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, 2024

☐ **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, 2024 (the last business day of the Registrant's second fiscal quarter), based upon the closing price of $23.51 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 19, 2025
Common stock, $0.0001 par value per share	60,275,561 shares

DOCUMENTS INCORPORATED BY REFERENCE

None.

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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) or rheumatoid arthritis (RA) that meaningfully improve both efficacy and convenience compared to today's standard of care and our ability to develop first-in-class therapeutics for RA; our plans to expand the development of our product candidates, including SPY002, to indications beyond IBD and RA; the SPY001 Phase 1 trial final data readouts not being consistent with or being different than the interim Phase 1 results; the planned 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; the expected design and timing of the platform Phase 2 trial, including timing of each cohort and data readouts; 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 foreign equivalents and further clinical evaluation of therapeutic combinations, 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; use of net proceeds from our public offerings; the timing and results of nonclinical studies and clinical trials, including commencement of first-in-human ("FIH") and Phase 2 trials and timing of data readouts; 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, geopolitical tensions between China and the United States 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 utilizing potential best-in-class antibody engineering, dose optimization, and rational therapeutic combinations to target improved efficacy and convenience in the treatment of IBD and other immune-mediated 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 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")

Next-generation monotherapies

Our next-generation monotherapy antibody candidates targeting α4ß7, TL1A, and IL-23 are engineered to match or exceed the potency of comparator first generation molecules, maintain selectivity, incorporate Fc domain modifications called YTE substitutions in order to increase pharmacokinetic half-life, and are formulated as high-concentration, citrate-free formulations. Combined, these attributes have the potential to enable infrequent subcutaneous ("SC") maintenance dosing compared to competitor molecules, 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.

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). 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.

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: RA, axial spondyloarthritis, psoriatic arthritis, 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 RA, with further validation from in-house in vivo experiments:

- TL1A is elevated in RA patients relative to healthy controls and increases with disease duration and severity
- TL1A administration exacerbates arthritis in murine models of RA 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 RA

If successful in development and in obtaining regulatory approval, SPY002's projected quarterly to twice-annual subcutaneous dosing in a single autoinjector has the potential to be the most convenient product available for RA and represents an attractive opportunity to expand the value of our portfolio.

Inflammatory Bowel Disease

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

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

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

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

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

Rheumatoid Arthritis

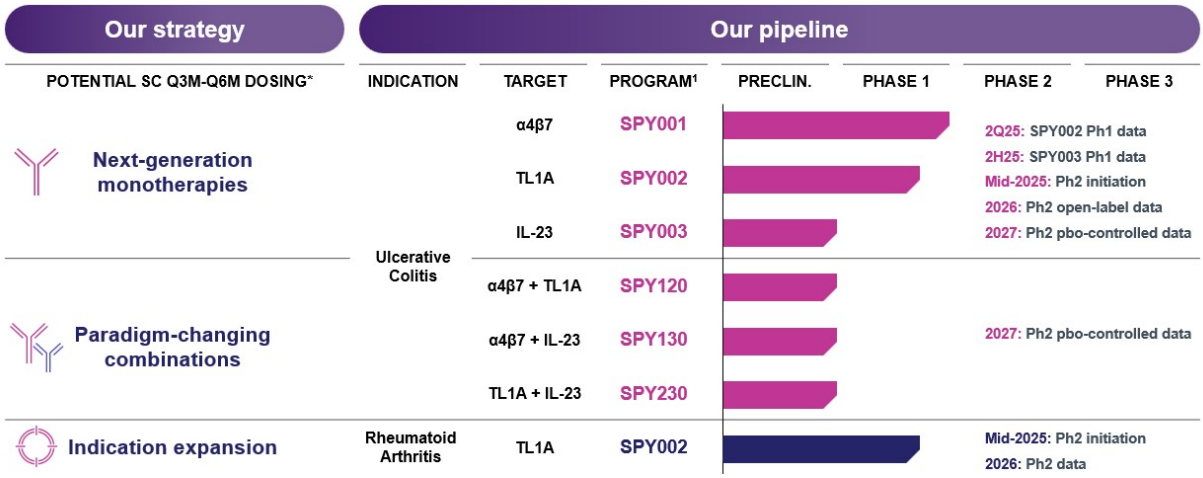
RA is a chronic inflammatory autoimmune condition that primarily affects the joints. It is characterized by pain, stiffness and swelling of one or more joints and can progress from mild swelling of the joints in early stages to severe deformations of the feet, ankles, and hands in late/severe stages. 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.

A range of pharmaceutical options exist including conventional synthetic disease-modifying antirheumatic drugs ("DMARDs") (methotrexate, leflunomide, sulfasalazine), biological DMARDs (TNF inhibitors, CD80/86 inhibitor, IL-6 inhibitors, CD20 inhibitors), and targeted synthetic DMARDs (JAKs). Despite available treatments, there remains substantial unmet need in RA 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
- Poor adherence to frequent and/or inconvenient dosing regimens

Our Portfolio

We are advancing a pipeline of monoclonal antibodies ("mAbs") for the treatment of IBD and other immune-mediated diseases. The following table summarizes our programs and strategy:



Through the Asset Acquisition, we received the option to license the intellectual property rights related to four research programs (collectively, the "Option") pursuant to the Paragon Agreement, and subsequently executed license agreements for our α4β7, TL1A, and IL-23 programs. As of the date of this Annual Report on Form 10-K, we have exercised our Option with respect to and nominated development candidates for our SPY001, SPY002, and SPY003 programs. We executed license agreements with Paragon for SPY001 (the "SPY001 License Agreement") and SPY002 (the "SPY002 License Agreement") in the second quarter of 2024 and we executed a license agreement with Paragon for SPY003 (the "SPY003 License Agreement" and, together with the SPY001 License Agreement and the SPY002 License Agreement, the "License Agreements") in the fourth quarter of 2024. The SPY001 and SPY002 licenses are indication agnostic, and the SPY003 license is restricted to IBD. We additionally have an exclusive option under the Paragon Agreement for a discovery stage program targeting a novel mechanism of action ("MOA") that also incorporates half-life extension (SPY004). See the section titled "Paragon Agreement" in this Annual Report on Form 10-K for more discussion about the Paragon Agreement and the License Agreements.

SPY001 – anti-α4β7 mAb

Our most advanced product candidate, SPY001, is a highly potent, highly selective, and humanized monoclonal immunoglobulin G1 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. This interaction is responsible for guiding lymphocytes from the bloodstream into the gut tissue, where they cause inflammation. 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 preclinical characterization studies were conducted in-house with support from third party vendors. SPY001 demonstrates similar potency and selectivity as synthesized vedolizumab in preclinical *in vitro* models including surface plasmon residence (n=5 concentrations) and cellular adhesion assays (see Figure 1, n=6 replicates per group). The 28-day GLP toxicity study in non-human primates ("NHPs") (n=42) for SPY001 was completed with the highest dose level tested determined as the no-observed-adverse-effect-level.

The Company initiated a FIH Phase 1 trial for SPY001 in June 2024. The SPY001 Phase 1 trial is a double blind, placebo-controlled trial in healthy volunteers and consists of a single-ascending dose (SAD) component and a multi-ascending dose (MAD) component. The trial design includes enrolling 56 healthy adult

participants into five SAD cohorts and two MAD cohorts in the main portion of the study. The primary endpoint is safety, with pharmacokinetics (PK) and anti-drug antibodies (ADA) serving as secondary endpoints. Additional cohorts have been added to the study to evaluate pharmacokinetics in healthy volunteers of various ethnicities to facilitate subsequent global clinical trials. Trial enrollment is now complete.

Interim results were presented in November 2024 with up to four months of follow up. Findings from the interim SAD and MAD portions of the Phase 1 trial were as follows:

- Safety (See Figure 2) - SPY001 was well tolerated across all dose groups (single doses of up to 1,000mg and multiple doses of up to 600 mg) with a favorable safety profile. The most common treatment-emergent adverse events ("TEAEs") were headache and nasopharyngitis.
- PK - SPY001 demonstrated a meaningfully differentiated PK profile relative to vedolizumab. The half-life is estimated at greater than 90 days by population PK modeling, which is approximately four times that of vedolizumab's 25-day human half-life in a cross-trial comparison (See Figure 3), supporting the potential for Q3M-Q6M SC maintenance dosing.
- Pharmacodynamics ("PD") - complete occupancy of α4β7 receptors was observed with a single dose of 300 mg up to Day 85 (See Figure 4), which was the longest follow up available at data cutoff.

Longer-term data from this Phase 1 trial will be presented at a medical meeting later this year. Based on these interim results, we plan to advance SPY001 to a Phase 2 clinical trial in UC patients in mid-2025.

Figure 1. Potency and selectivity of SPY001 relative to synthesized vedolizumab in cellular assays (Data on file).

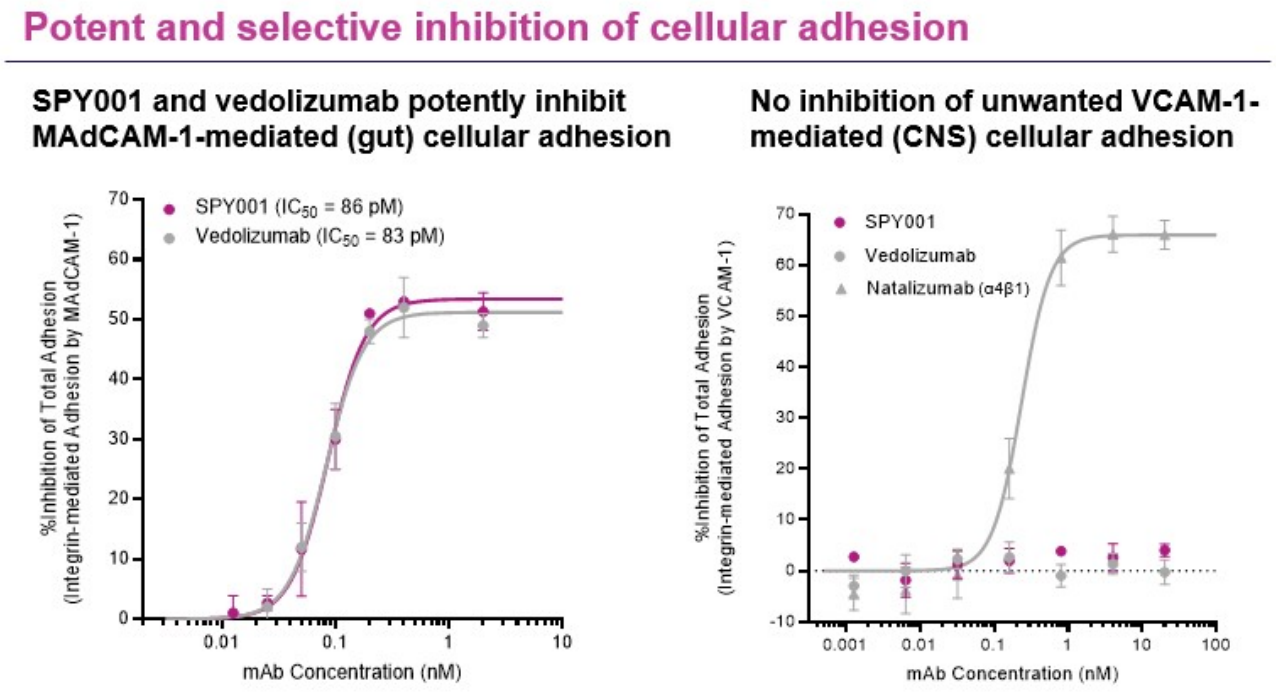


Figure 2. Interim SPY001 Phase 1 safety data

N (%)	100 mg	300 mg	600 mg	1000 mg	1000 mg	SAD Pooled	300 mg	600 mg	MAD Pooled
N=	8	8	8	8	8	**40**	8	8	**16**
At least one **TEAE**	1 (13%)	3 (38%)	2 (25%)	3 (38%)	0	**9 (23%)**	2 (25%)	3 (38%)	**5 (31%)**
At least one **TESAE**	0	0	0	0	0	**0**	0	0	**0**
At least one **Drug-related AE**[1]	0	0	0	1 (13%)	0	**1 (3%)**	0	0	**0**
At least one **≥Grade 2 TEAE**	0	0	0	0	0	**0**	0	0	**0**

TEAE=treatment-emergent adverse events. TESAE=treatment-emergent serious adverse events. [1]Injection site discomfort starting 6 hours after 4 SC injections and resolved 2 hours later without intervention.

Figure 3. Interim SPY001 simulated concentration-time profile compared to vedolizumab

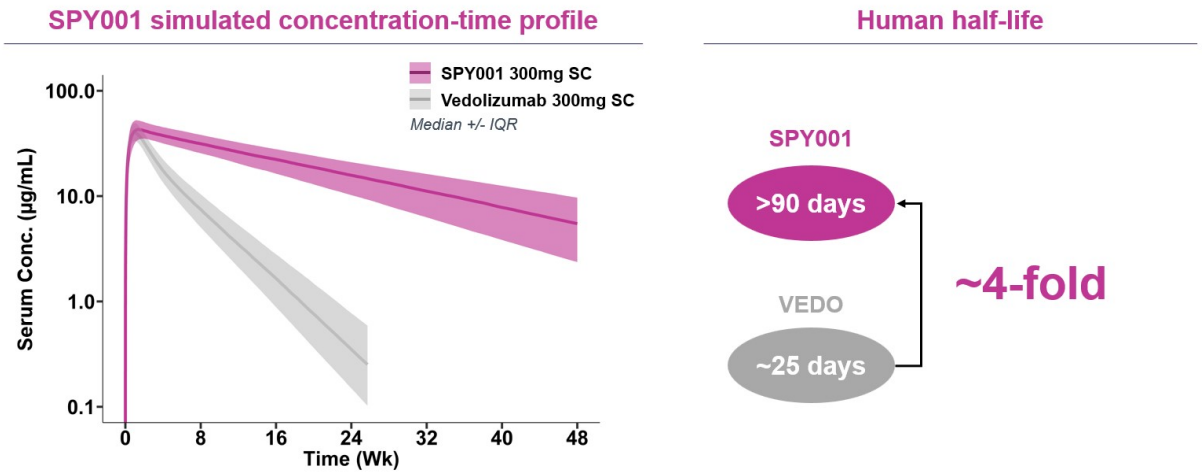
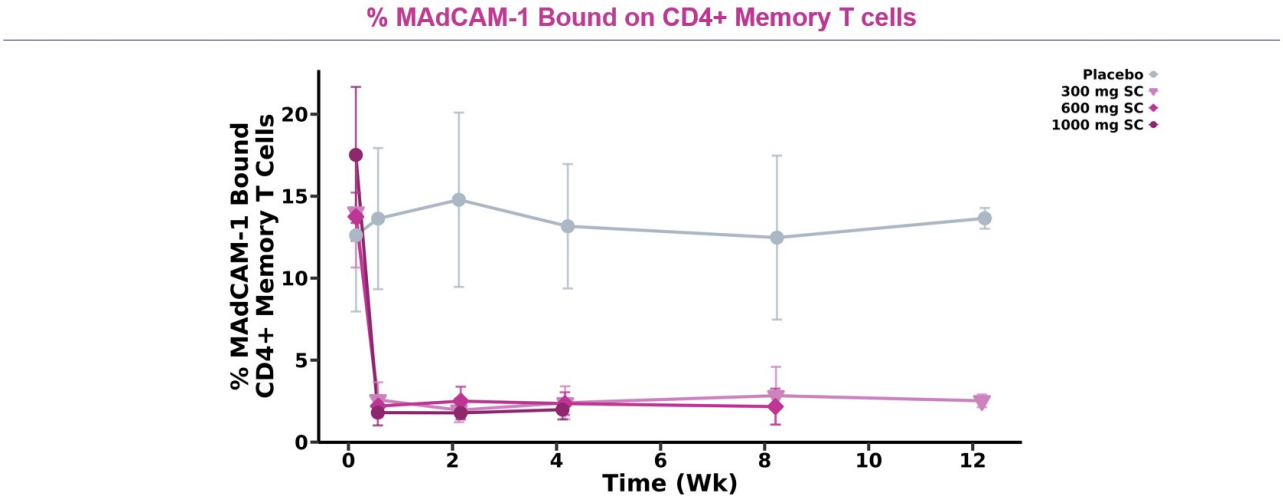


Figure 4. Interim SPY001 pharmacodynamic data



SPY002 – anti-TL1A mAb

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

SPY002 preclinical characterization studies were conducted in-house with support from third party vendors. Our extensive discovery campaign has identified two lead candidates which bind TL1A monomers and trimers and have subnanomolar potency in cellular assays (see Figure 5, n=4 replicates per group per study). The candidates also exhibited extended pharmacokinetic half-lives of greater than two to three-fold relative to synthesized competitor molecules in clinical development that do not incorporate half-life extending modifications, based on head-to-head preclinical studies in NHPs (see Figure 6, n=5 per group). The 42-day GLP toxicity studies in NHPs (n=42) for both SPY002 candidates were completed with the highest dose level tested determined as the no-observed-adverse-effect-level.

The Company initiated two FIH trials in healthy volunteers in the fourth quarter of 2024, one for each of our SPY002 candidates, with interim safety and PK data from these trials expected in the second quarter of 2025. If successful, one or more SPY002 candidates will then advance to Phase 2 clinical trials (UC and RA).

Figure 5. Inhibition of TL1A induced TF-1 cell apoptosis (left) and IFNγ secretion in primary human whole blood 1 donor of 4 donors profiled (right) (Data on file. Duvakitug was not benchmarked in IFNγ secretion assay; Duvakitug, RO7790121, and tulisokibart are synthesized comparator antibodies).

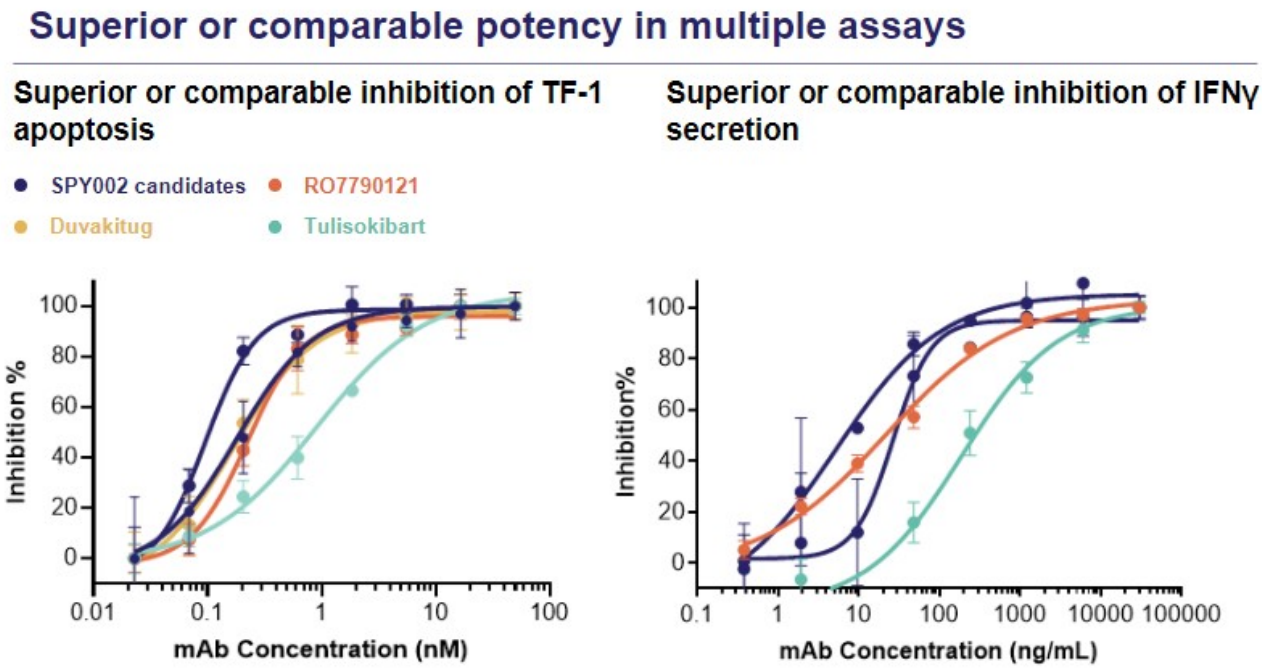
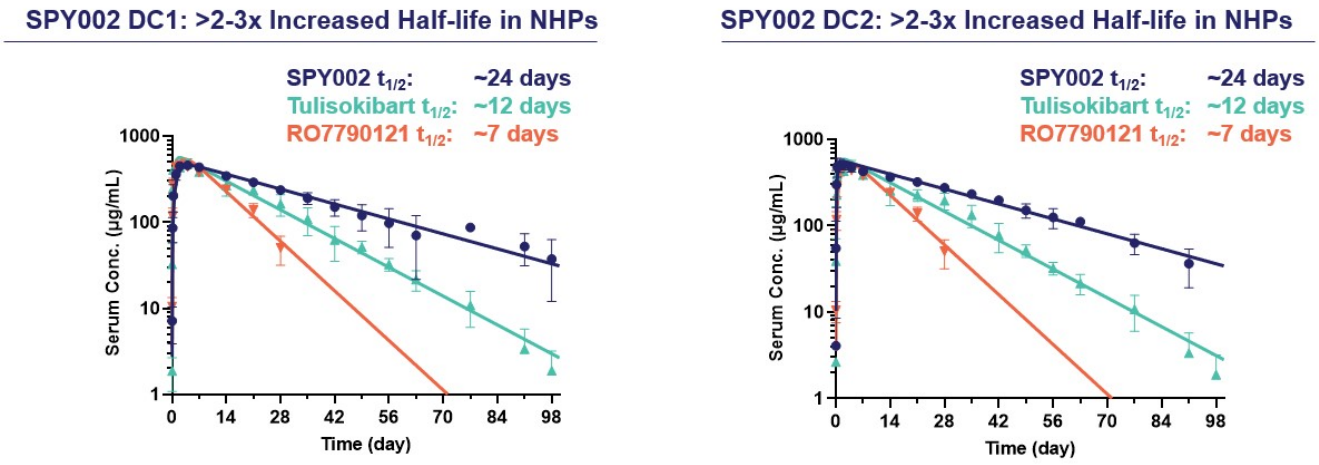


Figure 6. Pharmacokinetic concentration-time curves of SPY002 candidates compared to synthesized competing anti-TL1A molecules in non-human primates (Data on file. Group size was n=5 for SPY002 mAbs and tulisokibart at final endpoints for half-life determination; No RO7790121 detected after day 28. Duvakitug not compared in these models given low human half-life (7-10 days).).



SPY003 – anti-IL-23 mAb

SPY003 is a preclinical-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 preclinical characterization studies were conducted in-house with support from third party vendors. Our extensive discovery campaign has identified a lead candidate which binds to the p19 subunit of IL-23 with subnanomolar potency in cellular assays (see Figure 7, n=2 and n=3 for pSTAT assay and IL-17 assay, respectively). The development candidate also exhibited extended pharmacokinetic 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 NHPs (see Figure 8, n=4 per group with n=4 and n=3 at the final timepoint for half-life determination for SPY003 and risankizumab, respectively).

The Company expects to initiate a FIH trial in healthy volunteers in the first quarter of 2025, with interim safety and PK data from this trial expected in the second half of 2025. If successful, SPY003 will then advance to Phase 2 clinical trials.

Figure 7. Inhibition of IL-23 induced STAT3 phosphorylation in a human lymphoma cell line (DB) (left) and IL-23 induced IL-17 secretion in human peripheral blood mononuclear cells (right) by SPY003 and synthesized risankizumab (Data on file).

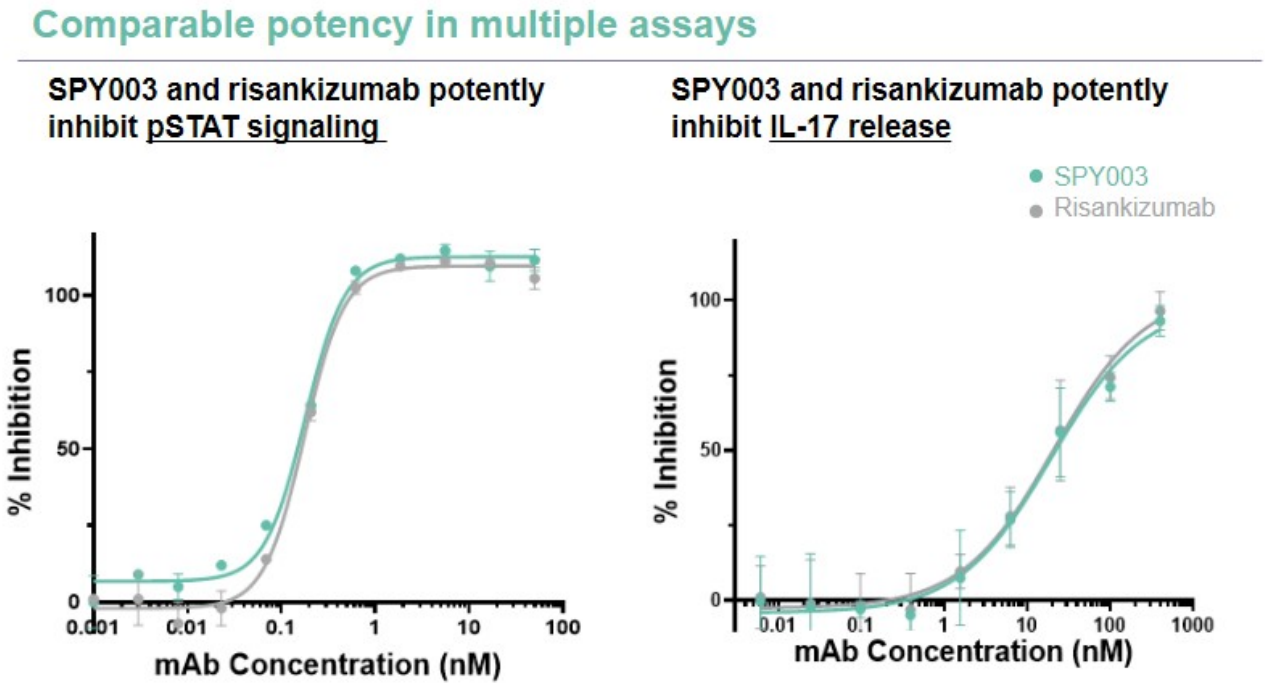
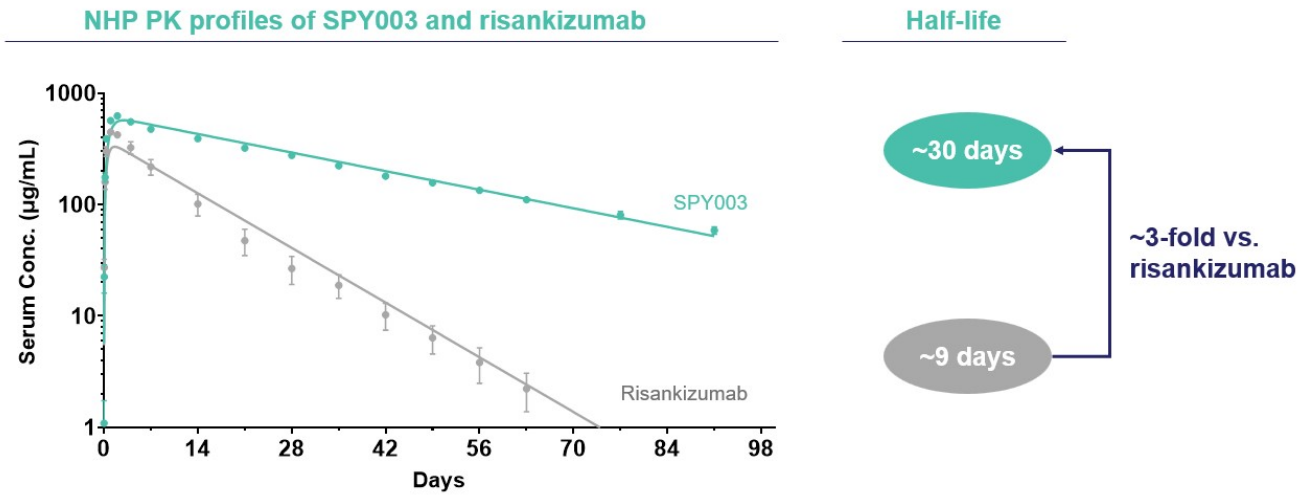


Figure 8. Pharmacokinetic concentration-time curves of SPY003 candidate compared to synthesized risankizumab comparator in non-human primates (Data on file. Group size was n=4 in the NHP studies with n=4 and n=3 at the final timepoint for half-life determination for SPY003 and risankizumab, respectively).



SPY004 – novel MOA mAb

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

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

SPY120 combines SPY001 (anti-α4β7) and SPY002 (anti-TL1A) antibodies, pairing two mechanisms studied in third-party clinical trials targeting non-overlapping sites of action. We are currently evaluating SPY120 in nonclinical studies, and have initiated combination toxicology studies. Subject to regulatory feedback, we intend to initiate clinical trials in 2025 that will include SPY120.

In February 2025, the Company presented new preclinical data demonstrating that combination therapy resulted in additive or greater than additive in vivo biological activity relative to either monotherapy in murine hapten reagent 2,4,6-trinitrobenzene sulfonic acid (TNBS) and anti-CD40 colitis models (Figure 9). In addition, coadministration of SPY001 and SPY002 in NHPs demonstrated no drug effects on PK (Figure 10).

Figure 9. Combined inhibition of anti-TL1A and anti-ß7 (anti-α4β7 murine surrogate) is superior to either monotherapy in mouse models of colitis

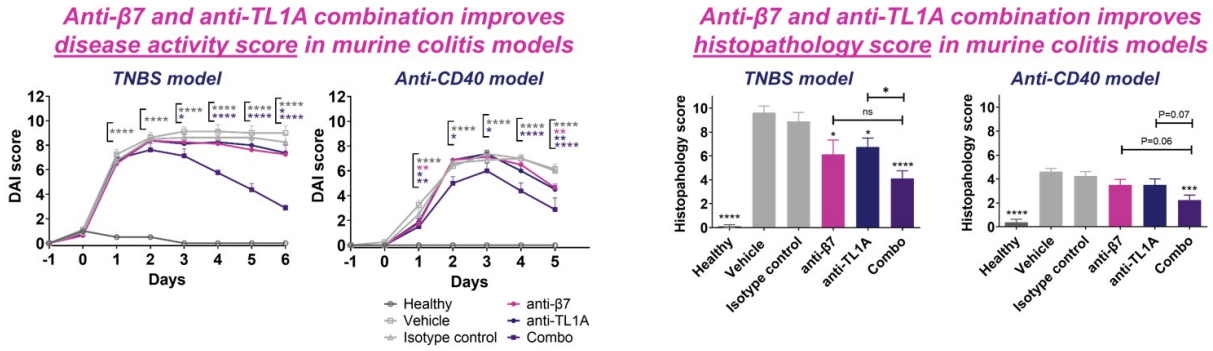
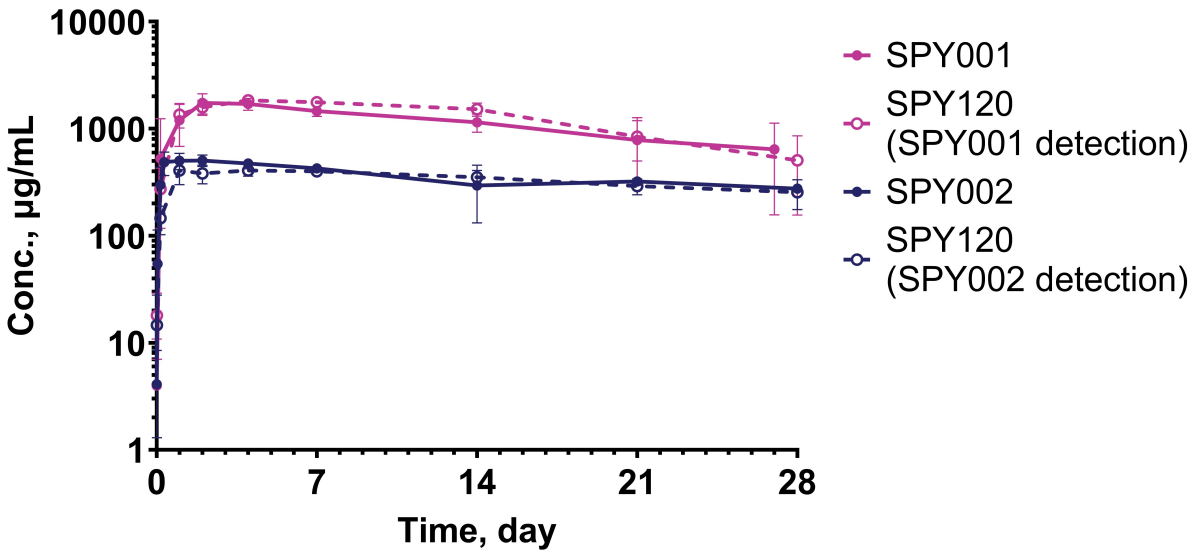


Figure 10. Coadministration of SPY001 and SPY002 demonstrates no drug-drug effects on exposure in NHPs



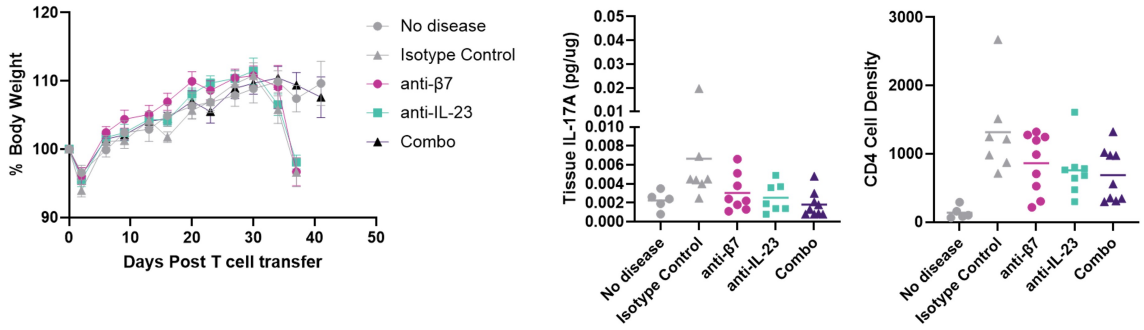
SPY130 - combination anti-α4β7 and anti-IL-23 mAbs

SPY130 combines SPY001 (anti-α4ß7) and SPY003 (anti-IL-23) antibodies, pairing two commercially validated mechanisms targeting non-overlapping sites of action. We are currently evaluating SPY130 in

nonclinical studies and initiated combination toxicology studies in 2024. Subject to regulatory feedback, we intend to initiate clinical trials in 2025 that will include SPY130.

In October 2024, the Company presented new preclinical data, demonstrating in a T-cell transfer model of IBD, that combination therapy with anti-IL-23 and anti-α4ß7 improved body weight and reduced colonic CD4+ infiltration and IL-17 levels relative to monotherapy (Figure 11).

Figure 11. Combination of anti-ß7 (anti-α4β7 murine surrogate) and anti-IL-23 increases efficacy and PD in T-cell transfer colitis model.

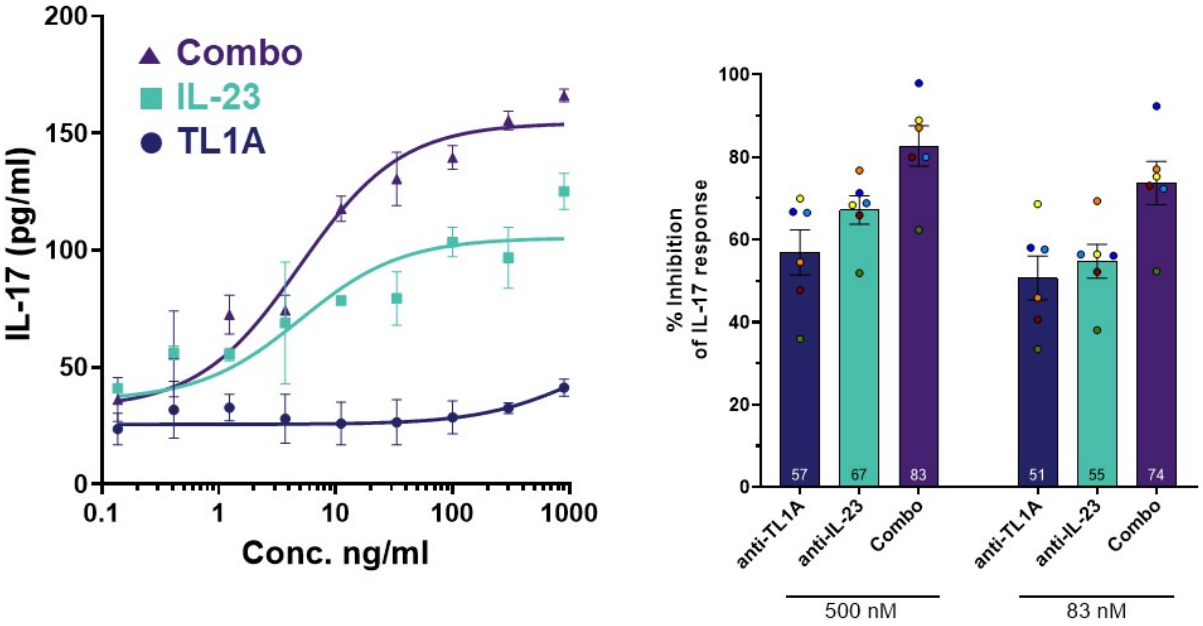


SPY230 – combination anti-TL1A and anti-IL-23 mAbs

SPY230 combines SPY002 (anti-TL1A) and SPY003 (anti-IL-23) antibodies, pairing two complementary mechanisms of action with potential to address overlapping and non-overlapping triggers of inflammation. We are currently evaluating SPY230 in nonclinical studies and initiated combination toxicology studies in 2024. Subject to regulatory feedback, we intend to initiate clinical trials in 2025 that will include SPY230.

In October 2024, the Company presented new 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 (Figure 12).

Figure 12. Combination of anti-TL1A and anti-IL-23 offers superior inhibition of IL-17 release in vitro



Employees and Human Capital Resources

As of December 31, 2024, we had 65 employees, all of whom were employed full time. We also engage temporary employees and consultants to augment our existing workforce. None of our employees are represented by a labor union or covered under a collective bargaining agreement. We consider our relationship with our employees to be good.

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

Commercial

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

Manufacturing 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”).

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

Biologics Master Services Agreement

In April 2023, Paragon and WuXi Biologics entered into the WuXi Biologics MSA, which was subsequently novated to us by Paragon on September 19, 2023 pursuant to the Novation Agreement. The WuXi Biologics MSA 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.

Paragon Agreement

In May 2023, Pre-Merger Spyre entered into the Paragon Agreement with Paragon and Parapyre. Pursuant to the Paragon Agreement, the Option provided for the right to acquire the intellectual property rights related to four research programs from Paragon in accordance with a license agreement to be entered into following each exercise of the Option.

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) and TL1A (SPY002 program) 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) 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. Our Option available under the Paragon Agreement with respect to the SPY004 program remains unexercised.

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 $3 million upon the first dosing of a human patient in a Phase 2 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 SPY004 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 RO7790121, 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) and SOR102 targeting TNF and IL-23 (Sorriso).

If approved for the treatment of patients with moderate-to-severe rheumatoid arthritis, SPY002 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 Anaptys' rosnilimab, Johnson and Johnson's JNJ-4703, and Gilead's GS-0151 PD-1 agonists; FcRn inhibitors including IMVT-1402 (Immunovant), a nipocalimab and certolizumab combination (Johnson and Johnson); RIPK1 inhibitors including Lilly's ocadusertib; additional TNF inhibitors including Zenas' ZB002 half-life extended antibody and Sanofi's oral small molecule SAR441566; BTLA agonist GS-0272 (Gilead); Treg cell therapy SBT-77-7101 (Sonoma Biotherapeutics); IgG degrader BHV-1300 (Biohaven); and bispecific fusion proteins including plamotamab/XmAb-13676 (Xencor).

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 ("GLP") regulation;
- submission to the FDA of an IND, which must become effective before clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an independent 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 GCPs; and
- FDA review and approval of a BLA to permit commercial marketing of the product for particular indications for use in the United States.

Preclinical and Clinical Development

Prior to beginning any clinical trial with a product candidate in the United States, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol or protocols for preclinical studies and clinical trials. The IND also includes results of animal and in vitro

studies assessing the toxicology, pharmacokinetics, pharmacology and pharmacodynamic characteristics of the product, chemistry, manufacturing and controls information, and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

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

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

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

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

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

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the BLA. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the

product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

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

BLA Submission and Review

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

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

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

Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with 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. 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 medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. The fast track program is intended to expedite or facilitate the process for reviewing new products that meet certain criteria. Specifically, new products are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and data demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. 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. 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 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 one pill, that is known as a fixed dose combination product and it is reviewed pursuant to the FDA's Combination Rule at 21 CFR 300.50. The rule provides that two or more drugs may be combined in a single dosage form when each component contributes to the claimed effects and the dosage of each component (amount, frequency, duration) is such that the combination is safe and effective for a significant patient population requiring such concurrent therapy as defined in the labeling for the drug.

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

Regulation of Combination Products

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

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

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

- injunctions or the imposition of civil or criminal penalties.

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

Biosimilars and Reference Product Exclusivity

The 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 study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. A product shown to be biosimilar or interchangeable with an FDA-approved reference biological product may rely in part on the FDA's previous determination of safety and effectiveness for the reference product for approval, which can potentially reduce the cost and time required to obtain approval to market the product. Complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA. 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. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

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

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

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

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

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

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

The AKS prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, to induce, or in return for, either the referral of an individual, or the purchase or recommendation of an item or service for which payment may be made under any federal healthcare program. The term remuneration has been interpreted broadly to include anything of value. The AKS has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand, and prescribers and purchasers on the other. The government often takes the position that to violate the AKS, only one purpose of the remuneration need be to induce referrals, even if there are other legitimate purposes for the remuneration. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from AKS prosecution, but they are drawn narrowly and practices that involve remuneration, such as consulting agreements, that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor

does not make the conduct per se illegal under the AKS. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

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

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

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

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

We are also subject to federal price reporting laws and federal consumer protection and unfair competition laws. Federal price reporting 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. Federal consumer protection and unfair competition laws broadly regulate marketplace activities and activities that potentially harm consumers.

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

Data Privacy and Security

Numerous state, federal, and foreign laws govern the collection, dissemination, use, access to, confidentiality, and security of personal information, including health-related information. In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations, govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. For example, HIPAA, as amended by the Health Information Technology for

Economic and Clinical Health ("HITECH"), and their respective implementing regulations imposes data privacy, security, and breach notification obligations on certain health care providers, health plans, and health care clearinghouses, known as covered entities, as well as their business associates and their covered subcontractors that perform certain services that involve using, disclosing, creating, receiving, maintaining, or transmitting individually identifiable protected health information ("PHI") for or on behalf of such covered entities. These requirements imposed by HIPAA and the HITECH Act on covered entities and business associates include entering into agreements that require business associates protect PHI provided by the covered entity against improper use or disclosure, among other things; following certain standards for the privacy of PHI, which limit the disclosure of a patient's past, present, or future physical or mental health or condition or information about a patient's receipt of health care if the information identifies, or could reasonably be used to identify, the individual; ensuring the confidentiality, integrity, and availability of all PHI created, received, maintained, or transmitted in electronic form, to identify and protect against reasonably anticipated threats or impermissible uses or disclosures to the security and integrity of such PHI; and reporting of breaches of PHI to individuals and regulators. Entities that are found to be in violation of HIPAA may be subject to significant civil, criminal, and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with the U.S. Department of Health and Human Services ("HHS") to settle allegations of HIPAA non-compliance. A covered entity or business associate is also liable for civil money penalties for a violation that is based on an act or omission of any of its agents, which may include a downstream business associate, as determined according to the federal common law of agency. HITECH also increased the civil and criminal penalties applicable to covered entities and business associates and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions. To the extent that we submit electronic healthcare claims and payment transactions that do not comply with the electronic data transmission standards established under HIPAA and HITECH, payments to us may be delayed or denied.

In addition, state health information privacy laws, such as California's Confidentiality of Medical Information Act and Washington's My Health My Data Act, govern the privacy and security of health-related information, specifically, may apply even when HIPAA does not and impose additional requirements.

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

In addition, certain state laws, such as the California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act of 2020 ("CCPA"), govern the privacy and security of personal information, including health-related information in certain circumstances, some of which are more stringent than HIPAA in various ways. Numerous other states have passed similar laws, but many differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. The CCPA applies to personal data of consumers, business representatives, and employees, and imposes obligations on certain businesses that do business in California, including to provide specific disclosures in privacy notices, and affords rights to California residents in relation to their personal information. Health information falls under the CCPA's definition of personal information where it identifies, relates to, describes, or is reasonably capable of being associated with or could reasonably be linked, directly or indirectly, with a particular consumer or household — unless it is subject to HIPAA — and is included under a new category of personal information, "sensitive personal information," which is offered greater protection. The numerous other comprehensive privacy laws that have passed or are being considered in other states, as well as at the federal and local levels, also exempt some data processed in the context of clinical trials; but others exempt covered entities and business associates subject to HIPAA altogether, further complicating compliance efforts, and increasing legal risk and compliance costs for us and the third parties upon whom we rely.

Additionally, our use of artificial intelligence and machine learning may be subject to laws and evolving regulations regarding the use of artificial intelligence and machine learning, controlling for data bias, and antidiscrimination.

Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in

investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

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

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

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

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

For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization.

In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost- containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. The IRA provides CMS with significant new authorities intended to curb drug costs and to encourage market competition. For the first time, CMS will be able to directly negotiate prescription drug prices and to cap out-of-pocket costs. Each year, CMS will select and negotiate a preset number of high-spend drugs and biologics that are covered under Medicare Part B and Part D that do not have generic or biosimilar competition. On August 29, 2023, HHS announced the list of the first ten drugs subject to price negotiations. These price negotiations occurred in 2024. In January 2025, CMS announced a

list of 15 additional Medicare Part D drugs that will be subject to price negotiations. The IRA also provides a new "inflation rebate" covering Medicare patients that took effect in 2023 and is intended to counter certain price increases in prescriptions drugs. The inflation rebate provision requires drug manufacturers to pay a rebate to the federal government if the price for a drug or biologic under Medicare Part B and Part D increases faster than the rate of inflation. To support biosimilar competition, beginning in October 2022, qualifying biosimilars may receive a Medicare Part B payment increase for a period of five years. Separately, if a biologic drug for which no biosimilar exists delays a biosimilar's market entry beyond two years, CMS will be authorized to subject the biologics manufacturer to price negotiations intended to ensure fair competition. Notwithstanding these provisions, the IRA's impact on commercialization and competition remains largely uncertain.

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

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

Healthcare Reform

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

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

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

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

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

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

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

Other Government Regulation Outside of the United States

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

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

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

Regulation in the European Union

European Data Laws

The collection and use of personal health data and other personal data in the 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.

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 UK is deemed to have an adequate data protection level. However, the adequacy decisions include a ‘sunset clause’ which entails that the decisions will automatically expire four years after their entry into force, unless renewed.

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 public disclosure obligations provided in the EU Clinical Trials Regulation No. 536/2014 (“CTR”), European Medical Agency ("EMA") disclosure initiatives and voluntary commitments by industry. Failure to comply with these obligations could lead to government enforcement actions and significant penalties against us, harm to our reputation, and adversely impact our business and operating results.

Additionally, following the UK’s withdrawal from the EU and the EEA, companies also have to comply with the UK’s data protection laws (including the UK GDPR (as defined in section 3(10) (as supplemented by section 205(4)) of the Data Protection Act 2018 (the “DPA 2018”)), the DPA 2018, and related data protection laws in the UK). Separate from the fines that can be imposed by the GDPR, the UK regime has the ability to fine up to the greater of £17.5 million or 4% of global turnover.

Companies are subject to specific transfer rules under the UK regime which broadly mirror the GDPR rules. On February 2, 2022, the UK Secretary of State laid before the UK Parliament the international data transfer agreement (“IDTA”) and the international data transfer addendum to the EC’s standard contractual clauses for international data transfers (Addendum) and a document setting out transitional provisions. The IDTA and Addendum came into force on March 21, 2022 and replaced the old SCCs for the purposes of the UK regime. 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.

Drug and Biologic Development Process

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

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

A more unified procedure will apply under the new CTR. A sponsor will be able to submit a single application for approval of a clinical trial through a centralized EU clinical trials portal (the Clinical Trials Information System or "CTIS”). One national regulatory authority (the reporting EU member state proposed by the applicant) will take the lead in validating and evaluating the application consult and coordinate with the other concerned EU Member States. If an application is rejected, it may be amended and resubmitted through the EU clinical trials portal. If an approval is issued, the sponsor may start the clinical trial in all concerned EU Member States. However, a concerned EU member state may in limited circumstances declare an “opt-out” from an approval and prevent the clinical trial from being conducted in such member state. The CTR also aims to streamline and simplify the rules on safety reporting, and introduces enhanced transparency requirements such

as mandatory submission of a summary of the clinical trial results to the EU Database. The CTR foresees a three-year transition period. EU Member States will work in CTIS immediately after the system has gone live. Since January 31, 2023, submission of initial clinical trial applications via CTIS is mandatory and CTIS serves as the single entry point for submission of clinical trial-related information and data. By January 31, 2025, all ongoing trials approved under the former Clinical Trials Directive will need to comply with the CTR and have to be transitioned to CTIS. On July 19, 2023, the EC published guidance concerning the steps to be taken in this transition. This guidance provides, among other things, that (i) documentation which was previously assessed will not be reassessed, (ii) templates that were developed and endorsed by the EU Clinical Trials Expert Group to provide compliance with the CTR do not need to be updated and (iii) there is no need to retrospectively create a site suitability form, which are only necessary for new trial sites.

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

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

Drug Marketing Authorization

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

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

On August 30, 2023, the MHRA published detailed guidance on its recently announced new International Reliance Procedure (“IRP”) for MAAs. The IRP applies since January 1, 2024 and replaces existing EU reliance procedures to apply for authorizations from seven international regulators (e.g. Health Canada, Swiss Medic, FDA, EMA, among others). The IRP allows medicinal products approved in other jurisdictions that meet certain criteria to undergo a fast-tracked MHRA review to obtain and/or update a MA in the UK. Applicants can submit initial MAAs to the IRP but the procedure can also be used throughout the lifecycle of a product for post-authorization procedures including line extensions, variations and renewals.

Centralized Authorization Procedure

The centralized procedure provides for the grant of a single MA that is issued by the EC following the scientific assessment of the application by the EMA that is valid for all EU Member States as well as in the three additional EEA Member States (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 not yet authorized in the EEA before May 20, 2004 and indicated for the treatment of other diseases, medicinal products that constitute significant therapeutic, scientific or technical innovations or for which the grant of a MA

through the centralized procedure would be in the interest of public health at EU level, an applicant may voluntarily submit an application for a MA through the centralized procedure.

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

Decentralized Authorization Procedure

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

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

Risk Management Plan

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

MA Validity Period

MAs have an initial duration of five years. After these five years, the authorization may subsequently be renewed on the basis of a reevaluation of the risk-benefit balance. Once renewed, the MA is valid for an unlimited period unless the EC or the national competent authority decides, on justified grounds relating to

pharmacovigilance, to proceed with only one additional five-year renewal. Applications for renewal must be made to the EMA at least nine months before the five-year period expires.

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

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

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

Advanced Therapy Medicinal Products

In the EU, medicinal products, including 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/Conditional Approval

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

Data and Market Exclusivity

As in the United States, it may be possible to obtain a period of market and / or data exclusivity in the EU that would have the effect of postponing the entry into the marketplace of a competitor’s generic, hybrid or biosimilar product (even if the pharmaceutical product has already received a MA) and prohibiting another

applicant from relying on the MA holder's pharmacological, toxicological and clinical data in support of another MA for the purposes of submitting an application, obtaining MA or placing the product on the market. Innovative medicinal products, referred to as New Chemical Entities ("NCEs"), approved in the EU qualify for eight years of data exclusivity and 10 years of marketing exclusivity.

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

The data exclusivity period begins on the date of the product's first MA in the EU. After eight years, a generic product application may be submitted and generic companies may rely on the MA holder's data. However, a generic product cannot launch until two years later (or a total of 10 years after the first MA in the EU of the innovator product), or three years later (or a total of 11 years after the first MA in the EU of the innovator product) if the MA holder obtains MA for a new indication with significant clinical benefit within the eight-year data exclusivity period. Additionally, another non-cumulative one-year period of data exclusivity can be added to the eight years of data exclusivity where an application is made for a new indication for a well-established substance, provided that significant pre-clinical or clinical studies were carried out in relation to the new indication. Another year of data exclusivity may be added to the eight years, where a change of classification of a pharmaceutical product has been authorized on the basis of significant pre-trial tests or clinical trials (when examining an application by another applicant for or holder of MA for a change of classification of the same substance the competent authority will not refer to the results of those tests or trials for one year after the initial change was authorized).

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

On April 26, 2023, the EC submitted a proposal for the reform of the European pharmaceutical legislation. The current draft envisages e.g., a shortening of the periods of data exclusivity, however, there is currently neither a final version of this draft nor a date for its entry into force. While the European Parliament adopted its approving position on the reform on April 10, 2024, no further required legislative steps have been taken since.

Orphan Designation and Exclusivity

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

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

are covered by the orphan drug designation. Upon the grant of a MA, orphan drug designation provides up to ten years of market exclusivity in the orphan indication.

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

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

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

Pediatric Development

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

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

PRIME Designation

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The Priority Medicines ("PRIME") scheme is

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

Post-Approval Regulation

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

Failure by us or by any of our third-party partners, including suppliers, manufacturers and distributors to comply with EU laws and the related national laws of individual EU Member States governing the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of MA, statutory health insurance, bribery and anti-corruption or other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

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

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

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

The manufacturing process for pharmaceutical products in the EU is highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC (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 GMP standards when manufacturing pharmaceutical products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU. 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. Similarly, the distribution of pharmaceutical products into and within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU Member States. The manufacturer or importer must have a qualified person who is responsible for certifying that each batch of product has been manufactured in accordance with GMP, before releasing the product for commercial distribution in the EU or for use in a clinical trial. Manufacturing facilities are subject to periodic inspections by the competent authorities for compliance with GMP.

Sales and Marketing Regulations

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

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

Anti-Corruption Legislation

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

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

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

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

Regulations in the UK and Other Markets

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

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

The MMDA supplements the UK Medical Devices Regulations 2002 (the "Regulations"), which are based on the EU Medical Devices Directive as amended to reflect the United Kingdom's post-Brexit regulatory regime. Notably, the Regulations do not include any of the revisions that have been made by the EU Medical Devices Regulation (EU) 2017/745, which has gained full application in all EU Member States since May 26, 2021 but is not applicable in the UK as "retained law". Additionally, the MHRA launched a comprehensive consultation in 2021 with proposals to amend the regulatory framework for medical devices in the United Kingdom. The stated objectives of the proposals include expansion of the scope of the Regulations (for example, by expanding the in vitro diagnostic medical device definition to include software and other products, including products without an intended medical purpose but with similar functioning and risk profiles) and potentially through use of internationally recognized definitions (for example, by excluding products that contain viable biological substances and excluding food), remove trade barriers, further the availability of medical devices and improve the favorability of the UK market. The consultation period closed on November 25, 2021 and on June 26, 2022, the MHRA published a response to its consultation, which sets out the proposed new UK regulatory framework for medical devices and in vitro diagnostic medical devices. The proposals are intended to improve patient safety and public health through appropriate regulatory oversight, improve the traceability of medical devices, improve the regulation of the rules governing software and AI as medical devices and introduce alternative routes to market to ensure the UK aligns with any superior international best practices. Core aspects of the new framework are expected to apply from July 1, 2025 with appropriate transitional measures and the introduction of secondary legislation.

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 nonclinical 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 trial designs and interpretation of data and its sufficiency to support safety and efficacy of our product candidates, patient recruitment or other clinical trial challenges, or unanticipated drug supply disruptions.
- We are substantially dependent on the success of the SPY001, SPY002 and SPY003 programs, alone or in combination, and may fail to achieve our projected 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 intraportfolio 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.
- The FDA may not accept data from clinical trials we conduct at sites outside the United States.

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 face difficulties from healthcare and other legislative reform measures and other changes in law.
- Our potential revenue may be adversely affected due to unfavorable regulations 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.

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.

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 security or data breaches or other improper access to our data.
- Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.
- We may fail to comply with privacy, 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.
- We may fail to maintain proper and effective internal controls. We have identified a material weakness in our internal control over financial reporting over financial reporting which could, if not remediated, 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.
- Our business could be adversely affected by macroeconomic conditions.

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, 2024, we had $603.1 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 rising interest rates and downturns 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 downturns. We may be unable to raise capital through public offerings of our common stock and may need to turn to alternative financing arrangements. Such arrangements, if we pursue them, could involve issuances of one or more types of securities, including common stock, preferred stock, convertible debt, warrants to acquire common stock or other securities. These securities could be issued at or below the then prevailing market price for our common stock. In addition, if we issue debt securities, the holders of the debt would have a claim to our assets that would be superior to the rights of stockholders until the principal, accrued and unpaid interest and any premium or make-whole has been paid. Interest on any newly-issued debt securities and/or newly-incurred borrowings would increase our operating costs and reduce our net income (or increase our net loss), and these impacts may be material. If the issuance of new securities results in diminished rights to holders of our common stock, the market price of our common stock could be materially and adversely affected.

We do not currently have any products approved for sale and do not generate any revenue from product sales. Accordingly, we expect to rely primarily on equity and/or debt financings to fund our continued operations. Our ability to raise additional funds will depend, in part, on the success of our 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 financial, economic and market conditions, many of which are beyond our control. There can be no assurances that sufficient funds will be available to us when required or on acceptable terms, if at all.

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

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

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

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

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

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

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

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

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

We are a biopharmaceutical company with a limited operating history. Since inception, we have incurred significant operating losses. For the years ended December 31, 2024, 2023 and 2022, we reported a net loss of $208.0 million, $338.8 million and $83.8 million, respectively. As of December 31, 2024, we had an accumulated deficit of $972.4 million. 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 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 and 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. 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 and remain outstanding as of December 31, 2024 due to beneficial ownership limitations.

Debt financing, if available, would likely involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, making additional product acquisitions, or declaring dividends. If we raise additional funds through strategic collaborations or licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates or future revenue streams or grant licenses on terms that are not favorable to us. We cannot

be assured that we will be able to obtain additional funding if and when necessary to fund our entire portfolio of product candidates to meet our projected plans. If we are unable to obtain funding on a timely basis, we may be required to delay or discontinue one or more of our development programs or the commercialization of any product candidates or be unable to expand our operations or otherwise capitalize on potential business opportunities, which could materially harm our business, financial condition, and results of operations.

Risks Related to Discovery, Development and Commercialization

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

The development and commercialization of drugs is highly competitive. Our product candidates, if approved, will face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration. We compete with a variety of multinational biopharmaceutical companies, specialized biotechnology companies and emerging biotechnology companies, as well as academic institutions, governmental agencies, and public and private research institutions, among others. Many of the companies with which we are currently competing or will 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 a competitive safety, efficacy, dosing and/or presentation profile. Our commercial opportunity and success will be reduced or eliminated if competing products are safer, more effective, have a more attractive dosing profile or presentation or are less expensive than the products we develop, or if our competitors develop competing products or if biosimilars enter the market more quickly than we do and are able to gain market acceptance. See the section titled “Business – Competition” in this Annual Report on Form 10-K for more discussion about our competitors.

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

Our product candidates are in clinical and nonclinical 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 nonclinical stages of development, and we have not completed any clinical trials. 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 complete any clinical trials, 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 and efficacy in humans of our programs 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 could 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 FDA, or ethics committees ("ECs")/institutional review boards ("IRBs") may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations ("CROs"), the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trial sites may deviate from trial protocol or drop out of a trial;
- clinical trials of any product candidates may fail to demonstrate safety or efficacy, or produce negative or inconclusive results, 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 third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators 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;
- 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 is subject to acceptance by the FDA of an IND or similar application and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA requires us to complete additional nonclinical studies or clinical trials or we are required to satisfy other FDA 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. Even if we conduct such additional nonclinical studies or 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 impose stricter approval conditions than we currently expect.

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 three most advanced programs, SPY001, SPY002 and SPY003, 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 three most advanced programs, SPY001, SPY002 and SPY003, alone or in combination. We exercised our Option with respect to the SPY001, SPY002 and SPY003 programs on July 12, 2023, December 14, 2023, and June 5, 2024, respectively. Additionally, 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) and TL1A (SPY002 program) 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) 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. We are investing a majority of our efforts and financial resources into the research and development of these programs. We initiated a Phase 1 clinical trial in healthy volunteers of SPY001 and announced the dosing of our first participant in June 2024. We also initiated a Phase 1 clinical trial in healthy volunteers of SPY002 in the fourth quarter of 2024. We anticipate initiating a Phase 1 clinical trial in healthy volunteers of SPY003 in the first quarter of 2025, subject to regulatory feedback and approval. We also plan to initiate a Phase 2 platform trial of our product candidates in IBD beginning with monotherapies in mid-2025 and subsequent planned addition of combination arms as well as a Phase 2 clinical trial of SPY002 in RA in mid-2025, each subject to regulatory feedback and approval. 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. This is based in part on the assumption that the longer half-lives observed in NHPs will translate into extended half-lives of our product candidates in humans. To the extent we do not observe these extended half-lives with favorable safety and efficacy profiles when we dose humans with our product candidates, it would significantly and adversely affect the clinical and commercial potential of our product candidates.

Our programs will require additional clinical development, evaluation of clinical, nonclinical and manufacturing activities, product development, marketing approval in multiple jurisdictions, substantial investment and significant marketing efforts before we generate any revenues from product sales. We are not

permitted to market or promote these programs, or any other programs, before we receive marketing approval from the FDA and comparable foreign regulatory authorities, and we may never receive such marketing approvals.

The success of our product candidates will depend on a variety of factors. We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any current or future collaborator. Accordingly, we cannot assure you that we will ever be able to generate revenue through the sale of these product candidates, even if approved. If we are not successful in commercializing SPY001, SPY002 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 for the anticipated completion of our Phase 1 clinical trials in healthy volunteers and topline data from our planned Phase 2 clinical trials in IBD and RA, 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 the research programs with respect to which we have signed a license agreement, exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Paragon Agreement, leverages

clinically validated mechanisms of action and incorporates advanced antibody engineering to optimize half-life and other properties designed to overcome limitations of existing therapies. Our programs are purposefully designed to improve upon existing product candidates and products while maintaining the same well-established mechanisms of action. However, the scientific research that forms the basis of our efforts to develop programs using half-life extension technologies, including YTE and LS amino acid substitutions, is ongoing and may not result in viable programs. We have limited clinical data on product candidates utilizing YTE and LS half-life extension technologies, especially in I&I indications, demonstrating whether they are safe or effective for long-term treatment in humans. The long-term safety and efficacy of these technologies and the extended half-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. Other than for our SPY001 program, we currently have only nonclinical data regarding the increased half-life properties of our programs and a similar half-life extension may not be seen in humans. In addition, programs using half-life extension technologies may demonstrate different chemical and pharmacological properties in participants than they do in laboratory studies. This technology and any programs resulting therefrom may not demonstrate the same chemical and pharmacological properties in humans and may interact with human biological systems in unforeseen, ineffective or harmful ways.

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

Nonclinical 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 nonclinical 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 nonclinical 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 nonclinical study or clinical trial process. For example, we depend on the availability of NHPs to conduct certain nonclinical 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 nonclinical 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 nonclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials. Moreover, nonclinical and clinical data are often susceptible to varying interpretations and analyses, and many

companies that have believed their product candidates performed satisfactorily in nonclinical 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. We plan to use the data from our ongoing and planned Phase 1 trials of our SPY001, SPY002 and SPY003 programs in healthy volunteers to support Phase 2 trials in IBD, RA and other I&I indications. 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, CTA 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. Events that may prevent successful or timely initiation or completion of clinical trials include: inability to generate sufficient nonclinical, toxicology or other in vivo or in vitro data; delays in reaching a consensus with regulatory authorities on trial design or implementation of the clinical trials; delays or failure in obtaining regulatory authorization to commence a trial; delays in reaching agreement on acceptable terms with current and prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites; CRO personnel changes which could lead to operational delays or complications; delays in identifying, recruiting and training suitable clinical investigators and their study teams; delays in obtaining required EC/IRB approval at each clinical trial site; delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of our product candidates or other supplies for use in clinical trials or the inability to do any of the foregoing; failure by our CROs, other third parties or us to adhere to clinical trial protocols; failure to perform in accordance with the FDA's or any other regulatory authority's good clinical practice requirements ("GCPs") or applicable regulatory guidelines in other countries; changes to the clinical trial protocols; clinical sites deviating from trial protocol or dropping out of a trial; changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data; transfer of manufacturing processes to facilities operated by a contract manufacturing organization ("CMO") and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and third parties being unwilling or unable to satisfy their contractual obligations to us.

We could also encounter delays if a 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, 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 combination therapies, 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 combination therapies, 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 combination therapy. 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 combination therapies, 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 combination therapies 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 current or future approval standards required for combination therapies or combination products, if we decided to administer or package a combination therapy 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 a combination therapy 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 a combination therapy or if we are unable to meet the FDA'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 if participants choose to enroll in clinical

trials, rather than using approved products, or if our competitors have ongoing clinical trials for programs that are under development for the same indications as our programs, and participants instead enroll in such clinical trials. Additionally, the number of participants required for clinical trials of our programs may be larger than we anticipate. 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.

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 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 non-clinical 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 non-clinical 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. Any of these occurrences could harm our business, financial condition, results of operations and prospects significantly.

Our product candidates have mechanisms of action 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 ulcerative colitis in adults and of moderately to severely active Crohn's disease in adults. In addition, mAbs targeting TL1A such as our product candidate SPY002, in clinical research are associated with patient adverse reactions that most commonly include headache, nasopharyngitis, 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 ulcerative colitis in adults and of moderately to severely active Crohn's disease in adults, the most common adverse reactions are upper respiratory infections, headache, arthalgia, injection site reactions, abdominal pain, anemia, pyrexia, back pain, arthropathy, and urinary tract infection in patients with Crohn's disease and arthralgia, pyrexia, injection site reactions, and rash in patients with UC. Patients in our clinical trials for SPY001, SPY002 and SPY003, or combinations thereof, may experience similar or additional adverse reactions.

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 the research programs with respect to which we have signed a licensed agreement for or exercised the Option to acquire intellectual property license rights to or have the Option to acquire intellectual property license rights to pursuant to the Paragon Agreement prove to be unsafe, our entire pipeline could be affected, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Because we have limited financial and managerial resources, we focus our research and development efforts on certain selected programs. For example, we are initially focused on our most advanced programs, SPY001, SPY002 and SPY003, including combinations thereof. 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 RA. 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 or RA. 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 in development for the same indication, IBD, and are planning to develop one product candidate (SPY002) for RA. We may in the future develop our programs for other I&I indications. Each such program targets a different mechanism of action. However, developing multiple programs for a single indication may negatively impact our business if the programs compete with each other. For example, if multiple programs are conducting clinical trials at the same time, they could compete for the enrollment of participants. In addition, if multiple product candidates are approved for the same indication, they may compete for market share, which could limit our future revenue.

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

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

Further, conducting international clinical trials presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled 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.

Risks Related to Government Regulation

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

The process of obtaining regulatory approvals, both in the United States and abroad, is unpredictable, expensive and typically takes many years following commencement of clinical trials, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. We cannot commercialize product candidates in the United States without first obtaining regulatory approval from the FDA. Similarly, we cannot commercialize product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of our product candidates, including our most advanced product candidates, SPY001, SPY002 and SPY003, 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.

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.

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 (the "ACA"), includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a highly similar or "biosimilar" product may not be submitted to the FDA until four years following the date that the reference product was first approved by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first approved. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own 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 is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

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

Any regulatory approvals that we may receive for our product candidates will require the submission of reports to regulatory authorities and surveillance to monitor the safety and efficacy of the product candidate, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval 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 face difficulties from healthcare legislative reform measures and other changes in law.

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. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, 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 government administration on us and the pharmaceutical industry as a whole is unclear. These government actions could cause delays in our business plans, increase cost of execution of our business plans or otherwise have a material adverse affect on our business. For example, if legislation similar to the BIOSECURE Act is passed with terms that require us to switch or move development of our product candidates from one CMO to another, we may incur additional development costs or delays in manufacturing product for clinical trials or commercialization. See the section titled “Business – Government Regulation – Healthcare Reform” in this Annual Report on Form 10-K for a more detailed description of healthcare reform measures that may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates.

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

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. See the section titled “Business – Government Regulation – Other Healthcare Laws and Compliance Requirements” in this Annual Report on Form 10-K for a more detailed description of the laws that may affect our ability to operate.

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

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

We intend to seek approval to market our product candidates in both the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. Our ability to successfully commercialize any product candidates that we may develop will depend in part on the extent to which reimbursement for these product

candidates and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. These entities may create preferential access policies for a competitor's product, including a branded or generic/biosimilar product, over our products in an attempt to reduce their costs, which may reduce our commercial opportunity. Additionally, if any of our product candidates are approved and we are found to have improperly promoted off-label uses of those product candidates, we may become subject to significant liability, which would materially adversely affect our business and financial condition. See the sections titled "Business – Government Regulation – Coverage and Reimbursement" and "Business – Government Regulation – Regulation in the European Union" in this Annual Report on Form 10-K 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, the U.S. Physician Payments Sunshine 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 regulatory authorities. The receipt of a designation for a product candidate may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify under one of FDA's designation programs, the FDA may later decide that the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. See the section titled "Business – Government Regulation – United States Biologics Regulation – Expedited Development and Review Programs" in this Annual Report on Form 10-K for a more detailed description of the process for seeking expedited designations such as fast track or breakthrough therapy designations.

Risks Related to Our Intellectual Property

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

We rely upon a combination of patents, trademarks, trade secret protection, confidentiality agreements, 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 and license may not afford us any meaningful competitive advantage.

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

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

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

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

Periodic maintenance fees, renewal fees, annuities fees and various other governmental fees on patents and/or patent applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent and/or patent application. The USPTO and various foreign governmental patent agencies also require compliance with a number of procedural, documentary, fee payment and other

similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our programs, our competitive position would be adversely affected.

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

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

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

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

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

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

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

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

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

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

Risks Related to Our Reliance on Third Parties

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

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

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

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

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

We currently rely, and plan to rely in the future, on third parties to conduct and support our 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 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 nonclinical studies and 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 these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our 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.

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 potential passing of an act similar to the previously proposed

BIOSECURE 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. If we are not able to secure supply of our product candidates as a result of applicable legislation, this could result in a material adverse effect on our Company.

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

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

We do not currently own any facility that may be used as our clinical or commercial manufacturing and processing facility and must currently rely on CMOs to manufacture our product candidates. We have not yet caused our product candidates to be manufactured on a commercial scale and may not be able to do so for any of our programs, if approved. We currently have a sole source relationship for our supply of the SPY001 and SPY003 programs and one of the molecules in our SPY002 program. 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. 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. 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 on Form

10-K for a more detailed description of our manufacturing plans and assumptions and the factors that may affect the success of our programs.

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

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

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

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

We are a clinical stage biotechnology company with a limited operating history, and, as of December 31, 2024, we had 65 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. 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, or those of any of our CROs, manufacturers, other contractors or consultants, third-party service providers, or potential future collaborators, may fail or suffer security or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations.

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

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

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

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

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

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

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

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

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

practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

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

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

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

We, and third parties who we work with, are or may become subject to numerous domestic and foreign laws, regulations, and standards relating to privacy, data protection, and data security, the scope of which is changing, subject to differing applications and interpretations, and may be inconsistent among countries, or conflict with other rules. We are or may become subject to the terms of contractual obligations related to privacy, data protection and data security. Our obligations may also change or expand as our business grows. The actual or perceived failure by us or third parties related to us to comply with such laws, regulations and obligations could increase our compliance and operational costs, expose us to regulatory scrutiny, actions, fines and penalties, result in reputational harm, lead to a loss of customers, result in litigation and liability, and otherwise cause a material adverse effect on our business, financial condition and results of operations. See the section titled “Business – Government Regulation – Data Privacy and Security” in this Annual Report on Form 10-K 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. Such changes, among others, may adversely affect our effective tax rate, results of operation and general business condition.

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

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

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

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

Risks Related to Our Common Stock

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

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

- our ability to obtain regulatory approvals for our product candidates, and delays or failures to obtain such approvals;
- failure of any of our product candidates, if approved, to achieve commercial success;
- failure to maintain our existing third-party license and supply agreements;
- changes in laws or regulations applicable to our product candidates;
- any inability to obtain adequate supply of our product candidates or the inability to do so at acceptable prices;
- adverse regulatory authority decisions;

- introduction of new products, services, or technologies by our competitors;
- failure to meet or exceed financial and development projections we may provide to the public and the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators, and the investment community;
- announcements of significant acquisitions, strategic collaborations, joint ventures, or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- additions or departures of key personnel;
- significant lawsuits, including patent or stockholder litigation;
- if securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our business and stock;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions, including global inflationary pressures, rising interest rates, general economic slowdown or a recession, changes in monetary policy, instability in financial institutions and the prospect of a shutdown of the U.S. federal government;
- geopolitical instability and government actions, including the ongoing military conflict in Ukraine, conflict between Israel and various other parties, geopolitical tensions between China and the United States, 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.

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 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 potential clinical trials for our product candidates. To raise capital, we may sell common stock, convertible securities, or other equity securities in one or more transactions at prices and in a manner we determine from time to time. As a result, our stockholders may experience additional dilution, which could cause our stock price to fall.

Pursuant to our equity incentive plans, we may grant equity awards and issue additional shares of our common stock to our employees, directors and consultants, and the number of shares of our common stock reserved for future issuance under certain of these plans will be subject to automatic annual increases in accordance with the terms of the plans. To the extent that new options 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 or will be 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.

We are not required to reflect the change in our smaller reporting company status and comply with the increased disclosure obligations until our quarterly report for the quarter ending March 31, 2025, the first quarter in our fiscal year ending December 31, 2025.

We will reassess, as of June 30, 2025, whether we continue to qualify as a large accelerated filer for filings beyond the fiscal year ending December 31, 2025.

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

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

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

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, and the rules and regulations of Nasdaq. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. 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. This requires that we incur substantial professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. We may experience difficulty in meeting these reporting requirements in a timely manner for each period.

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

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act, or if we are unable to maintain proper and effective internal controls, it could result in a material misstatement of our financial statements that would not be prevented or detected on a timely basis, which could require a

restatement, cause us to be subject to sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities, cause investors to lose confidence in our financial information, or cause our stock price to decline.

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

We have identified a material weakness in our internal control over financial reporting. If our remediation of the material weaknesses is not effective, or if we experience additional material weaknesses or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to accurately report our financial results in a timely manner, and we or our independent registered public accounting firm may conclude that our internal control over financial reporting is not effective, which may adversely affect investor confidence in us and materially and adversely affect our business and operating results.

Effective internal controls over financial reporting are necessary for us to provide reliable financial information and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our consolidated financial statements or identify other areas for further attention or improvement. 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 elsewhere in this Annual Report, we have identified a material weakness in our internal control over financial reporting related to the Company's accounting and reporting of complex financial instruments, resulting in a determination that the Company's issued preferred stock is common-like in nature and therefore we should apply the two-class method of calculating net loss per share and include our issued Series A Preferred Stock and Series B Preferred Stock in such calculation for our issued audited consolidated financial statements as of December 31, 2023 and for the year then ended, and our unaudited consolidated financial statements for the quarterly and year-to-date (as applicable) periods ended June 30, 2023, September 30, 2023, March 31, 2024, June 30, 2024 and September 30, 2024 (collectively, the "Affected Periods").

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. These remediation measures may be time-consuming and costly and there is no assurance that these initiatives will ultimately have the intended effects. While we believe that these efforts will improve our internal control over financial reporting, remediation of the material weaknesses will require validation and testing of the design and operating effectiveness of internal controls over a sustained period of financial reporting cycles. We cannot assure you that these measures will significantly improve or remediate the material weaknesses described above.

The material weakness resulted in the restatement of our financial statements for the Affected Periods. As a result of this material weakness, our management has concluded that our disclosure controls and procedures were not effective as of December 31, 2023 and 2024. See Part II, Item 9A. Controls and Procedures included in this Annual Report. While we are taking a number of measures to remediate the material weakness (as described above), if we identify additional material weaknesses, we may be unable to provide required financial information in a timely and reliable manner and we may incorrectly report financial information. Likewise, if our financial statements are not filed on a timely basis, we could be subject to sanctions or investigations by the stock exchange on which our shares of common stock are listed, the SEC or other regulatory authorities. The existence of material weaknesses in internal control over financial reporting could adversely affect our reputation or investor perceptions of us, which could have a negative effect on the trading

price of our stock. We can give no assurance that any additional material weaknesses or restatements of financial results will not arise in the future due to a failure to implement and maintain adequate internal control over financial reporting or circumvention of these controls. Even if we are successful in strengthening our controls and procedures, in the future those controls and procedures may not be adequate to prevent or identify irregularities or errors or to facilitate the fair presentation of our financial statements.

If we identify any new material weaknesses in the future, any such newly identified material weakness could limit our ability to prevent or detect a misstatement of our accounts or disclosures that could result in a material misstatement of our annual or interim financial statements. In such case, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting and our stock price may decline as a result. We cannot assure you that any measures we may take in the future, will be sufficient to avoid potential future material weaknesses.

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, and Israel and various other parties and other conflicts in the region, 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. For example, the COVID-19 pandemic resulted in widespread unemployment, economic slowdown and extreme volatility in the capital markets. 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, and 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 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.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 1C. CYBERSECURITY

In the ordinary course of our 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 National Institute of Standards and Technology ("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 Senior Vice President, Operations and 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. 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 periodic employee training that covers cyber and information security, among other topics. 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, Information Technology, who reports directly to our Senior Vice President, Operations, has over 25 years of experience managing information technology and cybersecurity matters and is certified as Certified Information Systems Security Professional. Together with our Senior Vice President, Operations and the other members of our senior leadership team, our Vice President, Information Technology 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 threats 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,” under the heading “Our internal information technology systems, or those of any of our CROs, manufacturers, other contractors or consultants, third-party service providers, or potential future collaborators, may fail or suffer security or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations.”

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, Information Technology, 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 19, 2025, there were approximately 26 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.

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

On December 31, 2024, in accordance with the Paragon Agreement and to settle the Company's 2024 obligations under the Parapyre Option Obligation (as defined below), we issued to Parapyre a warrant to purchase an aggregate of up to 848,184 shares of our common stock, with a per share exercise price equal to $23.28, which was the closing price of a share of the Company's common stock on December 31, 2024 (the "Issue Date"), the last business day of the calendar year-ended December 31, 2024, effective as of the Issue Date and an expiration date of the 10th anniversary of the Issue Date. We have relied on the exemption from registration requirements provided by Section 4(a)(2) under the Securities Act of 1933, as amended, relating to a transaction not involving any public offering to a single accredited investor.

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. If this research program is pursued non-provisionally and matures into issued patents, we would expect those patents to expire no earlier than 2044, subject to any disclaimers or extensions. On December 14, 2023, we exercised the Option under the Paragon Agreement to be granted an exclusive license to all of Paragon's rights, title and interest in and to intellectual property rights, including inventions, patents, sequence information and results, under SPY002, our TL1A program, to develop and commercialize antibodies and products worldwide in all therapeutics disorders. If this research program is pursued non-provisionally and matures into issued patents, we would expect those patents to expire no earlier than 2044, subject to any disclaimers or extensions. 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. If this research program is pursued non-provisionally and matures into issued patents, we would expect those patents to expire no earlier than 2045, subject to any disclaimers or extensions. 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, SPY004.

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 RA 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, 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, study 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 years ended December 31, 2023 and 2022, we recognized revenue of $0.9 million and $2.3 million, respectively, 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. For the year ended December 31, 2022, the revenue recognized was related to the PEACE Phase 3 trial and BLA package performance.

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. The upfront payment and contingent milestone payments if paid, net of expenses and adjustments, will be distributed to holders of our CVRs (as defined below) pursuant to 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.

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, 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 began the process of closing our subsidiaries in the United Kingdom and Ireland, both of which have 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 2023 tax year for us and our Former Subsidiaries. We will continue to have income tax reporting requirements for our two foreign subsidiaries until the closure process is completed.

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 study duration, may vary from our estimates, resulting in adjustments to research and development expense in future periods. Changes in these estimates that result in material changes to our accruals could materially affect our results of operations. However, there have been no material changes in estimates for the periods presented.

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 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 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 cash payments in the future calculated on the monetization or disposal of certain legacy assets owned by us prior to the Asset Acquisition (the "Legacy Assets") within the CVR period. Certain contingent payments under the CVR Agreement qualify as derivatives under ASC 815, Derivatives and Hedging, and are recorded as a liability on the balance sheet as of December 31, 2024 and December 31, 2023. The CVR liability is considered a Level 3 instrument that is initially measured at its estimated fair value on the transaction date and subsequently remeasured at each reporting date with changes recorded in the consolidated statement of operations. The determination of the initial and subsequent fair value of the CVR liability requires significant judgment by management. Changes in any of the inputs not related to facts and circumstances existing as of the transaction

date may result in a significant fair value adjustment, which can impact the results of operations in the period in which the adjustment is made. 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, 2024 compared to the year ended December 31, 2023 is presented below. A discussion and analysis of our financial condition and results of operations for the year ended December 31, 2023 compared with the year ended December 31, 2022 is included in Item 7 of Part II, “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our Annual Report on Form 10-K for the year ended December 31, 2023, filed with the U.S. Securities and Exchange Commission ("SEC") on February 29, 2024, as amended by Amendment No. 1 and Amendment No. 2, each on Form 10-K/A, filed with the SEC on March 1, 2024 and November 18, 2024, respectively.

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 a $43.4 million increase in manufacturing costs, a $34.0 million increase in nonclinical and clinical development, a $10.2 million increase in intellectual property license fees, and a $7.9 million increase in compensation costs primarily associated with an increase in research and development headcount, partially offset by a $23.2 million decrease in costs related to the Company's legacy rare disease pipeline.

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 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 a $9.8 million increase in stock-based compensation expense, inclusive of a $2.4 million acceleration expense related to legacy Aeglea officers and directors, partially offset by a $2.6 million reduction in compensation costs primarily associated with lower legacy severance costs, and $1.4 million reduction in lease termination costs that were incurred in the prior year.

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.

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.

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.

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, 2024, we have funded our operations by raising an aggregate of approximately $1.3 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, 2024, we had an accumulated deficit of $972.4 million.

Our primary use of cash is to fund the development of our product candidates and advance our pipeline. This includes both the research and development costs and the general and administrative expenses required to support those operations. 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 March 2021, we entered into the Immedica Agreement, pursuant to which Immedica licensed the product rights for commercialization of pegzilarginase in the European Economic Area, United Kingdom, Switzerland, Andorra, Monaco, San Marino, Vatican City, Turkey, Saudi Arabia, United Arab Emirates, Qatar, Kuwait, Bahrain, and Oman. In April 2021, we received an upfront payment of $21.5 million from Immedica. In July 2021, the Immedica Agreement was modified to include additional development services, up to $3.0 million, to support the PEACE Phase 3 trial and BLA package performance obligation. In July 2023, the Immedica Agreement was terminated through the sale of pegzilarginase to Immedica for $15.0 million in upfront cash proceeds and up to $100.0 million in contingent milestone payments.

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

In June 2023, we sold 721,452 shares of convertible Series A preferred stock 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 September 2024 and December 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 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.

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

	Year Ended December 31,	
	2024	2023
Net cash and cash equivalents (used in) provided by:		
Operating activities	$ (157,410)	$ (99,910)
Investing activities	(353,285)	(108,393)
Financing activities	410,906	361,077
Effect of exchange rate on cash, cash equivalents, and restricted cash	(3)	25
Net increase (decrease) in cash and cash equivalents	$ (99,792)	$ 152,799

Cash Used in Operating Activities

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 a $4.5 million net change in operating assets and liabilities and $11.4 million in net accretion of discount on marketable securities 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 operating activities for the year ended December 31, 2023 was $99.9 million and reflected a net loss of $338.8 million. Our net loss, coupled with a $5.2 million net change in operating assets and liabilities related to the continuing wind down of legacy operations, $16.4 million gain on the sale of IPR&D, and $2.3 million in net accretion of discount on marketable securities; partially offset by $262.9 million of non-cash items consisting of $130.2 million for acquired IPR&D, $83.5 million change in fair value of forward contract liability, $25.7 million in stock-based compensation, $19.0 million change in fair value of CVR liability, $2.6 million impairment loss on lease abandonment, and $1.9 million in depreciation, amortization and loss on disposal of long-lived assets.

Cash (Used in) Provided by Investing Activities

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

Cash Provided by Financing Activities

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, $20.5 million and $215.9 million in net proceeds from the issuance of common stock in connection with the Company's at-the-market offering program and the November 2024 underwritten offering, 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.

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

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 four 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, 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, 2024, we have paid milestone payments totaling $9.5 million for milestones achieved thus far under each License Agreement out of a total maximum of $66.0 million in potential milestone payments across all License Agreements. 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. As of December 31, 2024 we have incurred $0.7 million of sublicensing fees of which $0.5 million remain outstanding and payable.

As of the date of the filing of this Annual Report, the Option remains unexercised with respect to the one remaining research program, SPY004, under the Paragon Agreement. Should the Option for SPY004 be exercised and upon entry into a license agreement with respect to SPY004, we expect to be obligated to pay Paragon up to an additional $22.0 million based on certain development, regulatory and clinical milestones.

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, 2024, we held $603.1 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, 2024, 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

Report of Independent Registered Public Accounting Firm

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

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Spyre Therapeutics, Inc. and its subsidiaries (the "Company") as of December 31, 2024 and 2023, and the related consolidated statements of operations, of comprehensive loss, of changes in convertible preferred stock and stockholders' equity and of cash flows for each of the three years in the period ended December 31, 2024, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

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, 2024 and 2023, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2024 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company did not maintain, in all material respects, effective internal control over financial reporting as of December 31, 2024, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO because a material weakness in internal control over financial reporting existed as of that date related to the Company not designing and maintaining effective controls to evaluate the treatment of the Series A Preferred Stock and the Series B Preferred Stock for the purpose of calculating earnings per share under the two-class method.

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 the annual or interim financial statements will not be prevented or detected on a timely basis. The material weakness referred to above is described in Management's Annual Report on Internal Control Over Financial Reporting appearing under Item 9A. We considered this material weakness in determining the nature, timing, and extent of audit tests applied in our audit of the 2024 consolidated financial statements, and our opinion regarding the effectiveness of the Company's internal control over financial reporting does not affect our opinion on those consolidated financial statements.

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 management's report referred to above. Our responsibility is to express opinions on the Company's consolidated financial statements and 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 audits 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 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. 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 (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) 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 (iii) 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 Matters

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

Contingent Value Right (CVR) Liability

As described in Notes 1, 2, and 3 to the consolidated financial statements, in connection with the asset acquisition of Pre-Merger Spyre, a non-transferable contingent value right was distributed to certain legacy stockholders of record as of the close of business on July 3, 2023 entitling holders of the contingent value right to receive certain cash payments from proceeds received by the Company related to the disposition or monetization of the Company's legacy assets. Management determined that certain contingent payments under the Contingent Value Rights (CVR) Agreement qualified as derivatives, and as such, were recorded as a liability on the balance sheet. For derivative financial instruments accounted for as liabilities, the derivative instrument is initially recorded by management at its fair value and is then re-valued at each reporting date. The fair value of the CVR liability was determined using the probability weighted discounted cash flow method to estimate future cash flows associated with the sale of the legacy assets. The CVR liability value is based on significant inputs not observable in the market such as estimated cash flows, estimated probabilities of regulatory success, estimated reimbursement rates compared to the reimbursement target, and risk-adjusted discount rates. The CVR liability as of December 31, 2024 was $61.7 million and the Company recognized an increase in the CVR liability of $19.0 million for the year ended December 31, 2024 related to the change in fair value between December 31, 2023 and December 31, 2024 of $20.4 million offset by payments of $1.4 million.

The principal considerations for our determination that performing procedures relating to the valuation of the CVR liability is a critical audit matter are (i) the significant judgment by management when developing the fair value estimate of the CVR liability; (ii) a high degree of auditor judgment, subjectivity, and effort in performing procedures and evaluating management's significant assumptions related to the estimated probabilities of regulatory success, estimated reimbursement rates compared to the reimbursement target, and risk-adjusted discount rates; and (iii) the audit effort involved the use of professionals with specialized skill and knowledge.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to the valuation of the contingent value rights liability, including controls over the significant assumptions and underlying data. These procedures also included, among others (i) evaluating the terms of the CVR agreement; (ii) testing management's process for developing the fair value estimate of the CVR liability; (iii) evaluating the appropriateness of the probability weighted discounted cash flow method used by management; (iv) testing the completeness and accuracy of underlying data used by management in the probability weighted discounted cash flow method; and (v) evaluating the reasonableness of the significant assumptions used by management related to the estimated probabilities of regulatory success, estimated reimbursement rates compared to the reimbursement target, and risk-adjusted discount rates. Evaluating management's assumptions related to estimated probabilities of regulatory success and estimated reimbursement rates compared to the reimbursement target involved evaluating whether the assumptions used by management were reasonable considering the consistency with (i) external market and industry data and (ii) evidence obtained in other areas of the audit. Professionals with specialized skill and knowledge were used to assist in evaluating (i) the appropriateness of the probability weighted discounted cash flow method and (ii) the reasonableness of the risk-adjusted discount rate assumption.

/s/ PricewaterhouseCoopers LLP

Austin, Texas

February 27, 2025

We have served as the Company's auditor since 2014.

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

	December 31,	
	2024	2023
ASSETS		
CURRENT ASSETS		
Cash and cash equivalents	$ 89,423	$ 188,893
Marketable securities	513,665	150,384
Prepaid expenses and other current assets	5,386	2,251
Total current assets	608,474	341,528
Restricted cash	—	322
Other non-current assets	10	9
TOTAL ASSETS	$ 608,484	$ 341,859
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES		
Accounts payable	$ 666	$ 896
CVR liability	25,080	1,390
Accrued and other current liabilities	27,711	13,108
Related party accounts payable	603	16,584
Total current liabilities	54,060	31,978
Non-current CVR liability	36,620	41,310
TOTAL LIABILITIES	90,680	73,288
Commitments and Contingencies (Note 8, Note 9)		
Series B non-voting convertible preferred stock, $0.0001 par value; 150,000 shares authorized, issued, and outstanding as of December 31, 2023.	—	84,555
STOCKHOLDERS' EQUITY		
Series A non-voting convertible preferred stock, $0.0001 par value; 1,086,341 shares authorized as of December 31, 2024 and December 31, 2023; 346,045 and 437,037 shares issued and outstanding as of December 31, 2024 and December 31, 2023, respectively.	146,425	184,927
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, 2024.	9,395	—
Preferred stock, $0.0001 par value; 8,642,034 shares and 8,763,659 shares authorized as of December 31, 2024 and December 31, 2023, respectively; no shares issued and outstanding as of December 31, 2024 and December 31, 2023.	—	—
Common stock, $0.0001 par value; 400,000,000 shares authorized as of December 31, 2024 and December 31, 2023; 60,257,023 shares and 36,057,109 shares issued and outstanding as of December 31, 2024 and December 31, 2023, respectively.	13	10
Additional paid-in capital	1,334,223	763,191
Accumulated other comprehensive income	180	302
Accumulated deficit	(972,432)	(764,414)
TOTAL STOCKHOLDERS' EQUITY	517,804	184,016
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY	$ 608,484	$ 341,859

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,		
	2024	2023	2022
Revenue:			
Development fee and royalty	—	886	2,329
Total revenue	—	886	2,329
Operating expenses:			
Research and development [1]	162,790	89,504	58,579
General and administrative	45,776	39,946	28,531
Acquired in-process research and development	—	130,188	—
Gain on sale of in-process research and development asset	—	(16,449)	—
Total operating expenses	208,566	243,189	87,110
Loss from operations	(208,566)	(242,303)	(84,781)
Other income (expense):			
Interest income	21,312	6,147	837
Change in fair value of forward contract liability	—	(83,530)	—
Other expense, net	(20,713)	(19,130)	(7)
Total other income (expense)	599	(96,513)	830
Loss before income tax expense	(207,967)	(338,816)	(83,951)
Income tax (expense) benefit	(51)	26	136
Net loss	$ (208,018)	$ (338,790)	$ (83,815)
Net loss per share, basic and diluted, Series A Preferred Stock	$ (127.21)	$ (550.28)	$ —
Weighted-average Series A non-voting convertible preferred stock outstanding, basic and diluted	374,387	434,612	—
Net loss per share, basic and diluted, Series B Preferred Stock	$ (127.21)	$ (550.29)	$ —
Weighted-average Series B non-voting convertible preferred stock outstanding, basic and diluted	85,208	8,630	—
Net loss per share, basic and diluted, common	$ (3.18)	$ (13.76)	$ (24.86)
Weighted-average common shares outstanding, basic and diluted	47,027,638	6,897,065	3,371,231

[1] Includes $41.2 million and $48.5 million in related party expenses for the years ended December 31, 2024 and December 31, 2023, respectively, and no related party expenses for the year ended December 31, 2022.

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,		
	2024	2023	2022
Net loss	$ (208,018)	$ (338,790)	$ (83,815)
Other comprehensive income (loss):			
Foreign currency translation adjustment	4	37	(35)
Unrealized (loss) gain on marketable securities	(126)	313	7
Total comprehensive loss	$ (208,140)	$ (338,440)	$ (83,843)

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, 2021	—	$ —	—	$ —	—	$ —	1,974	$ 5	$ 425,765	$ (20)	$ (341,809)	$ 83,941
Issuance of common stock and pre-funded warrants in connection with registered direct offering, net of offering costs	—	—	—	—	—	—	430	1	42,873	—	—	42,874
Issuance of common stock in connection with exercise of pre-funded warrants	—	—	—	—	—	—	204	—	—	—	—	—
Issuance of common stock in connection with employee stock purchase plan	—	—	—	—	—	—	6	—	222	—	—	222
Stock-based compensation expense	—	—	—	—	—	—	—	—	7,111	—	—	7,111
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	(35)	—	(35)
Unrealized gain on marketable securities	—	—	—	—	—	—	—	—	—	7	—	7
Net loss	—	—	—	—	—	—	—	—	—	—	$ (83,815)	$ (83,815)
Balances—December 31, 2022	—	$ —	—	$ —	—	$ —	2,614	$ 6	$ 475,971	$ (48)	$ (425,624)	$ 50,305
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
Exchange of Series A non-voting convertible preferred stock for common stock	—	—	(91)	(38,502)	—	—	3,640	1	38,501	—	—	—
Conversion of Series B non-voting convertible preferred stock into common stock	—	—	—	—	(255)	(244,010)	10,198	1	244,009	—	—	—
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 follow-on offering, net of financing costs	—	—	—	—	—	—	8,366	1	215,673			215,674
Issuance of common stock in connection with exercise of pre-funded warrants	—	—	—	—	—	—	250	—	1	—	—	1
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
Vesting of restricted stock units	—	—	—	—	—	—	38	—	—	—	—	—
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	4	—	4
Unrealized gain 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

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,		
	2024	2023	2022
CASH FLOWS FROM OPERATING ACTIVITIES			
Net loss	$ (208,018)	$ (338,790)	$ (83,815)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	—	744	1,567
Stock-based compensation	44,833	25,675	7,111
Acquired in-process research and development	—	130,188	—
Change in fair value of CVR liability	20,430	18,986	—
Change in fair value of forward contract liability	—	83,530	—
Gain on sale of in-process research and development asset	—	(16,449)	—
Lease ROU asset and leasehold improvement impairment loss	—	2,580	—
Loss on disposal of long-lived assets	—	915	—
Net (accretion of discount) amortization of premium on marketable securities	(11,404)	(2,318)	(327)
Interest proceeds from maturities of zero coupon debt securities	1,283	—	—
Amortization of operating lease assets	—	220	397
Other	—	15	426
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	(2,932)	3,245	(1,144)
Accounts payable	(230)	218	(2,641)
Deferred revenue	—	575	(880)
Development receivables	—	375	440
Operating lease liabilities	—	(2,326)	(435)
Accrued and other liabilities	14,609	(4,891)	(843)
Related party accounts payable	(15,981)	(2,402)	—
Net cash used in operating activities	(157,410)	(99,910)	(80,144)
CASH FLOWS FROM INVESTING ACTIVITIES			
Cash assumed from asset acquisition of Spyre	—	3,035	—
Proceeds from sale of in-process research & development asset	—	15,000	—
Purchases of property and equipment	—	—	(38)
Proceeds from the sale of property plant and equipment	—	475	—
Purchases of marketable securities	(599,252)	(166,803)	(39,500)
Proceeds from maturities and sales of marketable securities	245,967	39,900	96,546
Net cash provided by (used in) investing activities	(353,285)	(108,393)	57,008
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	20,521	—	—
Proceeds from issuance of common stock in connection with follow-on offering, net of issuance costs	215,860	—	—
Payment of deferred offering costs in connection with shelf registration	(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	(1,430)	(5,786)	—
Proceeds from issuance of common stock and pre-funded warrants in registered direct offering, net of offering costs	1	—	42,874
Proceeds from employee stock option exercises and employee stock plan purchases	7,511	405	222
Principal payments on finance lease obligation	—	(16)	(418)
Net cash provided by financing activities	410,906	361,077	42,678
Effect of exchange rate on cash, cash equivalents, and restricted cash	(3)	25	(106)
NET INCREASE (DECREASE) IN CASH, CASH EQUIVALENTS, AND	(99,792)	152,799	19,436

CASH, CASH EQUIVALENTS, AND RESTRICTED CASH			
Beginning of period	189,215	36,416	16,980
End of period	$ 89,423	$ 189,215	$ 36,416
Supplemental Disclosure of Non-Cash Investing and Financing Information:			
Allocation of deferred offering costs against proceeds of issuance of common stock	$ 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	$ —
Leased assets obtained in exchange for lease obligations	$ —	$ —	$ 21
Reconciliation of Cash, Cash Equivalents, and Restricted Cash Reported in the Statement of Financial Position			
Cash and cash equivalents	89,423	188,893	$ 34,863
Restricted cash	$ —	$ 322	$ 1,553
Total cash, cash equivalents, and restricted cash shown in the statement of cash flows	$ 89,423	$ 189,215	$ 36,416

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

Spyre Therapeutics, Inc.
Notes to Consolidated Financial Statements

1. The Company and Basis of Presentation

Spyre Therapeutics, Inc., formerly Aeglea BioTherapeutics, Inc., (“Spyre” or the “Company”) is a 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 cash payments from proceeds received by the Company for a 3-year period related to the disposition or monetization of its legacy assets for a period of one-year following the closing of the Asset Acquisition. For additional information, see Note 3.

On November 21, 2023, the Company's stockholders approved the conversion of the Company's Series A non-voting convertible preferred stock to common stock. For additional information, see Note 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, 2024.

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 our 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 with TD Securities (USA) LLC (“TD Cowen”), 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 at an average price per share of $26.935, resulting in aggregate net proceeds of approximately $20.5 million after deducting $0.4 million in commissions paid to TD Cowen as sales agent and other offering costs.

On November 18, 2024, the Company entered into an underwriting agreement (the "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 "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 an 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.

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, 2024, the Company has funded our operations by raising an aggregate of approximately $1.3 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, 2024, Spyre had an accumulated deficit of $972.4 million, and cash, cash equivalents, and marketable securities of $603.1 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 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 operations in the United Kingdom for the period ended December 31, 2023. There were no restricted cash balances as of December 31, 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, 2024 and 2023, balances at the Company's U.S. banking institutions exceeded the FDIC limits. The Company has not experienced any losses on its deposits of cash, cash equivalents, and restricted cash and its accounts are monitored by management to mitigate risk. The Company is exposed to credit risk in the event of default by the financial institutions holding its cash, cash equivalents, and restricted cash, and bond issuers.

Property and Equipment

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

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

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

Impairment of Long-Lived Assets

Long-lived assets are reviewed for indications of possible impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparison of the carrying amounts to the future undiscounted cash flows attributable to these assets. An impairment loss is recognized to the extent an asset group is not recoverable, and the carrying amount exceeds the fair value. The Company recognized a $2.6 million impairment loss for the year ended December 31, 2023 related to its leased office space in Austin, Texas (see Note 11 and Note 17 for additional information). There were no impairments of long-lived assets for the years ended December 31, 2024 and 2022.

Accrued Research and Development Costs

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

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

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 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.

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 U.S. Food and Drug Administration ("FDA"), among other events. This fair value measurement is based on significant inputs not observable in the market and thus represents a Level 3 measurement as defined in ASC 820, Fair Value Measurement. The key assumptions used include the discount rate, probability of regulatory success, and reimbursement rates from certain government agencies. The estimated value of the CVR consideration is based upon available information and certain assumptions which the Company's management believes are reasonable under the circumstances. The ultimate payout under the CVRs may differ materially from the assumptions used in determining the fair value of the CVR consideration.

Income Taxes

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

A valuation allowance is established against the deferred tax assets to reduce their carrying value to an amount that is more likely than not to be realized. The deferred tax assets and liabilities are classified as noncurrent along with the related valuation allowance. Due to a lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance.

The Company recognizes benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on the technical merits, as the largest amount of benefits that is more likely than not to be realized upon the ultimate settlement. The Company’s policy is to recognize interest and penalties related to the unrecognized tax benefits as a component of income tax expense, if applicable. As of December 31, 2024 and 2023, the Company had no unrecognized tax benefits and there were no interest or penalties incurred by the Company in the years ended December 31, 2024, 2023, or 2022.

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

The Company early adopted the Financial Accounting Standards Board’s ("FASB") Accounting Standards Update 2020-06, Accounting for Convertible Instruments and Contracts in an Entity’s Own Equity (“ASU 2020-06”), effective as of January 1, 2023 using the modified retrospective method. Among other

amendments, ASU 2020-06 eliminates the cash conversion and beneficial conversion feature models in ASC 470-20 that required an issuer of certain convertible debt and preferred stock to separately account for embedded conversion features as a component of equity, as well as changes the accounting for diluted earnings-per-share for convertible instruments and contracts that may be settled in cash or stock. Additionally, ASU 2020-06 requires the if-converted method, which is more dilutive than the treasury stock method, be used for all convertible instruments. The Company applied ASU 2020-06 to all Series A Preferred Stock and Series B Preferred Stock during fiscal year 2023, and, accordingly, the Company did not apply the cash conversion or beneficial conversion feature models in its analysis of the Series A Preferred Stock and Series B Preferred Stock. The adoption of ASU 2020-06 did not have a material impact on the Company's consolidated financial statements.

The Company adopted the FASB Standards Update 2023-07, Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures ("ASU 2023-07") effective for fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024, with early adoption permitted. Among other amendments, ASU 2023-07 requires issuers to provide enhanced disclosures about significant segment expenses and information used to assess segment performance on an annual and interim basis. The ASU also requires companies with a single reportable segment, such as the Company, to provide all disclosures required by Topic 280 - Segment Reporting. The Company adopted this ASU with the fiscal year ending December 31, 2024, and applied the amendments retrospectively to all prior periods presented in the consolidated financial statements. See Note 19, Segment Reporting.

Not Yet Adopted Accounting Pronouncements

In December 2023, the FASB issued ASU 2023-09, Income Taxes (Topic 740): Improvements to Income Tax Disclosures. This ASU expands disclosures in an entity’s income tax rate reconciliation table and disclosures regarding taxes paid both in the U.S. and foreign jurisdictions. This update is effective for fiscal years beginning after December 15, 2024. This ASU will have no impact on the Company’s consolidated financial condition or results of operations. The Company is currently evaluating the impact to its income tax disclosures.

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.

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, 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

	December 31, 2023			
	Level 1	Level 2	Level 3	Total
Financial Assets				
Money market funds	$ 150,648	$ —	$ —	$ 150,648
U.S. government treasury securities	32,843	—	—	32,843
U.S. government agency securities	—	16,257		16,257
Commercial paper	—	104,141	—	104,141
Corporate bonds	—	33,064	—	33,064
Total financial assets	$ 183,491	$ 153,462	$ —	$ 336,953
Liabilities:				
CVR liability	$ —	$ —	$ 42,700	$ 42,700
Total liabilities	$ —	$ —	$ 42,700	$ 42,700

The Company measures the fair value of money market funds on quoted prices in active markets for identical asset or liabilities. The Level 2 assets include U.S. government agency securities, commercial paper and corporate bonds, and are valued based on quoted prices for similar assets in active markets and inputs other than quoted prices that are derived from observable market data.

The Company evaluates transfers 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, 2024 and 2023, the Company had $61.7 million and $42.7 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, 2024 and 2022.

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 CVR will be entitled to receive certain cash payments from proceeds received by the Company for a three-year period, if any, related to the disposition or monetization of the Company’s legacy assets for a period of one year following the closing of the Asset Acquisition.

The fair value of the CVR liability was determined using the probability weighted discounted cash flow method to estimate future cash flows associated with the sale of the legacy assets. Analogous to a dividend being declared/approved in one period and paid out in another, the liability was recorded at the date of approval, June 22, 2023, as a common stock dividend, returning capital to the Legacy Stockholders. Changes in fair value of the liability will be recognized as a component of Other income (expense) in the consolidated statement of operations and comprehensive loss in each reporting period. The liability value is based on significant inputs not observable in the market such as estimated cash flows, estimated probabilities of regulatory success, and discount rates, which represent a Level 3 measurement within the fair value hierarchy. The significant inputs used to estimate the fair value of the CVR liability were as follows:

	December 31, 2024
Estimated cash flow dates	5/28/25 - 06/22/26
Estimated probability of success	72% - 100%
Estimated reimbursement rate compared to reimbursement target	81% - 100%
Risk-adjusted discount rates	7.29% - 7.50%

The change in fair value between December 31, 2023 and December 31, 2024 was a $20.4 million increase, and was primarily driven by changes in the expected timing of achievement of certain milestones, changes in the likelihood of certain milestones related to the approval received from the European Medicines Agency by Immedica Pharma AB ("Immedica"), partially offset by a change in the likelihood of a successful disposition of pegtarviliase and updates to expenses and deductions.

The following table presents changes in the CVR liability for the periods presented (in thousands):

	CVR Liability
Beginning balance as of December 31, 2023	$ 42,700
Changes in the fair value of the CVR liability	20,430
Payments	(1,430)
Ending Balance as of December 31, 2024	$ 61,700

4. Cash Equivalents and Marketable Securities

The following tables summarize the estimated fair value of the Company's cash equivalents and marketable securities and the gross unrealized gains and losses (in thousands):

	December 31, 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

	December 31, 2023			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Cash equivalents:				
Money market funds	$ 150,648	$ —	$ —	$ 150,648
Commercial paper	24,950	5	—	24,955
U.S. government treasury securities	10,965	1	—	10,966
Total cash equivalents	$ 186,563	$ 6	$ —	$ 186,569
Marketable securities:				
Commercial paper	$ 79,124	$ 62	$ —	$ 79,186
Corporate bonds	32,984	81	(1)	33,064
U.S. government treasury securities	21,846	31	—	21,877
U.S. government agency securities	16,147	110	—	16,257
Total marketable securities	$ 150,101	$ 284	$ (1)	$ 150,384

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, 2024 and 2023, aggregated by major security type and length of time in a continuous unrealized loss position:

	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)

	December 31, 2023					
	Less Than 12 Months		12 Months or Longer		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
Corporate bonds	$ 9,907	$ (1)	$ —	$ —	$ 9,907	$ (1)
U.S. government treasury securities	4,831	—	—	—	4,831	—
Total marketable securities	$ 14,738	$ (1)	$ —	$ —	$ 14,738	$ (1)

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, 2024 and 2023, 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, 2024 and 2023.

There were $0.1 million net unrealized losses on marketable securities for the year ended December 31, 2024. For the years ended December 31, 2023 and 2022, there were $0.3 million and de minimis, respectively, net unrealized gains. There were no realized gains on marketable securities for the years ended December 31, 2024, 2023 and 2022.

Interest on marketable securities is included in interest income. Accrued interest receivable on available-for-sale debt securities totaled $3.4 million and $0.9 million as of December 31, 2024 and 2023, 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,	
	2024	2023
Due in one year or less	$ 338,442	$ 115,784
Due in 1 - 2 years	175,223	34,600
Total marketable securities	$ 513,665	$ 150,384

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, 2024 and 2023.

Depreciation and amortization expense for the years ended December 31, 2023 and 2022 was $0.7 million, and $1.4 million, respectively. There was no depreciation and amortization expense for the year ended December 31, 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,	
	2024	2023
Accrued compensation	$ 5,688	$ 4,054
Accrued contracted research and development costs	20,861	7,092
Accrued professional and consulting fees	661	1,474
Other	501	488
Total accrued and other current liabilities	$ 27,711	$ 13,108

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 SPY004 pursuant to the Paragon Agreement. Accordingly, the Company treated the Asset Acquisition as an asset acquisition for accounting purposes. Even if the transaction would have failed the screen test, Pre-Merger Spyre lacked the financial resources to have inputs, processes, and outputs to constitute a business under ASC 805.

The Company completed the Asset Acquisition of Pre-Merger Spyre, in accordance with the terms of the Acquisition Agreement. Under the terms of the Acquisition Agreement, the Company issued 517,809 shares of common stock and 364,887 shares of Series A Preferred Stock to former Pre-Merger Spyre security holders. In addition, outstanding and unexercised stock options to purchase 2,734 shares of common stock were assumed from the Amended and Restated Spyre 2023 Equity Incentive Plan.

At the acquisition date, the Company recorded forward contracts to represent the obligation to issue shares of the Company's common stock and shares of Series A Preferred Stock. The forward contract related to the common stock was recorded as Additional paid-in capital as the instrument is indexed to the Company's common stock. The forward contract related to the Series A Preferred Stock was recorded as a liability, as the underlying stock has a cash redemption feature. On July 7, 2023, both the shares of common stock and Series A Preferred Stock were issued and the forward contract liability associated with the Series A Preferred Stock was settled accordingly.

The Company concluded that the arrangement meets the definition of an asset acquisition rather than a business combination, as substantially all of the fair value of the gross assets acquired is concentrated in a single identifiable asset, the Option to exclusively license IPR&D. The Company determined that the Option to license IPR&D was a single asset as the Company's strategy relies on developing the entire portfolio of individual treatments to create combination treatments that simultaneously address different mechanisms of irritable bowel disease with a single treatment. The Company also determined that the pipeline candidates within the portfolio are similar in nature and risk profile. In addition, the Company did not obtain any substantive processes, assembled workforce, or employees capable of producing outputs in connection with the Asset Acquisition.

The Company determined that the cost to acquire the asset was $113.2 million which was recorded as acquired IPR&D. The fair value of the consideration issued consisted of the 364,887 shares of Series A Preferred Stock (14,595,480 shares of common stock on an as-converted basis) and 517,809 shares of common stock, valued at $291.08 per share and $7.277 per share, respectively.

The Asset Acquisition costs are shown on the following table (in millions):

	June 22, 2023
Consideration transferred in Series A Preferred Stock and common stock	$ 110.0
Transaction costs incurred by the Company	3.2
Total cost to acquire asset	$ 113.2

The allocation of the purchase price to net assets acquired is as a follows:

	June 22, 2023
Acquired in-process research and development	$ 130.2
Cash acquired	3.0
Assumed liabilities	(20.0)
Total cost to acquire asset	$ 113.2

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, 2024, the Company recognized expense of $9.5 million 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 years ended December 31, 2023 and 2022.

For the year ended December 31, 2024, the Company made cash milestone payments to Paragon totaling $9.5 million. There were no such payments for the years ended December 31, 2023 and 2022. As of December 31, 2024, there were no Paragon license milestone payments outstanding and payable to Paragon.

Additionally, the Company recognized $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, 2024. For the year ended December 31, 2024, the Company made sublicensing fees payments to Paragon totaling $0.2 million. There were no such payments for the years ended December 31, 2023 and 2022. As of December 31, 2024, $0.5 million in sublicensing fees were outstanding and payable to Paragon.

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,		
	2024	2023	2022
Reimbursable costs under the Paragon Agreement	$ 15.3	$ 37.1	$ —
License Agreements milestone and sublicensing fees	10.2	—	—
Total related party expense (excludes stock comp)	$ 25.5	$ 37.1	$ —

The following is the summary of Related party accounts payable and other current liabilities (in millions):

	December 31,	
	2024	2023
Reimbursable costs under the Paragon Agreement	$ 0.1	$ 16.6
License Agreements development milestone liability (see Note 9)	0.5	—
Total related party accounts payable	$ 0.6	$ 16.6

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. Our Option available under the Paragon Agreement with respect to the SPY004 program remains unexercised. 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, 2024 and 2023, the Company recognized expenses related to services provided by Paragon subsequent to the Asset Acquisition totaling $29.8 million and $48.5 million, which included $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, 2024 and December 31, 2023, the Company made payments totaling $31.8 million and $39.5 million, respectively, to Paragon. There were no such payments for the year ended December 31, 2022.

Parapyre Option Obligation

Pursuant to the Paragon Agreement, the Company agreed to issue 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

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, 2024 and December 31, 2023, the Company recognized $1.1 million and $0.1 million, respectively, in stock-based compensation expense related to Mr. McKenna's consulting agreement. There was no such expense for the year ended December 31, 2022.

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 its building lease in Austin, Texas. The negotiated termination agreement obligated the Company to pay the lessor a $2.0 million termination fee in exchange for releasing the Company of all further obligations under the lease including terminating the associated letter of credit.

The following table summarizes the lease costs pertaining to the Company's operating leases (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Operating lease cost	$ —	$ 455	$ 910
Variable lease cost	—	471	472
Total lease cost	$ —	$ 926	$ 1,382

Cash paid for amounts included in the measurement of operating lease liabilities during the years ended December 31, 2023 and 2022 was $0.5 million and $0.9 million, respectively, and was included within net cash used in operating activities in the cash flows.

As of December 31, 2024 and December 31, 2023, 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, 2024 and 2023, no common stock dividends had been declared by the board of directors.

Registered Direct Offering

In May 2022, the Company issued and sold 430,107 shares of common stock at an offering price of $40.00 per share and pre-funded warrants to purchase up to 694,892 shares of common ctock at an offering price of $39.9975 per warrant (representing the price per share of common stock sold in the offering minus the $0.0025 exercise price per warrant) in a registered direct offering pursuant to a shelf registration statement on Form S-3. The net proceeds to the Company from this offering were approximately $42.9 million, after deducting placement agent fees and offering costs of $2.1 million.

June 2023 PIPE

In June 2023, in connection with the Asset Acquisition, the Company issued and sold 721,452 shares of Series A Preferred Stock at $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 a sales agreement (the "Sales Agreement") with TD Cowen, 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 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 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. As of February 27, 2025, $179.1 million remained available for sale under the Sales Agreement.

November 2024 Underwritten Offering

On November 18, 2024, the Company entered into the Underwriting Agreement with the Underwriters, pursuant to which the Company sold an aggregate of 8,366,250 shares of common stock, 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.

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, 2024, 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, 2024, 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. Following the April 2024 Exchange, 346,045 shares of Series A Preferred Stock remained outstanding.

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 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.

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, 2024 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 members states of the European Economic Area, United Kingdom, Switzerland, Andorra, Monaco, San Marino, Vatican City, Turkey, Saudi Arabia, United Arab Emirates, Qatar, Kuwait, Bahrain, and Oman (the “Territory”);

ii. Complete the global pivotal PEACE (Pegzilarginase Effect on Arginase 1 Deficiency Clinical Endpoints) Phase 3 trial (“PEACE Trial”) and related Biologics License Application (“BLA”) package to file with the United States Food and Drug Administration (“FDA”), which will be leveraged by Immedica in obtaining the necessary regulatory approvals in the Territory; and

iii. Perform a Pediatric Investigation Plan trial (“PIP Trial”) in order for Immedica to be able to receive certain regulatory approvals within the Territory.

In addition, the Company and Immedica formed a Joint Steering Committee ("JSC") to provide oversight to the activities performed under the agreement; however, the substance of the Company's participation in the JSC does not represent an additional promised service, but rather, a right of the Company to protect its own interests in the arrangement.

Further, the Company agreed to supply to Immedica, and Immedica agreed to purchase from the Company, substantially all commercial requirements of the Product. The terms of the agreement do not provide for either (i) an option to Immedica to purchase the Product from the Company at a discount from the standalone selling price or (ii) minimum purchase quantities. Finally, Immedica will bear (i) all costs and expenses for any development or commercialization of the Product in the Territory subject to the License exclusive of the Company's promised goods and services summarized above and (ii) all costs and fees associated with applying for regulatory approval of the Product in the Territory. In July 2021, the Company modified the agreement with Immedica to provide certain additional services in relation to the PEACE Phase 3 Trial and BLA package performance obligation in exchange for the reimbursement of up to $3.0 million of the actual costs incurred in relation to such incremental services.

For the years ended December 31, 2023 and 2022, the Company recognized revenue of $0.9 million and $2.3 million, respectively, related to the PEACE Trial and BLA package performance obligation using a cost to cost model.

On July 27, 2023, the Company announced that it had entered into an agreement to sell the global rights to pegzilarginase to Immedica for $15.0 million in upfront cash proceeds and up to $100.0 million in contingent milestone payments. The sale of pegzilarginase to Immedica superseded and terminated the previous license agreement between the Company and Immedica. On July 27, 2023, the carrying value of the asset was zero as it was internally developed. Accordingly, the Company recognized a $16.4 million gain within Gain on Sale of in-process research and development, which is comprised of $15.0 million in upfront cash proceeds and the reimbursement of $1.8 million in pre-paid manufacturing costs that was contingent upon a favorable opinion being received by the CHMP, net of transaction costs and the derecognition of pegzilarginase related nonfinancial assets and liabilities totaling $0.4 million.

The milestone payments are contingent on formal reimbursement decisions by national authorities in key European markets and pegzilarginase approval by the FDA, among other events. The upfront payment and contingent milestone payments if paid, net of expenses and adjustments, will reduce the CVR liability and will be distributed to CVR holders pursuant to the CVR Agreement resulting from the Asset Acquisition.

Contract Balances from Customer Contract

The timing of revenue recognition, billings and cash collections results in contract assets and contract liabilities on the balance sheets. The Company recognizes license and development receivables based on billed services, which are derecognized upon reimbursement. When consideration is received, or such consideration is unconditionally due, from a customer prior to transferring goods or services to the customer under the terms of a contract, a contract liability is recorded. Contract liabilities are recognized as revenue after control of the goods or services is transferred to the customer and all revenue recognition criteria have been met.

The Company had no contract assets or liabilities during the years ended December 31, 2024 and 2023.

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

2015 Equity Incentive Plan

In March 2015, the Company adopted the 2015 Equity Incentive Plan ("2015 Plan"), administered by the board of directors, and provides for the Company to sell or issue shares of common stock or restricted common stock, or to grant incentive stock options or nonqualified stock options for the purchase of common

stock, to employees, members of the board of directors and consultants of the Company. Under the terms of the 2015 Plan, the exercise prices, vesting and other restrictions may be determined at the discretion of the board of directors, or their committee if so delegated, except that the exercise price per share of stock options may not be less than 100% of the fair market value of the share of common stock on the date of grant, the term of stock options may not be greater than ten years for all grants, and for grantees holding more than 10% of the total combined voting power of all classes of stock, the term may not be greater than five years.

The Company granted options under the 2015 Plan until April 2016 when it was terminated as to future awards, although it continues to govern the terms of options that remain outstanding under the 2015 Plan.

As of December 31, 2024, a total of 952 shares of common stock are subject to options outstanding under the 2015 Plan and will become available under the 2016 Equity Incentive Plan (as amended and restated, the “2016 Plan”), to the extent the options are forfeited or lapse unexercised.

2016 Equity Incentive Plan

The 2016 Plan became effective in April 2016 and serves as the successor to the 2015 Plan. Under the 2016 Plan, the Company may grant stock options, stock appreciation rights, restricted stock awards, restricted stock units, performance awards, and stock bonuses. The 2016 Plan provides for an initial reserve of 44,000 shares of common stock, plus 20,395 shares of common stock remaining under the 2015 Plan, and any share awards that subsequently are forfeited or lapse unexercised under the 2015 Plan. The shares reserved exclude shares of common stock reserved for issuance under the 2015 Plan.

In October 2018, the 2016 Plan was amended to increase the number of shares of common stock reserved for issuance thereunder by 70,384 shares, extend the term of the 2016 Plan through August 7, 2028, and provide for an automatic increase in the number of shares reserved for issuance thereunder on January 1 of each year for the remaining term of the plan equal to (a) 4.0% of the number of issued and outstanding shares of common stock on December 31 of the immediately preceding year, or (b) a lesser amount as approved by the board each year (the "Evergreen Provision").

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, 2024, 2023, and 2022, an additional 3,023,650, 104,561, and 78,968 shares, respectively, became available for issuance under the 2016 Plan.

As of December 31, 2024, the total number of shares reserved for issuance under the 2016 Plan was 7,193,219, of which 3,145,248 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 1,000,000 and 6,000,000 during the years ended December 31, 2024 and 2023, respectively.

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.

As of December 31, 2024, the total number of shares reserved for issuance under the 2018 Plan was 6,895,602, of which 6,219,622 shares were subject to outstanding awards.

Spyre 2023 Equity Incentive Plan

On June 22, 2023, in connection with the Asset Acquisition, the Company assumed the Amended and Restated Spyre 2023 Equity Incentive Plan (the "Spyre Equity Plan") and its outstanding and unexercised stock options, which were converted to options to purchase 2,734 shares of 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.

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. 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 similar expense for the years ended December 31, 2022.

As of December 31, 2024, the unamortized expense related to the Parapyre Option Obligation was nil.

The following table summarizes stock option activity for the year ended December 31, 2024:

	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, 2023	8,497,395	$ 12.13	8.40	$ 98,928
Granted	2,521,853	28.39		
Exercised	(912,382)	7.90		
Forfeited	(853,708)	32.78		
Outstanding as of December 31, 2024	9,253,158	$ 15.08	8.80	$ 90,016
Options vested and expected to vest as of December 31, 2024	9,253,158	$ 15.08	8.80	$ 90,016
Options exercisable as of December 31, 2024	2,529,495	$ 11.99	8.43	$ 31,518

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, 2024, 2023, and 2022, the weighted-average grant date fair value of options granted was $28.39, $9.67, and $1.80, per share, respectively. The total intrinsic value of options exercised during the years ended December 31, 2024, 2023 and 2022 was $22.7 million, $0.4 million and $0.7 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, 2022. For the year ended December 31, 2024 139,187 non-employee stock options vested in the period. There were no non-employee stock options vested during the years ended December 31, 2023 and 2022.

2016 Employee Stock Purchase Plan

The 2016 Employee Stock Purchase Plan ("2016 ESPP") became effective in April 2016. A total of 6,600 shares of common stock were reserved for issuance under the 2016 ESPP. Eligible employees may purchase shares of common stock under the 2016 ESPP at 85% of the lower of the fair market value of the common stock as of the first or the last day of each offering period. Employees are limited to contributing 15% of the employee's eligible compensation and may not purchase more than $25,000 of stock during any calendar year. The 2016 ESPP will terminate ten years from the first purchase date under the plan, unless terminated earlier by the board of directors.

In June 2018, the 2016 ESPP was amended to provide for an automatic annual increase in the number of shares reserved for issuance thereunder on January 1 of each year for the remaining term of the year equal to (a) 1.0% of the number of issued and outstanding shares of common stock on December 31 of the immediately preceding year, or (b) a lesser amount as approved by the board of directors each year. As a result of the operation of this provision, on January 1, 2024, 2023 and 2022, an additional 360,571, 26,140, and 19,742 shares, respectively, became available for issuance under the 2016 ESPP. As of December 31, 2024, the reserve remaining and available for future issuance under the 2016 ESPP was 416,592 shares.

In February 2023, the 2016 ESPP was amended to increase the maximum shares purchased during any one period from 80 shares to 400 shares or a lesser amount determined by the board of directors.

For the years ended December 31, 2024, 2023 and 2022, stock-based compensation expense related to the 2016 ESPP plan was $0.3 million, $0.1 million and $0.2 million, respectively.

Restricted Stock Units

The Company granted 153,865 service-based restricted stock units during the year ended December 31, 2023, of which 38,467 vested during the year ended December 31, 2024. There were no restricted stock units granted during the years ended December 31, 2024 and 2022.

The following table summarizes employee restricted stock unit activity for the year ended December 31, 2024:

	Shares	Weighted Average Grant Date Fair Value
Unvested restricted stock units as of December 31, 2023	153,865	$ 18.17
Granted	—	—
Vested	(38,467)	18.17
Forfeited	—	—
Unvested restricted stock units as of December 31, 2024	115,398	$ 18.17

There were no restricted stock units granted to non-employees during the years ended December 31, 2024, 2023, and 2022.

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, 2024, 2023, and 2022 was as follows (in thousands):

	Year Ended December 31,					
	2024		2023		2022	
	Employees	Non-Employees	Employees	Non-Employees	Employees	Non-Employees
Research and development [1]	$ 9,112	$ 14,459	$ 2,910	$ 11,328	$ 2,591	$ —
General and administrative	19,833	1,429	11,327	109	4,520	—
Total stock-based compensation expense [2]	$ 28,945	$ 15,888	$ 14,237	$ 11,437	$ 7,111	$ —

[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, 2022.

[2] Of the total $28.9 million, $14.2 million and $7.1 million of employee related stock-based compensation expense for the years ended December 31, 2024, 2023 and 2022, respectively, $3.6 million, $8.3 million and $6.9 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, 2024, 2023, and 2022 (see Note 18).

The awards contain both performance and service-based vesting conditions. No expense was recognized for the unvested awards with only a performance condition for the years ended December 31, 2024, 2023, and 2022. The performance-based vesting conditions represent specific performance targets. Compensation expense for share-based payment awards with performance conditions is recognized when the performance condition is deemed probable of achievement.

As of December 31, 2024, the Company had an aggregate of $85.2 million of unrecognized stock-based compensation expense for options outstanding, which is expected to be recognized over a weighted average period of 2.9 years.

In determining the fair value of the stock-based awards, the Company uses the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Expected Term

The Company's expected term represents the period that the Company's stock-based awards are expected to be outstanding and is determined using the simplified method (based on the midpoint between the vesting date and the end of the contractual term). The Company utilizes this method due to lack of historical exercise data and the plain-vanilla nature of the Company's stock-based awards.

Expected Volatility

Since the Company was privately held through April 2016 and transitioned from a clinical stage company to a pre-clinical stage company in 2023, it alone does not have the relevant company-specific historical data to support its expected volatility. As such, the Company has used an average of expected volatilities based on the volatilities of a representative group of publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. Subsequent to the Company's initial public offering, it began to consider the Company's own historic volatility. However, due to the transition from a clinical stage company to a pre-clinical stage company, the Company still uses peer company data to assist in this analysis. For purposes of identifying comparable companies, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. The Company intends to consistently apply this process using the same or similar comparable entities until a sufficient amount of historical information regarding the volatility of the Company's own share price post transition becomes available.

Risk-Free Interest Rate

The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend

The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

Valuation of Stock Options and 2016 ESPP

The fair value of the stock options granted under the 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,		
	2024	2023	2022
Stock Options Granted			
Expected term (in years)	6.03	5.88	6.00
Expected volatility	105%	107%	84%
Risk-free interest	4.06%	4.37%	2.93%
Dividend yield	0%	0%	0%
2016 ESPP			
Expected term (in years)	0.50	0.49	0.49
Expected volatility	84%	181%	84%
Risk-free interest	5.16%	4.99%	1.95%
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, 2024, 2023, 2022, the Company provided $0.5 million, $0.2 million, and $0.6 million, respectively, in contributions to the plan.

17. Restructuring Charges

Severance and Stock Compensation

On April 12, 2023, based on the review of the inconclusive interim results from the Company's Phase 1/2 clinical trial of pegtarviliase for the treatment of classical homocystinuria and other business considerations, the Company announced that it had initiated a process to explore strategic alternatives to maximize stockholder value and engaged an independent exclusive financial advisor to support this process.

As a result, the Company implemented a restructuring plan resulting in an approximate 83% reduction of the Company’s existing headcount by June 30, 2023. The Company recognized restructuring expenses consisting of cash severance payments and other employee-related costs of $6.4 million during the year ended December 31, 2023. Cash payments for employee related restructuring charges of $5.3 million were paid as of December 31, 2023. In addition, the Company recognized $1.0 million in non-cash stock-based compensation expense related to the accelerated vesting of stock-based awards for certain employees. The Company recorded these restructuring charges based on each employee’s role to the respective research and development and general and administrative operating expense categories on its consolidated statements of operations and comprehensive loss.

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

As of December 31, 2024 and 2023, nil and $1.1 million of restructuring costs remained outstanding and unpaid, respectively, under the restructuring plan described above.

18. Income Taxes

The following table summarizes the (loss) income before income tax expense by jurisdiction for the periods indicated:

	Year Ended December 31,		
	2024	2023	2022
Domestic	$ (207,965)	$ (338,942)	$ (84,113)
Foreign	(2)	126	162
Loss before income tax expense	$ (207,967)	$ (338,816)	$ (83,951)

For the years ended December 31, 2024 and 2023, the Company recognized no provision or benefit from income taxes. For the year ended December 31, 2022, the Company recognized an income tax expense of $0.1 million related to foreign subsidiaries income tax expense. 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	2022
Tax provision derived by applying the federal statutory rate to income before income taxes	$ (43,673)	$ (71,151)	$ (17,630)
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	1,042
Federal tax credits	(91)	(1)	(3,559)
State tax credits	—	—	(640)
Effect of tax rate on foreign jurisdiction	(2)	(53)	42
Other, net	191	—	—
Change in the valuation allowance	37,471	17,839	20,609
Income tax (benefit) expense	$ 51	$ (26)	$ (136)

The components of the deferred tax assets and liabilities consist of the following (in thousands):

	December 31,		
	2024	2023	2022
Deferred tax assets			
Net operating loss carryforward	$ 87,321	$ 74,454	$ 68,917
Capitalized 174 R&D costs	45,531	22,532	11,097
Intangible assets	2,117	47	52
Deferred revenue	—	—	566
Accrued expense	1,047	579	668
Stock-based compensation	7,114	4,246	3,293
Federal tax credits	18,196	21,914	21,914
State tax credits	1,631	1,631	1,631
Other	64	88	190
Total deferred tax assets	163,021	125,491	108,328
Deferred tax liabilities			
Unrealized gain	(92)	—	—
Depreciable assets	—	—	(676)
Total deferred tax liabilities	(92)	—	(676)
Less: Valuation allowance	(162,929)	(125,491)	(107,652)
Deferred tax assets, net	$ —	$ —	$ —

The Company has established a full federal and state valuation allowance equal to the net deferred tax assets due to uncertainties regarding the realization of the deferred tax asset based on the Company's lack of earnings history. The valuation allowance increased by $37.4 million, $17.8 million, and $20.6 million during the years ended December 31, 2024, 2023, and 2022, respectively, primarily due to continuing loss from operations.

As of December 31, 2024 and 2023, the Company had U.S. net operating loss carryforwards ("NOL") of $415.8 million and $354.5 million, 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.

For the year ended December 31, 2023, the Company had U.S. tax credit carryforwards and state tax credit carryforwards of $21.9 million and $2.1 million, respectively. Of the net operating loss and tax credit carryforwards $58.4 million and $21.9 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 2020 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, 2024 and 2023, there were no amounts recorded for uncertain tax positions. As of December 31, 2024, 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,		
	2024	2023	2022
Revenue	$ —	$ 886	$ 2,329
Less:			
Compensation	$ 21,780	$ 22,590	$ 25,776
Share-based compensation [1]	44,833	25,675	7,111
Research and development, excluding compensation and share-based compensation [2] [3]	127,491	65,282	40,700
Other segment items [4]	13,914	226,129	12,557
Segment net loss	$ 208,018	$ 338,790	$ 83,815
Reconciliation of net loss			
Adjustments and reconciling items	—	—	—
Consolidated net loss	$ 208,018	$ 338,790	$ 83,815

[1] Includes $15.6 million and $11.4 million in related party expenses for the years ended December 31, 2024 and 2023, respectively, and no related party expenses for the year ended December 31, 2022.

[2] Includes non-clinical study expenses, clinical trial expenses and manufacturing costs.

[3] Includes $25.5 million and $37.1 million in related party expenses for the years ended December 31, 2024 and 2023, respectively, and no related party expenses for the year ended December 31, 2022.

[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, 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.

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, 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)

	Year Ended December 31, 2022		
	Series A Preferred Stock	Series B Preferred Stock	Common Stock
Net loss per share, basic and diluted:			
Numerator			
Allocation of losses	$ —	$ —	$ (83,815)
Denominator			
Weighted-average shares outstanding	—	—	2,307,668
Weighted-average pre-funded warrants outstanding	—	—	1,063,563
Number of shares used in per share computation	—	—	3,371,231
Net loss per share, basic and diluted	$ —	$ —	$ (24.86)

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,		
	2024	2023	2022
Options to purchase common stock	3,212,734	2,583,226	346,331
Unvested restricted stock units	68,027	4,240	6,983
Outstanding Parapyre Warrants	686,724	5,625	—

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.

Our principal executive officer and principal financial officer evaluated the effectiveness of the Company’s disclosure controls and procedures and concluded that the Company’s disclosure controls and procedures were not effective as of December 31, 2024 because of the material weakness in internal control over financial reporting disclosed below in Management's Annual Report on Internal Control Over Financial Reporting.

Notwithstanding the material weakness in internal control over financial reporting, our management, including our principal executive officer and principal financial officer, have concluded that our consolidated financial statements present fairly, in all material respects, our financial position, results of our operations and our cash flows for the periods presented in this Annual Report, in conformity with U.S. GAAP.

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, 2024. 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.

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 the company's annual or interim financial statements will not be prevented or detected on a timely basis.

We did not design and maintain effective controls related to the earnings per share calculation, as there was not an effectively designed control in place to evaluate the treatment of the Series A Preferred Stock and the Series B Preferred Stock for the purpose of calculating earnings per share under the two-class method.

This material weakness resulted in the restatement of the Company's consolidated financial statements as of and for the year ended December 31, 2023, as well as the quarterly condensed consolidated financial information for the 2024 interim periods ended March 31, 2024, June 30, 2024, and September 30, 2024 related to earnings per share. Additionally, the material weakness could result in misstatements of the earnings per share calculation that would result in a material misstatement to the annual or interim financial statements that would not be prevented or detected.

Because of this material weakness, management concluded that the Company did not maintain effective internal control over financial reporting as of December 31, 2024.

The effectiveness of the Company's internal control over financial reporting as of December 31, 2024 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report which appears herein.

Remediation Plan

In order to address the material weakness described above, management, with direction from the Audit Committee, has:

- completed a comprehensive evaluation to identify the cause of the material weakness;
- completed the review and enhancement of the existing control designs relating to the calculation of the Company's net loss per share; and
- implemented the identified enhancements into impacted control processes.

While the Company has implemented the needed remediating processes described above, remediation requires the demonstration of effective control operation for a sufficient period of time. The material weakness will not be considered remediated until the applicable controls operate for a sufficient period of time, and management has concluded, through testing, that these controls are operating effectively.

Changes in Internal Control Over Financial Reporting

In the fourth quarter of 2024, we updated the design of our controls over the earnings per share calculation to include Series A and Series B Preferred Stock, and to evaluate the substance of financing arrangements for purposes of calculating earnings per share. We executed the newly designed control in connection with the disclosure controls and procedures for this Annual Report. Other than the remediation efforts disclosed above, there have been no additional changes in internal control over financial reporting that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

(b) None of our directors or executive officers adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement during the quarter ended December 31, 2024, as such terms are defined under Item 408(a) of Regulation S-K.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Management and Board of Directors

The following table sets forth the names, ages as of February 27, 2025, and positions of the individuals who currently serve as directors and executive officers of Spyre Therapeutics, Inc.

Name	Age	Position(s)
Executive Officers and Employee Director		
Cameron Turtle	35	Chief Executive Officer and Director
Scott Burrows	47	Chief Financial Officer
Heidy King-Jones	42	Chief Legal Officer and Corporate Secretary
Sheldon Sloan	67	Chief Medical Officer
Non-Employee Directors		
Mark McKenna	45	Director
Laurie Stelzer[(1)(2)]	57	Director
Jeffrey W. Albers[(2)(3)]	53	Director
Tomas Kiselak[(3)]	38	Director
Peter Harwin[(1)]	39	Director
Michael Henderson[(2)]	35	Director
Sandra Milligan[(1)(3)]	61	Director

(1) Member of the Nominating Committee

(2) Member of the Audit Committee

(3) Member of the Compensation Committee

Our business and affairs are managed by and under the direction of our Board, which currently consists of eight members. 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, Mark McKenna, Cameron Turtle and Laurie Stelzer, whose terms expire at the 2026 Annual Meeting of Stockholders; two Class II directors, Jeffrey W. Albers and Tomas Kiselak, whose terms expire at the 2027 Annual Meeting of Stockholders; and three Class III directors, Peter Harwin, Michael Henderson and Sandra Milligan, whose terms expire at the 2025 Annual Meeting of Stockholders. Our executive officers are elected by the Board and serve at the Board's discretion.

The following is a biographical summary of the experience of our executive officers and directors:

Executive Officers and Employee Director

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

several awards, including a Rhodes Scholarship, Goldwater Scholarship, Forbes 30 Under 30 and San Francisco Business Times 40 Under 40.

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

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, develop lifecycle strategy for lead and follow on compounds, investor interface, business development support, and building a Phase 3 medical infrastructure including Clinical Development, Pharmacovigilance, Bioinformatics, Medical Affairs and Clinical Pharmacology. From March 2022 to January 2023, Dr. Sloan was Vice President and Program Lead for etrasimod UC at Pfizer, Inc. (NYSE: PFE), a biopharmaceutical company, where he was responsible for leading the etrasimod UC cross functional team and overseeing NDA and MM submission. From November 2019 to March 2022, Dr. Sloan was Vice President and Program Lead for etrasimod GI at Arena Pharmaceuticals, Inc., a Nasdaq-listed biopharmaceutical company that was acquired by Pfizer in March 2022, where he was responsible for leading the cross functional etrasimod UC team for the Phase 3 program. Between September 1997 and October 2019, Dr. Sloan held different leadership positions at Johnson and Johnson (NYSE: JNJ), a pharmaceutical and medical technologies company, in Medical Affairs, Research and Development, and Science Policy, including Global Medical Affairs Leader for IBD, leading the global launch strategy and execution for CD and UC for Stelara. He holds a Doctor of Medicine from Rush Medical College, Chicago, a Master of Bioethics from the University of Pennsylvania and a Bachelor of Science from University of Illinois Urbana-Champaign. Dr. Sloan currently serves on the Columbia University Masters of Bioethics Advisory Board, the Drexel University Dornsife School of Public Health Dean's Impact, Advancement and Learning Council, and the American Gastroenterological Association Ethics Committee.

Non-employee Directors

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.

Laurie Stelzer. Ms. Stelzer has served as a director since November 2023. Ms. Stelzer has served as Chief Financial Officer of Kailera Therapeutics, Inc., a biotechnology company focused on developing therapies for obesity, since January 2025. Prior to joining Kailera, Ms. Stelzer served as Chief Financial Officer of Orna Therapeutics, Inc., a biotechnology company focused on RNA therapeutics, from May 2024 to January 2025. Prior to joining Orna, Ms. Stelzer served as Chief Financial Officer of ReNAgade Therapeutics, Inc., a biotechnology company focused on RNA therapeutics, from September 2023 to May 2024. Prior to joining ReNAgade, Ms. Stelzer served as Chief Financial Officer of Mirati Therapeutics, Inc. (Nasdaq: MRTX), a commercial-stage targeted oncology company, from May 2022 to September 2023. Prior to joining Mirati Therapeutics, Ms. Stelzer served as Executive Vice President and Chief Financial Officer of Arena Pharmaceuticals, Inc. (acquired by Pfizer Inc.), a biopharmaceutical company, from March 2020 until the completion of Pfizer's acquisition in March 2022. Prior to joining Arena Pharmaceuticals, Ms. Stelzer served as Chief Financial Officer at 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 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.

Jeffrey Albers. Mr. Albers has served as a director since November 2023. Mr. Albers has over 25 years of experience working in the biopharmaceutical industry and bringing important new medicines to patients with cancer and rare diseases. He has served as Chairman of Blueprint Medicines Corporation (Nasdaq: BPMC), a global precision therapy company, since June 2021, and Venture Partner at Atlas Venture, a venture capital firm focused on investment in biotechnology companies, since January 2023. Mr. Albers served as Chief Executive Officer, President and Chairman of Blueprint Medicines from June 2021 to April 2022, Executive Chairman from

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

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

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

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

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

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

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

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

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

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

Code of Business Conduct and Ethics

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

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 Stock Market (“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.

Audit Committee and Audit Committee Financial Expert

We have a separately designated standing Audit Committee. The members of our Audit Committee are Laurie Stelzer (Chair), Jeffrey W. Albers and Michael Henderson, each of whom qualifies as an “independent” director for audit committee purposes, as defined under Nasdaq listing rules and the rules and regulations established by the SEC. 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.

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires our directors, officers and persons who beneficially own more than 10% of a registered class of our equity securities to file with the SEC initial reports of ownership and

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

ITEM 11. EXECUTIVE COMPENSATION

Overview

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

Our named executive officers for 2024 were:

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

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

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

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

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

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

Summary Compensation Table

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

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

(1) For 2024, the amount reported in this column reflects a sign-on bonus for Dr. Sloan in connection with the commencement of his employment with the Company during 2024, as described in more detail under “Narrative Disclosure to Summary Compensation Table—Offer Letters” below.

(2) Amounts reported in this column for 2024 represent the aggregate grant date fair value of stock options granted to our NEOs, as computed in accordance with ASC 718. See Note 15 to our consolidated financial statements in this Annual Report for more information regarding the assumptions used in calculating the grant date fair value of stock options.

(3) Amounts reported in this column for 2024 represent the annual bonuses earned under the 2024 annual bonus program, as described in more detail under “Narrative Disclosure to Summary Compensation Table —Elements of Compensation—Annual Bonus Program” below.

(4) Amounts reported in this column for 2024 include matching contributions under our 401(k) plan made during 2024.

Narrative Disclosure to Summary Compensation Table

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

Peer Group

In October 2023, our Compensation Committee, in consultation with Alpine, its independent compensation consultant, established a peer group that focuses on U.S.-based, pre-clinical or early clinical biotechnology/pharmaceutical companies (with priority placed on companies with a similar therapeutic focus) with a market capitalization ranging from $250 million to $2 billion and less than 100 employees. The peer

group, which was approved by the Board and used in establishing executive compensation for 2024, includes the following companies:

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

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

Elements of Compensation

Base Salary

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

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

Annual Bonus Program

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

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

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

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

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

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

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

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

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

Long-Term Incentive Compensation

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

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

Offer Letters

We have entered into offer letters with each of our NEOs in connection with their appointments (and, for Dr. Turtle, his promotion to Chief Executive Officer), which for Dr. Turtle was further amended in February 2024

(collectively, the "Offer Letters"). Each Offer Letter provides for an initial base salary, target bonus opportunity and stock option grant. Under the Offer Letters, the NEOs are eligible for certain payments or benefits upon certain terminations of employment, as described under "Additional Narrative Disclosure-Potential Payments Upon Termination of Change in Control" below. Mr. Burrows' Offer Letter also provided for a sign-on bonus of $115,000, which was subject to repayment in the event of a termination for cause or resignation without good reason prior to September 1, 2024, and Dr. Sloan's Offer Letter also provided for a sign-on bonus of $120,000, which is subject to repayment in the event of a termination for cause or resignation without good reason prior to October 1, 2025.

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

Outstanding Equity Awards at December 31, 2024

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

		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	709,457	1,182,430[2]	$7.50	6/22/2033		
	11/22/2023	101,291	272,709[3]	$10.39	11/22/2033		
	2/1/2024	57,864	219,886[2]	$25.86	2/1/2034		
	[4]					333,893[5]	7,773,029
Sheldon Sloan	10/1/2024	—	400,000[3]	$27.46	10/1/2034		
Scott Burrows	9/1/2023	126,517	287,340[3]	$14.50	9/1/2033		
	2/1/2024	14,583	55,417[2]	$25.86	2/1/2024		
	12/22/2023					101,214[6]	2,356,262

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

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

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

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

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

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

Additional Narrative Disclosure

Retirement Benefits

We maintain a tax-qualified 401(k) defined contribution plan that provides eligible U.S. employees, including our NEOs, with an opportunity to save for retirement on a tax-advantaged basis. Eligible employees may make voluntary contributions from their eligible pay, up to certain applicable annual limits set by the Internal Revenue Code of 1986, as amended. We provide matching contributions equal to 100% of the first 3% of eligible compensation contributed by each employee, and 50% of the next 2% of eligible compensation contributed by each employee. All company matching contributions are immediately and fully vested. We do not maintain, and have not historically maintained, any non-qualified deferred compensation or defined benefit pension plan.

Potential Payments Upon Termination or Change in Control

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

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

As used in the Offer Letters:

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

Clawback Policy and Restatement Analysis

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

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

Equity Grant Timing Policy and Practices

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

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

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

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

Director Compensation

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

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

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

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

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

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

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)[1]	Total ($)
Jeffrey W. Albers	84,354	353,221	437,575
Russell J. Cox[2]	35,962	—	35,962
Peter Harwin	47,888	353,221	401,109
Michael Henderson	50,000	353,221	403,221
Tomas Kiselak	47,500	353,221	400,721
Alison Lawton[3]	4,396	—	4,396
Mark McKenna[4]	36,593	838,124	874,717
Sandra Milligan, M.D., J.D.[5]	33,445	703,512	736,957
Laurie Stelzer	65,000	353,221	418,221

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

(2) Mr. Cox did not stand for reelection at the 2024 Annual Meeting of Stockholders.

(3) Ms. Lawton resigned from the Board effective as of February 1, 2024.

(4) Mr. McKenna was appointed to the Board effective as of February 1, 2024.

(5) Dr. Milligan was appointed to the Board effective as of May 14, 2024.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The following table sets forth information, to the extent known by us or ascertainable from public filings, with respect to the beneficial ownership of our common stock as of February 19, 2025 by:

- each of our directors;
- 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 60,275,561 shares of our common stock outstanding as of February 19, 2025.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock subject to options that are currently exercisable or exercisable within 60 days of the date of this table or subject to conversion of preferred stock up to applicable beneficial ownership limitations are considered outstanding and beneficially owned by the person holding the options or preferred stock, as applicable, for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise indicated in the table below,

addresses of named beneficial owners are in care of Spyre Therapeutics, Inc., 221 Crescent Street, Building 23, Suite 105, Waltham, MA 02453.

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

*Represents beneficial ownership of less than one percent.

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

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

Fairmount GP, Peter Harwin and Tomas Kiselak disclaim beneficial ownership of such shares, except to the extent of any pecuniary interest therein. The address of each of these persons and entities is 200 Barr Harbor Drive, Suite 400, West Conshohocken, PA.

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

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

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

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

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

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

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

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

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

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

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

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

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

Securities Authorized for Issuance Under Equity Compensation Plans

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

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

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

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

(3) This column reflects the total shares of our common stock remaining available for issuance under the listed equity compensation plan as of December 31, 2024.

(4) No further awards may be made under the 2015 Equity Incentive Plan (the “2015 Plan”); however, shares of common stock that are subject to outstanding awards under the 2015 Plan that expire or are forfeited for any reason without having been exercised in full will generally be available for future grant and issuance under the 2016 Plan.

(5) The 2016 Plan provides for an automatic increase in the number of shares reserved for issuance thereunder on January 1 of each year through January 1, 2028 equal to (a) 5% of the number of issued and outstanding shares of common stock on December 31 of the immediately preceding year, or (b) a lesser amount as approved by the Board each year. Pursuant to this provision, the number of shares reserved for grant and issuance under the 2016 Plan increased by 3,814,905 shares on January 1, 2025.

(6) No further awards may be made under the 2023 Equity Incentive Plan, which was assumed in connection with the Asset Acquisition.

(7) The ESPP provides for an automatic annual increase in the number of shares reserved for issuance thereunder on January 1 of each year for through January 1, 2026 equal to (a) 1% of the number of issued and outstanding shares of common stock on December 31 of the immediately preceding year, or (2) a lesser amount as approved by the Board each year. Pursuant to this provision, the number of shares reserved for grant and issuance under the ESPP increased by 602,570 shares on January 1, 2025.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

Certain Relationships and Related Transactions

Other than the executive officer and director compensation arrangements disclosed above under "Item 11. Executive Compensation," below we describe the transactions to which we were a party since January 1, 2024, in which the amount involved exceeded $120,000 and in which our directors, executive officers, holders of more than 5% of our common stock, or members of their immediate family had a direct or indirect material interest.

Related Party Transactions

Spyre's Relationships with Paragon, Parapyre and Fairmount

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

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

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

In June 2024, we exercised our option available under the Paragon Agreement with respect to the SPY003 research program and in October 2024, we entered into the SPY003 License Agreement, which was subsequently amended and restated in February 2025. Under the terms of the SPY003 License Agreement, we are obligated to pay Paragon up to $22.0 million based on specific development, regulatory and clinical milestones for the first Company product to reach such milestones, including a $1.5 million fee for nomination of a development candidate, as applicable, and a further milestone payment of $2.5 million upon the first dosing of a human patient in a Phase 1 trial.

Subject to the execution of the option to acquire the intellectual property rights related to the SPY004 research program pursuant to the Paragon Agreement, we expect to be obligated to make similar payments upon and following the execution of a license agreement with respect to such research program. Our option available under the Paragon Agreement with respect to the SPY004 program remains unexercised.

Private Placement Transactions

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

Consulting Agreement

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

Exchange Agreement

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

Related Party Transaction Policy

Our Board has a written policy regarding the review and approval or ratification by our Audit Committee of related person transactions. For purposes of our policy only, a related person transaction is a transaction, arrangement or relationship or any series of similar transactions, arrangements or relationships between us or any of our subsidiaries and any related person in which the aggregate amount involved since the beginning of our last completed fiscal year exceeds or is expected to exceed $120,000 and such related person has or will have a direct or indirect interest. A related person is defined to include any executive officers, directors or director nominees or beneficial owner of more than 5% of our common stock and any immediate family member of any of the foregoing persons. In determining to approve or ratify any such transaction, our Audit Committee is expected to take into account, among other factors it deems appropriate, whether the transaction is on terms no less favorable than terms generally available to an unaffiliated third-party under the same or similar circumstances and the extent of the related person's interest in the transaction. Transactions involving compensation for services provided to us as an employee or director, among other limited exceptions, are deemed under the terms of the policy to have standing pre-approval by the Audit Committee but may be specifically reviewed if appropriate in light of the facts and circumstances. Any director who is a related person

with respect to a transaction under review is not permitted to participate in the deliberations (other than to provide information concerning the transaction to the Audit Committee) or vote on approval of the transaction.

Director Independence

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

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

All members of our Audit Committee, Compensation Committee and Nominating Committee must be independent directors under the Nasdaq listing rules. Members of the Audit Committee and Compensation Committee also must satisfy the independence criteria set forth in Rule 10A-3 and Rule 10C, respectively, under the 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.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Our independent registered public accounting firm is PricewaterhouseCoopers LLP, Austin, Texas, Auditor Firm ID: 238.

PricewaterhouseCoopers LLP ("PwC") served as our independent auditor since 2014. The following table summarizes the audit fees billed and expected to be billed by PwC for the indicated fiscal years and the fees billed by PwC for all other services rendered during the indicated fiscal years. All services associated with such fees were pre-approved by our Audit Committee in accordance with the “Pre-Approval Policies and Procedures” described below.

	Year Ended December 31,	
Fee Category	**2024**	**2023**
Audit Fees[1]	$ 1,574,031	$ 1,513,184
Audit-Related Fees[2]	—	—
Tax Fees[3]	67,990	70,923
All Other Fees[4]	2,125	2,125
Total Fees	$ 1,644,146	$ 1,586,232

(1) Consists of fees for professional services rendered for the audit of our financial statements, review of our interim condensed financial statements, professional consultations with respect to accounting matters and assistance with registration statements filed with the SEC and services that are normally provided by PwC in connection with statutory and regulatory filings or engagements. Included in our 2024 and 2023 audit fees are fees of $218,000 and $40,000 respectively, related to comfort letter fees.

(2) Consists of fees for assurance and related services reasonably related to the performance of the audit or review of our financial statements.

(3) Consists of fees for professional services for tax compliance, tax advice and tax planning.

(4) Consists of fees for all other services.

Pre-Approval Policies and Procedures

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

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					X
4.5	Form of Warrant to Purchase Common Stock (Parapyre Warrant 2023)	10-Q	001-37722	5/9/2024	4.2	
4.6	Form of Warrant to Purchase Common Stock (Parapyre Warrant 2024)					X
10.1	Form of Indemnification Agreement	S-1/A	333-276251	2/5/2024	10.19	

Exhibit Number	Description of Document	Incorporate by Reference				Filed Herewith
		Form	File No.	Date of Filing	Exhibit No.	
10.2‡	2015 Equity Incentive Plan and forms of award agreements	S-1	333-276251	12/22/2023	10.7	
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‡	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	
10.6‡	Spyre Therapeutics, Inc. 2018 Equity Inducement Plan and the First Amendment, Second Amendment, Third Amendment and Fourth Amendment thereto	S-1/A	333-276251	2/5/2024	10.10	
10.7‡	Fifth Amendment to the Spyre Therapeutics, Inc. 2018 Equity Inducement Plan	10-Q	001-37722	11/7/2024	10.4	
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-!	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, 2024, by and between the Company and WuXi Biologics (Hong Kong) Limited	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.	
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.					X
10.26	Sales Agreement, dated September 6, 2024, between Spyre Therapeutics, Inc. and TD Securities (USA) LLC	S-3	333-281975	9/6/2024	1.2	
19.1	Spyre Therapeutics, Inc. Insider Trading Policy					X
21.1	Subsidiaries of the Registrant					X
23.1	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-14(a) of the Securities Exchange Act of 1934					X
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

Exhibit Number	Description of Document	Incorporate by Reference				Filed Herewith
		Form	File No.	Date of Filing	Exhibit No.	
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 27, 2025

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 27, 2025
/s/ Scott Burrows Scott Burrows	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	February 27, 2025
/s/ Jeffrey W. Albers Jeffrey W. Albers	Chairman of the Board	February 27, 2025
/s/ Peter Harwin Peter Harwin	Director	February 27, 2025
/s/ Michael Henderson, M.D. Michael Henderson, M.D.	Director	February 27, 2025
/s/ Tomas Kiselak Tomas Kiselak	Director	February 27, 2025
/s/ Mark McKenna Mark McKenna	Director	February 27, 2025
/s/ Sandra Milligan Sandra Milligan	Director	February 27, 2025
/s/ Laurie Stelzer Laurie Stelzer	Director	February 27, 2025