon Agreement.

On July 12, 2023, December 14, 2023, and June 5, 2024, the Company exercised the Option available under the Paragon Agreement with respect to the SPY001, SPY002 and SPY003 research programs, respectively. The Option with respect to one additional program remains unexercised under the Paragon Agreement. Please refer to Note 9 for additional information on the License Agreements related to the exercised options.

On May 14, 2024, the Company, Paragon and Parapyre entered into a second amended and restated antibody discovery and option agreement that amends and restates that certain amended and restated antibody discovery and option agreement, dated September 29, 2023, by and between Paragon, Parapyre and Spyre Therapeutics, LLC, in order to, among other things, (i) replace the Company's subsidiary with the Company as a party to the agreement and (ii) amend certain terms related to the SPY003 research program, including without limitation, (a) establishing an SPY003 antibody selection process pursuant to which the Company and Paragon shall alternate in turn to select a project antibody to be included and excluded, respectively, from the Company's rights under its option to license certain intellectual property rights related to SPY003 from Paragon until all project antibodies under the SPY003 research program have been selected; (b) reducing the development costs invoiced to the Company for the SPY003 research program incurred from and after April 1, 2024 through completion of the SPY003 antibody selection process by 50%; (c) requiring Paragon to reimburse the Company for 50% of the development costs for the SPY003 research program incurred prior to April 1, 2024; provided, that Paragon receives rights to at least one SPY003 project antibody following completion of the SPY003 antibody selection process; (d) obligating the Company to exercise its option to license the intellectual property rights to SPY003 project antibodies and technology following the completion of the SPY003 antibody selection process; and (e) establishing a license agreement term sheet for the SPY003 research program with substantially similar milestone payment terms and royalty payment terms as the SPY001 License Agreement. Please refer to Note 9 for additional disclosures.

For the years ended December 31, 2025, 2024 and 2023, the Company recognized expenses related to services provided by Paragon subsequent to the Asset Acquisition totaling $0.1 million and $29.8 million and $48.5 million, which included nil, $14.5 million and $11.4 million of stock-based compensation expense, respectively, and were recorded as Research and development expenses in the consolidated statements of operations. Included within the expenses recognized for services provided by Paragon for the year ended December 31, 2024, is a $5.9 million reduction in Research and development expenses related to the reimbursement of 50% of the development costs for the SPY003 research program by Paragon.

For the years ended December 31, 2025, 2024 and 2023, the Company made payments totaling $0.2 million and $31.8 million and $39.5 million, respectively, to Paragon.

Parapyre Option Obligation

Pursuant to the Paragon Agreement, the Company issued Parapyre an annual equity grant of warrants, on the last business day of each of the years ended December 31, 2023 and December 31, 2024, to purchase 1% of the then outstanding shares of the Company's common stock, on a fully diluted basis, during the term of the Paragon Agreement. See Note 15 for disclosures related to the Parapyre Option Obligation.

Paragon License Agreements

See Note 9 for disclosures related to the License Agreements entered into with Paragon.

December 2023 PIPE

On December 11, 2023, the Company completed December 2023 PIPE. The December 2023 PIPE Investors included Fairmount, a related party. Fairmount's participation in the December 2023 PIPE was approved by the Company's board of directors. Fairmount's investment accounted for $10.0 million of the $180.0 million gross proceeds raised in the December 2023 PIPE. See Note 1 for disclosures related to the December 2023 PIPE.

Mark McKenna Option Grant

On February 1, 2024, the Board appointed Mark McKenna as a Class I director. Mr. McKenna and the Company are parties to a consulting agreement, pursuant to which Mr. McKenna agreed to continue to provide consulting services as an independent contractor to the Company, with an effective date of August 1, 2023 (the "Vesting Commencement Date"). As compensation for Mr. McKenna's consulting services, on November 22, 2023, he was granted non-qualified stock options to purchase 477,000 shares of the Company's common stock under the Company's equity incentive plan with an exercise price of $10.39 per share, which vest as to 25% on the one year anniversary of the Vesting Commencement Date and thereafter vest and become exercisable in 48th equal monthly installments, subject to Mr. McKenna's continued service to the Company through each applicable vesting date. For the years ended December 31, 2025, 2024 and 2023, the Company recognized $1.0 million, $1.1 million and $0.1 million, respectively, in stock-based compensation expense related to Mr. McKenna's consulting agreement.

11. Leases

Prior to the Company's restructuring, as described in Note 17, the Company leased certain office space, laboratory facilities, and equipment. These leases required monthly lease payments that were subject to annual increases throughout the lease term. Certain of these leases also included renewal options at the election of the Company to renew or extend the lease for an additional three to five years. These optional periods were not considered in the determination of the right-of-use assets or lease liabilities associated with these leases as the Company did not consider it reasonably certain it would exercise the options. The Company performed evaluations of its contracts and determined it has both operating and finance leases. Variable lease expense for these leases primarily consisted of common area maintenance and other operating costs.

In April 2019, the Company entered into a lease agreement (the "Las Cimas Lease") for its corporate headquarters and laboratory space located in Austin, Texas. The Las Cimas Lease included approximately 30,000 square feet and commenced on April 30, 2019, with an expiration on April 30, 2028. The Company posted a customary letter of credit in the amount of $1.5 million as security, which is subject to automatic reductions per the terms of the Las Cimas Lease. A tenant allowance of up to $1.0 million was provided by the lessor and fully reimbursed to the Company.

In August 2023, the Company terminated the Las Cimas Lease. The negotiated termination agreement obligated the Company to pay the lessor a $2.0 million termination fee in exchange for releasing the Company of all further obligations under the lease including terminating the associated letter of credit.

The following table summarizes the lease costs pertaining to the Company's operating leases (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Operating lease cost	$ —	$ —	$ 455
Variable lease cost	—	—	471
Total lease cost	$ —	$ —	$ 926

Cash paid for amounts included in the measurement of operating lease liabilities during the years ended December 31, 2023 was $0.5 million, respectively, and was included within net cash used in operating activities in the cash flows. There were no such payments for the years ended December 31, 2025 and 2024.

As of December 31, 2025 and 2024, the Company had no operating or finance lease obligations.

12. Convertible Preferred Stock and Stockholders' Equity

The Company is authorized to issue 410,000,000 shares of capital stock of which 400,000,000 shares are designated as common stock and 10,000,000 shares are designated as preferred stock, all with a par value of $0.0001 per share. Each holder of common stock is entitled to one vote for each share of common stock

held. The common stock is not entitled to preemptive rights, and is not subject to conversion, redemption or sinking fund provisions. Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of common stock are entitled to receive dividends out of funds legally available if the board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that the board of directors may determine.

As of December 31, 2025 and 2024, no common stock dividends had been declared by the board of directors.

June 2023 PIPE

In June 2023, in connection with the Asset Acquisition, the Company issued and sold 721,452 shares of Series A Preferred Stock at $291.08 per share through a private placement to a group of accredited investors. The net proceeds from this offering were approximately $197.3 million, after deducting placement agent fees and offering costs of $12.7 million.

December 2023 PIPE

In December 2023, the Company issued and sold 6,000,000 shares of common stock at an offering price of $15.00 per share and 150,000 shares of Series B Preferred Stock at $600 per share through a private placement to a group of accredited investors. The net proceeds from this offering were approximately $169.1 million, after deducting placement agent fees and offering costs of $10.9 million.

March 2024 PIPE

On March 18, 2024, in connection with the March 2024 PIPE, the Company filed a certificate of amendment to its Series B Certificate of Designation to increase the number of authorized shares of Series B Preferred Stock from 150,000 to 271,625.

On March 20, 2024, as part of the March 2024 PIPE, the Company completed a private placement of 121,625 shares of Series B Preferred Stock at an offering price of $1,480 per share. The net proceeds from this offering were approximately $168.9 million, after deducting placement agent fees and offering costs of $11.2 million.

September 2024 ATM Facility

On September 6, 2024, the Company filed a new shelf registration statement on Form S-3 that was declared effective by the SEC for the potential offering, issuance and sale by the Company of up to $500.0 million of the Company's common stock, preferred stock, debt securities, warrants and/or units consisting of all or some of these securities. Concurrent with the filing of the shelf-registration statement, the Company entered into the Sales Agreement, pursuant to which the Company may issue and sell shares of its common stock for an aggregate offering price of up to $200.0 million under an ATM offering program included in the shelf registration.

During the twelve months ended December 31, 2024, the Company sold an aggregate of 777,432 shares of common stock under the ATM offering program at an average price per share of $26.935 resulting in net proceeds of $20.5 million, after deducting sales agent commissions and other offering costs of $0.4 million.

During the three and twelve months ended December 31, 2025, the Company sold an aggregate of 445,668 shares of common stock under the ATM offering program at an average price per share of $33.772 resulting in net proceeds of $14.8 million, after deducting sales agent commissions and other offering costs of $0.3 million.

As of February 12, 2026, $154.1 million remained available for sale under the Sales Agreement.

November 2024 Underwritten Offering

On November 18, 2024, the Company entered into the November 2024 Underwriting Agreement with the November 2024 Underwriters, pursuant to which the Company sold an aggregate of 8,366,250 shares of common stock, inclusive of 1,091,250 shares pursuant to the full exercise of the underwriters' over-allotment option, at a public offering price per share of $27.50, resulting in net proceeds of approximately $215.9 million after deducting approximately $14.2 million of underwriting discounts and other offering costs. The November 2024 Offering closed on November 20, 2024 and the over-allotment option was exercised in full on November 26, 2024 and closed on November 29, 2024.

October 2025 Underwritten Offering

On October 13, 2025, the Company entered into the October 2025 Underwriting Agreement with the October 2025 Underwriters, pursuant to which the Company sold an aggregate of 17,094,594 shares of common stock, inclusive of 2,229,729 shares pursuant to the full exercise of the underwriters' over-allotment option, at a public offering price per share of $18.50, resulting in net proceeds of approximately $296.4 million after deducting approximately $19.9 million of underwriting discounts and other offering costs. The over-allotment option was exercised in full on October 14, 2025 and the transaction closed on October 15, 2025.

Parapyre Warrants

The Company settled its 2024 and 2023 obligations under the Parapyre Option Obligation by issuing Parapyre 848,184 and 684,407 warrants, respectively, to purchase the Company's common stock, at an exercise price per share per warrant of $23.28 and $21.52, respectively. As of December 31, 2025, none of the warrants issued under the Parapyre Option Obligation have been exercised. See Note 15 for additional information on the Parapyre Option Obligation.

Pre-Funded Warrants

In May 2022, the Company issued pre-funded warrants to purchase shares of its common stock in underwritten public offerings at the offering price of the common stock, less the $0.0025 per share exercise price of each warrant. The warrants were recorded as a component of stockholders’ equity within additional paid-in capital and have no expiration date. Per the terms of the warrant agreements, the outstanding warrants to purchase shares of the Company's common stock may not be exercised if the holder’s ownership of the Company's common stock would exceed 4.99% (“Maximum Ownership Percentage”) or 9.99% for certain holders. By written notice to the Company, each holder may increase or decrease the Maximum Ownership Percentage to any other percentage (not in excess of 19.90% for the majority of such warrants). The revised Maximum Ownership Percentage would be effective 61 days after the notice is received by the Company. As of December 31, 2025, all pre-funded warrants have been exercised and none remain outstanding.

Series A Non-Voting Convertible Preferred Stock

On June 22, 2023, the Company filed a Certificate of Designation of Preferences, Rights and Limitations of the Series A Preferred Stock with the Secretary of State of the State of Delaware (the “Series A Certificate of Designation”) in connection with the Asset Acquisition and the June 2023 PIPE.

Pursuant to the Series A Certificate of Designation, holders of Series A Preferred Stock are entitled to receive dividends on shares of Series A Preferred Stock equal to, on an as-if-converted-to-common stock basis, and in the same form as, dividends actually paid on shares of the Company's common stock. Except as provided in the Series A Certificate of Designation or as otherwise required by law, the Series A Preferred Stock does not have voting rights. However, as long as any shares of Series A Preferred Stock are outstanding, the Company will not, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series A Preferred Stock: (a) alter or change adversely the powers, preferences or rights given to the Series A Preferred Stock, or alter or amend the Series A Certificate of Designation, amend or repeal any provision of, or add any provision to, the Company’s Certificate of Incorporation or its Bylaws, or file any articles of amendment, certificate of designations, preferences, limitations and relative rights of any series of preferred stock, if such action would adversely alter or change the preferences, rights, privileges or powers of, or restrictions provided for the benefit of the Series A Preferred Stock, regardless of whether any of the foregoing actions will be by means of amendment to the Certificate of Incorporation or by merger, consolidation, recapitalization, reclassification, conversion or otherwise, (b) issue further shares of Series A Preferred Stock or increase or

decrease (other than by conversion) the number of authorized shares of Series A Preferred Stock, (c) prior to the stockholder approval of the conversion of the Series A Preferred Stock into shares of common stock in accordance with Nasdaq Stock Market Rules (the “Series A Conversion Proposal”) or at any time while at least 30% of the originally issued Series A Preferred Stock remains issued and outstanding, consummate (x) any Fundamental Transaction (as defined in the Series A Certificate of Designation) or (y) any merger or consolidation of the Company with or into another entity or any stock sale to, or other business combination in which our stockholders immediately before such transaction do not hold at least a majority of our capital stock immediately after such transaction or (d) enter into any agreement with respect to any of the foregoing. The Series A Preferred Stock does not have a preference upon any liquidation, dissolution or winding-up of the Company.

The Company held a stockholders’ meeting to submit the following matters to its stockholders for their consideration: (i) the approval of the Series A Conversion Proposal, and (ii) if deemed necessary or appropriate by the Company or as otherwise required by law or contract, the approval of an amendment to the Certificate of Incorporation to authorize sufficient shares of common stock for the conversion of the Series A Preferred Stock issued pursuant to the Acquisition Agreement. In connection with these matters, the Company filed with the SEC a definitive proxy statement and other relevant materials.

On June 26, 2023, the Company completed a private placement of 721,452 shares of June 2023 PIPE Securities at $291.08 per share in exchange for net proceeds of $197.3 million after deducting placement agent fees and offering costs of $12.7 million.

On July 7, 2023, the Company issued 364,887 shares of Series A Preferred Stock as part of its consideration transferred in connection with the Asset Acquisition that closed on June 22, 2023 which settled the related forward contract liability. For additional information, see Note 3.

On November 21, 2023, the Company's stockholders approved the Series A Conversion Proposal, among other matters, at a special meeting of stockholders. As a result of the approval of the Series A Conversion Proposal, all conditions that could have required cash redemption of the Series A Preferred Stock were satisfied. Since the Series A Preferred Stock is no longer redeemable, the associated balances of the Series A Preferred Stock were reclassified from mezzanine equity to permanent equity during the fourth quarter of 2023.

Following stockholder approval of the Series A Conversion Proposal, each share of Series A Preferred Stock automatically converted into 40 shares of the Company's common stock, subject to certain limitations, including that a holder of Series A Preferred Stock is prohibited from converting shares of Series A Preferred Stock into shares of common stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (established by the holder between 0.0% and 19.9%) of the total number of shares of common stock issued and outstanding immediately after giving effect to such conversion. 649,302 shares of Series A Preferred Stock automatically converted to 25,972,080 shares of common stock; 437,037 shares of Series A Preferred Stock did not automatically convert and remained outstanding following the conversion. This conversion was recorded as a reclassification between Series A Preferred Stock and common stock based on the historical per-share contributed capital amount of the Series A Preferred Stock.

On April 23, 2024, in connection with the April 2024 Exchange, the Stockholder agreed to exchange an aggregate of 90,992 shares of Series A Preferred Stock for an aggregate of 3,639,680 shares of the Company's common stock. This exchange was recorded as a reclassification between Series A Preferred Stock and common stock based on the historical per-share contributed capital amount, inclusive of any forward-contract valuation adjustments, of the Series A Preferred Stock. The April 2024 Exchange closed on April 25, 2024, with 346,045 shares of Series A Preferred Stock remaining outstanding following closing.

Series B Non-Voting Convertible Preferred Stock

On December 8, 2023, the Company filed a Certificate of Designation of Preferences, Rights and Limitations of Series B Non-Voting Convertible Preferred Stock with the Secretary of State of the State of Delaware (the “Series B Certificate of Designation”) in connection with the December 2023 PIPE.

Pursuant to the Series B Certificate of Designation, holders of Series B Preferred Stock are entitled to receive dividends on shares of Series B Preferred Stock equal to, on an as-if-converted-to-common stock basis, and in the same form as, dividends actually paid on shares of Company common stock. Except as provided in the Series B Certificate of Designation or as otherwise required by law, the Series B Preferred Stock does not have voting rights. However, as long as any shares of Series B Preferred Stock are outstanding, the Company will not, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series B Preferred Stock, alter or change adversely the powers, preferences or rights given to the Series B Preferred Stock, or alter or amend the Series B Certificate of Designation, amend or repeal any provision of, or add any provision to, the Company's Certificate of Incorporation or its Bylaws, or file any articles of amendment, certificate of designations, preferences, limitations and relative rights of any series of preferred stock, if such action would adversely alter or change the preferences, rights, privileges or powers of, or restrictions provided for the benefit of the Series B Preferred Stock, regardless of whether any of the foregoing actions will be by means of amendment to the Certificate of Incorporation or by merger, consolidation, recapitalization, reclassification, conversion or otherwise. The Series B Preferred Stock does not have a preference upon any liquidation, dissolution or winding-up of the Company.

On December 11, 2023, as part of the December 2023 PIPE, the Company completed a private placement of 150,000 shares of Series B Preferred Stock at $600 per share in exchange for net proceeds of $84.6 million after deducting placement and offering costs of $5.4 million.

On March 18, 2024, in connection with the March 2024 PIPE, the Company filed a certificate of amendment to its Series B Certificate of Designation to increase the number of authorized shares of Series B Preferred Stock from 150,000 to 271,625.

On March 20, 2024, as part of the March 2024 PIPE, the Company completed a private placement of 121,625 shares of Series B Preferred Stock at $1,480 per share in exchange for net proceeds of approximately $168.9 million, after deducting placement agent fees and offering costs of $11.2 million.

On May 14, 2024, the Company's stockholders approved the issuance of Company common stock upon the conversion of all issued and outstanding Series B Preferred Stock into shares of common stock in accordance with the Nasdaq Stock Market Rules (the "Series B Conversion Proposal"), among other matters, at its 2024 annual meeting of stockholders. As a result of the approval of the Series B Conversion Proposal, all conditions that could have required cash redemption of the Series B Preferred Stock were satisfied. Since the Series B Preferred Stock were no longer redeemable, the associated balances of the Series B Preferred Stock were reclassified from mezzanine equity to permanent equity during the second quarter of 2024. A total of 254,958 shares of Series B Preferred Stock automatically converted to 10,198,320 shares of common stock; 16,667 shares of Series B Preferred Stock did not automatically convert and remained outstanding as of December 31, 2025.

Following stockholder approval of the Series B Conversion Proposal, each share of Series B Preferred Stock will automatically convert into 40 shares of the Company's common stock, subject to certain limitations, including that a holder of Series B Preferred Stock is prohibited from converting shares of Series B Preferred Stock into shares of common stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (established by the holder between 0% and 19.9%) of the total number of shares of common stock issued and outstanding immediately after giving effect to such conversion. 254,958 shares of Series B Preferred Stock automatically converted to 10,198,320 shares of common stock; 16,667 shares of Series B Preferred Stock did not automatically convert and remain outstanding as of December 31, 2025 due to beneficial ownership limitations. This conversion was recorded as a reclassification between Series B Preferred Stock and common stock based on the historical per-share contributed capital amount of the Series B Preferred Stock.

13. Strategic License Agreements

Immedica Pharma AB License and Development Agreement

On March 21, 2021, the Company entered into an exclusive license and supply agreement with Immedica Pharma AB ("Immedica"). By entering into this agreement, the Company agreed to provide Immedica the following goods and services:

i. Deliver an exclusive, sublicensable, license and know-how (the "License") to develop and commercialize pegzilarginase (the "Product") in the territory comprising the member states of the European Economic Area, United Kingdom, Switzerland, Andorra, Monaco, San Marino, Vatican City, Turkey, Saudi Arabia, United Arab Emirates, Qatar, Kuwait, Bahrain, and Oman (the "Territory");

ii. Complete the global pivotal PEACE (Pegzilarginase Effect on Arginase 1 Deficiency Clinical Endpoints) Phase 3 trial ("PEACE Trial") and related Biologics License Application ("BLA") package to file with the United States Food and Drug Administration ("FDA"), which will be leveraged by Immedica in obtaining the necessary regulatory approvals in the Territory; and

iii. Perform a Pediatric Investigation Plan trial ("PIP Trial") in order for Immedica to be able to receive certain regulatory approvals within the Territory.

In addition, the Company and Immedica formed a Joint Steering Committee ("JSC") to provide oversight to the activities performed under the agreement; however, the substance of the Company's participation in the JSC does not represent an additional promised service, but rather, a right of the Company to protect its own interests in the arrangement.

Further, the Company agreed to supply to Immedica, and Immedica agreed to purchase from the Company, substantially all commercial requirements of the Product. The terms of the agreement do not provide for either (i) an option to Immedica to purchase the Product from the Company at a discount from the standalone selling price or (ii) minimum purchase quantities. Finally, Immedica will bear (i) all costs and expenses for any development or commercialization of the Product in the Territory subject to the License exclusive of the Company's promised goods and services summarized above and (ii) all costs and fees associated with applying for regulatory approval of the Product in the Territory. In July 2021, the Company modified the agreement with Immedica to provide certain additional services in relation to the PEACE Phase 3 Trial and BLA package performance obligation in exchange for the reimbursement of up to $3.0 million of the actual costs incurred in relation to such incremental services.

For the year ended December 31, 2023, the Company recognized revenue of $0.9 million related to the PEACE Trial and BLA package performance obligation using a cost to cost model.

On July 27, 2023, the Company announced that it had entered into an agreement to sell the global rights to pegzilarginase to Immedica for $15.0 million in upfront cash proceeds and up to $100.0 million in contingent milestone payments. The sale of pegzilarginase to Immedica superseded and terminated the previous license agreement between the Company and Immedica. On July 27, 2023, the carrying value of the asset was zero as it was internally developed. Accordingly, the Company recognized a $16.4 million gain within Gain on Sale of in-process research and development, which is comprised of $15.0 million in upfront cash proceeds and the reimbursement of $1.8 million in pre-paid manufacturing costs that was contingent upon a favorable opinion being received by the CHMP, net of transaction costs and the derecognition of pegzilarginase related nonfinancial assets and liabilities totaling $0.4 million.

The milestone payments are contingent on formal reimbursement decisions by national authorities in key European markets and pegzilarginase approval by the FDA, among other events. The upfront payment and contingent milestone payments if paid, net of expenses and adjustments, will reduce the CVR liability and will be distributed to CVR holders pursuant to the CVR Agreement resulting from the Asset Acquisition.

During the twelve months ended December 31, 2025, the Company recognized a gain of $10.0 million within Gain on Sale of in-process research and development, for achieving certain reimbursement decision

milestones during the period. As of December 31, 2025, $3.0 million remains outstanding and reflected in Prepaid expenses and other current assets. There was no similar gain during the twelve months ended or similar receivable as of December 31, 2024.

Contract Balances from Customer Contract

The timing of revenue recognition, billings and cash collections results in contract assets and contract liabilities on the balance sheets. The Company recognizes license and development receivables based on billed services, which are derecognized upon reimbursement. When consideration is received, or such consideration is unconditionally due, from a customer prior to transferring goods or services to the customer under the terms of a contract, a contract liability is recorded. Contract liabilities are recognized as revenue after control of the goods or services is transferred to the customer and all revenue recognition criteria have been met.

The Company had no contract assets or liabilities during the years ended December 31, 2025 and 2024.

14. Novation of Manufacturing Agreements

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

Biologics Master Services Agreement

In April 2023, Paragon and WuXi Biologics entered into the WuXi Biologics MSA, which was subsequently novated to the Company by Paragon on September 19, 2023 pursuant to the Novation Agreement. The WuXi Biologics MSA was subsequently amended and restated in October 2024. The WuXi Biologics MSA governs certain development activities and GMP manufacturing and testing for the SPY001, SPY002, and SPY003 programs, as well as potential future programs, on a work order basis. Under the WuXi Biologics MSA, the Company is obligated to pay WuXi Biologics a service fee and all non-cancellable obligations in the amount specified in each work order associated with the agreement for the provision of services.

The WuXi Biologics MSA terminates on the later of (i) October 14, 2029 or (ii) the completion of services under all work orders executed by the parties prior to October 14, 2029, unless terminated earlier. The term of each work order terminates upon completion of the services under such work order, unless terminated earlier. The Company can terminate the WuXi Biologics MSA or any work order at any time upon 30 days' prior written notice and immediately upon written notice if WuXi Biologics fails to obtain or maintain required material governmental licenses or approvals. The Company can also terminate the WuXi Biologics MSA, or any work order, in the event that any law is enacted that has, or could be reasonably expected to have, a material adverse effect on the Company or any of its products that is the subject of the WuXi Biologics MSA, in each case, as a result of WuXi Biologics providing services under the WuXi Biologics MSA or the Company being a party to the WuXi Biologics MSA. Either party may terminate a work order (i) at any time upon six months prior notice with reasonable cause, provided however that if WuXi Biologics terminates a work order in such manner, no termination or cancellation fees shall be paid by the Company and (ii) immediately for cause upon (a) the other party’s material breach that remains uncured for 30 days after notice of such breach, (b) the other party’s bankruptcy or (c) a force majeure event that prevents performance for a period of at least 90 days.

Cell Line License Agreement

In April 2023, Paragon and WuXi Biologics entered into the Cell Line License Agreement, which was subsequently novated to the Company by Paragon pursuant to the Novation Agreement. The Cell Line License Agreement was subsequently amended and restated in October 2024. Under the Cell Line License Agreement, the Company received a non-exclusive, worldwide, sublicensable license to certain of WuXi Biologics’s know-how, cell line, biological materials (the “WuXi Biologics Licensed Technology”) and media and feeds to make, have made, use, sell and import certain therapeutic products produced through the use of the cell line licensed by WuXi Biologics under the Cell Line License Agreement (the “WuXi Biologics Licensed Products”).

Specifically, the WuXi Biologics Licensed Technology is used in certain manufacturing activities in support of the SPY001, SPY002, and SPY003 programs.

In consideration for the license, the Company agreed to pay WuXi Biologics a non-refundable license fee of $0.2 million. Additionally, if the Company manufactures all of its commercial supplies of bulk drug product with a manufacturer other than WuXi Biologics or its affiliates, the Company is required to make royalty payments to WuXi Biologics of less than one percent of global net sales of WuXi Biologics Licensed Products manufactured by a third-party manufacturer (the “Royalty”). If the Company manufactures part of its commercial supplies of the WuXi Biologics Licensed Products with WuXi Biologics or its affiliates, then the Royalty will be reduced accordingly on a pro rata basis. Subject to the terms of the Cell Line License Agreement, royalties owed under the Cell Line License Agreement may be bought out on a product-by-product basis for a lump-sum payment.

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

15. Stock-Based Compensation

2016 Equity Incentive Plan

The 2016 Plan became effective in April 2016 and serves as the successor to the 2015 Equity Incentive Plan ("2015 Plan"). Under the 2016 Plan, the Company may grant stock options, stock appreciation rights, restricted stock awards, restricted stock units, performance awards, and stock bonuses. The 2016 Plan provides for an initial reserve of 44,000 shares of common stock, plus 20,395 shares of common stock remaining under the 2015 Plan, and any share awards that subsequently are forfeited or lapse unexercised under the 2015 Plan. The shares reserved exclude shares of common stock reserved for issuance under the 2015 Plan.

In October 2018, the 2016 Plan was amended to increase the number of shares of common stock reserved for issuance thereunder by 70,384 shares, extend the term of the 2016 Plan through August 7, 2028, and provide for an automatic increase in the number of shares reserved for issuance thereunder on January 1 of each year for the remaining term of the plan equal to (a) 4.0% of the number of issued and outstanding shares of common stock on December 31 of the immediately preceding year, or (b) a lesser amount as approved by the board each year (the "Evergreen Provision").

In November 2023, the 2016 Plan was amended to (i) increase the number of shares of common stock reserved for issuance thereunder by 4,481,152 shares, (ii) revise the annual limit on non-employee director compensation from 4,000 shares to (a) $750,000 in total value or (b) $1,000,000 in the year of the director’s initial service as a non-employee director or in any year a director serves as chairman of the Board of Directors, in either case, applicable to fees paid in both cash and equity, (iii) remove the fixed termination date of the 2016 Plan and, (iv) revise the Evergreen Provision from 4% to 5% of issued and outstanding shares of Company common stock on December 31 of the preceding calendar year and to include shares issuable upon the exercise of pre-funded warrants and the conversion of outstanding shares of non-voting convertible preferred stock in the calculation.

As a result of the Evergreen Provision, on January 1, 2025, 2024, and 2023, an additional 3,814,905, 3,023,650, and 104,561 shares, respectively, became available for issuance under the 2016 Plan.

As of December 31, 2025, the total number of shares reserved for issuance under the 2016 Plan was 10,810,714, of which 4,827,082 shares were subject to outstanding option awards and restricted unit awards.

2018 Equity Inducement Plan

In February 2018, the board of directors approved and adopted the 2018 Equity Inducement Plan (as amended, the “2018 Plan”), which became effective on the same date. The board of directors approved an initial reserve of 44,000 shares of common stock to be used exclusively for individuals who were not previously employees or directors, or following a bona fide period of non-employment, as an inducement material to the individual entering into employment with the Company. Nonqualified stock options or restricted stock units may be granted under the 2018 Plan at the discretion of the Compensation Committee or the board of directors. The Company did not seek stockholder approval of the 2018 Plan pursuant to Nasdaq Rule 5635(c)(4).

The 2018 Plan was amended to increase the number of shares of common stock reserved for issuance by 750,000 and 1,000,000 during the years ended December 31, 2025 and 2024, respectively.

As of December 31, 2025, the total number of shares reserved for issuance under the 2018 Plan was 7,460,440, of which 6,620,097 shares were subject to outstanding awards.

Under the 2016 Plan and 2018 Plan, the Company may grant stock-based awards with service conditions (“service-based” awards), performance conditions (“performance-based” awards), and market conditions (“market-based” awards). Service-based awards granted under the 2018 Plan, 2016 Plan, and 2015 Plan generally vest over four years and expire after ten years, although awards have been granted with vesting terms less than four years.

Spyre 2023 Equity Incentive Plan

On June 22, 2023, in connection with the Asset Acquisition, the Company assumed the Amended and Restated Spyre 2023 Equity Incentive Plan (the "Spyre Equity Plan") and its outstanding and unexercised stock options, which were converted to options to purchase 2,734 shares of the Company's common stock. The acquisition-date fair value of these grants will be recognized as an expense on a pro-rata basis over the vesting period. As of December 31, 2025, none of the stock options under the 2023 Plan remained outstanding.

Parapyre Option Obligation

On June 22, 2023, in connection with the Asset Acquisition, the Company assumed the Parapyre Option Obligation which provided for an annual equity grant of warrants for Parapyre to purchase 1% of the then outstanding shares of Pre-Merger Spyre's common stock, on a fully diluted basis, on the last business day of each calendar year during the term of the Paragon Agreement, at the fair market value determined by the board of directors of Pre-Merger Spyre.

On September 29, 2023, the Company amended the Paragon Agreement to amend and restate certain terms of the option grant pertaining to the Parapyre Option Obligation, including but not limited to (i) defining that the annual equity grant of warrants is based on the outstanding shares of the Company’s common stock, on a fully-diluted basis, (ii) establishing the grant date as the last business day of 2023 and 2024, and (iii) defining the term of the warrants granted as ten years. The Company determined that the 2023 and 2024 grants are two separate grants, as there would be no obligation for the 2024 grant had the Company exercised or terminated all of the options under the Paragon Agreement prior to December 31, 2023. The service inception period for the grant precedes the grant date, with the full award being vested as of the grant date with no post-grant date service requirement. Accordingly, a liability related to the Parapyre Option Obligation was recorded pursuant to the amended Paragon Agreement during the 2023 and 2024 interim periods. The Company settled its 2024 and 2023 obligations under the Parapyre Option Obligation by issuing Parapyre 848,184 and 684,407 warrants, respectively, to purchase the Company's common stock at an exercise price per share per warrant of $23.28 and $21.52, respectively. There was no similar expense for the year ended December 31, 2025.

The following table summarizes stock option activity for the year ended December 31, 2025:

	Shares Issuable Under Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
			(in years)	(in thousands)
Outstanding as of December 31, 2024	9,253,158	$ 15.08	8.80	$ 90,016
Granted	2,623,217	19.98		
Exercised	(307,673)	8.68		
Forfeited	(198,455)	33.38		
Outstanding as of December 31, 2025	11,370,247	$ 16.06	8.16	$ 191,198
Options vested and expected to vest as of December 31, 2025	11,370,247	$ 16.06	8.16	$ 191,198
Options exercisable as of December 31, 2025	5,164,959	$ 14.50	7.95	$ 95,153

The aggregate intrinsic value of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the fair value of the Company's common stock as of the reporting date.

For the years ended December 31, 2025, 2024, and 2023, the weighted-average grant date fair value of options granted was $19.98, $28.39, and $9.67, per share, respectively. The total intrinsic value of options exercised during the years ended December 31, 2025, 2024 and 2023 was $4.0 million, $22.7 million and $0.4 million, respectively.

There were 10,000 and 477,000 stock options issued to non-employees during the years ended December 31, 2024 and 2023, respectively. There were no stock options issued to non-employees during the year ended December 31, 2025. For the year ended December 31, 2025 and 2024, 119,250 and 139,187 non-employee stock options vested in the period, respectively. There were no non-employee stock options vested during the years ended 2023.

2016 Employee Stock Purchase Plan

The 2016 Employee Stock Purchase Plan ("2016 ESPP") became effective in April 2016. A total of 6,600 shares of common stock were reserved for issuance under the 2016 ESPP. Eligible employees may purchase shares of common stock under the 2016 ESPP at 85% of the lower of the fair market value of the common stock as of the first or the last day of each offering period. Employees are limited to contributing 15% of the employee's eligible compensation and may not purchase more than $25,000 of stock during any calendar year. The 2016 ESPP will terminate ten years from the first purchase date under the plan, unless terminated earlier by the board of directors.

In June 2018, the 2016 ESPP was amended to provide for an automatic annual increase in the number of shares reserved for issuance thereunder (the "Evergreen Provision") on January 1 of each year for the remaining term of the year equal to (a) 1.0% of the number of issued and outstanding shares of common stock on December 31 of the immediately preceding year, or (b) a lesser amount as approved by the board of directors each year. As a result of the operation of this provision, on January 1, 2025, 2024 and 2023, an additional 602,570, 360,571, and 26,140 shares, respectively, became available for issuance under the 2016 ESPP. As of December 31, 2025, the reserve remaining and available for future issuance under the 2016 ESPP was 972,775 shares.

In February 2023, the 2016 ESPP was amended to increase the maximum shares purchased during any one period (the "ESPP Limit") from 80 shares to 400 shares or a lesser amount determined by the board of directors and in January 2024, the 2016 ESPP was further amended to increase the ESPP Limit to 2,000 shares or a lesser amount determined by the Compensation Committee.

Effective January 1, 2026, the 2016 ESPP was amended and restated (as amended and restated, the "AR 2016 ESPP") to remove the Evergreen Provision, extend the term of the 2016 ESPP indefinitely and re-establish the offering periods, among other changes. The Company plans to submit the AR 2016 ESPP for stockholder approval at its 2026 Annual Meeting of Stockholders.

For the years ended December 31, 2025 and 2024, stock-based compensation expense related to the 2016 ESPP plan was $0.3 million and $0.1 million for the year ended December 31, 2023.

Restricted Stock Units

The following table summarizes employee restricted stock unit activity for the year ended December 31, 2025:

	Shares	Weighted Average Grant Date Fair Value
Unvested restricted stock units as of December 31, 2024	115,398	$ 18.17
Vested	(38,466)	18.17
Unvested restricted stock units as of December 31, 2025	76,932	$ 18.17

There were no restricted stock units granted during the year ended December 31, 2025.

Stock-Based Compensation Expense

Total stock-based compensation expense recognized from the Parapyre Option Obligation, the Company's equity incentive plans, 2018 Plan, and the 2016 ESPP for the years ended December 31, 2025, 2024, and 2023 was as follows (in thousands):

	Year Ended December 31,					
	2025		2024		2023	
	Employees	Non-Employees	Employees	Non-Employees	Employees	Non-Employees
Research and development [1]	$ 16,270	$ —	$ 9,112	$ 14,459	$ 2,910	$ 11,328
General and administrative	20,318	1,026	19,833	1,429	11,327	110
Total stock-based compensation expense [2]	$ 36,588	$ 1,026	$ 28,945	$ 15,888	$ 14,237	$ 11,438

[1] For the years ended December 31, 2024 and 2023, $14.5 million and $11.4 million, respectively, was recognized as stock compensation expense related to the Parapyre Option Obligation. There was no such expense for the year ended December 31, 2025.

[2] Of the total $36.6 million, $28.9 million and $14.2 million of employee related stock-based compensation expense for the years ended December 31, 2025, 2024 and 2023, respectively, nil, $3.6 million and $8.3 million is related to legacy Aeglea employees and directors who no longer served the Company as of the end of the respective period.

No related tax benefits were recognized for the years ended December 31, 2025, 2024, and 2023 (see Note 18).

All outstanding awards as of December 31, 2025, under the 2016 Plan and 2018 Plan, have service-based vesting conditions only.

As of December 31, 2025, the Company had an aggregate of $81.3 million of unrecognized stock-based compensation expense for options outstanding, which is expected to be recognized over a weighted average period of 2.3 years.

In determining the fair value of the stock-based awards, the Company uses the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Expected Term

The Company's expected term represents the period that the Company's stock-based awards are expected to be outstanding and is determined using the simplified method (based on the midpoint between the vesting date and the end of the contractual term). The Company utilizes this method due to lack of historical exercise data and the plain-vanilla nature of the Company's stock-based awards.

Expected Volatility

The Company has limited relevant company-specific historical data to support its expected volatility since the Company's 2023 strategy and pipeline reset . As such, the Company has used an average of expected volatilities based on the volatilities of a representative group of publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. For purposes of identifying comparable companies, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. The Company intends to consistently apply this process using the same or similar comparable entities until a sufficient amount of historical information regarding the volatility of the Company's own share price post transition becomes available.

Risk-Free Interest Rate

The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend

The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

Valuation of Stock Options and 2016 ESPP

The fair value of the stock options granted under the Company's equity incentive plans, as well as the shares available for purchase under the 2016 ESPP were determined using the Black-Scholes option-pricing model. The following table summarizes the weighted-average assumptions used in calculating the fair value of the awards:

	Year Ended December 31,		
	2025	2024	2023
Stock Options Granted			
Expected term (in years)	5.99	6.03	5.88
Expected volatility	76%	105%	107%
Risk-free interest	4.33%	4.06%	4.37%
Dividend yield	0%	0%	0%
2016 ESPP			
Expected term (in years)	0.44	0.50	0.49
Expected volatility	70%	84%	181%
Risk-free interest	4.22%	5.16%	4.99%
Dividend yield	0%	0%	0%

16. Defined Contribution Plan

The Company sponsors a 401(k) retirement plan in which substantially all of its full-time employees are eligible to participate. Participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. During the years ended December 31, 2025, 2024, 2023, the Company provided $0.8 million, $0.5 million, and $0.2 million, respectively, in contributions to the plan.

17. Restructuring Charges

Severance and Stock Compensation

On April 12, 2023, based on the review of the inconclusive interim results from the Company's Phase 1/2 clinical trial of pegtarviliase for the treatment of classical homocystinuria and other business considerations, the Company announced that it had initiated a process to explore strategic alternatives to maximize stockholder value and engaged an independent exclusive financial advisor to support this process.

As a result, the Company implemented a restructuring plan resulting in an approximate 83% reduction of the Company's existing headcount by June 30, 2023. The Company recognized restructuring expenses consisting of cash severance payments and other employee-related costs of $6.4 million during the year ended December 31, 2023. Cash payments for employee related restructuring charges of $5.3 million were paid as of December 31, 2023. In addition, the Company recognized $1.0 million in non-cash stock-based compensation expense related to the accelerated vesting of stock-based awards for certain employees. The Company recorded these restructuring charges based on each employee's role to the respective research and development and general and administrative operating expense categories on its consolidated statements of operations and comprehensive loss.

Sale of Assets

During the second quarter of 2023, the Company sold various lab equipment, consumables, and furniture and fixtures for total consideration of $0.5 million. After recording the disposal of all the Company's property and equipment net of proceeds, the Company recorded a $0.7 million and $0.2 million loss on disposal of long-lived assets which is included in Research and development and General and administrative expenses, respectively.

Lease Right-of-use Asset and Leasehold Improvement Impairment

Effective June 30, 2023, the Company abandoned its leased office space in Austin, Texas. As a result, the Company recognized an impairment loss of $0.9 million related to the operating lease right-of-use asset and $1.7 million related to leasehold improvements. On August 7, 2023, the Company terminated its building lease in Austin, Texas. The negotiated termination agreement obligated the Company to pay the lessor a $2.0 million termination fee in exchange for releasing the Company of all further obligations under the lease.

All charges related to the restructuring activities were recognized during the second quarter of 2023. No further restructuring charges will be incurred under the restructuring plan. A summary of the charges related to the restructuring activities is as follows (in thousands):

	Severance Related Expenses	Stock Compensation Expenses	Loss on Disposal of Long-Lived Assets	Lease Asset Impairment	Total Restructuring Costs
Research and development	$ 3,182	$ 123	$ 749	$ 1,405	$ 5,459
General and administrative	3,266	870	182	1,175	5,493
Total	$ 6,448	$ 993	$ 931	$ 2,580	$ 10,952

18. Income Taxes

The following table summarizes the (loss) income before income tax expense by jurisdiction for the periods indicated (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Domestic	$ (155,255)	$ (207,965)	$ (338,942)
Foreign	37	(2)	126
Loss before income tax expense	$ (155,218)	$ (207,967)	$ (338,816)

The difference between the Company's provision for income taxes and the amounts computed by applying the statutory federal income tax rate to income before income taxes for the year ended December 31, 2025 is as follows (in thousands):

	Year Ended December 31, 2025	
	Amount	%
Income taxes (benefit) at statutory federal rate	$ (32,596)	21.00 %
State and local taxes, net of federal income tax effect	—	— %
Foreign tax effects		
Other foreign	(23)	0.01 %
Changes in valuation allowance	37,622	(24.24)%
Non-taxable or nondeductible items		
Stock compensation	773	(0.50)%
Change in fair market value of contingent value right	(6,251)	4.03 %
Limitation on officers' compensation	2,860	(1.84)%
Permanent and other items	114	(0.07)%
Other		
Other	10	(0.01)%
Stock based compensation - deferred only	(2,524)	1.63 %
Provision / (benefit) for income taxes	$ (15)	0.01 %

As disclosed for the years ended December 31, 2024 and 2023, prior to the adoption of ASU 2023-09, the difference between the Company's provision for income taxes and the amounts computed by applying the statutory federal income tax rate to income before income taxes is as follows (in thousands):

	Year Ended December 31,	
	2024	2023
Tax provision derived by applying the federal statutory rate to income before income taxes	$ (43,673)	$ (71,151)
Loss on forward contract valuation	—	17,541
Acquired IPR&D	—	27,340
Loss on CVR revaluation	4,290	3,987
Other permanent differences	1,865	4,472
Federal tax credits	(91)	(1)
Effect of tax rate on foreign jurisdiction	(2)	(53)
Other, net	191	—
Change in the valuation allowance	37,471	17,839
Income tax (benefit) expense	$ 51	$ (26)

The amounts of cash income taxes paid by the company are as follows:

	Year Ended December 31, 2025
Federal	$ —
State	—
Foreign	(15)
Total	$ (15)

The components of the deferred tax assets and liabilities consist of the following (in thousands):

	December 31,		
	2025	2024	2023
Deferred tax assets			
Net operating loss carryforward	$ 118,511	$ 87,321	$ 74,454
Capitalized 174 R&D costs	44,465	45,531	22,532
Intangible assets	4,070	2,117	47
Accrued expense	1,625	1,047	579
Stock-based compensation	12,943	7,114	4,246
Federal tax credits	18,196	18,196	21,914
State tax credits	1,631	1,631	1,631
Other	87	64	88
Total deferred tax assets	201,528	163,021	125,491
Deferred tax liabilities			
Unrealized gain	(183)	(92)	—
Total deferred tax liabilities	(183)	(92)	—
Less: Valuation allowance	(201,345)	(162,929)	(125,491)
Deferred tax assets, net	$ —	$ —	$ —

The Company has established a full federal and state valuation allowance equal to the net deferred tax assets due to uncertainties regarding the realization of the deferred tax asset based on the Company's lack of earnings history. The valuation allowance increased by $38.4 million, $37.4 million, and $17.8 million during the years ended December 31, 2025, 2024, and 2023, respectively, primarily due to continuing loss from operations.

As of December 31, 2025 and 2024, the Company had U.S. net operating loss carryforwards (“NOL”) of $560.1 million and $415.8 million, respectively.

For the year ended December 31, 2025, the Company had U.S. tax credit carryforwards and state tax credit carryforwards of $18.2 million and $2.1 million, respectively. Of the net operating loss and tax credit carryforwards $58.4 million and $20.3 million will begin to expire in 2033 and 2034, respectively.

For the year ended December 31, 2024, the Company had U.S. tax credit carryforwards and state tax credit carryforwards of $18.2 million and $2.1 million, respectively. Of the net operating loss and tax credit carryforwards $58.4 million and $20.3 million will begin to expire in 2033 and 2034, respectively, if not utilized. Any remaining net operating loss will carry forward indefinitely and can be utilized to offset up to 80% of the taxable income in any tax year. The net operating loss and credit carryforwards are subject to Internal Revenue Service adjustments until the statute closes on the year the net operating loss or tax credits are utilized.

The Company has not completed a study to assess whether an ownership change has occurred or whether there have been multiple ownership changes since the Company’s formation due to the complexity and cost associated with such a study, and the fact that there may be additional such ownership changes in the future. If the Company has experienced an ownership change at any time since its formation, utilization of the NOL or research and development credit carryforwards would be subject to an annual limitation under Section 382 or 383 of the Internal Revenue Code, which is determined by first multiplying the value of the Company’s stock at the time of the ownership change by the applicable long-term, tax-exempt rate, and then could be subject to additional adjustments, as required. Additionally, the separate return limitation year (“SRLY”) rules may apply to losses of the Company’s eight wholly owned U.S. subsidiary corporations that have now been merged with the parent company. The SRLY rules limit the consolidated group’s use of a subsidiary corporation’s net operating losses to the amount of income generated by the subsidiary corporation after it becomes a member of the group. Any limitation may result in expiration of a portion of the NOL or research and development credit carryforwards before utilization. Further, until a study is completed and any limitation known, no amounts are being considered as an uncertain tax position or disclosed as an unrecognized tax benefit. Additionally, the Company does not expect any unrecognized tax benefits to change significantly over the next twelve months. Due to the existence of the valuation allowance, future changes in the Company’s unrecognized tax benefits will not impact its effective tax rate. Any carryforwards that will expire prior to utilization as a result of such limitations will be removed from deferred tax assets with a corresponding reduction of the valuation allowance.

The Company is subject to examination by taxing authorities in its significant jurisdictions for the year ended 2021 and subsequent years. However, due to NOL and tax attribute carryovers, the taxing authorities have the ability to adjust the NOLs and other tax attributes related to closed years. As of December 31, 2025 and 2024, there were no amounts recorded for uncertain tax positions. As of December 31, 2025, undistributed earnings of the Company’s incorporated foreign subsidiaries are immaterial. Under the Global Intangible Low-Taxed Income (“GILTI”) provisions of the 2017 Tax Cuts and Jobs Act, U.S. income taxes have been incurred on the undistributed earnings of the foreign subsidiaries and therefore, the tax impact upon distribution is limited to state income and withholding taxes and is not material.

19. Segment Reporting

The Company operates under a single operating and reportable segment, which is the development of biopharmaceutical products for the treatment of patients with IBD and other immune-mediated diseases. The Company's Chief Operating Decision Maker ("CODM") is the Company's Chief Executive Officer. The Company's CODM uses consolidated Net loss as the measure of segment profit or loss and uses consolidated Total Assets as reported on the balance sheet as the measure of segment assets. The Company's CODM compares Net loss against budgeted and/or forecasted amounts to track the Company's financial performance against expectations and to inform, along with development timelines and scientific and commercial considerations, their decisions regarding resource allocations to fund the Company's development of its pipeline.

The following table sets forth the significant expenses provided to the CODM on a regular basis (in thousands):

	Year Ended December 31,		
	2025	2024	2023
Revenue	$ —	$ —	$ 886
Less:			
Compensation	$ 34,794	$ 21,780	$ 22,590
Stock-based compensation [1]	37,614	44,833	25,675
Research and development, excluding compensation and stock-based compensation [2] [3]	132,490	127,491	65,282
Other segment items [4] [5]	(49,695)	13,914	226,129
Segment net loss	$ 155,203	$ 208,018	$ 338,790
Reconciliation of net loss			
Adjustments and reconciling items	—	—	—
Consolidated net loss	$ 155,203	$ 208,018	$ 338,790

[1] Includes $1.0 million, $15.6 million and $11.5 million in related party expenses for the years ended December 31, 2025, 2024 and 2023, respectively.

[2] Includes non-clinical study expenses, clinical trial expenses and manufacturing costs.

[3] Includes $10.5 million, $25.5 million and $37.1 million in related party expenses for the years ended December 31, 2025, 2024 and 2023, respectively.

[4] Includes general and administrative expenses such as audit, legal, and other professional fees, interest income, and Other expense, net. For the year ended December 31, 2025, includes a gain recognized in connection with the sale of pegzilarginase to Immedica. For the year ended December 31, 2023, includes acquired IPR&D expense related to the Asset Acquisition, a gain on sale related to sale of Pegzilarginase to Immedica, and changes in the forward-contract liability related to the Asset Acquisition.

[5] Includes a $29.8 million decrease, a $20.4 million increase and a $18.9 million increase in fair value of CVR liability for the years ended December 31, 2025, 2024 and 2023, respectively.

20. Net Loss Per Share

The Company computes net loss per share of common stock, Series A Preferred Stock, and Series B Preferred Stock using the two-class method required for multiple classes of common stock and other participating securities.

The two-class method is an earnings (loss) allocation method under which earnings (loss) per share is calculated for each class of common stock. The Company has determined that the Series A Preferred Stock and Series B Preferred Stock do not have preferential rights when compared to the Company's common stock and therefore it must allocate losses to these other classes of common stock, as illustrated in the table below.

Basic and diluted net loss per share is computed by dividing the net loss by the weighted-average number of shares and pre-funded warrants outstanding during the period, without consideration of potential dilutive securities. The pre-funded warrants are included in the computation of basic net loss per share as the exercise price is negligible and they are fully vested and exercisable. For periods in which the Company generated a net loss, the Company does not include potential shares of common stock in diluted net loss per share when the impact of these items is anti-dilutive. The Company has generated a net loss for all periods presented, therefore diluted net loss per share is the same as basic net loss per share since the inclusion of potential shares of common stock would be anti-dilutive.

The following table sets forth the computation of basic and diluted net loss per share of common stock, Series A Preferred Stock, and Series B Preferred Stock (in thousands, except share and per share amounts):

	Year Ended December 31, 2025		
	Series A Preferred Stock	Series B Preferred Stock	Common Stock
Net loss per share, basic and diluted:			
Numerator			
Allocation of losses	$ (27,344)	$ (1,317)	$ (126,541)
Denominator			
Weighted-average shares outstanding	346,045	16,667	64,056,442
Net loss per share, basic and diluted	$ (79.02)	$ (79.02)	$ (1.98)

	Year Ended December 31, 2024		
	Series A Preferred Stock	Series B Preferred Stock	Common Stock
Net loss per share, basic and diluted:			
Numerator			
Allocation of losses	$ (47,624)	$ (10,839)	$ (149,555)
Denominator			
Weighted-average shares outstanding	374,387	85,208	46,940,206
Weighted-average pre-funded warrants outstanding	—	—	87,432
Number of shares used in per share computation	374,387	85,208	47,027,638
Net loss per share, basic and diluted	$ (127.21)	$ (127.21)	$ (3.18)

	Year Ended December 31, 2023		
	Series A Preferred Stock	Series B Preferred Stock	Common Stock
Net loss per share, basic and diluted:			
Numerator			
Allocation of losses	$ (239,158)	$ (4,749)	$ (94,883)
Denominator			
Weighted-average shares outstanding	434,612	8,630	6,201,954
Weighted-average pre-funded warrants outstanding	—	—	695,111
Number of shares used in per share computation	434,612	8,630	6,897,065
Net loss per share, basic and diluted	$ (550.28)	$ (550.29)	$ (13.76)

The following weighted-average equity instruments were excluded from the calculation of diluted net loss per share because their effect would have been anti-dilutive for the periods presented:

	Year Ended December 31,		
	2025	2024	2023
Options to purchase common stock	1,785,568	3,212,734	2,583,226
Unvested restricted stock units	27,806	68,027	4,240
Outstanding Parapyre Warrants	1,532,591	686,724	5,625.00

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Management’s Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our board of directors, management and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting standards. Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect our transactions and dispositions of our assets;

- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and

- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management, with the participation of our principal executive officer and principal financial officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2025. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in its 2013 Internal Control – Integrated Framework. Based on our assessment, our management has concluded that, as of December 31, 2025, our internal control over financial reporting was effective based on those criteria.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2025 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

Trading Plans

During the fiscal quarter ended December 31, 2025, no director or Section 16 officer adopted or terminated any Rule 10b5-1 trading arrangement or non-Rule 10b5-1 trading arrangement (in each case, as defined in Item 408(a) of Regulation S-K), except as described below.

On November 10, 2025, Scott Burrows, our Chief Financial Officer, terminated a trading plan dated April 15, 2024 intended to satisfy Rule 10b5-1(c) to sell up to 180,000 shares of our common stock over a period ending November 19, 2026, subject to certain conditions, and adopted a trading plan intended to satisfy Rule 10b5-1(c) to sell up to 180,000 shares of our common stock over a period ending February 3, 2028, subject to certain conditions.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item is incorporated herein by reference from the applicable information set forth in the Proxy Statement with respect to our 2026 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K (the "2026 Proxy Statement"), including the sections titled "Information Regarding Director Nominees and Continuing Directors," "Executive Officers," "Corporate Governance," and, if applicable, "Delinquent Section 16(a) Reports."

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is incorporated herein by reference from the applicable information set forth in our 2026 Proxy Statement, including the sections titled "Executive Compensation" and "Corporate Governance."

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item is incorporated herein by reference from the applicable information set forth in our 2026 Proxy Statement, including the sections titled "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" and "Securities Authorized for Issuance Under Equity Compensation Plans."

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item is incorporated herein by reference from the applicable information set forth in our 2026 Proxy Statement, including the sections titled "Certain Relationships and Related Party Transactions" and "Director Independence."

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this item is incorporated herein by reference from the applicable information set forth in our 2026 Proxy Statement, including the section titled "Ratification of Independent Auditor Appointment."

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

The following documents are filed as part of this report:

1. Financial Statements

See Index to Financial Statements at Item 8 herein.

2. Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. Exhibits

		Incorporate by Reference				
Exhibit Number	Description of Document	Form	File No.	Date of Filing	Exhibit No.	Filed Herewith
2.1	Agreement and Plan of Merger, dated June 22, 2023, by and among the Company, Aspen Merger Sub I, Inc., Sequoia Merger Sub II, LLC and Spyre Therapeutics, Inc.	S-1	333-276251	12/22/2023	2.1	
3.1	Second Amended and Restated Certificate of Incorporation of the Company, effective as of May 14, 2024	8-K	001-37722	5/15/2024	3.2	
3.2	Amended and Restated Bylaws	S-1/A	333-276251	2/5/2024	3.2	
3.3	Certificate of Designations of Series A Non-Voting Convertible Preferred Stock	S-1	333-276251	12/22/2023	3.3	
3.4	Certificate of Designations of Series B Non-Voting Convertible Preferred Stock	S-1	333-276251	12/22/2023	3.4	
3.5	Certificate of Amendment to Certificate of Designation of Series B Non-Voting Convertible Preferred Stock	8-K	001-37722	3/18/2024	3.2	
4.1	Form of Registration Rights Agreement, by and among the Company and certain purchasers (December 2023 PIPE)	S-1/A	333-276251	2/5/2024	4.1	
4.2	Form of Common Stock Certificate	S-1	333-276251	12/22/2023	4.2	
4.3	Form of Registration Rights Agreement, by and among the Company and certain purchasers (June 2023 PIPE)	S-1/A	333-276251	2/5/2024	4.4	
4.4	Description of the Registrant's securities	10-K	001-37722	2/27/2025	4.4	
4.5	Form of Warrant to Purchase Common Stock (Parapyre Warrant 2023)	10-Q	001-37722	8/5/2025	4.1	
4.6	Form of Warrant to Purchase Common Stock (Parapyre Warrant 2024)	10-Q	001-37722	8/5/2025	4.2	
10.1	Form of Indemnification Agreement	S-1/A	333-276251	2/5/2024	10.19	
10.2‡	2015 Equity Incentive Plan and forms of	S-1	333-276251	12/22/2023	10.7	

Exhibit Number	Description of Document	Incorporate by Reference				Filed Herewith
		Form	File No.	Date of Filing	Exhibit No.	
	award agreements					
10.3‡	Spyre Therapeutics, Inc. 2016 Equity Incentive Plan, As Amended and Restated Effective November 21, 2023	S-1	333-276251	12/22/2023	10.8	
10.4‡	Form of Stock Option Agreement under the Amended and Restated Spyre Therapeutics, Inc. 2016 Equity Incentive Plan	10-Q	001-37722	8/7/2024	10.6	
10.5‡	Form of Restricted Stock Unit Award Agreement under the Amended and Restated Spyre Therapeutics, Inc. 2016 Equity Incentive Plan					X
10.6‡	Spyre Therapeutics, Inc. 2016 Employee Stock Purchase Plan, as amended by the First Amendment on January 31, 2024	10-K	001-37722	2/29/2024	10.4	
10.7‡	Spyre Therapeutics, Inc. 2018 Equity Inducement Plan and the First Amendment, Second Amendment, Third Amendment, Fourth Amendment, Fifth Amendment and Sixth Amendment thereto	10-Q	001-37722	8/5/2025	10.1	
10.8‡	Form of Stock Option Agreement under the Amended and Restated 2018 Equity Inducement Plan	S-1	333-276251	12/22/2023	10.11	
10.9‡	Form of Restricted Stock Unit Award Agreement under the Amended Spyre Therapeutics, Inc. 2018 Equity Inducement Plan	10-Q	001-37722	8/7/2024	10.7	
10.10‡	Spyre Therapeutics, Inc. 2023 Equity Incentive Plan	S-1	333-276251	12/22/2023	10.12	
10.11‡	Form of Stock Restriction Agreement	S-1	333-276251	12/22/2023	10.13	
10.12‡	Form of Severance Agreement	S-1	333-276251	12/22/2023	10.14	
10.13‡	Amended and Restated Offer Letter, dated November 22, 2023 and as amended on February 1, 2024, by and between the Company and Cameron Turtle	S-1/A	333-276251	2/5/2024	10.4	
10.14‡	Offer Letter, dated August 10, 2023, by and between the Company and Scott Burrows	S-1	333-276251	12/22/2023	10.16	
10.15‡	Offer Letter, dated August 18, 2023, by and between the Company and Heidy King-Jones	10-K	001-37722	2/29/2024	10.19	
10.16‡	Offer Letter, dated September 20, 2024, by and between the Company and Sheldon Sloan	10-Q	001-37722	11/7/2024	10.5	
10.17‡	Consulting Agreement by and between the Company and Mark McKenna, effective August 1, 2023	10-K	001-37722	2/29/2024	10.20	
10.18†	Amended and Restated Biologics Master Services Agreement, dated October 14,	8-K	001-37722	10/15/2024	10.2	

Exhibit Number	Description of Document	Incorporate by Reference				Filed Herewith
		Form	File No.	Date of Filing	Exhibit No.	
	2024, by and between the Company and WuXi Biologics (Hong Kong) Limited					
10.19†	Amended and Restated Cell Line License Agreement, dated October 14, 2024, by and between the Company and WuXi Biologics (Hong Kong) Limited	8-K	001-37722	10/15/2024	10.3	
10.20	Novation Agreement, dated September 19, 2023, by and between Paragon Therapeutics, Inc., the Company and WuXi Biologics (Hong Kong) Limited	S-1	333-276251	12/22/2023	10.3	
10.21	Amendment No. 1 to Novation Agreement, dated April 25, 2024, by and between Paragon Therapeutics, Inc., the Company and WuXi Biologics (Hong Kong) Limited	10-Q	001-37722	5/9/2024	10.6	
10.22†	Second Amended and Restated Antibody Discovery and Option agreement, dated May 14, 2024, by and between the Company, Paragon Therapeutics, Inc. and Parapyre Holding LLC	10-Q	001-37722	8/7/2024	10.5	
10.23†	α4ß7 (SPY001) License Agreement, dated May 14, 2024, by and between the Company and Paragon Therapeutics, Inc.	10-Q	001-37722	8/7/2024	10.3	
10.24†	TL1A (SPY002) License Agreement, dated May 14, 2024, by and between the Company and Paragon Therapeutics, Inc.	10-Q	001-37722	8/7/2024	10.4	
10.25†	Amended and Restated IL-23 (SPY003) License Agreement, dated February 24, 2025, by and between the Company and Paragon Therapeutics, Inc.	10-K	001-37722	2/27/2025	10.25	
10.26	Sales Agreement, dated September 6, 2024, between Spyre Therapeutics, Inc. and TD Securities (USA) LLC	S-3	333-285341	2/27/2025	1.2	
16.1	Letter from PricewaterhouseCoopers LLP, dated March 6, 2025	8-K	001-37722	3/6/2025	16.1	
19.1	Spyre Therapeutics, Inc. Insider Trading Policy	10-K	001-37722	2/27/2025	19.1	
21.1	Subsidiaries of the Registrant					X
23.1	Consent of KPMG LLP					X
23.2	Consent of PricewaterhouseCoopers LLP					X
24.1	Power of Attorney					X
31.1	Certification of the Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934					X
31.2	Certification of the Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-					X

Exhibit Number	Description of Document	Incorporate by Reference				Filed Herewith
		Form	File No.	Date of Filing	Exhibit No.	
	14(a) of the Securities Exchange Act of 1934					
32.1	Certification of the Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
97	Spyre Therapeutics, Inc. Compensation Recoupment (Clawback) Policy	10-K	001-37722	2/29/2024	97	
101.INS	Inline XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					X
104	The cover page of this Annual Report on Form 10-K for the year ended December 31, 2024, formatted in Inline XBRL and contained in Exhibit 101					

† Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

‡ Indicates management contract or compensatory plan.

(1) The certifications on Exhibit 32 hereto are deemed not “filed” for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of that Section. Such certifications will not be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act, regardless of any general incorporation language contained in such filing.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: February 19, 2026

SPYRE THERAPEUTICS, INC.

By: /s/ Scott Burrows

Scott Burrows

Chief Financial Officer

(Principal Financial Officer and Principal Accounting Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Dr. Cameron Turtle and Mr. Scott Burrows, jointly and severally, his or her attorneys-in-fact, each with the power of substitution, for him or her in any and all capacities, to sign any amendments to this Report on Form 10-K and to file same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Cameron Turtle, D.Phil Cameron Turtle, D.Phil	President and Chief Executive Officer and Director (Principal Executive Officer)	February 19, 2026
/s/ Scott Burrows Scott Burrows	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	February 19, 2026
/s/ Jeffrey W. Albers Jeffrey W. Albers	Chairman of the Board	February 19, 2026
/s/ Peter Harwin Peter Harwin	Director	February 19, 2026
/s/ Michael Henderson, M.D. Michael Henderson, M.D.	Director	February 19, 2026
/s/ Tomas Kiselak Tomas Kiselak	Director	February 19, 2026
/s/ Mark McKenna Mark McKenna	Director	February 19, 2026
/s/ Sandra Milligan Sandra Milligan	Director	February 19, 2026
/s/ Laurie Stelzer Laurie Stelzer	Director	February 19, 2026

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

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

Filed by the Registrant ☒
Filed by a Party other than the Registrant ☐
Check the appropriate box:

☐ Preliminary Proxy Statement
☐ Confidential, for Use of the Commission Only (as permitted by Rule 14a-6(e)(2))
☒ Definitive Proxy Statement
☐ Definitive Additional Materials
☐ Soliciting Material under §240.14a-12

Spyre Therapeutics, Inc.
(Name of Registrant as Specified In Its Charter)
(Name of Person(s) Filing Proxy Statement if other than the Registrant)

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

☒ No fee required.
☐ Fee paid previously with preliminary materials.
☐ Fee computed on table in exhibit required by Item 25(b) per Exchange Act Rules 14a-6(i)(1) and 0-11.



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

NOTICE OF THE 2026 ANNUAL MEETING OF STOCKHOLDERS TO BE HELD ON MAY 27, 2026

To the Stockholders of Spyre Therapeutics:

Spyre Therapeutics, Inc. (the "Company") will hold its 2026 Annual Meeting of Stockholders (the "Annual Meeting") on Wednesday, May 27, 2026, at 12:00 p.m. Eastern Time. The Annual Meeting will be a virtual meeting conducted exclusively online via live audio webcast at *www.virtualshareholdermeeting.com/SYRE2026*. The Annual Meeting will be held for the following purposes, as more fully described in the accompanying proxy statement (the "Proxy Statement"):

(1) To elect the three Class I director nominees named in the Proxy Statement to serve until the 2029 Annual Meeting of Stockholders and until their successors are duly elected and qualified;

(2) To approve, on a non-binding, advisory basis, the compensation of the Company's named executive officers;

(3) To ratify the appointment of KPMG LLP as the Company's independent registered public accounting firm for the year ending December 31, 2026;

(4) To approve the Company's amended and restated 2016 Employee Stock Purchase Plan; and

(5) To transact any other matters that may properly come before the Annual Meeting or any adjournments or postponements thereof.

The Board of Directors has fixed April 2, 2026 as the Record Date. Only stockholders of record at the close of business on that date will be entitled to notice of, and to vote at, the Annual Meeting or any adjournment or postponement thereof.

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

By Order of the Board of Directors,

/s/ Cameron Turtle
Cameron Turtle, D.Phil.
Chief Executive Officer and Director

Waltham, Massachusetts
April 10, 2026

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

TABLE OF CONTENTS

	Page
QUESTIONS AND ANSWERS ABOUT THE PROXY MATERIALS AND VOTING	4
PROPOSAL 1: ELECTION OF DIRECTORS	9
PROPOSAL 2: NON-BINDING ADVISORY VOTE ON EXECUTIVE COMPENSATION	13
PROPOSAL 3: RATIFICATION OF INDEPENDENT AUDITOR APPOINTMENT	14
PROPOSAL 4: APPROVAL OF AMENDED AND RESTATED 2016 EMPLOYEE STOCK PURCHASE PLAN	17
CORPORATE GOVERNANCE	21
EXECUTIVE OFFICERS	28
COMPENSATION DISCUSSION & ANALYSIS	30
CERTAIN INFORMATION ABOUT OUR COMMON STOCK	47
CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS	50
OTHER MATTERS	52
ANNEX A	A-1

LEGAL MATTERS

Important Notice Regarding the Availability of Proxy Materials for the 2026 Annual Meeting of Stockholders to Be Held on May 27, 2026. The Proxy Statement and Annual Report for the year ended December 31, 2025 are available at *www.proxyvote.com*.

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

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

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



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

PROXY STATEMENT
FOR THE 2026 ANNUAL MEETING OF STOCKHOLDERS

QUESTIONS AND ANSWERS ABOUT THE PROXY MATERIALS AND VOTING

What Is the Purpose of These Proxy Materials?

We are making these proxy materials available to you in connection with the solicitation of proxies by the Board of Directors (the "Board") of Spyre Therapeutics, Inc. ("we," "us," "our" or the "Company") for use at the 2026 Annual Meeting of Stockholders (the "Annual Meeting") to be held virtually on May 27, 2026 at 12:00 p.m. Eastern Time, or at any other time following adjournment or postponement thereof. You are invited to participate in the Annual Meeting and to vote on the proposals described in this proxy statement (the "Proxy Statement"). The proxy materials are being made available to our stockholders beginning on or about April 10, 2026.

Why Did I Receive a Notice of Internet Availability?

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

Why Are We Holding a Virtual Annual Meeting?

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

Who Can Vote?

Only stockholders of record at the close of business on April 2, 2026 (the "Record Date") are entitled to notice of the Annual Meeting and to vote on the proposals described in this Proxy Statement. At the close of business on the Record Date, 78,784,358 shares of our common stock were issued and outstanding. Shares of our preferred stock generally do not have voting rights and holders of our preferred stock are therefore not entitled to vote at the Annual Meeting.

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

Registered Stockholder: Shares Registered in Your Name

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

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

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

How Can I Participate in the Virtual Annual Meeting?

Stockholders of record as of the close of business on the Record Date are entitled to participate in and vote at the Annual Meeting. To participate in the Annual Meeting, including to vote and ask questions, stockholders of record should go to the meeting website at *www.virtualshareholdermeeting.com/SYRE2026*, enter the 16-digit control number found on your proxy card or Notice, and follow the instructions on the website. If your shares are held in street name and your voting instruction form or Notice indicates that you may vote those shares through *www.proxyvote.com*, then you may access, participate in and vote at the Annual Meeting with the 16-digit access code indicated on that voting instruction form or Notice. Otherwise, stockholders who hold their shares in street name should contact their bank, broker or other nominee (preferably at least five days before the Annual Meeting) and obtain a "legal proxy" in order to be able to attend, participate in or vote at the Annual Meeting.

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

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

What Am I Voting on?

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

(1) Election of three Class I director nominees to serve until the 2029 Annual Meeting of Stockholders ("**Proposal 1**");

(2) Approval, on a non-binding, advisory basis, of the compensation of the Company's named executive officers ("**Proposal 2**");

(3) Ratification of the appointment of KPMG LLP as the Company's independent auditor for 2025 ("**Proposal 3**"); and

(4) Approval of the Company's Amended and Restated 2016 Employee Stock Purchase Plan ("**Proposal 4**").

How Does the Board Recommend That I Vote?

The Board recommends that you vote your shares "**FOR**" each director nominee in Proposal 1 and "**FOR**" Proposals 2, 3 and 4.

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

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

How Many Votes Do I Have?

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

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

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

How Do I Vote?

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

Registered Stockholder: Shares Registered in Your Name

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

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

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

What Happens If I Do Not Vote?

Registered Stockholder: Shares Registered in Your Name

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

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

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

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

Registered Stockholder: Shares Registered in Your Name

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

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

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

Can I Change My Vote after I Submit My Proxy?

Registered Stockholder: Shares Registered in Your Name

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

(1) You may complete and submit a new proxy card, but it must bear a later date than the original proxy card;

(2) You may submit new proxy instructions via telephone or the Internet;

(3) You may send a timely written notice that you are revoking your proxy to our Corporate Secretary at the address set forth on the first page of this Proxy Statement; or

(4) You may vote by attending the Annual Meeting virtually. However, your virtual attendance at the Annual Meeting will not, by itself, revoke your proxy.

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

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

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

What Is the Quorum Requirement?

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

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

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

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

Proposal 1: Election of Directors

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

Proposal 2: Non-Binding Advisory Vote on Executive Compensation

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

Proposal 3: Ratification of Independent Auditor Appointment

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

Proposal 4: Approval of Amended and Restated 2016 Employee Stock Purchase Plan

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

Who Is Paying for This Proxy Solicitation?

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

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

How Can I Find out the Voting Results?

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

PROPOSAL 1: ELECTION OF DIRECTORS

In accordance with our Certificate of Incorporation and Bylaws, the Board has fixed the number of directors constituting the Board at eight. At the Annual Meeting, the stockholders will vote to elect the three Class I director nominees named in this Proxy Statement to serve until the 2029 Annual Meeting of Stockholders and until their successors are duly elected and qualified or until their earlier resignation or removal. Our Board has nominated Mark McKenna, Cameron Turtle and Laurie Stelzer for election to our Board. Mr. McKenna was appointed to the Board in February 2024 and was initially identified for a position on our Board by management and other directors, and Ms. Stelzer was appointed to the Board in November 2023 and was initially identified for a position on our Board by a third-party search firm.

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

Information Regarding Director Nominees and Continuing Directors

Our Board is divided into three classes, with members of each class holding office for staggered three-year terms. There are currently three Class I directors, who are up for election at this meeting for a term expiring at the 2029 Annual Meeting of Stockholders; two Class II directors, whose terms expire at the 2027 Annual Meeting of Stockholders; and three Class III directors, whose terms expire at the 2028 Annual Meeting of Stockholders.

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

Name	Class	Age (as of April 10)	Position
Mark McKenna	I	46	Director
Cameron Turtle	I	36	Chief Executive Officer and Director
Laurie Stelzer[1][2]	I	58	Director
Jeffrey Albers[2][3]	II	54	Director
Tomas Kiselak[3]	II	39	Director
Peter Harwin[1]	III	40	Director
Michael Henderson[2]	III	36	Director
Sandra Milligan[1][3]	III	62	Director

(1) Member of the Nominating Committee
(2) Member of the Audit Committee
(3) Member of the Compensation Committee

Class I Director Nominees

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

General Manager of its U.S. Vision Care business. Mr. McKenna holds a B.S. in marketing from Arizona State University and an M.B.A. from Azusa Pacific University. Mr. McKenna was Ernst & Young's Entrepreneur of the Year in 2023.

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

Cameron Turtle, D. Phil. Dr. Turtle joined us as Chief Operating Officer in June 2023, and was appointed as our Chief Executive Officer and a director in November 2023. Prior to joining the Company, Dr. Turtle was an advisor to Pre-Merger Spyre from May 2023 to June 2023. Previously, he served as Venture Partner at Foresite Labs, a life sciences investment firm, from July 2022 to May 2023; Chief Strategy Officer of BridgeBio Pharma (Nasdaq: BBIO), a biopharmaceutical company, from January 2021 to April 2022; and Chief Business Officer of Eidos Therapeutics (Nasdaq: EIDX), a biopharmaceutical company, from November 2018 to January 2021, where he led business development, investor relations, and multiple operational functions as the company advanced an investigational medicine for a form of heart failure. Prior to joining BridgeBio and Eidos, he was a consultant at McKinsey & Company, where he worked with pharmaceutical and medical device companies on topics including M&A, growth strategy, clinical trial strategy, and sales force optimization. Dr. Turtle has served as a member of the board of directors of Damora Therapeutics, Inc. (Nasdaq: DMRA), a biotechnology company, since March 23, 2026 and Oruka Therapeutics, Inc. (Nasdaq: ORKA), a biotechnology company, from August 2024 to December 2025. Dr. Turtle received his B.S. with honors in Bioengineering from the University of Washington and his D.Phil. in Cardiovascular Medicine from the University of Oxford, St. John's College. He is the recipient of several awards, including a Rhodes Scholarship, Goldwater Scholarship, Forbes 30 Under 30 and San Francisco Business Times 40 Under 40.

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

Laurie Stelzer. Ms. Stelzer has served as a director since November 2023. Ms. Stelzer served as Chief Financial Officer of Kailera Therapeutics, Inc., a biotechnology company focused on developing therapies for obesity, from January 2025 to October 2025. Prior to joining Kailera, Ms. Stelzer served as Chief Financial Officer of Orna Therapeutics, Inc., a biotechnology company focused on RNA therapeutics, from May 2024 to January 2025. Prior to joining Orna, Ms. Stelzer served as Chief Financial Officer of ReNAgade Therapeutics, Inc., a biotechnology company focused on RNA therapeutics, from September 2023 to May 2024. Prior to joining ReNAgade, Ms. Stelzer served as Chief Financial Officer of Mirati Therapeutics, Inc. (Nasdaq: MRTX), a commercial-stage targeted oncology company, from May 2022 to September 2023. Prior to joining Mirati Therapeutics, Ms. Stelzer served as Executive Vice President and Chief Financial Officer of Arena Pharmaceuticals, Inc. (acquired by Pfizer Inc.), a biopharmaceutical company, from March 2020 until the completion of Pfizer's acquisition in March 2022. Prior to joining Arena Pharmaceuticals, Ms. Stelzer served as Chief Financial Officer at Halozyme Therapeutics, Inc. (Nasdaq: HALO), a biopharma technology platform company, from June 2015 to March 2020, where she led the Finance, Information Technology, Business Development, Project Management and Site Operations organizations. Prior to joining Halozyme Therapeutics, Ms. Stelzer held senior management roles at Shire Plc (acquired by Takeda Pharmaceutical), including Senior Vice President of Finance, Division Chief Financial Officer for the Regenerative Medicine Division and Head of Investor Relations. Previously, she also worked at Amgen, Inc. (Nasdaq: AMGN), a global biopharmaceutical company, for 15 years, serving in positions of increasing responsibility in the areas of Finance, Treasury, Global Accounting and International/Emerging Markets. Ms. Stelzer has served as a member of the board of directors of MBX Biosciences, Inc. (Nasdaq: MBX), a clinical-stage biopharmaceutical company, since January 2026, Sionna Therapeutics (Nasdaq: SION), a clinical-stage cystic fibrosis company, since 2024, PMV Pharmaceuticals, Inc. (Nasdaq: PMVP), a precision oncology company, since 2020, Surface Oncology, Inc. (Nasdaq: SURF), a clinical-stage immune-oncology company, from 2018 until its acquisition by Coherus in September 2023 and Longboard Pharmaceuticals, a clinical-stage neurology company from 2020 to 2021. Ms. Stelzer received her B.S. in Accounting from Arizona State University and her M.B.A. from University of California, Los Angeles, Anderson School of Management.

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

Class II Directors Continuing in Office

Jeffrey Albers. Mr. Albers has served as a director since November 2023. Mr. Albers has over 25 years of experience working in the biopharmaceutical industry and bringing important new medicines to patients with cancer and rare diseases. He currently serves as Venture Partner at Atlas Venture, a venture capital firm focused on investment in biotechnology

companies, since January 2023. Mr. Albers served as Chairman of Blueprint Medicines Corporation (Nasdaq: BPMC), a global precision therapy company, from June 2021 to July 2025, Executive Chairman from April 2022 to December 2022 and as Chief Executive Officer, President and Director from July 2014 to June 2021. Prior to joining Blueprint Medicines in July 2014, Mr. Albers was President of Algeta ASA, a Norwegian biotechnology company from January 2012 to April 2014, where he oversaw the U.S. business. Prior to Algeta ASA, from July 2005 to November 2011, Mr. Albers was at Genzyme Corporation, a biotechnology company that is now a wholly owned subsidiary of Sanofi S.A., most recently as Vice President of the U.S. hematology and oncology business unit. Mr. Albers serves on the board of directors of Kymera Therapeutics, Inc. (Nasdaq: KYMR) and several private companies, and previously served on the board of directors of Magenta Therapeutics, Inc. (which later became Dianthus Therapeutics, Inc. (Nasdaq: DNTH)) from July 2017 to September 2023. Mr. Albers received a B.S. from Indiana University and an M.B.A. and a J.D. from Georgetown University.

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

Tomas Kiselak. Mr. Kiselak has served as a director since June 2023. Mr. Kiselak is a Founding Partner at Fairmount Funds Management LLC, a healthcare investment firm he co-founded in April 2016. Prior to Fairmount, Mr. Kiselak was a managing director at RA Capital Management, LLC, a healthcare and life science investment firm. Mr. Kiselak currently serves as the chairman of the board of directors of Viridian Therapeutics, Inc. (Nasdaq: VRDN) since October 2020 and as a director for Apogee Therapeutics, Inc. (Nasdaq: APGE) since July 2023, Jade Biosciences, Inc. (Nasdaq: JBIO) since April 2025, and Zenas BioPharma, Inc. (Nasdaq: ZBIO) since September 2024, as well as several private companies. Mr. Kiselak previously served as a director for Dianthus Therapeutics, Inc. (Nasdaq: DNTH) from September 2023 to March 2025. He received a B.S. in neuroscience and economics from Amherst College.

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

Class III Directors Continuing in Office

Peter Harwin. Mr. Harwin has served as a director since June 2023. Mr. Harwin is a Founding Partner at Fairmount Funds Management LLC, a healthcare investment firm he co-founded in April 2016. Prior to Fairmount, Mr. Harwin was a member of the investment team at Boxer Capital, LLC, an investment fund that was part of the Tavistock Group, based in San Diego. Mr. Harwin also serves as chairman of the board of directors of Cogent Biosciences, Inc. (Nasdaq: COGT), where he has served as a director since July 2020 and Crescent Biopharma, Inc. (Nasdaq: CBIO), where he has served as a director since June 2025, and has served as a director of Apogee Therapeutics, Inc. (Nasdaq: APGE) since July 2023, Damora Therapeutics, Inc. (Nasdaq: DMRA) since November 2025, Oruka Therapeutics, Inc. (Nasdaq: ORKA) since August 2024 and Paragon Therapeutics, Inc. ("Paragon"), a private company. Mr. Harwin previously served as a director for Viridian Therapeutics, Inc. (Nasdaq VRDN) from October 2020 to March 2025. Mr. Harwin holds a B.B.A. from Emory University.

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

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

on the board of directors of ARYA Sciences Acquisition Corp IV (Nasdaq: ARYD), a special purpose acquisition company focused on the healthcare industry, from February 2021 to August 2024. Dr. Henderson received his B.A. in global health from Harvard University and his M.D. from Stanford University.

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

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

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

Board Recommendation

The Board recommends a vote "**FOR**" the election of each of the Class I director nominees set forth above.

PROPOSAL 2: NON-BINDING ADVISORY VOTE ON EXECUTIVE COMPENSATION

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

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

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

We are required to hold a say-on-pay vote at least once every three years, and we have determined to hold a say-on-pay vote every year. Unless the Board modifies its policy on the frequency of holding say-on-pay advisory votes, the next say-on-pay vote is expected to occur in 2027.

Board Recommendation

The Board recommends a vote "**FOR**" this proposal.

PROPOSAL 3: RATIFICATION OF INDEPENDENT AUDITOR APPOINTMENT

Our Audit Committee has appointed KPMG LLP ("KPMG") as the Company's independent registered public accounting firm for the year ending December 31, 2026. In this Proposal 3, we are asking stockholders to vote to ratify this appointment. Representatives of KPMG are expected to be present at the Annual Meeting. They will have the opportunity to make a statement, if they desire to do so, and are expected to be available to respond to appropriate questions from stockholders.

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

Recent Change in Independent Auditor

Dismissal of Independent Registered Public Accounting Firm

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

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

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

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

Appointment of New Independent Registered Public Accounting Firm

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

During the Company's fiscal years ended December 31, 2024 and 2023 and the subsequent interim period from January 1, 2025 to February 28, 2025, neither the Company nor anyone on its behalf consulted KPMG regarding: (i) the application of accounting principles to a specified transaction, either completed or proposed, or the type of audit opinion that might be rendered on the Company's financial statements, and neither a written report nor oral advice was provided to the Company that KPMG concluded was an important factor considered by the Company in reaching a decision as to any accounting, auditing or financial reporting issue; or (ii) any matter that was the subject of a disagreement (as defined in Item 304(a)(1)(iv) of Regulation S-K and the related instructions thereto) or a reportable event (as described in Item 304(a)(1)(v) of Regulation S-K).

Fees for the fiscal years ended December 31, 2025 and 2024

The following table summarizes the audit fees billed and expected to be billed by KPMG and PwC for the fiscal years ended December 31, 2025 and 2024, respectively, and the fees billed by KPMG and PwC for all other services rendered during the fiscal years ended December 31, 2025 and 2024, respectively. All services associated with such fees were pre-approved by our Audit Committee in accordance with the "Pre-Approval Policies and Procedures" described below.

	Year Ended December 31,	
Fee Category	**2025**	**2024**
Audit Fees[1]	$ 1,032,594	$ 1,855,000
Audit-Related Fees[2]	—	—
Tax Fees[3]	116,025	67,990
All Other Fees[4]	—	2,125
Total Fees	$ 1,148,619	$ 1,925,115

(1) Consists of fees for professional services rendered for the integrated audit of our financial statements, review of our interim condensed financial statements, professional consultations with respect to accounting matters and assistance with registration statements filed with the SEC and services that are normally provided by KPMG and PwC in connection with statutory and regulatory filings or engagements. Included in our 2025 and 2024 audit fees are fees of $100,000 and $115,000 respectively, related to comfort letter fees. 2024 also includes $280,969 in fees billed subsequent to the filing of the proxy statement for our 2025 annual meeting of stockholders.

(2) Consists of fees for assurance and related services reasonably related to the performance of the audit or review of our financial statements.

(3) Consists of fees for professional services for tax compliance, tax advice and tax planning.

(4) Consists of fees for all other services.

Pre-Approval Policies and Procedures

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

Report of the Audit Committee

The Audit Committee has reviewed and discussed the audited financial statements for the year ended December 31, 2025 with the Company's management and with KPMG. The Audit Committee has discussed with KPMG the matters required to be discussed by the applicable standards of the Public Company Accounting Oversight Board ("PCAOB") and the SEC. The Audit Committee has also received the written disclosures and the letter from KPMG pursuant to applicable PCAOB requirements regarding its communications with the Audit Committee concerning independence, and the Audit Committee has discussed with KPMG its independence. Based on the foregoing, the Audit Committee recommended to the Board that the audited financial statements be included in the Company's Annual Report on Form 10-K for the year ended December 31, 2025 for filing with the SEC.

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

Laurie Stelzer (Chair)
Jeffrey Albers
Michael Henderson

Board Recommendation

The Board recommends a vote "**FOR**" this proposal.

PROPOSAL 4: APPROVAL OF THE AMENDED AND RESTATED 2016 EMPLOYEE STOCK PURCHASE PLAN

General

The Spyre Therapeutics, Inc. 2016 Employee Stock Purchase Plan was originally effective in April 2016 in connection with our initial public offering and subsequently amended effective June 7, 2018 and January 31, 2024 (the "2016 ESPP"). The 2016 ESPP was scheduled to terminate on April 6, 2026. In order to continue offering the ability to participate in an employee stock purchase plan uninterrupted, on September 3, 2025, the Board of Directors approved an amendment and restatement of the 2016 ESPP (the "A&R 2016 ESPP") to be effective January 1, 2026, subject to stockholder approval.

The purpose of the A&R 2016 ESPP is to provide eligible employees with a means of acquiring an equity interest in the Company and to enhance such employees' sense of participation in the Company's affairs. The A&R 2016 ESPP, and the rights of participants to make purchases thereunder, is intended to qualify under Section 423 of the Code; however, offerings that do not meet the requirements of Section 423 of the Code may be established for the benefit of eligible employees of non-U.S. subsidiaries of the Company (the "Non-Section 423 Component").

In addition to removing the expiration of the 2016 ESPP, the A&R 2016 ESPP provides for the reservation of 1,056,096 shares of common stock for issuance and incorporates other ministerial changes.

If the A&R 2016 ESPP is not approved, the ongoing offering period will be terminated and accumulated contributions will be returned to participants. If the A&R 2016 ESPP is approved, we will file with the SEC a registration statement on Form S-8 to register the shares available for issuance thereunder.

Summary of the A&R 2016 ESPP

The following description of the A&R 2016 ESPP is not intended to be complete and is qualified in its entirety by the complete text of the A&R 2016 ESPP, a copy of which is attached as Annex A to this proxy statement. Stockholders are urged to read the A&R 2016 ESPP in its entirety.

Administration

The A&R 2016 ESPP is administered by the Compensation Committee or another committee designated by the Board of Directors to administer, which is referred to herein as the "Administrator." All questions of interpretation or application of the A&R 2016 ESPP are determined by the Administrator, whose decisions are final and binding upon all participants. The Administrator may adopt rules or procedures relating to the operation and administration of the A&R 2016 ESPP to accommodate the specific requirements of local laws and procedures, including for participants outside of the United States pursuant to the Non-Section 423 Component.

Stock Subject to ESPP

A total of 1,056,096 shares of common stock is reserved for issuance under the A&R 2016 ESPP, subject to certain adjustments in the event of a change in the Company's capitalization. Shares of common stock issued under the A&R 2016 ESPP may be shares of authorized but unissued common stock, common stock held as treasury shares, or common stock acquired in an open-market transaction.

If the total number of shares to be purchased by all participants on any exercise date (as defined below) exceeds the number of shares remaining available for issuance under the A&R 2016 ESPP, the Administrator may make a pro rata allocation of the remaining available number of shares in as uniform a manner as possible and as the Administrator determines to be equitable.

The closing price of our common stock, as reported on Nasdaq as of April 2, 2026, was $47.58.

Eligibility

All employees of the Company or a participating subsidiary of the Company who customarily work for more than 20 hours per week and more than five months in any calendar year and satisfy the requirements set forth in the A&R 2016 ESPP will be eligible to participate in the A&R 2016 ESPP. However, any employee who would own (or pursuant to Section 424(d) of the Code would be deemed to own) more than 5% of the voting power or value of the common stock immediately after a grant under the A&R 2016 ESPP is not eligible to participate. The Administrator may also, in its

discretion, establish additional requirements for participation, subject to the limitations set forth in Section 423 of the Code. No participant may purchase more than $25,000 of common stock in any one calendar year or more than the maximum number of shares established by the Administrator prior to the commencement of such offering period. For the initial offering, the maximum number of shares per participant is 2,000 shares. As of April 2, 2026, approximately 111 employees are eligible to participate in the A&R 2016 ESPP.

Offering Periods

The A&R 2016 ESPP is generally implemented by a series of "offering periods". The first offering period began on January 1, 2026 and will end on June 30, 2026 with subsequent offering periods and purchase periods lasting for six months and ending every December 31 and June 30.

Payroll Deductions

For the initial offering period, all participants of the offering period under the 2016 ESPP that ended immediately prior to its amendment and restatement on January 1, 2026 were automatically enrolled unless the participant chose to withdraw from the A&R 2016 ESPP. To participate in a future offering period, an eligible employee must submit an enrollment agreement prior to the applicable enrollment date (or such earlier date as determined by the Administrator). Once enrolled in the A&R 2016 ESPP, a participant can purchase shares of common stock with payroll deductions at the end of the applicable offering period. Once an offering period is over, a participant is automatically enrolled in the next offering period unless the participant chooses to withdraw from the A&R 2016 ESPP.

Each enrollment agreement will request a deduction in an amount expressed as a whole percentage between 1% and 15% and all payroll deductions will be credited to the eligible employee's account. No interest will be paid on any amount held in the account of any eligible employee.

Option Grant

On the first trading day of each offering period, each eligible employee automatically will be granted an option to acquire shares of common stock on the exercise date. All participants granted options under the A&R 2016 ESPP will have the same rights and privileges consistent with the requirements set forth in Section 423 of the Code. No eligible employee will be permitted to purchase more than shares of common stock during each purchase period.

Purchase Price

The price per share at which shares are purchased under the A&R 2016 ESPP is 85% of the lesser of the fair market value of the common stock on the first day of the offering period or the fair market value of the common stock on the last day of the offering period.

Exercise of Options

At the end of each offering period, unless the participant has withdrawn from the A&R 2016 ESPP, payroll deductions are applied automatically to purchase shares of common stock at the price described above. The number of shares purchased is determined by dividing the payroll deductions by the applicable purchase price, rounded down to the nearest whole share.

Any payroll deductions accumulated in a participant's account that are not sufficient to purchase a full share will be returned to the participant, without interest; however, the Administrator may determine that such amounts may be carried forward into the next offering period. Any other amounts of payroll deductions in a participant's account that are not used for the purchase of shares of common stock, whether because of the participant's withdrawal, because the amount would enable the participant to purchase more than the maximum number of shares, or for any other reason, will be returned to the participant, without interest, as soon as administratively practicable after such withdrawal, exercise date or other event, as applicable.

Cancellation and Withdrawal

Participants may cancel all (but not less than all) of their options and terminate their enrollment by submitting a signed and completed withdrawal form before any deadline established by the Administrator for such offering period. Upon such withdrawal, the balance in the participant's account will be returned to the participant, without interest.

Termination of Employment or Eligibility

Upon the termination of a participant's employment with the Company (or a participating subsidiary, as applicable) for any reason or if a participant loses eligibility to participate in the A&R 2016 ESPP, the participant's participation in the A&R 2016 ESPP is immediately terminated, the balance in the participant's account will be returned to the participant (or his or her estate or designated beneficiary in the event of the participant's death), without interest, as soon as administratively practicable, and the participant will have no other rights under the A&R 2016 ESPP.

Transferability

Rights to purchase common stock under the A&R 2016 ESPP and accumulated contributions may not be assigned, transferred, pledged or otherwise disposed of in any way (other than by will or the laws of descent and distribution) by a participant, and rights to purchase common stock under the A&R 2016 ESPP may be exercised during a participant's lifetime only by the participant.

Adjustments Upon Capital Changes

In the event of any stock dividends, recapitalizations, stock splits, reverse stock splits, subdivisions, combinations, reclassifications or similar changes in the capital structure of the Company without consideration, the Administrator will appropriately adjust the number and class of shares available under the A&R 2016 ESPP, the share limits under the A&R 2016 ESPP and the applicable purchase price of such shares in any ongoing offering period.

Corporate Transactions

If we experience a corporate transaction, any offering period that commenced prior to the closing of the proposed change in control transaction will be shortened and terminated on a new purchase date. The new purchase date will occur prior to the closing of the proposed change in control transaction and our A&R 2016 ESPP will then terminate on the closing of the proposed change in control.

Amendment and Termination

The Administrator may amend, suspend or terminate the A&R 2016 ESPP at any time and, in the event of a termination of the A&R 2016 ESPP, may terminate all outstanding offering periods (and return each participant's account balance to the participant) or allow outstanding offering periods to expire in accordance with their terms. The A&R 2016 ESPP will continue in effect until terminated by the Administrator.

Federal Income Tax Consequences

The following is a brief description of the federal income tax treatment that will generally apply to the grant and exercise of rights under the A&R 2016 ESPP that qualify under Section 423 of the Code, based on federal income tax laws in effect on the date of this proxy statement/prospectus. The exact federal income tax treatment of options under the A&R 2016 ESPP will depend on the specific nature of any such option and the individual tax attributes of the participant. The following summary is not intended to be exhaustive and, among other considerations, does not describe gift, estate, social security, state, local or international tax consequences. In addition, if an offering under the Non-Section 423 Component is established for employees of non-U.S. subsidiaries, the tax rules may be different than discussed below.

The A&R 2016 ESPP is intended to qualify as an "employee stock purchase plan" under Section 423 of the Code and, as a result, employees who participate in the A&R 2016 ESPP will be afforded favorable tax treatment subject to meeting certain requirements specified by the Code. In general, there are no federal income tax consequences to a participant upon the grant of the option to purchase shares under the A&R 2016 ESPP at the beginning of an option period or upon its exercise on the exercise date at the end of an option period. Upon the disposition of shares of common stock acquired upon exercise of an option, the participant will generally be subject to tax and the nature and amount of the tax will depend on whether the employee has satisfied the statutory holding period.

If the employee holds shares acquired under the A&R 2016 ESPP for at least two years from the grant date of his or her option and at least one year from the date he or she acquired the shares (referred to as the "statutory holding period"), any gain on the sale of the shares will be taxed as ordinary income to the extent of the lesser of (i) the amount by which the fair market value of the shares on the grant date (i.e., the first day of the option period) exceeded the exercise price for the option, or (ii) the amount by which the fair market value of the shares on the date of sale exceeds the exercise price of the option. Any additional gain or loss will be taxed as long-term capital gain or loss.

If the participant sells or otherwise disposes of the shares before the expiration of the statutory holding period, then in the year of such "disqualifying" disposition, the participant will be required to recognize ordinary income equal to the difference between the fair market value of the shares on the date of the exercise of the option and the exercise price of the option. Any additional gain or loss will be short-term or long-term capital gain or loss depending on the length of time the employee has held the shares.

The Company is not entitled to any deduction with respect to the difference between the fair market value of the common stock and the option exercise price if the participant satisfies the statutory holding period described above. If shares are sold before the statutory holding period is satisfied, the Company (or, if applicable, the affiliate employer) is entitled to a tax deduction for any ordinary income recognized by the participant.

2016 ESPP Benefits

The table below shows the number of shares purchased under the 2016 ESPP by the individuals and groups identified below since its inception (giving effect to our reverse stock split in September 2023). No non-employee directors have ever participated in the 2016 ESPP.

Name and Position	Number of Shares Purchased
Cameron Turtle, Chief Executive Officer	1,033
Scott Burrows, Chief Financial Officer	—
Sheldon Sloan, Chief Medical Officer	—
Heidy King-Jones, Chief Legal Officer and Corporate Secretary	2,159
All current executive officers as a group (4 persons)	3,192
All current employees other than executive officers as a group	58,200

New Plan Benefits

The benefits that will be received by or allocated to eligible employees under the A&R 2016 ESPP cannot be determined at this time because the amount of payroll deductions contributed to purchase shares of common stock under the A&R 2016 ESPP is entirely within the discretion of each participant (subject to the limitations discussed above). With respect to the offering period that commenced on January 1, 2026, Heidy King-Jones and 37 other employees have elected to participate, but the number of shares of common stock that may be acquired is not determinable until the completion of the offering period on June 30, 2026.

For information about our equity compensation plans as of December 31, 2025, see "Securities Authorized for Issuance under Equity Compensation Plans" on page 49.

Board Recommendation

The Board recommends a vote "**FOR**" this proposal.

CORPORATE GOVERNANCE

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

Our Governance Structure and Philosophy

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

- **Classified board:** our directors serve three-year terms, with approximately 1/3 of the Board (instead of the entire Board) elected at each annual meeting. This helps to provide stability and continuity, permitting directors to develop and share institutional knowledge and focus on the long term, and encourages stockholders to engage directly with the Board and management team regarding significant corporation transactions.

- **Supermajority voting:** the voting standard for most items is a majority of shares present and entitled to vote on the proposal, but 2/3 of the outstanding shares are needed to amend certain provisions of our Certificate of Incorporation and Bylaws and remove directors. This helps protect against a small group of stockholders acting to amend our governing documents or to remove directors for reasons that may not be in the best interests of all stockholders.

- **Plurality voting for directors:** our directors are elected by a plurality of votes cast (instead of a majority of votes cast), meaning the nominees with the most votes are elected. This helps avoid potential disruption to the Board and management team as a result of a "failed election."

- **Stockholders cannot call special meetings or act by written consent:** stockholders can propose business at each annual meeting (in accordance with our advance notice bylaws and Rule 14a-8) but cannot call a stockholder vote in between annual meetings or act by written consent. This helps avoid unnecessary diversion of Board and management time (potentially at the request of a limited number of stockholders acting to further short-term special interests) from executing on our long-term strategy.

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

Board Composition

Director Nomination Process

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

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

Criteria for Board Membership

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

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

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

Board Diversity

The Board and the Nominating Committee seek to achieve a variety of perspectives, experiences and occupational and personal backgrounds on the Board. As part of the search process for new directors, the Nominating Committee endeavors to include women and minority candidates within its broader pool of candidates from which Board nominees ultimately are considered holistically and chosen through a merit-based process.

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

Director Time Commitments

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

Stockholder Recommendations for Directors

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

Board Leadership Structure

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

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

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

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

Director Independence

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

Applying these standards, our Board reviews the independence of our directors, taking into account all relevant facts and circumstances. Our Board has determined that the following members of our Board are currently independent under Nasdaq listing rules: Drs. Henderson and Milligan, Ms. Stelzer and Messrs. Albers, Harwin and Kiselak. Dr. Turtle is not independent as he is our CEO, and Mr. McKenna is not independent due to his consulting arrangement with the Company.

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

Board Committees

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

Name	Audit Committee	Compensation Committee	Nominating Committee
Jeffrey Albers	X	Chair	
Peter Harwin			X
Michael Henderson	X		
Tomas Kiselak		X	
Mark McKenna			
Sandra Milligan		X	Chair
Laurie Stelzer	Chair		X
Cameron Turtle			
# of Meetings in 2025	5	5	2

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

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

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

The Compensation Committee may delegate its duties and responsibilities to one or more subcommittees. The committee may also delegate authority to review and approve the compensation of our employees to certain of our executive officers. Even where the committee does not delegate authority, our executive officers will typically make recommendations to the committee regarding compensation to be paid to our employees and the size of equity awards under our equity incentive plans but will not be present during voting or deliberations on their own compensation. The committee has the authority to engage outside advisors, such as compensation consultants, to assist it in carrying out its responsibilities. The committee engaged Alpine Rewards, LLC in 2025 ("Alpine") to provide advice regarding the amount and form of executive and director compensation. The committee reviewed Alpine's independence in light of SEC rules and has affirmatively determined that the work performed by Alpine does not raise any conflict of interest.

Nominating Committee. The primary responsibilities of our Nominating Committee are to engage in succession planning for the Board, identify individuals qualified to become members of the Board, recommend director candidates to

the Board, including for election or reelection to the Board at each annual stockholders' meeting, and perform a leadership role in shaping the Company's corporate governance. In addition, the committee is responsible for developing and recommending to the Board criteria for identifying and evaluating qualified director candidates and developing and recommending to the Board a set of corporate governance principles. The committee is also responsible for making recommendations to the Board concerning the size, structure, composition and functioning of the Board and its committees and oversees sustainability matters relevant to the Company's business, including Company policies, activities and opportunities.

Board Risk Oversight

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

- **The Audit Committee** has overall responsibility for overseeing the Company's practices with respect to risk assessment and management. Additionally, the committee is responsible for overseeing management of risks related to our financial statements and financial reporting process, compliance and information technology and cybersecurity.

- **The Compensation Committee** is responsible for overseeing management of risks related to our compensation policies and programs and human capital management practices.

- **The Nominating Committee** is responsible for overseeing management of risks related to director succession planning, corporate governance practices and sustainability matters.

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

Other Corporate Governance Practices and Policies

Director Attendance

The Board met seven (7) times during 2025. Each member of the Board attended at least 75% of the aggregate number of meetings of the Board and the committees on which he or she served during the period in which he or she was on the Board or committee.

Directors are encouraged to attend the annual meeting of stockholders. Eight (8) of our directors then serving on the Board attended our 2025 Annual Meeting of Stockholders.

Stockholder Communications

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

To enable the Company to speak with a single voice, as a general matter, senior management serves as the primary spokesperson for the Company and is responsible for communicating with various constituencies, including stockholders, on behalf of the Company. Directors may participate in discussions with stockholders and other constituencies on issues where Board-level involvement is appropriate. In addition, the Board oversees the Company's stockholder engagement efforts.

Code of Business Conduct and Ethics

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

Insider Trading Policy

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

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

Compensation Committee Interlocks

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

DIRECTOR COMPENSATION

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

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

Each non-employee director who initially joins our Board receives an initial grant of stock options having an aggregate grant date value of approximately $700,000 that vests in equal monthly installments over three years. Each non-employee director who is serving as of the date of the Annual Meeting will receive a grant of stock options with an aggregate grant date value approximately $350,000. Annual stock option grants vest in equal monthly installments over one year or, if earlier, upon the next Annual Meeting of Stockholders; however, beginning in 2026, such grants will instead vest in full upon the earlier of the first anniversary of the grant date or the next Annual Meeting of Stockholders. A director is only eligible to receive an annual stock option grant if the Annual Meeting is more than six months following the director's appointment to the Board. On May 29, 2025, each of our non-employee directors received a grant of stock options to

purchase 25,000 shares of our common stock. As shown below, the aggregate grant date value of such option awards granted to each non-employee director was $248,675; such amount was lower than the $350,000 aggregate grant date value prescribed by the program in light of stock price volatility between the date on which the number of options was calculated and the date of grant and responsible equity use considerations.

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

The following table provides information for the year ended December 31, 2025 regarding all compensation awarded to, earned by or paid to each person who served as a non-employee director for some portion of 2025. Employees who served on our Board during 2025 did not receive additional compensation for such service.

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)[1]	Total ($)
Jeffrey Albers	100,000	248,675	348,675
Peter Harwin	45,000	248,675	293,675
Michael Henderson	50,000	248,675	298,675
Tomas Kiselak	47,500	248,675	296,175
Mark McKenna	40,000	248,675	288,675
Sandra Milligan, M.D., J.D.	57,500	248,675	306,175
Laurie Stelzer	65,000	248,675	313,675

(1) The amounts reported in this column represent the aggregate grant date fair value of stock options granted to our non-employee directors during 2025, as computed in accordance with Accounting Standards Codification Topic 718 ("ASC 718"). For more information regarding the assumptions underlying the grant date fair value of stock options, please read Note 15 to our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2025. Note that the amounts reported in this column reflect the aggregate accounting cost for these awards, and do not necessarily correspond to the actual economic value that may be received by the non-employee directors from the awards. As of December 31, 2025, our non-employee directors held the following number of outstanding stock options: (i) Mr. Albers, 86,323; (ii) Mr. Harwin, 114,323; (iii) Dr. Henderson, 114,323; (iv) Mr. Kiselak, 114,323; (v) Mr. McKenna, 542,000 (including 477,000 options granted to Mr. McKenna in November 2023 for his service as a consultant prior to joining our Board, which vest over four years); (vi) Dr. Milligan, 46,980; and (vii) Ms. Stelzer, 86,323.

EXECUTIVE OFFICERS

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

Name	Age (as of April 10)	Position
Cameron Turtle[(1)]	36	Chief Executive Officer and Director
Scott Burrows	49	Chief Financial Officer
Heidy King-Jones	43	Chief Legal Officer and Corporate Secretary
Sheldon Sloan	68	Chief Medical Officer

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

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

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

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

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

COMPENSATION DISCUSSION & ANALYSIS

This Compensation Discussion and Analysis, or CD&A, provides an overview of our executive compensation philosophy, objectives, and design and each element of our executive compensation program with regard to the compensation awarded to, earned by, or paid to our named executive officers, or NEOs, during the fiscal year ended December 31, 2025. For 2025, all of our executive officers were NEOs, including:

Name	Title
Cameron Turtle	Chief Executive Officer
Scott Burrows	Chief Financial Officer
Sheldon Sloan	Chief Medical Officer
Heidy King-Jones	Chief Legal Officer and Corporate Secretary

Executive Summary

The Company's accomplishments in 2025 are directly tied to the performance of the Company's NEOs, and thus were an important factor in determining NEO compensation in 2025. During the year, the Company was able to achieve all of its objectives with respect to advancing its IBD and ex-IBD programs and establishing and resourcing the Company as a leader in the Immunology and Inflammation space.

In 2025, the Company significantly advanced its clinical programs. The Company successfully initiated a first-in-human trial evaluating SPY003 in healthy volunteers and reported positive interim phase 1 results for SPY002, SPY072 and SPY003. The Company also successfully initiated its Phase 2 SKYLINE and SKYWAY clinical trials in IBD and rheumatic diseases, respectively, in a timely manner.

The Company also successfully developed and executed on its 2025 investor relations, science communications and human resources plans, including maintaining robust investor and clinical community engagement throughout the year and growing its employee base to support the increased scale and complexity of the business. The Company further bolstered its financial resources by successfully raising over $310 million in net proceeds through an underwritten public offering and sales under its at-the-market offering program during 2025.

2025 Executive Compensation Highlights

In 2025, our compensation committee structured pay decisions for the NEOs to align with our compensation philosophy, stockholder interests, and overall business strategy, including:

- **Base salaries** – We made incremental adjustments to 2025 base salaries of our NEOs based on our review of roles, responsibilities and market competitiveness;
- **Annual bonuses** – Our annual bonus program was based on goals tied to advancing the portfolio and pipeline, plus broader corporate metrics. In 2025, we achieved each target result, all stretch goals and additional expansions of our pipeline and financial resources which resulted in an annual bonus payout of 130% of target; and
- **Equity grants** – Consistent with our annual grant practices since the closing of our reverse merger in 2023, we granted stock options to our NEOs in 2025 to align with stockholder interests and long-term company performance.

Overview of our Executive Compensation Program

The Compensation Committee annually reviews and either recommends to the Board (for our Chief Executive Officer) or approves (for our other executives) each NEO's compensation. The Compensation Committee is responsible for ensuring that compensation for the NEOs is consistent with the objectives of attracting and retaining highly qualified executives, tying pay to performance and Company strategy, aligning NEOs' incentives with long-term stockholder interests, and encouraging internal pay equity.

The Compensation Committee determines the appropriate level for each compensation component based on these overall compensation objectives. The Compensation Committee's philosophy is to strive to provide market competitive compensation and emphasize at-risk cash bonus opportunities and equity compensation that reflect the Company's performance goals and are commensurate with each NEO's scope of responsibility within the organization.

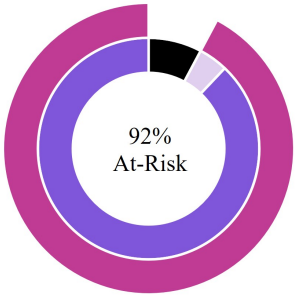
In overseeing our executive compensation program, our Compensation Committee seeks to ensure that our program is aligned with Company performance, our short- and long-term strategic priorities and stockholder interests. Accordingly, our executive compensation program aims to achieve the following objectives:

- **Motivate** our executives to achieve short-term and long-term financial and business objectives, reflecting our "pay for performance" culture
- **Attract and retain** executives by providing a total compensation package that is competitive with companies we compete with for talent.
- **Reward** our executives while keeping a significant portion of compensation at-risk.
- **Recognize** individual and company performance as a means to promote value creation for the Company and stockholders.

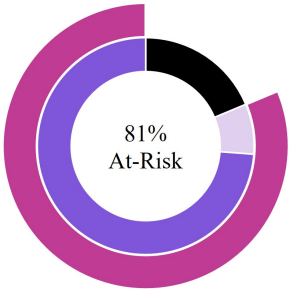
Compensation Mix

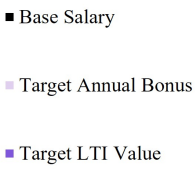
Given the significance of pay and performance alignment to our executive compensation philosophy, long-term equity incentive compensation makes up the largest component of each NEO's total target compensation each year, resulting in 92% of our Chief Executive Officer's compensation and 81% of the average of our other NEOs' compensation being "at risk." Total target compensation includes each NEO's base salary, target annual bonus and target long-term incentive award value, which in 2025 was granted as stock options. The Compensation Committee does not have any formal policies for allocating total compensation among the various components. Instead, the Compensation Committee relies on its judgment as well as the advice from its independent compensation consultant, including peer group practices. The pay mix for our NEOs reflected in the charts below was based on our compensation philosophy and practices described above, which is designed to be aligned with market competitive practices.

2025 CEO Target Compensation Mix



2025 Average Other NEO Target Compensation Mix





Our executive compensation program includes a number of governance best practices:

What We Do	What We Don't Do
• Majority of our NEOs' target compensation is "at risk" • Align executive pay with Company performance and stockholder interests • Retain an independent compensation consultant • Maintain an equity grant timing policy • Hold an annual say-on-pay vote • Employ a compliant clawback policy	• No excessive perquisites • No current dividend payments on unvested equity awards • No tax gross-ups on severance or perquisites • No excessive risk-taking in compensation programs • No hedging or pledging of our common stock

Process for Setting Executive Compensation

Role of Compensation Committee

Our executive compensation program is developed and overseen by our Compensation Committee. The purpose of our Compensation Committee is to assist the Board in discharging its responsibilities relating to compensation of the Company's executive officers and directors, including by overseeing our overall rewards philosophy, policies, and programs, evaluating the compensation and performance of our executive officers, and reviewing, approving, and modifying the terms of our compensation and benefit plans and programs as appropriate. Subject in certain circumstances to approval by the Board, our Compensation Committee has the sole authority to make final decisions with respect to our executive compensation program. For more information regarding the authority and responsibilities of our Compensation Committee, please refer to its charter, which is available via our Investor Relations website at ir.spyre.com.

Role of Chief Executive Officer and Management

In making decisions regarding our executive compensation program, our Compensation Committee takes into account the views and recommendations of management. Our Chief Executive Officer makes recommendations to our Compensation Committee with respect to the compensation for our NEOs, other than himself, based on market data provided by Alpine and his evaluation of each other NEO's individual performance and contributions to the Company, including recommendations regarding target annual compensation, annual incentive plan performance measures and long-term equity awards. Our Chief Executive Officer does not participate in, and is not present during, any deliberations or determinations of the Compensation Committee or the Board regarding his compensation. From time to time, various other members of management and other employees may be invited by the Compensation Committee to make presentations, to provide financial or other background information or advice or to otherwise participate in Compensation Committee meetings.

Compensation Consultant

During 2025, our Compensation Committee engaged Alpine Rewards ("Alpine") as its independent compensation consultant. Alpine assisted our Compensation Committee in designing the executive compensation program for 2025, which included review and recommendations regarding our 2025 peer group described below, a review and analysis of our target compensation levels and practices relative to the 2025 peer group, an evaluation of our non-employee director compensation program, and recommendations regarding the design of our annual and long-term incentive compensation, and an annual risk assessment. Other than its services as independent compensation consultant, Alpine did not provide any other services to us during 2025. After taking into consideration the factors listed in Nasdaq Listing Rule 5605(d)(3)(D), our Compensation Committee concluded that there are no conflicts of interest with respect to the engagement of Alpine by our Compensation Committee.

Peer Group

In September 2024, our Compensation Committee, in consultation with Alpine, reviewed our peer group to be used in establishing executive compensation for 2025. Our peer group focuses on U.S.-based, earlier-stage clinical biotechnology/ pharmaceutical companies (with priority placed on companies with a similar therapeutic focus) with a market capitalization ranging from $500 million to $4.5 billion and an employee population of less than 200 employees. Based on its review,

ACELYRIN, Aclaris Therapeutics, Inc., Allakos Inc., Alpine Immune Sciences, Inc., Cabaletta Bio, Inc., Morphic Holdings, Inc., RAPT Therapeutics, Inc., and Ventyx Biosciences, Inc. were removed from our peer group and Contineum Therapeutics, Inc., Disc Medicine, Inc., Dyne Therapeutics, Inc., Keros Therapeutics, Inc., Nurix Therapeutics, Inc., Stoke Therapeutics, Inc., Structure Therapeutics Inc., and Xencor Inc. were added to ensure the peer group remains appropriate. The 2025 peer group, which was approved by the Board, includes the following companies:

AnaptysBio, Inc.	Disc Medicine, Inc.	Nurix Therapeutics, Inc.
Apogee Therapeutics, Inc.	Dyne Therapeutics, Inc.	Pliant Therapeutics, Inc.
Arcellx, Inc.	IGM Biosciences, Inc.	Stoke Therapeutics, Inc.
Astria Therapeutics, Inc.	Janux Therapeutics, Inc.	Structure Therapeutics Inc.
Celldex Therapeutics, Inc.	Keros Therapeutics, Inc.	Vera Therapeutics, Inc.
Contineum Therapeutics, Inc.	Kymera Therapeutics, Inc.	Xencor Inc.

At the time of approval in September 2024, the Company ranked at the 48th percentile in market capitalization and the 20th percentile in employee population based on information available.

In August 2025, our Compensation Committee, in consultation with Alpine, evaluated our peer group and re-focused it on U.S.-based, pre-commercial biotechnology/pharmaceutical companies (with priority placed on companies with a similar therapeutic focus) with a market capitalization ranging from $400 million to $4.0 billion and an employee population of less than 200 employees. Based on its evaluation, 89bio, Inc., Dianthus Therapeutics, Inc., and Oruka Therapeutics, Inc. were added and Contineum Therapeutics, Inc., IGM Biosciences, Inc., and Pliant Therapeutics, Inc. were removed for the peer group used in establishing executive compensation for 2026 in order to ensure that the peer group appropriately reflects companies having a similar market capitalization, pipeline stage, employee population and other relevant factors.

Say-on-Pay Vote

Each year, we provide our stockholders the opportunity to cast a non-binding advisory vote on the compensation of our NEOs (commonly known as a "say-on-pay" vote). Our Board and our Compensation Committee consider the results of the say-on-pay vote in determining the compensation of our NEOs. At our 2025 Annual Meeting of Stockholders, approximately 93% of the votes cast approved the compensation of NEOs, a significant increase following our 2024 Annual Meeting of Stockholders, which saw only 62% of votes cast supporting our say-on-pay vote. In light of the significant support, our Board and our Compensation Committee did not make any material changes to the executive compensation program in response to the results of the say-on-pay vote.

Elements of Compensation

Base Salary

Each NEO's base salary is a fixed annual amount that is intended to compensate the NEO for performing specific job responsibilities and is based on the NEO's level of experience and requisite skills. Our Compensation Committee annually evaluates and approves (or recommends to the Board for approval for our Chief Executive Officer) each NEO's base salary. As part of this annual evaluation in December 2024, the Compensation Committee determined to increase the base salary for each of our NEOs in light of market data from our 2025 peer group provided by Alpine and their individual and Company performance. The table below sets forth the base salary as of December 31, 2025 for each NEO:

Named Executive Officer	Base Salary as of 12/31/2024	Base Salary as of 12/31/2025	Percentage Increase
Cameron Turtle	$ 625,000	$ 665,000	6.5%
Scott Burrows	$ 475,000	$ 490,000	3.2%
Sheldon Sloan	$ 496,000	$ 503,000	1.4%
Heidy King-Jones	$ 480,000	$ 490,000	2.1%

Annual Bonus Program

We provide our NEOs with the opportunity to earn annual cash incentives to encourage the achievement of corporate objectives. We established our annual bonus program to motivate our executives to achieve short-term financial and

business objectives, reflecting our "pay for performance" culture, resulting in a significant portion of NEO compensation tying directly to Company achievements. For each NEO, the target annual bonus opportunity is determined as a percentage of his or her base salary (as indicated in the table below) and is established by the Compensation Committee in consultation with Alpine, based on market data from companies in our peer group. No changes were made to our NEOs' target bonuses for 2025, which are set forth below:

Named Executive Officer	2025 Target Bonus (as a % of Base Salary)
Cameron Turtle	55 %
Scott Burrows	40 %
Sheldon Sloan	40 %
Heidy King-Jones	40 %

The Board approved the objectives and key targeted results and stretch goals applicable to the 2025 annual bonus program for our executives in December 2024. These milestones were intended to measure our performance in the following categories: Portfolio and Corporate, as further described below. The level of attainment of these performance milestones determines our NEOs' earned annual bonuses.

#	Objective	Weight	Summary of Key Result	Timing	Achieved
1	Portfolio: Advance IBD and ex-IBD Programs	80%	Readout topline Phase 1 data for SPY002 and SPY003 Prepare regulatory submissions for IBD and RA programs, execute on site activation plan for SKYLINE trial and commence RA study Advance preparations for Phase 3 development	Q2-Q4	100%
2	Portfolio: Additional Advancement of Pipeline	Stretch 10%	Evaluate additional product candidates Execute on site activation and patient enrollment plans for SKYLINE and RA trials	Q3-Q4	100%
3	Corporate: Establish and Resource Spyre as an I&I Leader	20%	Secure company investment and continue development and execution of plans across Finance and Human Resources functions to support Spyre's growth and business plans	Q1-Q4	100%
4	Corporate: Additional Support	Stretch 10%	Secure additional company investment	Q4	100%

At the end of 2025, the Board and the Compensation Committee reviewed the Company's performance against these performance measures and determined that performance was achieved at an aggregate of 130% of target, including 120% of target to recognize the timely achievement of each target result and all stretch goals, and an additional 10% of target to recognize the Company's additional performance of expanding its RA study to include RA, axSpA and PsA and securing additional company investment materially beyond stretch goal expectations. As a result, each NEO received an annual bonus for 2025 equal to 130% of target, as follows:

Named Executive Officer	2025 Target Bonus	2025 Annual Bonus
Cameron Turtle	$365,750	$475,475
Scott Burrows	$196,000	$254,800
Sheldon Sloan	$201,200	$261,560
Heidy King-Jones	$196,000	$254,800

Long-Term Incentive Compensation

For 2025, after taking into account the results of Alpine's market assessment, reviewing the practices of companies in our peer group and considering the important retentive value and performance alignment of our long-term incentive strategy, our Compensation Committee determined that it was appropriate to continue to use stock options as 100% of the annual long-term incentive awards granted to our NEOs.

In determining the target value of our NEOs' long-term incentive awards, the Compensation Committee considered the value of each NEO's existing outstanding equity awards and market data regarding the 50th and 75th percentiles of long-term incentive award values for similar executives at other companies in our peer group.

In light of these considerations, our Compensation Committee targeted a grant value of approximately $7,500,000 for Dr. Turtle and $1,950,000 for each of our other NEOs and the number of stock options to be granted to each NEO was calculated as explained in Note (2) of the table below. Accordingly, on January 15, 2025, Dr. Turtle received stock options to purchase 370,000 shares of our common stock and each of our other NEO's received stock options to purchase 95,500 shares of our common stock. The number of stock options granted were determined based on a 30-day average December 31, 2024. The annual stock options vest in equal monthly installments through the fourth anniversary of the grant date.

Named Executive Officer	2025 Target LTI Value ($)[(1)]	2025 Annual Stock Options Granted[(2)]	Grant Date Fair Value of Options Granted ($)[(3)]
Cameron Turtle	7,500,000	370,000	5,552,886
Scott Burrows	1,950,000	95,500	1,433,245
Sheldon Sloan	1,950,000	95,500	1,433,245
Heidy King-Jones	1,950,000	95,500	1,433,245

(1) Peer group information based on pre-commercial U.S.-based, earlier stage clinical biotechnology/pharmaceutical companies (with priority placed on companies with a similar therapeutic focus) with a market capitalization ranging from $500 million to $4.5 billion and an employee population of less than 200 employees.

(2) The number of stock options granted was calculated by converting the 2025 target long-term incentive value based on a 30-day average closing stock price of $24.94 per share as of December 31, 2024 and a Black-Scholes factor of approximately 81.92%. As a result, the 2025 target long-term incentive value differs from the grant date fair value reflected in this table and the "Summary Compensation Table" and "Grants of Plan-Based Awards Table" below.

(3) Amounts reported in this column represent the aggregate grant date fair value of stock options granted to the NEOs, as computed in accordance with FASB ASC Topic 718. See Note 15 to our consolidated financial statements in our Annual Report on Form 10-K for the year ended December 31, 2025 for more information regarding the assumptions used in calculating the grant date fair value of stock options.

Other Benefits and Perquisites

We maintain a tax-qualified 401(k) defined contribution plan that provides eligible U.S. employees, including our NEOs, with an opportunity to save for retirement on a tax-advantaged basis. Eligible employees may make voluntary contributions from their eligible pay, up to certain applicable annual limits set by the Internal Revenue Code of 1986, as amended. For 2025, we provided fully vested matching contributions equal to 100% of the first 3% of eligible compensation contributed by each employee, and 50% of the next 2% of eligible compensation contributed by each employee. Effective January 1, 2026, we provide fully vested matching contributions equal to 100% of all eligible compensation contributed by each employee up to a maximum of $14,000 per calendar year. Our NEOs are also eligible to participate in our other benefit programs generally available to all of our employees, including health and welfare benefits and our employee stock purchase plan, which allows our employees to purchase shares of our common stock at a discount using accumulated payroll contributions. We do not maintain, and have not historically maintained, any non-qualified deferred compensation or defined benefit pension plan, and we do not provide any material perquisites to our NEOs.

Other Compensation-Related Policies and Matters

Clawback Policy

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

Equity Grant Timing Policy and Practices

We maintain an Equity Grant Timing Policy (the "Equity Grant Policy"), which provides that it is the Company's policy to generally grant equity awards, including stock options, outside of blackout periods under our insider trading policy. With respect to grants of stock options to our named executive officers and to the extent a grant during a closed window is deemed necessary or appropriate by the Compensation Committee, awards typically may not occur during the period beginning four business days before and ending one business day after the filing of a Form 10-K or Form 10-Q or the filing or furnishing of a Form 8-K that contains material non-public information ("MNPI"). Under the Equity Grant Policy, annual equity grants to the Company's employees are typically granted within one week following the first regularly scheduled Compensation Committee meeting each year (or, with respect to grants to the Chief Executive Officer, within one week following the first regularly scheduled Board meeting each year). Grants to new hires generally occur on the first business day of each month for new hires who commenced employment during the previous month. Employees, including the named executive officers, may enroll to purchase shares under the terms of our ESPP, with purchase dates generally in June and December of each year using payroll deductions accumulated during the prior six-month period. During 2025, we did not time the disclosure of MNPI for the purpose of affecting the value of executive compensation.

Risk Assessment

Alpine provided an independent risk assessment of our compensation policies and programs in 2025. The assessment found that our executive and broad-based compensation policies and practices do not create risks that are reasonably likely to have a material adverse effect on the Company. Our Compensation Committee reviewed the results and does not believe that our executive and broad-based compensation policies and practices encourage excessive or unnecessary risk taking, and any risk inherent in our compensation programs is unlikely to have a material adverse effect on us.

COMPENSATION COMMITTEE REPORT

The Compensation Committee has reviewed and discussed with management the Compensation Discussion and Analysis required by Item 402(b) of Regulation S-K. Based on this review and discussion, the Compensation Committee recommended to the Board of Directors that the foregoing Compensation Discussion and Analysis be included in this Proxy Statement and incorporated by reference in our Annual Report on Form 10-K for the fiscal year ended December 31, 2025.

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

Jeffrey Albers (Chair)
Tomas Kiselak
Sandra Milligan, M.D., J.D.

EXECUTIVE COMPENSATION TABLES

Summary Compensation Table

The following table provides information regarding all plan and non-plan compensation awarded to, earned by or paid to each of our named executive officers for the years ended December 31, 2025, 2024 and 2023.

Name and Principal Position	Year	Salary ($)	Bonus ($)	Stock Awards ($)	Option Awards ($)[1]	Non-Equity Incentive Plan Compensation ($)[2]	All Other Compensation ($)[3]	Total ($)
Cameron Turtle	2025	665,000	—	—	5,552,886	475,475	14,000	6,707,361
Chief Executive Officer	2024	625,000	—	—	5,914,353	412,500	8,333	6,960,186
	2023	272,850	141,000	—	15,500,492	—	5,203	15,919,545
Scott Burrows	2025	490,000	—	—	1,433,245	254,800	14,000	2,192,045
Chief Financial Officer	2024	475,000	—	—	1,490,566	228,000	13,800	2,207,366
	2023	154,589	175,700	2,452,096	4,767,637	—	1,517	7,551,539
Sheldon Sloan	2025	503,000	—	—	1,433,245	261,560	14,000	2,211,805
Chief Medical Officer	2024	124,000	120,000	—	9,075,480	59,500	9,760	9,388,740
Heidy King-Jones	2025	490,000	—	—	1,433,245	254,800	14,000	2,192,045
Chief Legal Officer and Corporate Secretary	2024	480,000	—	—	1,341,509	230,400	—	2,051,909
	2023	168,724	62,700	—	6,356,857	—	—	6,588,281

(1) Amounts reported in this column for 2025 represent the aggregate grant date fair value of stock options granted to the NEOs, as computed in accordance with FASB ASC Topic 718. See Note 15 to our consolidated financial statements in our Annual Report on Form 10-K for the year ended December 31, 2025 for more information regarding the assumptions used in calculating the grant date fair value of stock options.

(2) Amounts reported in this column for 2025 represent the annual bonuses earned by the NEOs under the 2025 annual bonus program.

(3) Amounts reported in this column for 2025 include matching contributions under our 401(k) plan made during 2025.

Grants of Plan-Based Awards Table

The following table includes information regarding (i) annual bonus awards and (ii) stock options granted under the 2016 Plan, in each case, to the NEOs during 2025.

Name	Grant Date	Estimated Future Payouts Under Non-Equity Incentive Plan Awards (1)			All Other Option Awards: Number of Securities Underlying Options (#)(2)	Exercise or Base Price of Option Awards ($/Sh)	Grant Date Fair Value of Stock and Option Awards ($)(3)
		Threshold ($)	Target ($)	Maximum ($)			
Cameron Turtle		—	365,750	—			
	1/15/2025				370,000	21.66	5,552,886
Scott Burrows		—	196,000	—			
	1/15/2025				95,500	21.66	1,433,245
Sheldon Sloan		—	201,200	—			
	1/15/2025				95,500	21.66	1,433,245
Heidy King-Jones		—	196,000	—			
	1/15/2025				95,500	21.66	1,433,245

(1) Amounts in these columns represent the target potential payouts under the 2025 annual bonus program. The 2025 annual bonus program does not have a threshold or maximum potential payout. Please read "Compensation Discussion & Analysis—Elements of Compensation—Annual Bonus Program" above for more information.

(2) The stock options reflected in this column vest in equal monthly installments through the fourth anniversary of the grant date, subject to the NEO's continued service.

(3) Amounts reported in this column represent the aggregate grant date fair value of stock options granted to the NEOs, as computed in accordance with FASB ASC Topic 718. See Note 15 to our consolidated financial statements in our Annual Report on Form 10-K for the year ended December 31, 2025 for more information regarding the assumptions used in calculating the grant date fair value of stock options.

Narrative Disclosure to Summary Compensation Table and Grants of Plan-Based Awards Table

We have entered into offer letters with each of our NEOs in connection with their appointments (and, for Dr. Turtle, his promotion to Chief Executive Officer), which for Dr. Turtle was further amended in February 2024 (collectively, the "Offer Letters"). Each Offer Letter provides for an initial base salary, target bonus opportunity and stock option grant. Under the Offer Letters, the NEOs are eligible for certain payments or benefits upon certain terminations of employment, as described under "—Potential Payments Upon Termination of Change in Control" below. Dr. Sloan's Offer Letter also provided for a sign-on bonus of $120,000, which was subject to repayment in the event of a termination for cause or resignation without good reason prior to October 1, 2025.

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

Outstanding Equity Awards at December 31, 2025

The following table presents information regarding outstanding stock options, restricted stock units ("RSUs") and restricted stock held by each named executive officers as of December 31, 2025.

		Option Awards				Stock Awards	
Name	Grant Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested ($)[1]
Cameron Turtle	6/22/2023	1,182,429	709,458[2]	$7.50	6/22/2033		
	11/22/2023	194,791	179,209[3]	$10.39	11/22/2033		
	2/1/2024	127,302	150,448[2]	$25.86	2/1/2034		
	1/15/2025	84,791	285,209[2]	$21.66	1/15/2035		
	[4]					159,713[5]	5,232,198
Scott Burrows	9/1/2023	227,731	177,126[3]	$14.50	9/1/2033		
	2/1/2024	32,083	37,917[2]	$25.86	2/1/2034		
	1/15/2025	21,885	73,615[2]	$21.66	1/15/2035		
	12/22/2023					67,476[6]	2,210,514
Sheldon Sloan	10/1/2024	116,666	283,334[3]	$27.46	10/1/2034		
	1/15/2025	21,885	73,615[2]	$21.66	1/15/2035		
Heidy King-Jones	9/1/2023	303,642	236,168[3]	$14.50	9/1/2033		
	2/1/2024	28,875	34,125[2]	$25.86	2/1/2034		
	1/15/2025	21,885	73,615[2]	$21.66	1/15/2035		

(1) The market value was determined by multiplying the number of shares by $32.76, the closing price of our common stock as reported on the Nasdaq Global Select Market on December 31, 2025.

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

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

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

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

(6) These RSUs vest in equal installments on each of September 1, 2026 and September 1, 2027, subject to the NEO's continued service.

Option Exercises and Stock Vested Table

The following table reflects RSUs and restricted stock held by the NEOs which vested during 2025. No NEOs exercised any stock options during 2025.

Name	Stock Awards	
	Number of Shares Acquired on Vesting (#)	Value Realized on Vesting ($) [1]
Cameron Turtle	174,180	3,413,202
Scott Burrows	33,738	556,340
Sheldon Sloan	—	—
Heidy King-Jones	—	—

(1) The value of vested restricted stock and shares acquired from RSUs is determined based on the closing price of our common stock on the applicable vesting date.

Potential Payments Upon Termination or Change in Control

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

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

In addition, under each Offer Letter, in the event of the NEO's death or disability, all outstanding time-based equity awards will fully accelerate.

As used in the Offer Letters:

- "Cause" generally means (i) the NEO's dishonest statements or acts with respect to the Company or any affiliate of the Company, or any current or prospective customers, suppliers, vendors or other third parties with which such entity does business that results in or is reasonably anticipated to result in material harm to the Company; (ii) the NEO's conviction or plea of no contest to a felony or misdemeanor involving moral turpitude, deceit, dishonesty or fraud; (iii) the NEO's failure to perform his or her duties or responsibilities, subject to a 30-day cure period; (iv) the NEO's gross negligence, willful misconduct that results in or is reasonably anticipated to result in material harm to the Company; or (v) the NEO's violation of any material provision of any agreement with the Company or any written Company policies.

- "Change in Control" generally means (i) acquisition by any person of 50% or more of the total voting power of the Company, (ii) sale of all or substantially all of the Company's assets, (iii) the consummation of a merger or consolidation of the Company with any other corporation, other than a merger or consolidation where the holders of the Company's voting securities immediately prior thereto continue to represent at least 50% of the total voting power of the surviving entity in such transaction, (iv) any other transaction which qualifies as a "corporate transaction" under Section 424 of the Internal Revenue Code, or (v) a change in the effective control of the Company that occurs on the date that a majority of members of the Board is replaced during any 12 month period

by members of the Board whose appointment or election is not endorsed by a majority of the members of the Board prior to the date of the appointment or election.

- "Good Reason" generally means (i) a material diminution in the NEO's base salary or target bonus (excluding across-the-board reductions of less than 10%); (ii) a material geographic relocation or requirement to change the NEO's remote work location; (iii) a material reduction in the NEO's duties, authority or responsibilities; (or, for Dr. Sloan, a requirement that he report to any person other than the Chief Executive Officer); (iv) the failure of the Company to obtain the assumption of the Offer Letter by a successor; or (v) the material breach of any agreement between the NEO and the Company, in each case, subject to standard notice and cure periods.

Equity Awards

In addition to the accelerated vesting of certain outstanding equity awards as provided under each NEO's offer letter, Dr. Turtle's outstanding shares of restricted stock will fully vest upon a "Company Sale," which generally includes the sale of all or substantially all of the outstanding shares of capital stock, assets or businesses of the Company.

Quantification of Potential Payments

The table below sets forth the aggregate amounts that would have been payable to each NEO under their respective offer letter, as described above, assuming the applicable termination event, Change in Control or Company Sale occurred on December 31, 2025.

Name	Involuntary Termination ($)	CIC Involuntary Termination ($)	Company Sale ($)	Death / Disability ($)
Cameron Turtle				
Severance	1,030,750	1,546,125	—	—
COBRA Subsidy (1)	24,211	36,317	—	—
Equity Awards (2)	20,776,931	31,365,923	5,232,198	31,365,923
Total	**21,831,892**	**32,948,365**	**5,232,198**	**31,365,923**
Scott Burrows				
Severance	686,000	931,000	—	—
COBRA Subsidy (1)	34,416	51,625	—	—
Equity Awards (2)	3,339,205	6,523,588	—	6,523,588
Total	**4,059,622**	**7,506,213**	**—**	**6,523,588**
Sheldon Sloan				
Severance	578,450	704,200	—	—
COBRA Subsidy (1)	—	—	—	—
Equity Awards (2)	—	2,318,797	—	2,318,797
Total	**578,450**	**3,022,997**	**—**	**2,318,797**
Heidy King-Jones				
Severance	686,000	931,000	—	—
COBRA Subsidy (1)	34,416	51,625	—	—
Equity Awards (2)	2,837,929	5,365,017	—	5,365,017
Total	**3,558,346**	**6,347,641**	**—**	**5,365,017**

(1) Amounts in this row are based on premiums and individual elections in effect as of December 31, 2025, which are assumed for purposes of these calculations to remain in effect throughout the duration of the period in which the subsidization of COBRA benefits continues.

(2) Amounts in this row reflect the stock options, RSUs and restricted that would become vested upon the occurrence of the applicable event based on a per share price of $32.76, the closing price of our common stock on December 31, 2025, less the exercise price, if applicable.

CEO PAY RATIO

The 2025 annual total compensation of the median compensated of all our employees, other than Dr. Turtle, our Chief Executive Officer, was $437,242; Dr. Turtle's 2025 annual total compensation was $6,707,361; and the ratio of these amounts was approximately 1 to 15.

The pay ratio reported above is a reasonable estimate calculated in a manner consistent with SEC rules. For these purposes, we identified the median compensated employee using the sum of base salary paid in 2025 and bonus earned for 2025, which we annualized for all employees who were hired during 2025 and were employed as of December 31, 2025, but did not serve a full year with the Company. We identified our employee population as of December 31, 2025 based on our payroll records, resulting in an employee population of 102.

The SEC's rules for identifying the median compensated employee and calculating the pay ratio based on that employee's annual total compensation allow companies to adopt a variety of methodologies, to apply certain exclusions and to make reasonable estimates and assumptions that reflect their employee populations and compensation practices. As a result, the pay ratio reported by other companies may not be comparable to the pay ratio reported above, as other companies have different employee populations and compensation practices and may utilize different methodologies, exclusions, estimates and assumptions in calculating their own pay ratios.

PAY VERSUS PERFORMANCE

Our Compensation Committee approves and administers our executive compensation program to align executive compensation with stockholder interests by linking pay to performance. Our overall compensation program includes a mix of short-term and long-term components through our annual incentive plan and equity awards.
As required by Item 402(v) of Regulation S-K, we are providing the following information about the compensation reported to the NEOs in the Summary Compensation Table ("SCT"), the compensation actually paid ("CAP") to the NEOS and certain aspects of our financial performance. We did not use any financial performance measure to link CAP to the NEOs to our performance in 2025; accordingly, this disclosure does not present a company-selected measure in the table below.

During 2023, the Company completed a reverse merger, which brought in an entirely new pipeline of product candidates targeting IBD, and refreshed the Board and executive team to lead development of this new pipeline and sunset legacy asset development. Additionally, the Company has since expanded its pipeline into RD. As a result, pre-reverse merger performance is not relevant to the Company's current pipeline and strategy.

Pay-Versus-Performance Table

Year	Summary Compensation Table Total for Dr. Quinn ($)[1]	Summary Compensation Table Total for Mr. Kastenmayer ($)[1]	Summary Compensation Table Total for Mr. Goldberg ($)[1]	Summary Compensation Table Total for Mr. Alspaugh ($)[1]	Summary Compensation Table Total for Dr. Turtle ($)[1]	Compensation Actually Paid to Dr. Quinn ($)	Compensation Actually Paid to Mr. Kastenmayer ($)	Compensation Actually Paid to Mr. Goldberg ($)	Compensation Actually Paid to Mr. Alspaugh ($)	Compensation Actually Paid to Dr. Turtle ($)[3]
2025	N/A	N/A	N/A	N/A	$6,707,361	N/A	N/A	N/A	N/A	$13,869,330
2024	N/A	N/A	N/A	N/A	$6,960,186	N/A	N/A	N/A	N/A	$14,289,377
2023	N/A	N/A	$830,207	$8,360,029	$15,919,545	N/A	N/A	$122,206	$13,594,354	$48,710,501
2022	$2,392,254	$865,785	$1,832,485	N/A	N/A	$431,085	$318,380	$564,676	N/A[6]	N/A
2021	$2,623,186	N/A	N/A	N/A	N/A	$361,504	N/A	N/A	N/A[6]	N/A

			Value of Initial Fixed $100 Investment Based On:		
Year	Average Summary Compensation Table Total for Non-PEO NEOs ($)[2]	Average Compensation Actually Paid to Non-PEO NEOs ($)[3]	Total Stockholder Return Based on Initial Fixed $100 Investment ($)[4]	Peer Group Total Shareholder Return ($)[3]	Net Income (in thousands) ($)[5]
2025	$ 2,198,632	$ 3,144,403	$ 16.65	$ 124.75	$ (155,200)
2024	$ 5,798,053	$ 5,566,084	$ 11.83	$ 93.49	$ (208,018)
2023	$ 7,069,877	$ 9,563,596	$ 10.94	$ 94.03	$ (338,790)
2022	$ 1,049,862	$ 202,299	$ 5.72	$ 89.90	$ (83,815)
2021	$ 1,365,778	$ 712,689	$ 60.36	$ 100.02	$ (65,801)

(1) During years 2021-2025, the following individuals served as "principal executive officer" during the time periods set forth below:

Name	Dates as PEO During Years 2021 through 2025
Dr. Anthony Quinn	January 1, 2022 through August 23, 2022
Jim Kastenmayer	August 23, 2022 through November 29, 2022
Jeffrey M. Goldberg	November 29, 2022 through May 16, 2023
Jonathan Alspaugh	May 16, 2023 through August 31, 2023
Cameron Turtle	August 31, 2023 through December 31, 2025

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

(2) The dollar amounts reported in this column represent the average amount of total compensation report for our NEOs as a group (excluding our PEOs) for each covered fiscal year in the "Total" column of the SCT for each applicable

year. Please refer to "Executive Compensation Tables—Summary Compensation Table" above. The names of each NEO included for these purposes in each applicable year are as follows: (i) for 2025, Dr. Sheldon Sloan, Mr. Burrows, and Ms. King-Jones; (ii) for 2024, Dr. Sheldon Sloan and Mr. Burrows; (iii) for 2023, Mr. Burrows and Ms. King-Jones; (iv) for 2022, Mr. Alspaugh and Dr. Leslie Sloan; and (v) for 2021, Mr. Hanley and Dr. Leslie Sloan.

(3) The dollar amounts reported in these columns represent the amount of "compensation actually paid" to our PEOs or our NEOs as a group (excluding our PEOs), as computed in accordance with Item 402(v) of Regulation S-K, for each covered fiscal year. In accordance with these rules, these amounts reflect total compensation as set forth in the SCT, adjusted as shown below for 2025. Also shown below are the adjustments made to the compensation as set forth in the SCT for Dr. Turtle for 2023 and 2024, as the amounts previously reported in our proxy statement for the 2024 and 2025 Annual Meetings inadvertently excluded the change in value of his outstanding restricted stock awards. Equity values are calculated in accordance with FASB ASC Topic 718, and the valuation assumptions used to calculate fair values did not materially differ from those disclosed at the time of grant. The dollar amounts do not reflect the actual amount of compensation earned or received by or paid to the PEOs during the applicable fiscal year.

	Dr. Turtle			Average Non-PEO NEOs
	2023	**2024**	**2025**	**2025**
Summary Compensation Table Total	$ 15,919,545	$ 6,960,186	$ 6,707,361	$ 2,198,632
Less, value of "Stock Awards" and "Option Awards" reported in Summary Compensation Table	$ (15,500,492)	$ (5,914,353)	$ (5,552,886)	$ (1,433,245)
Plus, year-end fair value of outstanding and unvested equity awards granted in the year	$ 43,424,910	$ 4,152,217	$ 5,407,734	$ 1,395,785
Plus, fair value as of vesting date of equity awards granted and vested in the year	$ 2,479,557	$ 1,381,127	$ 1,080,512	$ 278,889
Plus (less), year over year change in fair value of outstanding and unvested equity awards granted in prior years	$ 2,386,981	$ 2,716,690	$ 9,132,676	$ 1,276,928
Plus (less), change in fair value from last day of prior fiscal year to vesting date for equity awards granted in prior years that vested in the year	$ —	$ 4,993,510	$ (2,906,067)	$ (572,586)
Compensation Actually Paid to PEOs	$ 48,710,501	$ 14,289,377	$ 13,869,330	$ 3,144,403

(4) Cumulative total stockholder return ("TSR") is calculated by dividing (a) the sum of (i) the cumulative amount of dividends during the measurement period, assuming dividend reinvestment, and (ii) the difference between our stock price at the end of the applicable measurement period and the beginning of the measurement period by (b) our stock price at the beginning of the measurement period. The beginning of the measurement period for each year in the table is December 31, 2020.

(5) The peer group used for this purpose is the following published industry index: NASDAQ Biotechnology (Total Return) Index, which is the Company's industry index utilized in the performance graph set forth in our Annual Report on Form 10-K for fiscal year 2025.

(6) The dollar amounts reported represent the amount of net income (loss) reflected in our audited financial statements for each covered fiscal year.

Financial Performance Measures

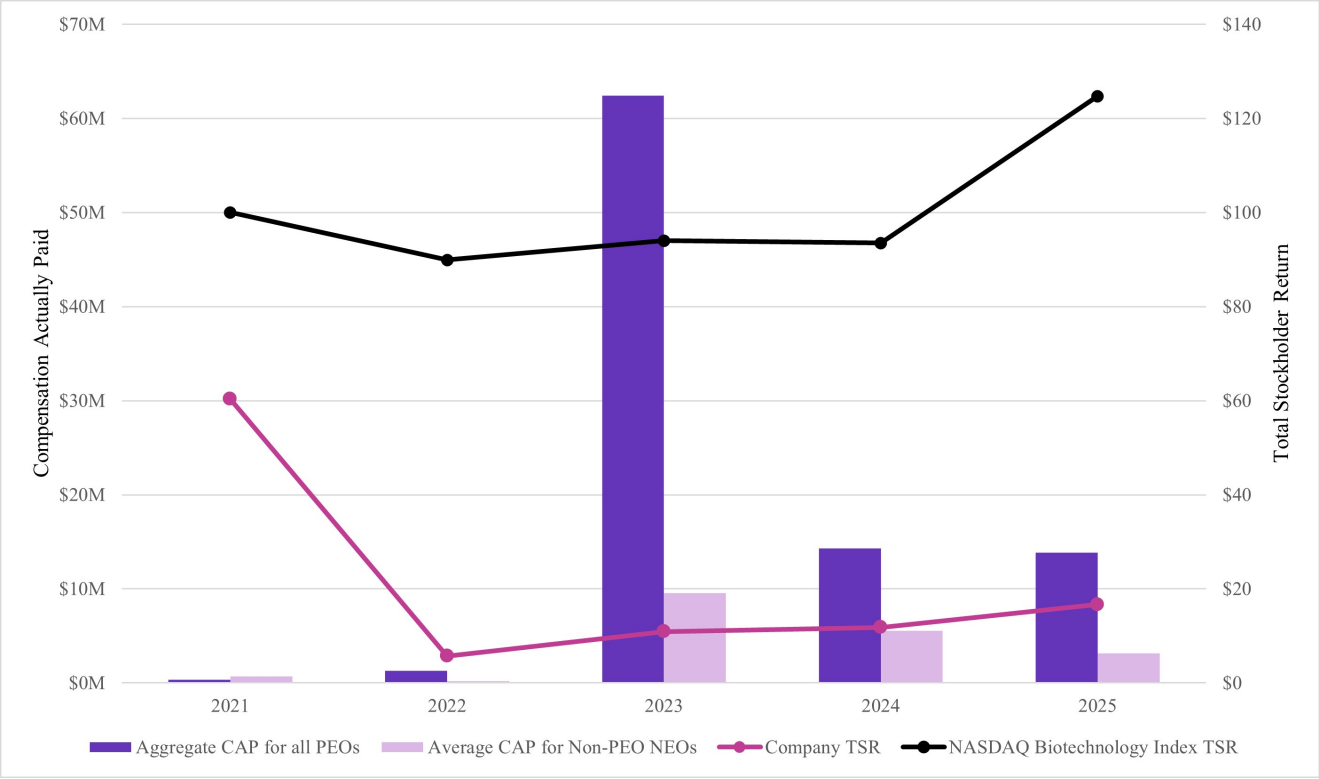
The Company's executive compensation program reflects a pay-for-performance philosophy. As a pre-revenue clinical stage biotechnology company, financial performance measures are not a component used to link executive compensation actually paid to the Company's performance. Instead, our annual bonus program uses solely strategic, non-financial performance metrics, including pre-clinical and clinical development of our pipeline, establishment of company investment

and progress towards the development and execution of our business plans, aimed at incentivizing our NEOs to develop our pipeline. For more information regarding the performance measures used in our executive compensation program, see "Compensation Discussion & Analysis—Elements of Compensation—Annual Bonus Program," above.

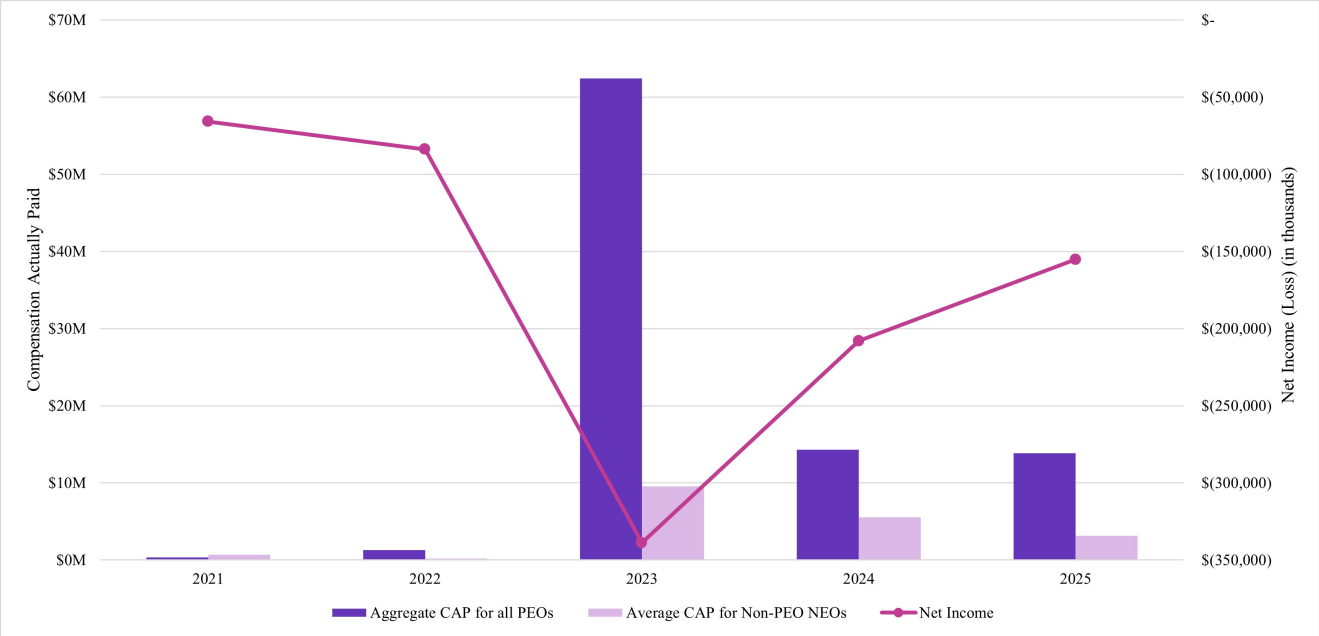
Analysis of Information Presented in the Pay Versus Performance Table

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

Compensation Actually Paid, Company TSR and Peer Group TSR



Compensation Actually Paid and Net Income



CERTAIN INFORMATION ABOUT OUR COMMON STOCK

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

The following table sets forth information, to the extent known by us or ascertainable from public filings, with respect to the beneficial ownership of our common stock as of February 12, 2026 by:

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

The column entitled "Shares Beneficially Owned" is based on a total of 78,540,164 shares of our common stock outstanding as of February 12, 2026.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock subject to options that are currently exercisable or exercisable within 60 days of the date of this table or subject to conversion of preferred stock up to applicable beneficial ownership limitations are considered outstanding and beneficially owned by the person holding the options or preferred stock, as applicable, for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise indicated in the table below, addresses of named beneficial owners are in care of Spyre Therapeutics, Inc., 221 Crescent Street, Building 23, Suite 105, Waltham, MA 02453.

Name of beneficial owner	Shares beneficially owned	
	Number	Percentage
5% Stockholders:		
Fairmount Healthcare Fund II L.P. [(1)]	8,271,021	9.99%
FMR LLC [(2)]	7,623,881	9.71%
BlackRock, Inc. [(3)]	3,962,635	5.05%
Named Executive Officers and Directors:		
Scott Burrows [(4)]	364,008	*
Heidy King-Jones [(5)]	421,515	*
Sheldon Sloan [(6)]	186,604	*
Cameron Turtle [(7)]	2,467,741	3.07%
Jeffrey Albers [(8)]	98,404	*
Peter Harwin [(1)(9)]	8,787,215	10.60%
Michael Henderson, M.D. [(10)]	278,762	*
Tomas Kiselak [(1)(11)]	8,787,215	10.60%
Mark McKenna [(12)]	327,971	*
Sandra Milligan [(13)]	34,265	*
Laurie Stelzer [(14)]	71,044	*
All current executive officers and directors as a group (11 persons) [(15)]	13,553,723	15.69%

* Represents beneficial ownership of less than one percent.

(1) Based solely upon a Schedule 13D/A filed on October 17, 2025 and the Company's records. Consists of (i) 4,018,101 shares of common stock and (ii) 4,252,920 shares of common stock issuable upon the conversion of 106,323 shares of Series A Preferred Stock held by Fairmount Healthcare Fund II LP ("Fund II"). Excludes shares of common stock issuable upon the conversion of shares of Series A Preferred Stock and Series B Preferred Stock held by Fund II in excess of the beneficial ownership limitation of 9.99%, which such limitation restricts Fairmount and its affiliates from converting those shares of preferred stock that would result in Fairmount and its affiliates owning, after conversion, a number of shares of common stock in excess of the applicable ownership limitation. Fairmount serves as investment manager for Fund II. Fund II has delegated to Fairmount Funds Management LLC ("Fairmount") the sole power to vote and the sole power to dispose of all securities held in Fund II's portfolio. Because Fund II has divested itself of voting and investment power over the securities it holds and may not revoke that delegation on less than 61 days' notice, Fund II disclaims beneficial ownership of the securities it holds. As managing members of Fairmount, Peter Harwin and Tomas Kiselak may be deemed to have voting and investment power over the shares held by Fund II. Fairmount, Peter Harwin and Tomas Kiselak disclaim beneficial ownership of such shares, except to the extent of any pecuniary interest therein. The address of each of these persons and entities is 200 Barr Harbor Drive, Suite 400, West Conshohocken, PA 19428.

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

(3) Based solely upon a Schedule 13G/A filed on July 16, 2025 (the "BlackRock 13G/A"). According to the BlackRock 13G/A, includes sole voting power with respect to 3,869,094 shares, shared voting power with respect to 0 shares, sole dispositive power with respect to 3,962,635 shares, and shared dispositive power with respect to 0 shares. The business address of BlackRock, Inc. is 50 Hudson Yards New York, NY 10001.

(4) Consists of (i) 30,518 shares of common stock held by Mr. Burrows and (ii) options exercisable for 333,490 shares of common stock within 60 days of the date of this table.

(5) Consists of (i) 2,159 shares of common stock held by Ms. King-Jones and (ii) options exercisable for 419,356 shares of common stock within 60 days of the date of this table.

(6) Consists of options exercisable for 186,604 shares of common stock within 60 days of the date of this table.

(7) Consists of (i) 657,540 shares of common stock held by Dr. Turtle and (ii) options exercisable for 1,810,201 shares of common stock within 60 days of the date of this table.

(8) Consists of (i) 27,360 shares of common stock held by Sessions LLC, which may be deemed to be indirectly beneficially owned by Mr. Albers, and (ii) options exercisable for 71,044 shares of common stock within 60 days of the date of this table.

(9) Includes (i) 406,038 shares of common stock held by Mr. Harwin; and (ii) options exercisable for 110,156 shares of common stock within 60 days of the date of this table.

(10) Consists of (i) 168,606 shares of common stock held by Dr. Henderson; and (ii) options exercisable for 110,156 shares of common stock within 60 days of the date of this table.

(11) Includes (i) 406,038 shares of common stock held by Mr. Kiselak; and (ii) options exercisable for 110,156 shares of common stock within 60 days of the date of this table.

(12) Consists of options exercisable for 327,971 shares of common stock within 60 days of the date of this table.

(13) Consists of options exercisable for 34,265 shares of common stock within 60 days of the date of this table.

(14) Consists of options exercisable for 71,044 shares of common stock within 60 days of the date of this table.

(15) Consists of (i) 5,716,360 shares of common stock; (ii) 4,252,920 shares of common stock issuable upon the exercise of Series A Preferred Stock; and (iii) options exercisable for 3,584,443 shares of common stock within 60 days of the date of this table.

Securities Authorized for Issuance Under Equity Compensation Plans

The following table presents information as of December 31, 2025 with respect to compensation plans under which shares of our common stock may be issued.

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights (#)[1]	Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights ($)[2]	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (a)) (#)[3]
	(a)	(b)	(c)
Equity Compensation Plans Approved by Security Holders:			
2016 Equity Incentive Plan	4,827,082	$ 18.40	5,983,632[4]
2016 Employee Stock Purchase Plan	—	N/A	1,056,096
Equity Compensation Plans Not Approved by Security Holders:			
2018 Equity Inducement Plan	6,620,097	$ 14.33	840,343
Total	**11,447,179**	**$ 16.05**	**7,880,071**

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

(2) This column reflects the weighted-average exercise price of stock options granted under the listed equity compensation plan that were outstanding as of December 31, 2025. RSUs reflected in column (a) are not reflected in this column as they do not have an exercise price.

(3) This column reflects the total shares of our common stock remaining available for issuance under the listed equity compensation plan as of December 31, 2025.

(4) The 2016 Plan provides for an automatic increase in the number of shares reserved for issuance thereunder on January 1 of each year through January 1, 2028 equal to (a) 5% of the number of issued and outstanding shares of common stock on December 31 of the immediately preceding year, or (b) a lesser amount as approved by the Board each year. Pursuant to this provision, the number of shares reserved for grant and issuance under the 2016 Plan increased by 4,711,544 shares on January 1, 2026.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Other than the executive officer and director compensation arrangements disclosed above under "Corporate Governance—Director Compensation" and "Compensation Discussion & Analysis," below we describe the transactions to which we were a party since January 1, 2025, in which the amount involved exceeded $120,000 and in which our directors, executive officers, holders of more than 5% of our common stock, or members of their immediate family had a direct or indirect material interest.

Related Party Transactions

Spyre's Relationships with Paragon, Parapyre and Fairmount

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

In connection with the Asset Acquisition, we assumed the rights and obligations of Pre-Merger Spyre under that certain antibody discovery and option agreement, dated May 25, 2023 and subsequently amended and restated on September 29, 2023 and May 14, 2024, by and among the Company, Paragon and Parapyre (the "Paragon Agreement"), pursuant to which we have exercised the option to acquire intellectual property license rights to or have the option to acquire intellectual property license rights with respect to certain research programs, including with respect to our product candidates. Under the Paragon Agreement, we are obligated to compensate Paragon on a quarterly basis for its services performed under each research program based on the actual costs incurred with mark-up costs pursuant to the terms of the Paragon Agreement. As of the date of the Asset Acquisition, Pre-Merger Spyre had incurred total expenses of $19.0 million under the Paragon Agreement since inception, inclusive of a $3.0 million research initiation fee that was due upon signing of the Paragon Agreement and $16.0 million of reimbursable expenses under the Paragon Agreement for historical costs incurred by Paragon. As of the closing of the Asset Acquisition, $19.0 million was unpaid and was assumed by us through the Asset Acquisition. As of the year ended December 31, 2025, approximately $14 thousand was unpaid and owed to Paragon under the Paragon Agreement. Furthermore, following our amendment and restatement of the Paragon Agreement on September 29, 2023, we were obligated to provide certain equity grants to Parapyre upon the completion of each of the calendar years ending on December 31, 2023 and December 31, 2024 to purchase 1% of the then outstanding shares of our common stock, on a fully diluted basis, on the last business day of each applicable calendar year, at the fair market value determined by the Board (the "Parapyre Option Obligation"). We settled such 2023 and 2024 obligations by issuing Parapyre warrants to purchase 684,407 and 848,184 shares of common stock, respectively, less the $21.52 and $23.28 per share exercise price of each warrant, respectively. As of December 31, 2024, none of the warrants issued to Parapyre have been exercised.

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

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

milestones, including a $1.5 million fee for nomination of a development candidate, as applicable, and a further milestone payment of $2.5 million upon the first dosing of a human patient in a Phase 1 trial.

Subject to the execution of the option to acquire the intellectual property rights related to an additional research program pursuant to the Paragon Agreement, we expect to be obligated to make similar payments upon and following the execution of a license agreement with respect to such research program. Our option available under the Paragon Agreement with respect to such additional program remains unexercised.

Related Party Transaction Policy

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

OTHER MATTERS

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

Pursuant to Rule 14a-8 of the Exchange Act, stockholders who wish to submit proposals for inclusion in the proxy statement for the 2027 Annual Meeting of Stockholders must send such proposals to our Corporate Secretary at the address set forth on the first page of this Proxy Statement. Such proposals must be received by us as of the close of business (6:00 p.m. Eastern Time) on December 11, 2026 and must comply with Rule 14a-8 of the Exchange Act. The submission of a stockholder proposal does not guarantee that it will be included in the proxy statement.

As set forth in our Bylaws, if a stockholder intends to make a nomination for director election or present a proposal for other business (other than pursuant to Rule 14a-8 of the Exchange Act) at the 2027 Annual Meeting of Stockholders, the stockholder's notice must be received by our Corporate Secretary at the address set forth on the first page of this Proxy Statement no earlier than the 120th day and no later than the close of business on the 90th day before the anniversary of the last annual meeting; provided, however, that if the date of the annual meeting is more than 30 days before or more than 60 days after such anniversary date, the stockholder's notice must be delivered not earlier than the close of business on the 120th day prior to such annual meeting and not later than the close of business on the later of the 90th day prior to such annual meeting or the 10th day following the date on which the first public announcement of the date of such annual meeting is made by the Company. Therefore, unless the 2027 Annual Meeting of Stockholders is more than 30 days before or more than 60 days after the anniversary of the Annual Meeting, notice of proposed nominations or proposals (other than pursuant to Rule 14a-8 of the Exchange Act) must be received by our Corporate Secretary no earlier than January 27, 2027 and no later than the close of business on February 26, 2027. Any such director nomination or stockholder proposal must be a proper matter for stockholder action and must comply with the terms and conditions set forth in our Bylaws (which includes the timing and information required under Rule 14a-19 of the Exchange Act). If a stockholder fails to meet these deadlines or fails to satisfy the requirements of Rule 14a-4 of the Exchange Act, we may exercise discretionary voting authority under proxies we solicit to vote on any such proposal as we determine appropriate. We reserve the right to reject, rule out of order or take other appropriate action with respect to any nomination or proposal that does not comply with these and other applicable requirements.

Delivery of Documents to Stockholders Sharing an Address

A number of brokerage firms have adopted a procedure approved by the SEC called "householding." Under this procedure, certain stockholders who have the same address and do not participate in electronic delivery of proxy materials will receive only one copy of the proxy materials, including this Proxy Statement, the Notice and our Annual Report on Form 10-K for the year ended December 31, 2025, until such time as one or more of these stockholders notifies us that they wish to receive individual copies. This procedure helps to reduce duplicate mailings and save printing costs and postage fees, as well as natural resources. If you received a "householding" mailing this year and would like to have additional copies of the proxy materials mailed to you, please send a written request to our Corporate Secretary at the address set forth on the first page of this Proxy Statement, or call (617) 651-5940, and we will promptly deliver the proxy materials to you. Please contact your broker if you received multiple copies of the proxy materials and would prefer to receive a single copy in the future, or if you would like to opt out of "householding" for future mailings.

Availability of Additional Information

We will provide, free of charge, a copy of our Annual Report on Form 10-K for the year ended December 31, 2025, including exhibits, on the written or oral request of any stockholder of the Company. Please send a written request to our Corporate Secretary at the address set forth on the first page of this Proxy Statement, or call the number above.

ANNEX A

SPYRE THERAPEUTICS, INC.

AMENDED AND RESTATED 2016 EMPLOYEE STOCK PURCHASE PLAN

(as amended and restated effective January 1, 2026)

1. **PURPOSE.** Spyre Therapeutics, Inc. originally adopted this Plan effective as of the date of the initial public offering of the Common Stock and has subsequently amended and restated this Plan to be effective as of January 1, 2026 (the "***Effective Date***"). The purpose of this Plan is to provide eligible employees of the Company and the Participating Corporations with a means of acquiring an equity interest in the Company and to enhance such employees' sense of participation in the Company's affairs. Capitalized terms not defined elsewhere in the text are defined in Section 28.

2. **ESTABLISHMENT OF PLAN; SHARE RESERVE**.

(a) The Company proposes to grant rights to purchase shares of Common Stock to eligible employees of the Company and its Participating Corporations pursuant to this Plan. The Company intends this Plan to qualify as an "employee stock purchase plan" under Section 423 of the Code (including any amendments to or replacements of such Section), and this Plan shall be so construed, although the Company makes no undertaking or representation to maintain such qualification. Any term not expressly defined in this Plan but defined in Section 423 of the Code shall have the definition provided by Section 423 of the Code. In addition, with regard to offers of options to purchase shares of Common Stock under the Plan to employees working for a Subsidiary or an Affiliate outside the United States, this Plan authorizes the grant of options under a Non-Section 423 Component that is not intended to meet the requirements of Section 423 of the Code provided that, to the extent necessary under Section 423 of the Code, the other terms and conditions of this Plan are met.

(b) Subject to Section 14, as of the Effective Date, a total of 1,056,096 shares of Common Stock is reserved for issuance under this Plan. The number of shares initially reserved for issuance under this Plan and the maximum number of shares that may be issued under this Plan shall be subject to adjustments effected in accordance with Section 14. Any or all such shares may be granted under the Section 423 Component.

3. **ADMINISTRATION.** The Plan will be administered by the Committee. Subject to the provisions of this Plan and the limitations of Section 423 of the Code or any successor provision in the Code, all questions of interpretation or application of this Plan shall be determined by the Committee and its decisions shall be final and binding upon all eligible employees and Participants. The Committee will have full and exclusive discretionary authority to construe, interpret and apply the terms of this Plan, to determine eligibility, to designate the Participating Corporations, to determine whether Participating Corporations shall participate in the Section 423 Component or Non-Section 423 Component and to decide upon any and all claims filed under the Plan. Every finding, decision and determination made by the Committee will, to the full extent permitted by law, be final and binding upon all parties. Notwithstanding any provision to the contrary in this Plan, the Committee may adopt rules, sub-plans, and/or procedures relating to the operation and administration of this Plan designed to comply with local laws, regulations or customs or to achieve tax, securities law or other objectives for eligible employees outside of the United States. The Committee will have the authority to determine the Fair Market Value of the Common Stock (which determination shall be final, binding and conclusive for all purposes) in accordance with Section 8 below and to interpret Section 8 of this Plan in connection with circumstances that impact the Fair Market Value. Members of the Committee shall receive no compensation for their services in connection with the administration of this Plan, other than standard fees as established from time to time by the Board for services rendered by Board members serving on Board committees. All expenses incurred in connection with the administration of this Plan shall be paid by the Company. For purposes of this Plan, the Committee may designate separate offerings under the Plan (the terms of which need not be identical) in which eligible employees of one or more Participating Corporations will participate, even if the dates of the applicable Offering Periods of each such offering are identical.

4. **ELIGIBILITY**.

(a) Any employee of the Company or the Participating Corporations is eligible to participate in an Offering Period under this Plan, except that one or more of the following categories of employees may be

excluded from eligibility under this Plan by the Committee (other than where such exclusion is prohibited by applicable law):

(i) employees who are customarily employed for 20 hours or less per week;

(ii) employees who are customarily employed for five months or less in a calendar year; and

(iii) employees who do not meet any other eligibility requirements that the Committee may choose to impose (within the limits permitted by the Code).

For purposes of the Plan, the employment relationship shall be treated as continuing intact while the individual is on sick leave or other leave of absence approved by the Company. Where the period of leave exceeds 90 days and the individual's right to reemployment is not guaranteed either by statute or by contract, the employment relationship shall be deemed to have terminated on the 91st day of such leave. Notwithstanding the foregoing, an individual shall not be eligible if his or her participation in this Plan is prohibited by the law of any country having jurisdiction over him or her, if complying with the laws of the applicable country would cause the Plan to violate Section 423 of the Code, or if he or she is subject to a collective bargaining agreement that does not provide for participation in this Plan.

(b) No employee who, together with any other person whose stock would be attributed to such employee pursuant to Section 424(d) of the Code, owns stock or holds options to purchase stock possessing 5% or more of the total combined voting power or value of all classes of stock of the Company or its Parent or Subsidiary or who, as a result of being granted an option under this Plan with respect to such Offering Period, would own stock or hold options to purchase stock possessing 5% or more of the total combined voting power or value of all classes of stock of the Company or its Parent or Subsidiary shall be granted an option to purchase Common Stock under this Plan. Notwithstanding the foregoing, the rules of Section 424(d) of the Code shall apply in determining share ownership and the extent to which shares held under outstanding equity awards are to be treated as owned by the employee.

5. **OFFERING DATES**.

(a) Each Offering Period of this Plan may be of up to 27 months' duration and shall commence and end at the times designated by the Committee. Each Offering Period shall consist of one Purchase Period during which Contributions made by Participants are accumulated under this Plan.

(b) An Offering Period shall commence on the Effective Date and shall end with the Purchase Date that occurs on June 30, 2026 or another date selected by the Committee which is approximately six months after the commencement of the initial Offering Period, but no more than 27 months after the commencement of the initial Offering Period. The initial Offering Period shall consist of one Purchase Period. Thereafter, a six-month Offering Period shall commence on each July 1 and January 1, with each such Offering Period also consisting of one six-month Purchase Period, except as otherwise provided by an applicable sub-plan, or on such other date determined by the Committee. The Committee may at any time establish a different duration for an Offering Period or Purchase Period to be effective after the next scheduled Purchase Date, up to a maximum duration of 27 months.

(c) To the extent applicable, if the Fair Market Value on the first day of the current Offering Period in which a Participant is enrolled is higher than the Fair Market Value on the first day of any subsequent Purchase Period, the current Offering Period shall end, and Participant shall be automatically enrolled in the subsequent Offering Period, as specified under Section 5(a) or Section 5(b), as applicable. Any funds accumulated in a Participant' s account prior to the first day of such subsequent Offering Period will be applied to the purchase of shares on the Purchase Date immediately prior to the first day of such subsequent Offering Period, if any.

6. **PARTICIPATION IN THIS PLAN**.

(a) Any employee who is an eligible employee determined in accordance with Section 4 and was a participant of the offering period under the Plan that ended immediately prior to its amendment and restatement on January 1, 2026 will be automatically enrolled in the initial Offering Period under this Plan. With respect to

subsequent Offering Periods, any eligible employee determined in accordance with Section 4 will be eligible to participate in this Plan, subject to the requirement of Section 6(b) hereof and the other terms and provisions of this Plan.

(b) With respect to Offering Periods after the initial Offering Period, a Participant may elect to participate in this Plan by submitting an enrollment agreement prior to the commencement of the Offering Period (or such earlier date as the Committee may determine) to which such agreement relates.

(c) Once an employee becomes a Participant in an Offering Period, then such Participant will automatically participate in each subsequent Offering Period commencing immediately following the last day of the prior Offering Period unless the Participant withdraws or is deemed to withdraw from this Plan or terminates further participation in an Offering Period as set forth in Section 11 below. A Participant who is continuing participation pursuant to the preceding sentence is not required to file any additional enrollment agreement in order to continue participation in this Plan; a Participant who is not continuing participation pursuant to the preceding sentence is required to file an enrollment agreement prior to the commencement of the Offering Period (or such earlier date as the Committee may determine) to which such agreement relates.

7. **GRANT OF OPTION ON ENROLLMENT**. Becoming a Participant with respect to an Offering Period will constitute the grant (as of the Offering Date) by the Company to such Participant of an option to purchase on the Purchase Date up to that number of shares of Common Stock of the Company determined by a fraction, the numerator of which is the amount accumulated in such Participant's Contribution account during such Purchase Period and the denominator of which is the Purchase Price (as described in Section 8 below). The maximum amount that the Participant may contribute during any Purchase Period shall be 15% of the Participant's Compensation for such Purchase Period or such other percentage as determined by the Committee prior to the start of the Purchase Period, and the number of shares of Common Stock subject to any option granted pursuant to this Plan shall not exceed the lesser of (x) the maximum number of shares set by the Committee pursuant to Section 10(b) below with respect to the applicable Purchase Date, or (y) the maximum number of shares which may be purchased pursuant to Section 10(a) below with respect to the applicable Purchase Date.

8. **PURCHASE PRICE**. The Purchase Price per share at which a share of Common Stock will be sold in any Offering Period shall be 85% of the lesser of:

(a) The Fair Market Value on the Offering Date; or

(b) The Fair Market Value on the Purchase Date.

9. **PAYMENT OF PURCHASE PRICE; CONTRIBUTION CHANGES; SHARE ISSUANCES**.

(a) The Purchase Price shall be accumulated by regular payroll deductions made during each Offering Period, unless the Committee determines with respect to categories of Participants outside the United States that Contributions may be made in another form due to local legal requirements. The Contributions are made as a percentage of the Participant's Compensation in 1% increments not less than 1%, nor greater than 15% or such other limit set by the Committee. "***Compensation***" shall mean base salary (or in foreign jurisdictions, equivalent cash compensation); however, the Committee may at any time prior to the beginning of an Offering Period determine that for that and future Offering Periods, Compensation shall mean all cash compensation reported on the employee's Form W-2 or corresponding local country tax return, including without limitation base salary or regular hourly wages, bonuses, incentive compensation, commissions, overtime, shift premiums, and draws against commissions. For purposes of determining a Participant's Compensation, any election by such Participant to reduce his or her regular cash remuneration under Sections 125 or 40l(k) of the Code (or in foreign jurisdictions, equivalent salary deductions) shall be treated as if the Participant did not make such election. Contributions shall commence on the first payday following the last Purchase Date and shall continue to the end of the Offering Period unless sooner altered or terminated as provided in this Plan. Notwithstanding the foregoing, the terms of any sub-plan may permit matching shares without the payment of any purchase price.

(b) A Participant may decrease the rate of Contributions during an Offering Period by filing with the Company or a third party designated by the Company a new authorization for Contributions, with the new rate to become effective no later than the second payroll period commencing after the Company's receipt of the authorization and continuing for the remainder of the Offering Period unless changed as described below. A

decrease in the rate of Contributions may be made once during an Offering Period, but up to twice during the initial Offering Period, or more frequently under rules determined by the Committee. A Participant may increase or decrease the rate of Contributions for any subsequent Offering Period by filing with the Company or a third party designated by the Company a new authorization for Contributions prior to the beginning of such Offering Period, or such other time period as specified by the Committee.

(c) A Participant may reduce his or her Contribution percentage to zero during an Offering Period by filing with the Company or a third party designated by the Company a request for cessation of Contributions. Such reduction shall be effective beginning no later than the second payroll period after the Company' s receipt of the request and no further Contributions will be made for the duration of the Offering Period. Contributions credited to the Participant's account prior to the effective date of the request shall be used to purchase shares of Common Stock in accordance with Subsection (e) below. A reduction of the Contribution percentage to zero shall be treated as such Participant' s withdrawal from such Offering Period and the Plan, effective as of the day after the next Purchase Date following the filing date of such request with the Company.

(d) All Contributions made for a Participant are credited to his or her book account under this Plan and are deposited with the general funds of the Company, except to the extent local legal restrictions outside the United States require segregation of such Contributions. No interest accrues on the Contributions, except to the extent required due to local legal requirements. All Contributions received or held by the Company may be used by the Company for any corporate purpose, and the Company shall not be obligated to segregate such Contributions, except to the extent necessary to comply with local legal requirements outside the United States.

(e) On each Purchase Date, so long as this Plan remains in effect and provided that the Participant has not submitted a signed and completed withdrawal form before that date which notifies the Company that the Participant wishes to withdraw from that Offering Period under this Plan and have all Contributions accumulated in the account maintained on behalf of the Participant as of that date returned to the Participant, the Company shall apply the funds then in the Participant's account to the purchase of whole shares of Common Stock reserved under the option granted to such Participant with respect to the Offering Period to the extent that such option is exercisable on the Purchase Date. The Purchase Price per share for such automatic purchase shall be as specified in Section 8 of this Plan. Any fractional share, as calculated under this Subsection (e), shall be rounded down to the next lower whole share, unless the Committee determines with respect to all Participants that any fractional share shall be credited as a fractional share. Any amount remaining in a Participant's account on a Purchase Date that is less than the amount necessary to purchase a full share of Common Stock shall be returned to the Participant, without interest (except to the extent necessary to comply with local legal requirements outside the United States); however, the Committee may provide that such amounts may be carried forward into the next Purchase Period or Offering Period, as the case may be. In the event that this Plan has been oversubscribed, all funds not used to purchase shares on the Purchase Date shall be returned to the Participant, without interest (except to the extent required due to local legal requirements outside the United States). No Common Stock shall be purchased on a Purchase Date on behalf of any employee whose participation in this Plan has terminated prior to such Purchase Date, except to the extent required due to local legal requirements outside the United States.

(f) As promptly as practicable after the Purchase Date, the Company shall issue shares for the Participant's benefit representing the shares purchased upon exercise of his or her option to purchase shares hereunder.

(g) During a Participant's lifetime, his or her option to purchase shares hereunder is exercisable only by him or her. The Participant will have no interest or voting right in shares covered by his or her option until such option has been exercised.

(h) To the extent required by applicable federal, state, local or foreign law, a Participant shall make arrangements satisfactory to the Company and the Participating Corporation employing the Participant for the satisfaction of any withholding tax obligations that arise in connection with the Plan. The Company or any Subsidiary or Affiliate, as applicable, may withhold, by any method permissible under the applicable law, the amount necessary for the Company or Subsidiary or Affiliate, as applicable, to meet applicable withholding obligations, including any withholding required to make available to the Company or Subsidiary or Affiliate, as applicable, any tax deductions or benefits attributable to the sale or early disposition of shares of Common Stock by a Participant. The Company shall not be required to issue any shares of Common Stock under the Plan until such obligations are satisfied.

10. **LIMITATIONS ON SHARES TO BE PURCHASED**.

(a) Any other provision of the Plan notwithstanding, no Participant shall purchase Common Stock with a Fair Market Value in excess of the following limit:

(i) In the case of Common Stock purchased during an Offering Period that commenced in the current calendar year, the limit shall be equal to (A) $25,000 minus (B) the Fair Market Value of the Common Stock that the Participant previously purchased in the current calendar year (under this Plan and all other employee stock purchase plans of the Company or any Parent or Subsidiary).

(ii) In the case of Common Stock purchased during an Offering Period that commenced in the immediately preceding calendar year, the limit shall be equal to (A) $50,000 minus (B) the Fair Market Value of the Common Stock that the Participant previously purchased (under this Plan and all other employee stock purchase plans of the Company or any Parent or Subsidiary) in the current calendar year and in the immediately preceding calendar year.

For purposes of this Subsection (a), the Fair Market Value of Common Stock shall be determined in each case as of the beginning of the Offering Period in which such Common Stock is purchased. Employee stock purchase plans not described in Section 423 of the Code shall be disregarded. If a Participant is precluded by this Subsection (a) from purchasing additional Common Stock under the Plan, then his or her Contributions shall automatically be discontinued and shall automatically resume at the beginning of the earliest Purchase Period that will end in the next calendar year (if he or she then is an eligible employee), provided that when the Company automatically resumes such Contributions, the Company must apply the rate in effect immediately prior to such suspension.

(b) The Committee shall establish a maximum number of shares that may be purchased on any one Purchase Date. The Committee will communicate the applicable limit to Participants prior to commencement of the Offering Period for which it is effective.

(c) If the number of shares to be purchased on a Purchase Date by all Participants exceeds the number of shares then available for issuance under this Plan, then the Company will make a pro rata allocation of the remaining shares in as uniform a manner as shall be reasonably practicable and as the Committee shall determine to be equitable. In such event, the Company will give notice of such reduction of the number of shares to be purchased under a Participant' s option to each Participant affected.

(d) Any Contributions accumulated in a Participant' s account that are not used to purchase stock due to the limitations in this Section 10, and not subject to the automatic purchase provision of Section 9(e), shall be returned to the Participant as soon as practicable after the end of the applicable Purchase Period, without interest (except to the extent required due to local legal requirements outside the United States).

11. **WITHDRAWAL**.

(a) Each Participant may withdraw from an Offering Period under this Plan pursuant to a method specified for such purpose by the Company. Such withdrawal may be elected at any time prior to the end of an Offering Period, or such other time period as specified by the Committee.

(b) Upon withdrawal from this Plan, the accumulated Contributions shall be returned to the withdrawn Participant, without interest (except to the extent required due to local legal requirements outside the United States), and his or her interest in this Plan shall terminate. In the event a Participant voluntarily elects to withdraw from this Plan, he or she may not resume his or her participation in this Plan during the same Offering Period, but he or she may participate in any Offering Period under this Plan which commences on a date subsequent to such withdrawal by filing a new authorization for Contributions in the same manner as set forth in Section 6 above for initial participation in this Plan.

12. **TERMINATION OF EMPLOYMENT**. Termination of a Participant's employment for any reason, including retirement, death, disability, or the failure of a Participant to remain an eligible employee of the Company or of a Participating Corporation, immediately terminates his or her participation in this Plan (except as required due to local legal requirements outside the United States). In such event, accumulated Contributions credited to the Participant's account will be returned to him or her or, in the case of his or her

death, to his or her legal representative, without interest (except to the extent required due to local legal requirements outside the United States). For purposes of this Section 12, an employee will not be deemed to have terminated employment or failed to remain in the continuous employ of the Company or of a Participating Corporation in the case of sick leave, military leave, or any other leave of absence approved by the Company; provided that such leave is for a period of not more than ninety (90) days or reemployment upon the expiration of such leave is guaranteed by contract or statute. The Company will have sole discretion to determine whether a Participant has terminated employment and the effective date on which the Participant terminated employment, regardless of any notice period or garden leave required under local law.

13. **RETURN OF CONTRIBUTIONS**. In the event a Participant's interest in this Plan is terminated by withdrawal, termination of employment or otherwise, or in the event this Plan is terminated by the Board, the Company shall deliver to the Participant all accumulated Contributions credited to such Participant's account. No interest shall accrue on the Contributions of a Participant in this Plan (except to the extent required due to local legal requirements outside the United States).

14. **CAPITAL CHANGES**. If the number of outstanding shares is changed by a stock dividend, recapitalization, stock split, reverse stock split, subdivision, combination, reclassification or similar change in the capital structure of the Company, without consideration, then the Committee shall adjust the number and class of Common Stock that may be delivered under the Plan, the Purchase Price per share and the number of shares of Common Stock covered by each option under the Plan which has not yet been exercised, and the numerical limits of Sections 2 and 10 shall be proportionately adjusted, subject to any required action by the Board or the stockholders of the Company and in compliance with the applicable securities laws; provided that fractions of a share will not be issued.

15. **NONASSIGNABILITY.** Neither Contributions credited to a Participant's account nor any rights with regard to the exercise of an option or to receive shares under this Plan may be assigned, transferred, pledged or otherwise disposed of in any way (other than by will, the laws of descent and distribution or as provided in Section 22 below) by the Participant. Any such attempt at assignment, transfer, pledge or other disposition shall be void and without effect.

16. **USE OF PARTICIPANT FUNDS AND REPORTS.** The Company may use all Contributions received or held by it under the Plan for any corporate purpose, and the Company will not be required to segregate Participant Contributions (except to the extent required due to local legal requirements outside the United States). Until shares are issued, Participants will only have the rights of an unsecured creditor unless otherwise required under local law. Each Participant shall receive promptly after the end of each Purchase Period a report of his or her account setting forth the total Contributions accumulated, the number of shares purchased, the per share price thereof and the remaining cash balance, if any, carried forward to the next Purchase Period or Offering Period, as the case may be.

17. **NOTICE OF DISPOSITION.** Each U.S. taxpayer Participant shall notify the Company in writing if the Participant disposes of any of the shares purchased in any Offering Period pursuant to this Plan during the Notice Period. The Company may, at any time during the Notice Period, place a legend or legends on any certificate representing shares acquired pursuant to this Plan requesting the Company's transfer agent to notify the Company of any transfer of the shares. The obligation of the Participant to provide such notice shall continue notwithstanding the placement of any such legend on the certificates.

18. **NO RIGHTS TO CONTINUED EMPLOYMENT.** Neither this Plan nor the grant of any option hereunder shall confer any right on any employee to remain in the employ of the Company or any Participating Corporation, or restrict the right of the Company or any Participating Corporation to terminate such employee ' s employment.

19. **EQUAL RIGHTS AND PRIVILEGES.** All eligible employees granted an option under the Section 423 Component of this Plan shall have equal rights and privileges with respect to this Plan or within any separate offering under the Plan so that this Plan qualifies as an "employee stock purchase plan" within the meaning of Section 423 or any successor provision of the Code and the related regulations. Any provision of this Plan which is inconsistent with Section 423 or any successor provision of the Code, without further act or amendment by the Company, the Committee or the Board, shall be reformed to comply with the requirements of Section 423. This Section 19 shall take precedence over all other provisions in this Plan.

20. **NOTICES.** All notices or other communications by a Participant to the Company under or in connection with this Plan shall be deemed to have been duly given when received in the form specified by the Company at the location, or by the person, designated by the Company for the receipt thereof.

21. **TERM; STOCKHOLDER APPROVAL.** The amendment and restatement of the Plan shall be approved by the stockholders of the Company, in any manner permitted by applicable corporate law, within 12 months before or after the date this amendment and restatement of the Plan is adopted by the Board. The amendment and restatement of the Plan will become effective upon the Effective Date. No purchase of shares that are subject to such stockholder approval before becoming available under this Plan shall occur prior to stockholder approval of such shares and the Board or Committee may delay any Purchase Date and postpone the commencement of any Offering Period subsequent to such Purchase Date as deemed necessary or desirable to obtain such approval (provided that if a Purchase Date would occur more than 27 months after commencement of the Offering Period to which it relates, then such Purchase Date shall not occur and **i**nstead such Offering Period shall terminate without the purchase of such shares and Participants in such Offering Period shall be refunded their Contributions without interest). If the amendment and restatement of the Plan is not approved by the stockholders of the Company within 12 months before or after the date this amendment and restatement of the Plan is adopted by the Board, then it shall be null and void and the Plan shall continue in effect without the terms approved in the amendment and restatement. This Plan shall continue until the earlier to occur of (a) termination of this Plan by the Board (which termination may be effected by the Board at any time pursuant to Section 25 below) or (b) issuance of all of the shares of Common Stock reserved for issuance under this Plan.

22. **DESIGNATION OF BENEFICIARY**.

(a) Unless otherwise determined by the Committee, a Participant may file a written designation of a beneficiary who is to receive any cash from the Participant's account under this Plan in the event of such Participant's death prior to a Purchase Date. Such form shall be valid only if it was filed with the Company at the prescribed location before the Participant's death.

(b) If authorized by the Company, such designation of beneficiary may be changed by the Participant at any time by written notice filed with the Company at the prescribed location before the Participant's death. In the event of the death of a Participant and in the absence of a beneficiary validly designated under this Plan who is living at the time of such Participant' s death, the Company shall deliver such cash to the executor or administrator of the estate of the Participant or to the legal heirs of the Participant.

23. **CONDITIONS UPON ISSUANCE OF SHARES; LIMITATION ON SALE OF SHARES**. Shares shall not be issued with respect to an option unless the exercise of such option and the issuance and delivery of such shares pursuant thereto shall comply with all applicable provisions of law, domestic or foreign, including, without limitation, the U.S. Securities Act of 1933, as amended, the U.S. Securities Exchange Act of 1934, as amended, the rules and regulations promulgated thereunder, and the requirements of any stock exchange or automated quotation system upon which the shares may then be listed, exchange control restrictions and/or securities law restrictions outside the United States, and shall be further subject to the approval of counsel for the Company with respect to such compliance. Shares may be held in trust or subject to further restrictions as permitted by any subplan.

24. **APPLICABLE LAW.** The Plan shall be governed by the substantive laws (excluding the conflict of laws rules) of the State of Delaware.

25. **AMENDMENT OR TERMINATION**. The Committee, in its sole discretion, may amend, suspend, or terminate the Plan, or any part thereof, at any time and for any reason. Unless otherwise required by applicable law, if the Plan is terminated, the Committee, in its discretion, may elect to terminate all outstanding Offering Periods either immediately or upon completion of the purchase of shares of Common Stock on the next Purchase Date (which may be sooner than originally scheduled, if determined by the Committee in its discretion), or may elect to permit Offering Periods to expire in accordance with their terms (and subject to any adjustment pursuant to Section 14). If an Offering Period is terminated prior to its previously-scheduled expiration, all amounts then credited to Participants' accounts for such Offering Period, which have not been used to purchase shares of Common Stock, shall be returned to those Participants (without interest thereon, except as otherwise required under local laws) as soon as administratively practicable. Further, the Committee will be entitled to change the Purchase Periods and Offering Periods, limit the frequency and/or number of changes in the amount contributed during an Offering Period, establish the exchange ratio applicable

to amounts contributed in a currency other than U.S. dollars, permit payroll withholding in excess of the amount designated by a Participant in order to adjust for delays or mistakes in the administration of the Plan, establish reasonable waiting and adjustment periods and/or accounting and crediting procedures to ensure that amounts applied toward the purchase of Common Stock for each Participant properly correspond with amounts contributed from the Participant' s base salary and other eligible Compensation, and establish such other limitations or procedures as the Committee determines in its sole discretion advisable which are consistent with the Plan. Such actions will not require stockholder approval or the consent of any Participants. However, no amendment shall be made without approval of the stockholders of the Company (obtained in accordance with Section 21 above) within 12 months of the adoption of such amendment (or earlier if required by Section 21) if such amendment would: (a) increase the number of shares that may be issued under this Plan; or (b) change the designation of the employees (or class of employees) eligible for participation in this Plan. In addition, in the event the Board or Committee determines that the ongoing operation of the Plan may result in unfavorable financial accounting consequences, the Board or Committee may, in its discretion and, to the extent necessary or desirable, modify, amend or terminate the Plan to reduce or eliminate such accounting consequences including, but not limited to: (i) amending the definition of Compensation, including with respect to an Offering Period underway at the time; (ii) altering the Purchase Price for any Offering Period including an Offering Period underway at the time of the change in Purchase Price; (iii) shortening any Offering Period by setting a Purchase Date, including an Offering Period underway at the time of the Committee's action; (iv) reducing the maximum percentage of Compensation a Participant may elect to set aside as Contributions; and (v) reducing the maximum number of shares a Participant may purchase during any Offering Period. Such modifications or amendments will not require approval of the stockholders of the Company or the consent of any Participants.

26. **CORPORATE TRANSACTIONS.** In the event of a Corporate Transaction, the Offering Period for each outstanding right to purchase Common Stock will be shortened by setting a new Purchase Date and will end on the new Purchase Date. The new Purchase Date shall occur on or prior to the consummation of the Corporate Transaction, as determined by the Board or Committee, and the Plan shall terminate on the consummation of the Corporate Transaction.

27. **CODE SECTION 409A; TAX QUALIFICATION**.

(a) Options granted under the Plan generally are exempt from the application of Section 409A of the Code. However, options granted to U.S. taxpayers which are not intended to meet the Code Section 423 requirements are intended to be exempt from the application of Section 409A of the Code under the short-term deferral exception and any ambiguities shall be construed and interpreted in accordance with such intent. Subject to Subsection (b), options granted to U.S. taxpayers outside of the Code Section 423 requirements shall be subject to such terms and conditions that will permit such options to satisfy the requirements of the short-term deferral exception available under Section 409A of the Code, including the requirement that the shares of Common Stock subject to an option be delivered within the short-term deferral period. Subject to Subsection (b), in the case of a Participant who would otherwise be subject to Section 409A of the Code, to the extent the Committee determines that an option or the exercise, payment, settlement or deferral thereof is subject to Section 409A of the Code, the option shall be granted, exercised, paid, settled or deferred in a manner that will comply with Section 409A of the Code, including Treasury regulations and other interpretive guidance issued thereunder, including without limitation any such regulations or other guidance that may be issued after the Effective Date. Notwithstanding the foregoing, the Company shall have no liability to a Participant or any other party if the option that is intended to be exempt from or compliant with Section 409A of the Code is not so exempt or compliant or for any action taken by the Committee with respect thereto.

(b) Although the Company may endeavor to (i) qualify an option for favorable tax treatment under the laws of the United States or jurisdictions outside of the United States or (ii) avoid adverse tax treatment (e.g., under Section 409A of the Code), the Company makes no representation to that effect and expressly disavows any covenant to maintain favorable or avoid unfavorable tax treatment, notwithstanding anything to the contrary in this Plan, including Subsection (a). The Company shall be unconstrained in its corporate activities without regard to the potential negative tax impact on Participants under the Plan.

28. **DEFINITIONS**.

(a) "***Affiliate***" means any entity, other than a Subsidiary or Parent, (i) that, directly or indirectly, is controlled by, controls or is under common control with, the Company and (ii) in which the Company has a significant equity interest, in either case as determined by the Committee, whether now or hereafter existing.

(b) "***Board***" shall mean the Board of Directors of the Company.

(c) "***Code***" shall mean the U.S. Internal Revenue Code of 1986, as amended from time to time, and the rulings and regulations issued thereunder.

(d) "***Committee***" shall mean the Compensation Committee of the Board (or any successor committee), or such other committee as designated by the Board to administer the Plan under Section 3.

(e) "***Common Stock***" shall mean the common stock of the Company.

(f) "***Company***" shall mean Spyre Therapeutics, Inc. (f/k/a Aeglea BioTherapeutics, Inc.) and any successor corporation.

(g) "***Contributions***" means payroll deductions taken from a Participant's Compensation and used to purchase shares of Common Stock under the Plan and, to the extent payroll deductions are not permitted by applicable laws (as determined by the Committee in its sole discretion) contributions by other means, provided, however, that allowing such other contributions does not jeopardize the qualification of the Plan as an "employee stock purchase plan" under Section 423 of the Plan.

(h) "***Corporate Transaction***" means the occurrence of any of the following events: (i) any "person" (as such term is used in Sections 13(d) and 14(d) of the Exchange Act) becomes the "beneficial owner" (as defined in Rule 13d-3 of the Exchange Act), directly or indirectly, of securities of the Company representing 50% or more of the total voting power represented by the Company's then outstanding voting securities; or (ii) the consummation of the sale or disposition by the Company of all or substantially all of the Company's assets; or (iii) the consummation of a merger or consolidation of the Company with any other corporation, other than a merger or consolidation which would result in the voting securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or its parent) at least 50% of the total voting power represented by the voting securities of the Company or such surviving entity or its parent outstanding immediately after such merger or consolidation.

(i) "***Fair Market Value***" shall mean, as of any date, the value of a share of Common Stock determined as follows:

(i) if such Common Stock is publicly traded and is then listed on a national securities exchange, its closing price on the date of determination on the principal national securities exchange on which the Common Stock is listed or admitted to trading, or if there are no sales for such date, then the last preceding business day on which there were sales, as reported in *The Wall Street Journal* or such other source as the Board or the Committee deems reliable;

(ii) if such Common Stock is publicly traded but is not listed or admitted to trading on a national securities exchange, the average of the closing bid and asked prices on the date of determination as reported in The Wall Street Journal or such other source as the Board or the Committee deems reliable; or

(iii) if none of the foregoing is applicable, by the Board or the Committee in good faith.

(j) "***Non-Section 423 Component***" means the part of the Plan which is not intended to meet the requirements set forth in Section 423 of the Code.

(k) "***Notice Period***" shall mean within two years from the Offering Date or within one year from the Purchase Date on which such shares were purchased.

(l) "***Offering Date***" shall mean the first business day of each Offering Period.

(m) "***Offering Period***" shall mean a period with respect to which the right to purchase Common Stock may be granted under the Plan, as determined by the Committee pursuant to Section 5(a).

(n) "***Parent***" shall have the same meaning as " parent corporation" in Section 424(e) of the Code.

(o) "***Participant***" shall mean an eligible employee who meets the eligibility requirements set forth in Section 4 and who is either automatically enrolled in the initial Offering Period or who elects to participate in this Plan pursuant to Section 6(b).

(p) "***Participating Corporation***" shall mean any Parent, Subsidiary or Affiliate that the Committee designates from time to time as eligible to participate in this Plan. For purposes of the Section 423 Component, only the Parent and Subsidiaries may be Participating Corporations, provided, however, that at any given time a Parent or Subsidiary that is a Participating Corporation under the Section 423 Component shall not be a Participating Corporation under the Non-Section 423 Component. The Committee may provide that any Participating Corporation shall only be eligible to participate in the Non-Section 423 Component.

(q) "***Plan***" shall mean this Spyre Therapeutics, Inc. Amended and Restated 2016 Employee Stock Purchase Plan, as may be amended from time to time.

(r) "***Purchase Date***" shall mean the last business day of each Purchase Period.

(s) "***Purchase Period***" shall mean a period during which Contributions may be made toward the purchase of Common Stock under the Plan, as determined by the Committee pursuant to Section 8.

(t) "***Purchase Price***" shall mean the price at which Participants may purchase shares of Common Stock under the Plan, as determined pursuant to Section 8.

(u) "***Section 423 Component***" means the part of the Plan, which excludes the Non- Section 423 Component, pursuant to which options to purchase shares of Common Stock under the Plan that satisfy the requirements for "employee stock purchase plans" set forth in Section 423 of the Code may be granted to eligible employees.

(v) "***Subsidiary***" shall have the same meaning as "subsidiary corporation" in Section 424(f) of the Code.