

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, DC 20549**

**FORM 10-Q**

(Mark One)

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

For the quarterly period ended June 30, 2025  
OR

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  
(State or other jurisdiction of  
incorporation or organization)

46-4312787  
(I.R.S. Employer  
Identification No.)

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

(Address of principal executive offices including zip code)

Registrant's telephone number, including area code: (617) 651-5940  
Former name, former address and former fiscal year, if changed since last report: N/A

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)

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, 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	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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 is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes  No

As of July 31, 2025, the registrant had 60,400,960 shares of common stock, \$0.0001 par value per share, outstanding.

**SPYRE THERAPEUTICS, INC.**  
**QUARTERLY REPORT ON FORM 10-Q**  
**FOR THE QUARTER ENDED JUNE 30, 2025**  
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## NOTE ABOUT FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q for the quarter ended June 30, 2025 (this "Quarterly Report") contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 27A of the Securities Act of 1933, as amended (the "Securities Act"). All statements contained in this Quarterly Report other than statements of historical fact, including statements regarding any future payouts under our contingent value rights ("CVRs") issued in connection with the acquisition of Spyre Therapeutics, Inc. ("Pre-Merger Spyre") (the "Asset Acquisition"); our future results of operations and financial position; our business strategy, including our ability to develop best-in-class therapeutics for inflammatory bowel disease ("IBD") or rheumatic diseases ("RD") that meaningfully improve both efficacy and convenience compared to today's standard of care and our ability to develop first-in-class therapeutics for RD; our plans to expand the development of our product candidates, including SPY002 and SPY072, to indications beyond IBD and RD; the potential consistency of the SPY001, SPY002 and SPY072 Phase 1 trial final data readouts with previously disclosed interim Phase 1 results; the planned dosing regimen for SPY001, SPY002, SPY072 and our other product candidates, including the potential for a Q3M-Q6M dosing profile; the potential for increased or accelerated efficacy of our product candidates; our ongoing and future clinical development activities, including the expected design and timing of the planned SKYWAY-RD Phase 2 basket trial, including timing of data readouts, plans for and timing of monotherapy/combination arm enrollment, cohort initiation and data readouts for the ongoing SKYLINE-UC Phase 2 platform trial and further clinical evaluation of therapeutic combinations, enrollment of clinical trials, number of data readouts expected to be delivered in 2026 and 2027, the expected SPY003 Phase 1 trial readout in the fourth quarter of 2025 and advancements of SPY002 and SPY003 to the SKYLINE-UC Phase 2 platform trial and SPY072 to the SKYWAY-RD Phase 2 basket trial, and related regulatory feedback; 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; the potential efficacy, tolerability, convenience, commercial viability and safety profile of our product candidates, including in combinations; the potential therapeutic benefits and economic value of our product candidates as monotherapies or in combinations and their extended half-life; our ability to achieve the expected benefits or opportunities and related timing with respect to the Asset Acquisition; the expected impact of macroeconomic conditions, including inflation, increasing interest rates and volatile market conditions, current or potential bank failures, as well as global events, including the ongoing military conflict between Ukraine and Russia, the conflicts in the Middle East, and geopolitical tensions between the United States and other countries, including China, on our operations, and the implementation of changes in law, tariffs, sanctions, export or import controls, and other government measures that could impact our business operations, including restricting international trade by the United States, China or other countries; 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, but not limited to, uncertainties and risks arising from regulatory feedback, including potential disagreement by regulatory authorities with our clinical trial design, interpretation of data and our ongoing or planned clinical trials for our product candidates, including our planned SKYWAY-RD Phase 2 clinical trial design and our plans for and timing of cohort initiation for combination arms for the ongoing SKYLINE-UC Phase 2 platform trial across different jurisdictions; the potential for final clinical data not being consistent with or different than the previously disclosed data for our programs; the expected or potential impact of macroeconomic conditions, including inflationary pressures, rising interest rates, general economic slowdown or a recession, changes in tariff/trade and monetary policy, volatile market conditions, financial institution instability, as well as geopolitical instability, including the ongoing military conflicts between Ukraine and Russia, conflicts in the Middle East, and geopolitical tensions between the United States and other countries, including China, on our operations; the implementation of changes in law, tariffs, sanctions, export or import controls, and other government measures that could impact our business operations, including restricting international trade by the United States, China or other countries and the BIOSECURE Act or similar act if passed into law; and those uncertainties and factors described in Item 1A, "Risk Factors" included in this Quarterly 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

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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 Quarterly 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 Quarterly 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 Quarterly Report, the terms “Spyre,” “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 Quarterly 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 Quarterly Report refer to the research programs with respect to which we have signed a license agreement for 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”) (as amended, the “Paragon Agreement”).

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**PART I. – Financial Information**

**Item 1. Financial Statements (Unaudited).**

**Spyre Therapeutics, Inc.  
Condensed Consolidated Balance Sheets  
(Unaudited, in thousands, except share and per share amounts)**

	June 30, 2025	December 31, 2024
<b>ASSETS</b>		
<b>CURRENT ASSETS</b>		
Cash and cash equivalents	\$ 81,659	\$ 89,423
Marketable securities	444,921	513,665
Prepaid expenses and other current assets	12,252	5,386
Total current assets	538,832	608,474
Other non-current assets	—	10
<b>TOTAL ASSETS</b>	<b>\$ 538,832</b>	<b>\$ 608,484</b>
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
<b>CURRENT LIABILITIES</b>		
Accounts payable	\$ 3,712	\$ 666
CVR liability	59,900	25,080
Accrued and other current liabilities	19,416	27,711
Related party accounts payable	31	603
Total current liabilities	83,059	54,060
Non-current CVR liability	—	36,620
<b>TOTAL LIABILITIES</b>	<b>83,059</b>	<b>90,680</b>
<b>Commitments and Contingencies (Note 6 and 7)</b>		
<b>STOCKHOLDERS' EQUITY</b>		
Series A non-voting convertible preferred stock, \$0.0001 par value; 1,086,341 shares authorized as of June 30, 2025 and December 31, 2024; 346,045 shares issued and outstanding as of June 30, 2025 and December 31, 2024.	146,425	146,425
Series B non-voting convertible preferred stock, \$0.0001 par value; 271,625 shares authorized and 16,667 shares issued and outstanding as of June 30, 2025 and December 31, 2024.	9,395	9,395
Preferred stock, \$0.0001 par value; 8,642,034 shares authorized as of June 30, 2025 and December 31, 2024; no shares issued and outstanding as of June 30, 2025 and December 31, 2024.	—	—
Common stock, \$0.0001 par value; 400,000,000 shares authorized as of June 30, 2025 and December 31, 2024; 60,372,927 shares and 60,257,023 shares issued and outstanding as of June 30, 2025 and December 31, 2024, respectively.	13	13
Additional paid-in capital	1,353,408	1,334,223
Accumulated other comprehensive income	454	180
Accumulated deficit	(1,053,922)	(972,432)
<b>TOTAL STOCKHOLDERS' EQUITY</b>	<b>455,773</b>	<b>517,804</b>
<b>TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY</b>	<b>\$ 538,832</b>	<b>\$ 608,484</b>

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

**Spyre Therapeutics, Inc.**  
**Condensed Consolidated Statements of Operations**  
(Unaudited, in thousands, except share and per share amounts)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2025	2024	2025	2024
<b>Operating expenses:</b>				
Research and development <sup>(1)</sup>	\$ 40,145	\$ 32,636	81,768	67,564
General and administrative <sup>(2)</sup>	11,790	11,511	23,734	24,357
Gain on sale of in-process research and development asset	(10,000)	—	(10,000)	—
<b>Total operating expenses</b>	<b>41,935</b>	<b>44,147</b>	<b>95,502</b>	<b>91,921</b>
Loss from operations	(41,935)	(44,147)	(95,502)	(91,921)
<b>Other income:</b>				
Interest income	5,874	5,920	12,367	10,352
Other (expense) income, net	(656)	(610)	1,630	(1,093)
<b>Total other income</b>	<b>5,218</b>	<b>5,310</b>	<b>13,997</b>	<b>9,259</b>
Loss before income tax expense	(36,717)	(38,837)	(81,505)	(82,662)
Income tax benefit (expense)	—	—	15	(32)
<b>Net loss</b>	<b>\$ (36,717)</b>	<b>\$ (38,837)</b>	<b>\$ (81,490)</b>	<b>\$ (82,694)</b>
Net loss per share, basic and diluted, Series A Preferred Stock	\$ (19.62)	\$ (23.61)	\$ (43.57)	\$ (52.32)
Weighted-average Series A non-voting convertible preferred stock outstanding, basic and diluted	346,045	369,043	346,045	403,040
Net loss per share, basic and diluted, Series B Preferred Stock	\$ (19.62)	\$ (23.61)	\$ (43.57)	\$ (52.32)
Weighted-average Series B non-voting convertible preferred stock outstanding, basic and diluted	16,667	142,745	16,667	154,503
Net loss per share, basic and diluted, common	\$ (0.49)	\$ (0.59)	\$ (1.09)	\$ (1.31)
Weighted-average common stock outstanding, basic and diluted	60,333,838	45,316,264	60,300,073	40,914,463

(1) Includes de minimis and \$2.6 million in related party expenses for the three and six months ended June 30, 2025, respectively, and \$9.4 million and \$26.5 million related party expenses for the three and six months ended June 30, 2024, respectively.

(2) Includes \$0.2 million and \$0.5 million in related party expenses for both the three and six months ended June 30, 2025 and 2024, respectively.

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

**Spyre Therapeutics, Inc.**  
**Condensed Consolidated Statements of Comprehensive Loss**  
**(Unaudited, in thousands)**

	Three Months Ended June 30,		Six Months Ended June 30,	
	2025	2024	2025	2024
Net loss	\$ (36,717)	\$ (38,837)	\$ (81,490)	\$ (82,694)
Other comprehensive income (loss):				
Foreign currency translation adjustment	(36)	4	(22)	20
Unrealized (loss) gain on marketable securities	(192)	(194)	296	(875)
<b>Total comprehensive loss</b>	<b>\$ (36,945)</b>	<b>\$ (39,027)</b>	<b>\$ (81,216)</b>	<b>\$ (83,549)</b>

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

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

**Three and Six Months Ended June 30, 2025**

	Series A Non-Voting Convertible Preferred Stock		Series B Non-Voting Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount				
Balances - December 31, 2024	346	\$ 146,425	17	\$ 9,395	60,257	\$ 13	\$ 1,334,223	\$ 180	\$ (972,432)	\$ 517,804
Issuance of common stock in connection with exercise of stock options and employee stock purchase plan	—	—	—	—	19	—	335	—	—	335
Stock-based compensation expense	—	—	—	—	—	—	8,859	—	—	8,859
Cash settlement of stock option award	—	—	—	—	—	—	(117)	—	—	(117)
Foreign currency translation adjustment	—	—	—	—	—	—	—	14	—	14
Unrealized gain on marketable securities	—	—	—	—	—	—	—	488	—	488
Net loss	—	—	—	—	—	—	—	—	(44,773)	(44,773)
Balances - March 31, 2025	346	\$ 146,425	17	\$ 9,395	60,276	\$ 13	\$ 1,343,300	\$ 682	\$ (1,017,205)	\$ 482,610
Issuance of common stock in connection with exercise of stock options and employee stock purchase plan	—	—	—	—	97	—	730	—	—	730
Stock-based compensation expense	—	—	—	—	—	—	9,378	—	—	9,378
Foreign currency translation adjustment	—	—	—	—	—	—	—	(36)	—	(36)
Unrealized loss on marketable securities	—	—	—	—	—	—	—	(192)	—	(192)
Net loss	—	—	—	—	—	—	—	—	(36,717)	(36,717)
Balances - June 30, 2025	346	146,425	17	9,395	60,373	13	1,353,408	454	(1,053,922)	455,773

Three and Six Months Ended June 30, 2024

	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 Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount				
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	—	—	—	—	—	—	—	—	—	—
Issuance of common stock in connection with exercise of stock options and employee stock purchase plan	—	—	—	—	—	—	572	—	4,390	—	—	4,390
Stock-based compensation expense	—	—	—	—	—	—	—	—	8,385	—	—	8,385
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	16	—	16
Unrealized loss on marketable securities	—	—	—	—	—	—	—	—	—	(681)	—	(681)
Net loss	—	—	—	—	—	—	—	—	—	—	(43,857)	\$ (43,857)
Balances - March 31, 2024	272	\$ 253,405	437	\$ 184,927	\$ —	\$ —	36,629	\$ 10	\$ 775,966	\$ (363)	\$ (808,271)	\$ 152,269
Stockholder approval of the issuance of Common Stock upon conversion of Series B convertible non-voting preferred stock	(272)	(253,405)	—	—	272	253,405	—	—	—	—	—	253,405
Conversion of Series B non-voting convertible preferred stock into common stock	—	—	—	—	(255)	(244,010)	10,198	1	244,009	—	—	—
Exchange of Series A non-voting convertible preferred stock for common stock	—	—	(91)	(38,502)	—	—	3,640	1	38,501	—	—	—
Issuance of common stock in connection with exercise of pre-funded warrants	—	—	—	—	—	—	250	—	1	—	—	1
Issuance of common stock in connection with exercise of stock options and employee stock purchase plan	—	—	—	—	—	—	66	—	494	—	—	494
Stock-based compensation expense	—	—	—	—	—	—	—	—	7,243	—	—	7,243
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	4	—	4
Unrealized loss on marketable securities	—	—	—	—	—	—	—	—	—	(194)	—	(194)
Net loss	—	—	—	—	—	—	—	—	—	—	(38,837)	(38,837)
Balances - June 30, 2024	—	\$ —	346	\$ 146,425	\$ 17	\$ 9,395	50,783	\$ 12	\$ 1,066,214	\$ (553)	\$ (847,108)	\$ 374,385

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

**Spyre Therapeutics, Inc.**  
**Condensed Consolidated Statements of Cash Flows**  
(Unaudited, in thousands)

	Six Months Ended June 30,	
	2025	2024
<b>CASH FLOWS FROM OPERATING ACTIVITIES</b>		
Net loss	\$ (81,490)	\$ (82,694)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	18,237	22,517
Change in fair value of CVR liability	(1,800)	930
Gain on sale of in-process research and development asset	(10,000)	—
Net accretion of discount on marketable securities	(4,655)	(5,984)
Interest proceeds from maturities of zero coupon U.S. Treasury Bills	1,760	124
Changes in operating assets and liabilities:		
Accounts payable	3,046	2,335
Accrued and other liabilities	(8,299)	(7,623)
Related party accounts payable	(572)	(12,906)
Prepaid expenses and other assets	(3,784)	(7,489)
Net cash used in operating activities	(87,557)	(90,790)
<b>CASH FLOWS FROM INVESTING ACTIVITIES</b>		
Proceeds from maturities and sales of marketable securities	178,249	105,626
Purchases of marketable securities	(106,312)	(331,107)
Proceeds from sale of in-process research and development asset	7,000	—
Net cash provided by (used in) investing activities	78,937	(225,481)
<b>CASH FLOWS FROM FINANCING ACTIVITIES</b>		
Proceeds from issuance of Series B non-voting convertible preferred stock in connection with private placement, net of placement and other offering costs	—	169,070
Payments related to CVR	—	(1,430)
Payment of deferred offering costs in connection with shelf registration	(93)	—
Proceeds from employee stock option exercises and employee stock plan purchases	1,066	4,885
Cash settlement of employee stock option award	(117)	—
Net cash provided by financing activities	856	172,525
Effect of exchange rate on cash, cash equivalents, and restricted cash	—	(4)
NET DECREASE IN CASH, CASH EQUIVALENTS, AND RESTRICTED CASH	(7,764)	(143,750)
<b>CASH, CASH EQUIVALENTS, AND RESTRICTED CASH</b>		
Beginning of period	89,423	189,215
End of period	\$ 81,659	\$ 45,465
<b>Supplemental Disclosure of Non-Cash Financing Information:</b>		
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
Unpaid amounts related to issuance of Series B non-voting convertible preferred stock in connection with private placement	\$ —	\$ 220
<b>Reconciliation of Cash, Cash Equivalents, and Restricted Cash Reported in the Statement of Financial Position:</b>		
Cash and cash equivalents	\$ 81,659	\$ 45,144
Restricted cash	—	321
<b>Total cash, cash equivalents, and restricted cash shown in the statement of cash flows</b>	<b>\$ 81,659</b>	<b>\$ 45,465</b>

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

## Spyre Therapeutics, Inc.

### Notes to Unaudited Condensed 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 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 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"), 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 (as amended, the "Paragon Agreement") with Paragon Therapeutics, Inc. ("Paragon") and Parapyre Holding LLC ("Parapyre") (the "Asset Acquisition"). 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, merged with and into Pre-Merger Spyre, which existed at the time the Acquisition Agreement was entered into, and 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.

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"). Holders of the CVRs will be entitled to receive cash payments from proceeds received by the Company for a three-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.

On March 20, 2024, the Company completed a private placement of 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) (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 non-voting convertible preferred stock, par value of \$0.0001 per share ("Series A Preferred Stock"), par value of 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 June 30, 2025.

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

On November 18, 2024, the Company entered into an underwriting agreement (the "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 the Underwriters' over-allotment option, at a public offering price per share of \$27.50, resulting in net proceeds of approximately \$215.9 million after deducting approximately \$14.2 million of underwriting discounts and other offering costs (the "November 2024 Offering"). The November 2024 Offering closed on November 20, 2024 and the over-allotment option was exercised in full on November 26, 2024 and closed on November 29, 2024.

In February 2025, the Company filed a new shelf registration statement on Form S-3 (the "February 2025 Shelf Registration Statement") that was declared effective by the SEC for the potential offering, issuance and sale of up to \$500.0 million of shares of common stock, preferred stock, debt securities, warrants and/or units consisting of all or some of these securities. Concurrent with the effectiveness of the February 2025 Shelf Registration Statement, the offering of unsold securities under a previous shelf registration statement on Form S-3 (File No. 333-281975), which was initially filed with the SEC on September 6, 2024 and became effective on September 18, 2024, was deemed terminated pursuant to Rule 415(a)(6) under the Securities Act. The February 2025 Shelf Registration Statement contains a sales agreement prospectus supplement covering the offering, issuance and sale by the Company of up to \$179.1 million of shares of common stock that may be issued and sold under the Sales Agreement in connection with the ATM offering program. No shares were sold under the ATM offering program during the three months ended June 30, 2025. As of June 30, 2025, \$179.1 million remained available for sale under the Sales Agreement.

### **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 June 30, 2025, the Company has funded its 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 June 30, 2025, Spyre had an accumulated deficit of \$1.1 billion, and cash, cash equivalents, and marketable securities of \$526.6 million.

Based on its 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.

### ***Unaudited Interim Financial Information***

The interim condensed consolidated financial statements included in this Quarterly Report on Form 10-Q are unaudited. The unaudited interim financial statements have been prepared on the same basis as the annual financial statements and reflect, in the opinion of management, all adjustments of a normal and recurring nature that are necessary for a fair statement of the Company's financial position as of June 30, 2025, and its results of operations for the three and six months ended June 30, 2025 and 2024, changes in convertible preferred stock and stockholders' equity for the three and six months ended June 30, 2025 and 2024, and cash flows for the six months ended June 30, 2025 and 2024. The results of operations for the three and six months ended June 30, 2025, are not necessarily indicative of the results to be expected for the year ending December 31, 2025 or for any other future annual or interim period. The December 31, 2024 balance sheet was derived from audited financial statements, but does not include all disclosures required by U.S. GAAP for complete financial statements. These financial statements should be read in conjunction with the audited financial statements included in the Company's Form 10-K for the year ended December 31, 2024 (the "Annual Report") as filed with the SEC on February 27, 2025.

## **2. Summary of Significant Accounting Policies**

These interim condensed consolidated financial statements have been prepared in accordance with U.S. GAAP and SEC instructions for interim financial information, and should be read in conjunction with the Company's Annual Report. Significant accounting policies and other disclosures normally provided have been omitted since such items are disclosed in the Company's Annual Report. The Company uses the same accounting policies in preparing quarterly and annual financial statements.

There have been no significant changes from the significant accounting policies and estimates disclosed in the Notes titled "1. The Company and Basis of Presentation" and "2. Summary of Significant Accounting Policies" of the Company's Annual Report.

### ***Recently Adopted Accounting Pronouncements***

There have been no recent accounting pronouncements or changes in accounting pronouncements adopted during the six months ended June 30, 2025 that are of significance or potential significance to the Company.

### ***Not Yet Adopted Accounting Pronouncements***

In December 2023, the FASB issued Accounting Standards Update 2023-09 ("ASU 2023-09"), Income Taxes (Topic 740): Improvements to Income Tax Disclosures. ASU 2023-09 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. ASU 2023-09 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 Accounting Standards Update 2024-03 ("ASU 2024-03") Income Statement - Reporting Comprehensive Income - Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses to require more detailed information about specified categories of expenses (purchases of inventory, employee compensation, depreciation, amortization, and depletion) included in certain expense captions presented on the face of the income statement. ASU 2024-03 is effective for fiscal years beginning after December 15, 2026, and for interim periods within fiscal years beginning after December 15, 2027. Early adoption is permitted. The amendments may be applied either (1) prospectively to financial statements issued for reporting periods after the effective date of this ASU 2024-03 or (2)

retrospectively to all prior periods presented in the financial statements. The Company is currently evaluating the impact ASU 2024-03 will have 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):

	June 30, 2025			
	Level 1	Level 2	Level 3	Total
<b>Financial Assets:</b>				
Money market funds	\$ 79,957	\$ —	\$ —	\$ 79,957
U.S. government treasury securities	221,646	—	—	221,646
U.S. government agency securities	—	70,526	—	70,526
Commercial paper	—	89,178	—	89,178
Corporate bonds	—	63,571	—	63,571
<b>Total financial assets</b>	<b>\$ 301,603</b>	<b>\$ 223,275</b>	<b>\$ —</b>	<b>\$ 524,878</b>
<b>Liabilities:</b>				
CVR liability	\$ —	\$ —	\$ 59,900	\$ 59,900
<b>Total liabilities</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ 59,900</b>	<b>\$ 59,900</b>

	December 31, 2024			
	Level 1	Level 2	Level 3	Total
<b>Financial Assets:</b>				
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
<b>Total financial assets</b>	<b>\$ 293,146</b>	<b>\$ 308,259</b>	<b>\$ —</b>	<b>\$ 601,405</b>
<b>Liabilities:</b>				
CVR liability	\$ —	\$ —	\$ 61,700	\$ 61,700
<b>Total liabilities</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ 61,700</b>	<b>\$ 61,700</b>

The Company measures the fair value of money market funds and U.S. government treasury securities on quoted prices in active markets for identical assets or liabilities. The Level 2 assets include U.S. government agency securities, commercial paper and corporate bonds, and are valued based on quoted prices for similar assets in active markets and inputs other than quoted prices that are derived from observable market data. The Company evaluates transfers between levels at the end of each reporting period. There were no transfers between Level 1, Level 2, or Level 3 during the periods presented.

#### **CVR Liability**

In connection with the Asset Acquisition, a non-transferable CVR was distributed to the Legacy Stockholders. 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), net 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:

	June 30, 2025
Estimated cash flow dates	08/28/25 - 06/22/26
Estimated probability of success	72% - 100%
Estimated reimbursement rate compared to reimbursement target	49% - 100%
Risk-adjusted discount rates	9.38% - 9.48%

The change in fair value between December 31, 2024 and June 30, 2025 was a \$1.8 million decrease, primarily driven by changes in the likelihood of achievement of certain milestones and an increase in risk-adjusted discount rates, partially offset by time value of money adjustments.

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

	CVR Liability
Beginning balance as of December 31, 2024	\$ 61,700
Changes in the fair value of the CVR liability	(1,800)
Payments	—
Ending Balance as of June 30, 2025	\$ 59,900

#### 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):

	June 30, 2025			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
<b>Cash equivalents:</b>				
Money market funds	\$ 79,957	\$ —	\$ —	\$ 79,957
<b>Total cash equivalents</b>	<b>\$ 79,957</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ 79,957</b>
<b>Marketable securities:</b>				
Commercial paper	\$ 89,207	\$ 1	\$ (30)	\$ 89,178
Corporate bonds	63,544	54	(27)	63,571
U.S. government treasury securities	221,207	512	(73)	221,646
U.S. government agency securities	70,509	40	(23)	70,526
<b>Total marketable securities</b>	<b>\$ 444,467</b>	<b>\$ 607</b>	<b>\$ (153)</b>	<b>\$ 444,921</b>

December 31, 2024					
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	
<b>Cash equivalents:</b>					
Money market funds	\$ 65,902	\$ —	\$ —	\$ 65,902	
Commercial paper	21,832	6	—	21,838	
<b>Total cash equivalents</b>	<b>\$ 87,734</b>	<b>\$ 6</b>	<b>\$ —</b>	<b>\$ 87,740</b>	
<b>Marketable securities:</b>					
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	
<b>Total marketable securities</b>	<b>\$ 513,507</b>	<b>\$ 651</b>	<b>\$ (493)</b>	<b>\$ 513,665</b>	

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 June 30, 2025 and December 31, 2024, aggregated by major security type and length of time in a continuous unrealized loss position:

June 30, 2025						
	Less Than 12 Months		12 Months or Longer		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
Commercial paper	\$ 76,461	\$ (30)	\$ —	\$ —	\$ 76,461	\$ (30)
Corporate bonds	24,365	(27)	—	—	24,365	(27)
U.S. government treasury securities	48,575	(73)	—	—	48,575	(73)
U.S. government agency securities	21,211	(23)	—	—	21,211	(23)
<b>Total marketable securities</b>	<b>\$ 170,612</b>	<b>\$ (153)</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ 170,612</b>	<b>\$ (153)</b>

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)
<b>Total marketable securities</b>	<b>\$ 249,264</b>	<b>\$ (493)</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ 249,264</b>	<b>\$ (493)</b>

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 it will be required to sell the securities before recovery of the unamortized cost basis. As of June 30, 2025 and December 31, 2024, an allowance for credit losses had not been recognized. Given the Company's intent and ability to hold such securities until recovery, and the lack of significant change in credit risk of these

investments, the Company does not consider these marketable securities to be impaired as of June 30, 2025 and December 31, 2024.

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 June 30, 2025 and December 31, 2024, cash deposits at the Company's U.S. banking institutions exceeded the FDIC limits.

There were no realized gains or losses on marketable securities for both the three and six months ended June 30, 2025 and 2024. Interest on marketable securities is included in interest income. Accrued interest receivable on available-for-sale debt securities as of June 30, 2025 and December 31, 2024, was \$3.5 million and \$3.4 million, respectively, and is reflected in Prepaid expenses and other current assets.

The following table summarizes the contractual maturities of the Company's marketable securities at estimated fair value (in thousands):

	June 30, 2025	December 31, 2024
Due in one year or less	\$ 327,764	\$ 338,442
Due in 1 - 2 years	117,157	175,223
<b>Total marketable securities</b>	<b>\$ 444,921</b>	<b>\$ 513,665</b>

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. Accrued and Other Current Liabilities

Accrued and other current liabilities consist of the following (in thousands):

	June 30, 2025	December 31, 2024
Accrued compensation	\$ 3,289	\$ 5,688
Accrued contracted research and development costs	15,018	20,861
Accrued professional and consulting fees	867	661
Accrued other	242	501
<b>Total accrued and other current liabilities</b>	<b>\$ 19,416</b>	<b>\$ 27,711</b>

## 6. Licensing Agreements

On July 12, 2023, December 14, 2023, and June 5, 2024, the Company exercised the Option (as defined below) 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  $\alpha 4\beta 7$  integrin and (ii) a license agreement (the "SPY002 and SPY072 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, which includes the Company's SPY002 and SPY072 product candidates.

On October 11, 2024, the Company and Paragon entered into a license agreement (as amended, the "SPY003 License Agreement", and together with the SPY001 License Agreement and the SPY002 and SPY072 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.

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- $\alpha$ 4 $\beta$ 7 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 and SPY072 License Agreement only, on a product by product basis, the Company will pay sublicensing fees of up to approximately \$20 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.

The Company recognized expense related to Paragon license milestone payments, recorded within Research and development expenses, in the accompanying condensed statement of operations of nil and \$2.5 million for the three and six months ended June 30, 2025, respectively, and \$5.5 million for the three and six months ended June 30, 2024.

The Company paid milestone payments to Paragon totaling \$2.5 million for the three and six months ended June 30, 2025, and \$3.0 million for the three and six months ended June 30, 2024. As of June 30, 2025 and December 31, 2024, there were no milestone payments outstanding and payable to Paragon.

Additionally, there were no expenses recognized or payments made related to sublicensing fees for the three and six months ended June 30, 2025. The Company recognized and paid \$0.1 million related to sublicensing fees which were recorded as Research and development expenses in the accompanying condensed statement of operations for the three and six months ended June 30, 2024.

As of June 30, 2025 and December 31, 2024, nil and \$0.5 million in sublicensing fees were outstanding and payable to Paragon, respectively.

## 7. 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:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2025	2024	2025	2024
Reimbursable costs under the Paragon Agreement	\$ —	\$ 2.3	\$ 0.1	\$ 14.0
License Agreements milestone and sublicensing fees	—	5.6	2.5	5.6
Total related party expense (excludes stock-based compensation)	\$ —	\$ 7.9	\$ 2.6	\$ 19.6

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

	June 30, 2025	December 31, 2024
Reimbursable costs under the Paragon Agreement	\$ —	\$ 0.1
License Agreements development milestone liability (see Note 6)	—	0.5
Total related party accounts payable	\$ —	\$ 0.6

### Paragon Agreement

In connection with the Asset Acquisition, the Company assumed the rights and obligations of Pre-Merger Spyre under the Paragon Agreement. 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. Spyre was also obligated under the Paragon Agreement to issue Parapyre annual equity grants of warrants in accordance with the Parapyre Option Obligation (as defined below).

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. Please refer to Note 6 for additional information on the License Agreements.

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 6 for additional disclosures.

For the three and six months ended June 30, 2025, the Company recognized de minimis and \$0.1 million, respectively, of expenses related to services provided by Paragon, which were recorded as Research and development expenses in the consolidated statements of operations.

For the three and six months ended June 30, 2024, the Company recognized expenses related to services provided by Paragon subsequent to the Asset Acquisition totaling \$9.7 million and \$26.8 million, respectively, which included \$1.5 million and \$6.9 million, respectively, of stock-based compensation expense, and were recorded as Research and development expenses in the consolidated statements of operations.

During the second quarter of 2024, the SPY003 antibody selection process was completed and the Company recognized a \$5.9 million receivable and a corresponding reduction in Research and development expenses in its condensed consolidated statements of operations for the three and six ended June 30, 2024.

For the three and six months ended June 30, 2025, the Company made payments totaling de minimis and \$0.2 million, respectively, in connection with the Paragon Agreement. For the three and six months ended June 30, 2024, the Company made payments totaling \$11.3 million and \$29.5 million, respectively, in connection with the Paragon Agreement.

#### ***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 (the "Parapyre Option Obligation"). See Note 9 for disclosures related to the Parapyre Option Obligation.

#### ***Paragon License Agreements***

See Note 6 for disclosures related to the License Agreements entered into with Paragon.

#### ***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 2016 Plan (as defined in Note 9) 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 36 equal monthly installments, subject to Mr. McKenna's continued service to the Company through each applicable vesting date. For both the three and six months ended June 30, 2025 and 2024, the Company recognized \$0.2 million and \$0.5 million, respectively, in stock-based compensation expense related to Mr. McKenna's consulting agreement.

### **8. Convertible Preferred Stock and Stockholders' Equity**

#### ***Parapyre Warrants***

As of December 31, 2024, the Company settled its obligations under the Parapyre Option Obligation by issuing Parapyre 848,184 warrants to purchase the Company's common stock at an exercise price of \$23.28. As of June 30, 2025, a total of 1,532,591 warrants with a weighted-average exercise price of \$22.49 had been

issued to Parapyre under the Parapyre Option Obligation. As of June 30, 2025, none of the warrants issued under the Parapyre Option Obligation have been exercised and all remain outstanding.

#### **Series A Non-Voting Convertible Preferred Stock**

Pursuant to the Company's Certificate of Designation of Preferences, Rights and Limitations of the Series A Non-Voting Convertible Preferred Stock (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 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 or at any time while at least 30% of the originally issued Series A Preferred Stock remains issued and outstanding, consummate (x) any Fundamental Transaction (as defined in the Series A Certificate of Designation) or (y) any merger or consolidation of the Company with or into another entity or any stock sale to, or other business combination in which the Company's stockholders immediately before such transaction do not hold at least a majority of the Company's 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.

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 and are convertible into 13,841,800 common shares.

#### **Series B Non-Voting Convertible Preferred Stock**

Pursuant to the Company's Certificate of Designation of Preferences, Rights and Limitations of Series B Non-Voting Convertible Preferred Stock (as amended, the "Series B Certificate of Designation"), holders of Series B Preferred Stock are entitled to receive dividends on shares of Series B Preferred Stock equal to, on an as-if-converted-to-common stock basis, and in the same form as, dividends actually paid on shares of common stock. Except as provided in the Series B Certificate of Designation or as otherwise required by law, the Series B Preferred Stock does not have voting rights. However, as long as any shares of Series B Preferred Stock are outstanding, the Company will not, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series B Preferred Stock, alter or change adversely the powers, preferences or rights given to the Series B Preferred Stock, or alter or amend the Series B Certificate of Designation, amend or repeal any provision of, or add any provision to, the Company's Certificate of Incorporation or its Bylaws, or file any articles of amendment, certificate of designations, preferences, limitations and relative rights of any series of preferred stock, if such action would adversely alter or change the preferences, rights, privileges or powers of, or restrictions provided for the benefit of the Series B Preferred Stock, regardless of whether any of the foregoing actions will be by means of amendment to the Certificate of Incorporation or by merger, consolidation, recapitalization, reclassification, conversion or otherwise. The Series B Preferred Stock does not have a preference upon any liquidation, dissolution or winding-up of the Company.

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 \$1,480.00 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 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 automatically converted into 40 shares of common stock, subject to certain limitations, including that a holder of Series B Preferred Stock is prohibited from converting shares of Series B Preferred Stock into shares of common stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (established by the holder between 0% and 19.9%) of the total number of shares of common stock issued and outstanding immediately after giving effect to such conversion. 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 June 30, 2025 due to beneficial ownership limitations. This conversion was recorded as a reclassification between Series B Preferred Stock and common stock based on the historical per-share contributed capital amount of the Series B Preferred Stock. The remaining outstanding Series B Preferred Stock is convertible into 666,680 common shares as of June 30, 2025.

#### ***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 of up to \$500.0 million of the Company's common stock, preferred stock, debt securities, warrants and/or units consisting of all or some of these securities. Concurrent with the filing of the shelf-registration statement, the Company entered into the Sales Agreement, pursuant to which the Company may issue and sell up to \$200.0 million of shares of common stock under an ATM offering program included in the registration statement. During the twelve months ended December 31, 2024, the Company sold an aggregate of 777,432 shares of common stock under the ATM offering program resulting in net proceeds of \$20.5 million after deducting sales agent commissions and other offering costs.

In February 2025, 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 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 effectiveness of the February 2025 Shelf Registration Statement, the offering of unsold securities under the previous shelf registration statement on Form S-3 (described above), was deemed terminated pursuant to Rule 415(a)(6) under the Securities Act. The February 2025 Shelf Registration Statement contains a prospectus supplement covering the offering, issuance and sale by the Company of up to \$179.1 million of shares of common stock that may be issued and sold under the Sales Agreement in connection with the ATM program. No shares were sold under the ATM program during the three months ended June 30, 2025. As of June 30, 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.

## 9. Stock-Based Compensation

### 2016 Equity Incentive Plan

The Company's 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, as amended, provides 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) 5.0% of the number of issued and outstanding shares of common stock (including such shares issuable pursuant to the exercise or conversion, as applicable, of any outstanding pre-funded warrants and nonvoting convertible preferred stock) on December 31 of the immediately preceding year, or (b) a lesser amount as approved by the board each year (the "Evergreen Provision"). As a result of the Evergreen Provision, on January 1, 2025 and 2024, an additional 3,814,905 and 3,023,650 shares, respectively, became available for issuance under the 2016 Plan.

As of June 30, 2025, the 2016 Plan had 10,911,455 shares available for future issuance, of which 4,932,059 shares were subject to outstanding option awards.

### 2018 Equity Inducement Plan

The 2018 Equity Inducement Plan ("2018 Plan") became effective in February 2018.

During the second quarter of 2025, the Company amended the 2018 Plan to increase the number of shares of common stock reserved for issuance by 750,000. After this amendment and as of June 30, 2025, the 2018 Plan had 7,606,811 shares available for future issuance, of which 6,508,168 shares were subject to outstanding option awards and restricted unit awards.

Service-based awards granted under the 2018 Plan and 2016 Plan generally vest over four years and expire after ten years, although awards have been granted with vesting terms less than four years. Under the 2016 Plan and 2018 Plan, the Company may grant stock-based awards with service conditions, performance conditions, and market conditions.

### 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 "2023 Plan") and its outstanding and unexercised stock options, which were converted to options to purchase 2,734 shares of common stock. The acquisition-date fair value of these grants will be recognized as an expense on a pro-rata basis over the vesting period. As of June 30, 2025, none of the stock options under the 2023 Plan remained outstanding.

The following table summarizes the Company's stock awards granted under all equity incentive and inducement plans for each of the periods indicated:

	Three Months Ended June 30,				Six Months Ended June 30,			
	2025		2024		2025		2024	
	Grants	Weighted Average Grant Date Fair Value	Grants	Weighted Average Grant Date Fair Value	Grants	Weighted Average Grant Date Fair Value	Grants	Weighted Average Grant Date Fair Value
Stock options	427,800	\$ 15.29	387,695	\$ 36.42	2,325,717	\$ 20.32	1,432,353	\$ 29.19

### **Parapyre Option Obligation**

As of December 31, 2024, the Company settled its obligations under the Parapyre Option Obligation by issuing Parapyre 848,184 warrants to purchase the Company's common stock at an exercise price of \$23.28. As of June 30, 2025, a total of 1,532,591 warrants with a weighted-average exercise price of \$22.49 had been issued to Parapyre under the Parapyre Option Obligation. As of June 30, 2025 none of the warrants issued under the Parapyre Option Obligation have been exercised and all remain outstanding.

For the three and six months ended June 30, 2024, \$1.5 million and \$6.9 million, respectively, was recognized as stock compensation expense related to the Parapyre Option Obligation. There are no ongoing obligations under the Parapyre Option Obligation as of June 30, 2025.

### **2016 Employee Stock Purchase Plan**

Under the Company's 2016 Employee Stock Purchase Plan ("2016 ESPP"), the Company issued and sold 16,877 and 2,330 shares during the six months ended June 30, 2025 and 2024, respectively. There were no shares issued and sold during the three months ended June 30, 2025 and 2024. The aggregate cash proceeds were nil for the three months ended June 30, 2025 and 2024, and were \$0.3 million and de minimis for the six months ended June 30, 2025 and 2024, respectively.

### **Stock-based Compensation Expense**

Total stock-based compensation expense recognized from the Company's equity incentive plans, 2018 Plan, 2016 ESPP and Parapyre Option Obligation during the periods presented was as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2025	2024	2025	2024
Research and development <sup>(1)</sup>	\$ 4,100	\$ 3,451	\$ 7,612	\$ 10,308
General and administrative	5,278	5,231	10,625	12,209
Total stock-based compensation expense <sup>(2)</sup>	\$ 9,378	\$ 8,682	\$ 18,237	\$ 22,517

<sup>(1)</sup> For the three and six months ended June 30, 2024, \$1.5 million and \$6.9 million, respectively was recognized as stock compensation expense related to the Parapyre Option Obligation.

<sup>(2)</sup> Of the total \$8.7 million and \$22.5 million of stock-based compensation expense for the three and six months ended June 30, 2024, respectively, \$0.7 million and \$3.8 million is related to legacy Aeglea employees and directors who had been terminated as of the end of the period, respectively.

The following table summarizes the weighted-average Black-Scholes option pricing model assumptions used to estimate the fair value of stock options granted under the Company's equity incentive plans, and the shares purchased under the 2016 ESPP during the periods presented:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2025	2024	2025	2024
<b>Stock Options Granted</b>				
Expected term (in years)	5.74	5.92	5.97	6.00
Expected volatility	74%	104%	76%	105%
Risk-free interest	4.02%	4.35%	4.38%	4.01%
Dividend yield	—	—	—	—
<b>2016 ESPP</b>				
Expected term (in years)	—	—	0.50	0.50
Expected volatility	—	—	69%	98%
Risk-free interest	—	—	4.23%	5.31%
Dividend yield	—	—	—	—

#### 10. Sale of Pegzilarginase to Immedica

On July 27, 2023, the Company announced that it had entered into an agreement to sell the global rights to pegzilarginase to Immedica Pharma AB ("Immedica") for \$15.0 million in upfront cash proceeds and up to \$100.0 million in contingent milestone payments.

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. During the three and six months ended June 30, 2025, the Company recognized a gain of \$10.0 million within Gain on Sale of in-process research and development, for achieving certain reimbursement decision milestones during the period. The Company received cash of \$7.0 million during the three and six months ended June 30, 2025 with \$3.0 million remaining outstanding and reflected in Prepaid expenses and other current assets as of June 30, 2025. There was no similar gain during the three or six months ended June 30, 2024 or similar receivable as of December 31, 2024.

Milestone payments, 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.

#### 11. 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):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2025	2024	2025	2024
Compensation	\$ 8,120	\$ 4,881	\$ 15,111	\$ 9,055
Stock-based compensation <sup>(1)</sup>	9,378	8,682	18,237	22,517
Research and development, excluding compensation and stock-based compensation <sup>(2) (3)</sup>	30,749	26,808	64,300	52,910
Other segment items <sup>(4)</sup>	(11,530)	(1,534)	(16,158)	(1,788)
Segment net loss	\$ 36,717	\$ 38,837	\$ 81,490	\$ 82,694
<b>Reconciliation of net loss</b>				
Adjustments and reconciling items	—	—	—	—
Consolidated net loss	\$ 36,717	\$ 38,837	\$ 81,490	\$ 82,694

<sup>(1)</sup> Includes \$0.2 million and \$1.7 million in related party expenses for the three months ended June 30, 2025 and 2024, respectively. Includes \$0.5 million and \$7.4 million in related party expenses for the six months ended June 30, 2025 and 2024, respectively.

<sup>(2)</sup> Includes non-clinical study, clinical trial, and manufacturing expenses.

<sup>(3)</sup> Includes de minimis and \$7.9 million in related party expenses for the three months ended June 30, 2025 and 2024, respectively. Includes \$2.6 million and \$19.6 million in related party expenses for the six months ended June 30, 2025 and 2024, respectively.

<sup>(4)</sup> Includes general and administrative expenses such as audit, legal, and other professional fees, interest income, and other expense, net. Additionally, includes a \$10.0 million gain recognized in connection with the sale of pegzilarginase to Immedica.

## 12. 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):

	Three Months Ended June 30,					
	2025			2024		
	Series A Preferred Stock	Series B Preferred Stock	Common Stock	Series A Preferred Stock	Series B Preferred Stock	Common Stock
Net loss per share, basic and diluted:						
Numerator						
Allocation of losses	\$ (6,791)	\$ (327)	\$ (29,599)	\$ (8,714)	\$ (3,370)	\$ (26,753)
Denominator						
Weighted-average shares outstanding	346,045	16,667	60,333,838	369,043	142,745	45,214,616
Weighted-average pre-funded warrants outstanding	—	—	—	—	—	101,648
Number of shares used in per share computation	346,045	16,667	60,333,838	369,043	142,745	45,316,264
Net loss per share, basic and diluted	\$ (19.62)	\$ (19.62)	\$ (0.49)	\$ (23.61)	\$ (23.61)	\$ (0.59)

	Six Months Ended June 30,					
	2025			2024		
	Series A Preferred Stock	Series B Preferred Stock	Common Stock	Series A Preferred Stock	Series B Preferred Stock	Common Stock
Net loss per share, basic and diluted:						
Numerator						
Allocation of losses	\$ (15,078)	\$ (726)	\$ (65,686)	\$ (21,089)	\$ (8,084)	\$ (53,521)
Denominator						
Weighted-average shares outstanding	346,045	16,667	60,300,073	403,040	154,503	40,738,639
Weighted-average pre-funded warrants outstanding	—	—	—	—	—	175,824
Number of shares used in per share computation	346,045	16,667	60,300,073	403,040	154,503	40,914,463
Net loss per share, basic and diluted	\$ (43.57)	\$ (43.57)	\$ (1.09)	\$ (52.32)	\$ (52.32)	\$ (1.31)

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:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2025	2024	2025	2024
Options to purchase common stock	805,306	5,010,436	1,324,645	4,526,643
Unvested restricted stock units	—	79,870	11,943	71,368
Outstanding Parapyre warrants	—	684,407	—	684,407

## Item 2. 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 in conjunction with our unaudited condensed consolidated financial statements and related notes included in Part I, Item 1 of this Quarterly Report for the quarterly period ended June 30, 2025 (this "Quarterly Report") as well as the audited consolidated financial statements and notes and Management's Discussion and Analysis of Financial Condition and Results of Operations, included in our Annual Report on Form 10-K for the year ended December 31, 2024 (the "Annual Report") filed with the U.S. Securities and Exchange Commission (the "SEC") on February 27, 2025. This discussion and other parts of this Quarterly Report contain forward-looking statements that involve risks and uncertainties, such as statements regarding our expected results, outcomes, and the timing of these results and outcomes, plans, objectives, expectations and intentions. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Quarterly 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," 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 certain 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  $\alpha$ 4 $\beta$ 7 integrin program, to develop and commercialize antibodies and products worldwide in all therapeutics disorders. We expect any patents pursued non-provisionally and that mature into issued 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 (formerly SPY002-091) and SPY072 (formerly SPY002-072), our TL1A programs, to develop and commercialize antibodies and products worldwide in all therapeutics disorders. We expect any patents pursued non-provisionally and that mature into issued 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. We expect any patents pursued non-provisionally and that mature into issued patents to expire no earlier than 2045, subject to any disclaimers or extensions. The license agreements pertaining to SPY001 (the "SPY001 License Agreement") and SPY002 and SPY072 (the "SPY002 and SPY072 License Agreement") between the Company and Paragon were executed in the second quarter of 2024, and the license agreement pertaining to SPY003 (the "SPY003 License Agreement" and, together with the SPY001 License Agreement and the SPY002 and SPY072 License Agreement, the "License Agreements") between the Company and Paragon was executed in October 2024 and subsequently amended and restated on February 24, 2025. See the section titled "Paragon Agreement" in this Quarterly Report for more discussion about the Paragon Agreement and the License Agreements.



### 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 rheumatic diseases ("RD"), including

rheumatoid arthritis ("RA"), psoriatic arthritis ("PsA"), and axial spondyloarthritis ("axSpA"). Our portfolio of novel and proprietary monoclonal antibody product candidates has the potential to address unmet needs in IBD and RD care by improving efficacy, safety, and/or dosing convenience relative to products currently available or product candidates in development. We have engineered our product candidates with the aim to bind potently and selectively to their target epitopes and to exhibit extended pharmacokinetic ("PK") 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 combinations (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.

### Our Portfolio and Development Plan Updates

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

Trial	Indication	Program	Target	Phase 1	Phase 2	Phase 3	Anticipated Milestones	
	UC	SPY001	α4β7	[Phase 1 and 2 bars]			2026: Ph2 open-label POC 2027: Ph2 pbo-controlled data	
		SPY002	TL1A	[Phase 1 and 2 bars]				
		SPY003	IL-23	[Phase 1 bar]				
			SPY120	α4β7 + TL1A	[Phase 1 bar]			2027: Ph2 POC
			SPY130	α4β7 + IL-23	[Phase 1 bar]			
			SPY230	TL1A + IL-23	[Phase 1 bar]			
	RA	SPY072	TL1A	[Phase 1 and 2 bars]			2026: Ph2 POC	
	PsA			[Phase 1 and 2 bars]				
	axSpA			[Phase 1 and 2 bars]				

### SKYLINE-UC Phase 2 Platform Trial in UC

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

- **Part A:** Open-label assessment of the safety and preliminary efficacy of a single dose level of each investigational monotherapy.
- **Part B:** Randomized and placebo-controlled assessment of the safety and efficacy of monotherapies and combinations, designed to provide dose-ranging data on monotherapies, proof-of-concept and contribution of components for combinations.

SKYLINE-UC is currently enrolling subjects into the SPY001 arm of Part A.

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

SKYWAY-RD is a planned Phase 2 randomized and placebo-controlled basket trial of SPY072 in patients with moderately to severely active RA, PsA, or axSpA. Trial initiation is expected in the third quarter of 2025 and consists of three sub-studies:

- **RA sub-study:** Double-blind, placebo-controlled safety and efficacy study of two dose levels of SPY072 at Week 12 with open-label follow-up through Week 36.
- **PsA sub-study:** Double-blind, placebo-controlled safety and efficacy study of a single dose level of SPY072 at Week 16 with open-label follow-up through Week 40.
- **axSpA sub-study:** Double-blind, placebo-controlled safety and efficacy study of a single dose level of SPY072 at Week 16 with open-label follow-up through Week 40.

## SPY001 – anti- $\alpha$ 4 $\beta$ 7 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  $\alpha$ 4 $\beta$ 7 integrin being developed for the treatment of IBD (UC and CD). The  $\alpha$ 4 $\beta$ 7 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  $\alpha$ 4 $\beta$ 7 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  $\alpha$ 4 $\beta$ 7 integrin and MAdCAM-1, SPY001 aims to reduce the recruitment of immune cells to the gut, leading to a decrease in inflammation. Since it specifically targets the gut immune system, SPY001 is designed to minimize systemic immunosuppressive effects unrelated to IBD pathology.

SPY001 demonstrates similar potency and selectivity as synthesized vedolizumab in preclinical *in vitro* models including surface plasmon resonance and cellular adhesion assays. We initiated a first-in-human ("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 PK and anti-drug antibodies ("ADA") serving as secondary endpoints. Additional cohorts have been added to the study to evaluate PK in healthy volunteers of various ethnicities to facilitate subsequent global clinical trials. Trial enrollment is now complete.

Interim results were initially presented in November 2024, with additional data presented in May 2025 with up to eight months of follow up. To date, SPY001 has demonstrated a favorable safety profile across all dose groups, a meaningfully differentiated PK profile supporting potential quarterly or twice annual maintenance dosing, and rapid and complete saturation of  $\alpha$ 4 $\beta$ 7 receptors beyond six months with a single dose of 600mg. Based on these results, SPY001 was advanced into the SKYLINE-UC Phase 2 platform clinical trial, which initiated in May 2025.

## SPY002 and SPY072 – anti-TL1A mAbs

For our anti-TL1A program, we nominated two highly potent, highly selective, and fully human mAb candidates designed to bind to tumor necrosis factor-like ligand 1A ("TL1A"). SPY002 (formerly SPY002-091) is being developed for the treatment of IBD (UC and CD) and SPY072 (formerly SPY002-072) is being developed for the treatment of RD. TL1A is a protein that plays a role in regulating the immune system and is elevated in the gut tissue of individuals with IBD and serum or synovial tissue of individuals with RA, PsA, and axSpA. TL1A interacts with its receptor, death receptor 3 ("DR3"), which is expressed in various immune cells, including T cells and fibroblast-like synoviocytes. This interaction triggers signaling pathways that contribute to inflammation and joint injury in RD, leading to symptomology, such as pain and swelling. SPY002 and SPY072 have been designed to block the interaction between TL1A and DR3, and thereby inhibit the downstream signaling events

to dampen the inflammatory response. By neutralizing TL1A, we believe that SPY002 and SPY072 have the potential to modulate the immune response in IBD and RD patients, potentially reducing disease activity.

SPY002 and SPY072 bind TL1A monomers and trimers and have subnanomolar potency in preclinical cellular assays. We initiated FIH Phase 1 trials for SPY002 and SPY072 in the fourth quarter of 2024. The Phase 1 trials were each double blind, placebo-controlled evaluations in healthy volunteers, consisting of five SAD cohorts. Each trial enrolled 40 healthy adult participants across the five SAD cohorts in the main portion of the study. The primary endpoint is safety, with PK and ADAs serving as secondary endpoints, and PD markers as exploratory endpoints. Additional cohorts may be added to the SPY002 and SPY072 Phase 1 studies, for example to evaluate PK in healthy volunteers of various ethnicities, to facilitate subsequent global clinical trials.

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

#### **SPY003 – anti-IL-23 mAb**

SPY003 is a clinical-stage program designed to bind to Interleukin 23 (“IL-23”) and incorporates half-life extending modifications. IL-23 is a cytokine that is produced by immune cells and is involved in immune response regulation. IL-23 promotes the survival, expansion, and activity of Th17 cells. Th17 cells produce inflammatory cytokines, such as IL-17, which contribute to the inflammation seen in IBD. IL-23 also helps in the recruitment and activation of other immune cells, such as neutrophils, which further contribute to tissue damage in the gut.

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

We initiated a FIH trial in healthy volunteers in March 2025, with interim safety and PK data from this trial expected in the fourth quarter of 2025. If successful, SPY003 will advance to the SKYLINE-UC Phase 2 platform trial.

#### **SPY120 - combination, anti- $\alpha$ 4 $\beta$ 7 and anti-TL1A mAbs**

SPY120 combines SPY001 (anti- $\alpha$ 4 $\beta$ 7) 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 include SPY120 in the SKYLINE-UC Phase 2 platform trial.

In February and May 2025, we presented new preclinical data demonstrating that combinations resulted in additive or greater than additive in vivo biological activity relative to either monotherapy in mouse hapten reagent 2,4,6-trinitrobenzene sulfonic acid (“TNBS”) and anti-CD40 colitis models. In addition, coadministration of SPY001 and SPY002 in NHPs demonstrated no drug effects on PK.

#### **SPY130 - combination anti- $\alpha$ 4 $\beta$ 7 and anti-IL-23 mAbs**

SPY130 combines SPY001 (anti- $\alpha$ 4 $\beta$ 7) 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 include SPY130 in the SKYLINE-UC Phase 2 platform trial.

In October 2024, we presented new preclinical data, demonstrating in a T-cell transfer model of IBD, that combinations with anti-IL-23 and anti- $\alpha$ 4 $\beta$ 7 improved body weight and reduced colonic CD4+ infiltration and IL-17 levels relative to monotherapy. In March 2025, we presented additional preclinical data, demonstrating

that combinations resulted in additive or greater than additive in vivo biological activity relative to either monotherapy in mouse TNBS 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 include SPY230 in the SKYLINE-UC Phase 2 platform trial.

In October 2024, we 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. In March 2025, we presented additional preclinical data, demonstrating that combinations resulted in additive in vivo biological activity relative to either monotherapy in mouse TNBS model.

### **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 certain 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, SPY072 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  $\alpha 4\beta 7$  integrin (SPY001 program) and TL1A (SPY002 and SPY072 programs) 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.

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 and SPY072 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.

### **Critical Accounting Policies and Estimates**

Our condensed consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States ("U.S. GAAP"). The preparation of these condensed 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 discount rate, probabilities of success, and timing of estimated cash flows

in the valuation of the contingent value right ("CVR") liability and inputs used in the Black-Scholes model for stock-based compensation expense.

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. There have been no significant changes to our critical accounting policies and estimates as compared to the critical accounting policies and estimates disclosed in "Management's Discussion and Analysis of Financial Condition and Operations" included in our Annual Report.

## Results of Operations

### Comparison of the Three Months Ended June 30, 2025 and 2024

The following table summarizes our results of operations for the three months ended June 30, 2025 and 2024, together with the changes in those items in dollars and as a percentage:

	Three Months Ended June 30,		Increase/(Decrease)	% Change
	2025	2024		
	(in thousands)			
Operating expenses:				
Research and development	\$ 40,145	\$ 32,636	\$ 7,509	23 %
General and administrative	11,790	11,511	279	2 %
Gain on sale of in-process research and development asset	(10,000)	—	(10,000)	*
Total operating expenses	41,935	44,147	(2,212)	(5)%
Loss from operations	(41,935)	(44,147)	(2,212)	*
Other income:				
Interest income	5,874	5,920	(46)	*
Other (expense) income, net	(656)	(610)	(46)	*
Total other income	5,218	5,310	(92)	*
Loss before income tax expense	(36,717)	(38,837)	(2,120)	*
Income tax benefit (expense)	—	—	—	*
Net loss	\$ (36,717)	\$ (38,837)	\$ (2,120)	*

\* Percentage not meaningful

*Research and Development Expenses.* Research and development expenses increased by \$7.5 million, or 23%, to \$40.1 million for the three months ended June 30, 2025, from \$32.6 million for the three months ended June 30, 2024. The increase was primarily driven by higher clinical trial expenses and increased compensation costs, partially offset by lower early-stage R&D costs coupled with decreased intellectual property license and sub-licensing fees.

	Three Months Ended June 30,		Increase/(Decrease)	% Change
	2025	2024		
	(in thousands)			
<b>External research and development expenses:</b>				
Preclinical	\$ 4,078	\$ 11,857	\$ (7,779)	(66)%
IBD	23,178	14,296	8,882	62 %
Rheumatic diseases	3,120	—	3,120	*
Stock-based compensation <sup>(1)</sup>	—	1,439	(1,439)	(100)%
Legacy Aeglea assets	(23)	151	(174)	(115)%
<b>Total external research and development expense</b>	<b>30,353</b>	<b>27,743</b>	<b>2,610</b>	<b>9%</b>
<b>Internal research and development expenses:</b>				
Compensation	5,296	2,377	2,919	123%
Stock-based compensation	4,100	2,012	2,088	104%
Other	396	504	(108)	(21)%
<b>Total internal research and development expenses</b>	<b>9,792</b>	<b>4,893</b>	<b>4,899</b>	<b>100 %</b>
<b>Total research and development expense</b>	<b>\$ 40,145</b>	<b>\$ 32,636</b>	<b>\$ 7,509</b>	<b>23 %</b>

<sup>(1)</sup> For the three months ended June 30, 2024, \$1.5 million was recognized as stock compensation expense related to the Parapyre Option Obligation.

External research and development expenses include costs associated with third parties contracted to conduct research and development activities on our behalf, including through Paragon, contract research organizations ("CROs"), contract manufacturing organizations ("CMOs"), and third-party laboratories. For the three months ended June 30, 2025 and 2024, external research and development costs accounted for \$30.4 million and \$27.7 million, respectively. Preclinical expenses decreased primarily due to a reduction in early-stage R&D activities given our pipeline's advancement coupled with lower intellectual property license and sub-licensing fees. IBD expenses increased primarily due to an increase in clinical development activities related to ongoing or planned clinical trials partially offset by lower license and sub-licensing fees as well as lower manufacturing costs. Rheumatic diseases costs increased due to increases in manufacturing and clinical development costs. External stock-based compensation decreased due to our obligations ending under the Parapyre Option Obligation.

Internal research and development expenses include compensation and related costs associated with our research and development employees. For the three months ended June 30, 2025 and 2024, internal research and development costs accounted for \$9.8 million and \$4.9 million, respectively. The increase was primarily driven by an increase in research and development headcount.

**General and Administrative Expenses.** General and administrative expenses increased by \$0.3 million, or 2%, to \$11.8 million for the three months ended June 30, 2025, from \$11.5 million for the three months ended June 30, 2024. The increase was primarily attributable to an increase in compensation.

**Gain on Sale of In-Process Research and Development Asset.** During the three months ended June 30, 2025, the Company recognized a gain of \$10.0 million for achieved milestones related to the 2023 sale of the global rights of the legacy Aeglea asset pegzilarginase to Immedica, driven by a favorable reimbursement decision for pegzilarginase in Europe. There was no similar gain or loss during the three months ended June 30, 2024.

**Interest Income.** Interest income was \$5.9 million for both the three months ended June 30, 2025 and 2024, respectively.

*Other expense, net.* Other expense, net for the three months ended June 30, 2025 remained flat compared to the three months ended June 30, 2024. Changes in fair value of the CVR liability comprise the majority of Other expense, net.

#### Comparison of the Six Months Ended June 30, 2025 and 2024

The following table summarizes our results of operations for the six months ended June 30, 2025 and 2024, together with the changes in those items in dollars and as a percentage:

	Six Months Ended June 30,		Dollar Change	% Change
	2025	2024		
	(dollars in thousands)			
Operating expenses (income):				
Research and development	81,768	67,564	14,204	21 %
General and administrative	23,734	24,357	(623)	(3)%
Gain on sale of in-process research and development asset	(10,000)	—	(10,000)	*
Total operating expenses	<u>95,502</u>	<u>91,921</u>	<u>3,581</u>	*
Loss from operations	(95,502)	(91,921)	3,581	*
Other income:				
Interest income	12,367	10,352	2,015	*
Other income (expense), net	1,630	(1,093)	2,723	*
Total other income	<u>13,997</u>	<u>9,259</u>	<u>4,738</u>	*
Loss before income tax expense	(81,505)	(82,662)	(1,157)	*
Income tax benefit (expense)	15	(32)	47	*
Net loss	<u>\$ (81,490)</u>	<u>\$ (82,694)</u>	<u>\$ (1,204)</u>	*

\* Percentage not meaningful

*Research and Development Expenses.* Research and development expenses increased by \$14.2 million, or 21%, to \$81.8 million for the six months ended June 30, 2025, from \$67.6 million for the six months ended June 30, 2024. The increase was primarily driven by higher clinical development activities and increased compensation costs, partially offset by lower early-stage R&D costs coupled with decreased intellectual property license and sub-licensing fees.

	Six Months Ended June 30,		Dollar Change	% Change
	2025	2024		
	(in thousands)			
<b>External research and development expenses:</b>				
Preclinical	\$ 12,557	\$ 26,931	\$ (14,374)	(53)%
IBD	46,008	25,947	20,061	77 %
Rheumatic diseases	5,149	—	5,149	*
Stock-based compensation <sup>(1)</sup>	—	6,889	(6,889)	(100)%
Legacy Aeglea assets	178	(702)	880	(125)%
Total external research and development expense	63,892	59,065	4,827	8 %
<b>Internal research and development expenses:</b>				
Compensation	9,856	4,346	5,510	127 %
Stock-based compensation	7,612	3,419	4,193	123 %
Other	408	734	(326)	(44)%
Total internal research and development expenses	17,876	8,499	9,377	110 %
Total research and development expense	\$ 81,768	\$ 67,564	\$ 14,204	21 %

<sup>(1)</sup> For the six months ended June 30, 2024, \$6.9 million was recognized as stock compensation expense related to the Parapyre Option Obligation.

External research and development expenses include costs associated with third parties contracted to conduct research and development activities on our behalf, including through Paragon, contract research organizations, contract manufacturing organizations, and third-party laboratories. For the six months ended June 30, 2025 and 2024, external research and development costs accounted for \$63.9 million and \$59.1 million, respectively. Preclinical expenses decreased primarily due to a reduction in early-stage R&D activities given our pipeline's advancement coupled with lower intellectual property license and sub-licensing fees. IBD expenses increased primarily due to an increase in clinical development costs related to ongoing or planned clinical trials partially offset by decreased manufacturing costs. Rheumatic diseases costs increased due to increases in manufacturing and clinical development costs. External stock-based compensation decreased due to our obligations ending under the Parapyre Option Obligation.

Internal research and development expenses include compensation and related costs associated with our research and development employees. For the six months ended June 30, 2025 and 2024, internal research and development costs accounted for \$17.9 million and \$8.5 million, respectively. The increase was primarily driven by an increase in research and development headcount.

**General and Administrative Expenses.** General and administrative expenses decreased by \$0.6 million, or 3%, to \$23.7 million for the six months ended June 30, 2025, from \$24.4 million for the six months ended June 30, 2024. The decrease was primarily due to legacy Aeglea employee and director separation costs in the prior period.

**Gain on Sale of In-Process Research and Development Asset.** During the six months ended June 30, 2025, the Company recognized a gain of \$10.0 million for achieved milestones related to the 2023 sale of the global rights of the legacy Aeglea asset pegzilarginase to Immedica, driven by a favorable reimbursement decision for pegzilarginase in Europe. There was no similar gain or loss during the six months ended June 30, 2024.

**Interest Income.** Interest income was \$12.4 million and \$10.4 million for the six months ended June 30, 2025 and 2024, respectively. The increase was primarily due to higher investment balances.

*Other income, net.* Other income, net for the six months ended June 30, 2025 increased by \$2.7 million versus the six months ended June 30, 2024 primarily driven by changes in the fair value of the CVR liability.

## **Liquidity and Capital Resources**

We are a clinical stage biotechnology company with a limited operating history, and due to our significant research and development expenditures, we have generated operating losses since our inception and have not generated any revenue from the 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 our inception and through June 30, 2025, 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 June 30, 2025, we had an accumulated deficit of \$1.1 billion.

Our primary use of cash is to fund the development of our product candidates, and advance our pipeline. This includes both the research and development costs and the general and administrative expenses required to support those operations. Since we are a clinical stage biotechnology company, we have incurred significant operating losses since our inception and we anticipate such losses, in absolute dollar terms, to increase as we continue to pursue clinical development of our product candidates, prepare for the potential commercialization of our product candidates, and expand our development efforts in our pipeline of nonclinical candidates. Based on current operating plans, we have sufficient resources to fund operations for at least one year from the issuance date of the financial statements included in this Quarterly 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.

## **Sources of Liquidity**

In March 2024, we completed a private placement of 121,625 shares of Series B Preferred Stock at \$1,480.00 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 ATM offering program resulting in net proceeds of approximately \$20.5 million after deducting 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 the underwriters' 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.

## Cash Flows

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

	Six Months Ended June 30,	
	2025	2024
Net cash, cash equivalents, and restricted cash (used in) provided by:		
Operating activities	\$ (87,557)	\$ (90,790)
Investing activities	78,937	(225,481)
Financing activities	856	172,525
Effect of exchange rate on cash, cash equivalents, and restricted cash	—	(4)
Net (decrease) increase in cash, cash equivalents, and restricted cash	\$ (7,764)	\$ (143,750)

### Cash Used in Operating Activities

Cash used in operating activities for the six months ended June 30, 2025 was \$87.6 million and primarily reflected a net loss of \$81.5 million coupled with net loss adjustments of a \$10.0 million gain on sale of in-process-research and development and a \$9.6 million decrease in net operating assets and liabilities driven by timing of payments to vendors, partially offset by stock-based compensation of \$18.2 million.

Cash used in operating activities for the six months ended June 30, 2024 was \$90.8 million and reflected a net loss of \$82.7 million, coupled with net loss adjustments of a \$25.7 million decrease in net operating assets and liabilities driven by timing of payments to vendors and \$6.0 million in net accretion of discount on marketable securities, partially offset by stock-based compensation of \$22.5 million.

### Cash Provided By (Used in) Investing Activities

Cash provided by investing activities for the six months ended June 30, 2025 was \$78.9 million and primarily consisted of \$106.3 million in purchases of marketable securities, \$7.0 million in proceeds from the sale of in-process research & development asset, partially offset by \$178.2 million in maturities and sales of marketable securities.

Cash used in investing activities for the six months ended June 30, 2024, was \$225.5 million and primarily consisted of \$331.1 million in purchases of marketable securities, partially offset by \$105.6 million in maturities and sales of marketable securities.

### Cash Provided by Financing Activities

Cash provided by financing activities for the six months ended June 30, 2025 was \$0.9 million, which primarily consisted of proceeds from stock option exercises and sales of common stock under our Employee Stock Purchase Plan.

Cash provided by financing activities for the six months ended June 30, 2024, was \$172.5 million, which primarily consisted of the net proceeds from the issuance of the Series B Preferred Stock in the March 2024 PIPE of \$169.1 million and \$4.9 million from proceeds from stock option exercises and sales of common stock under our Employee Stock Purchase Plan.

### Contingent Contractual Obligations

Through the Asset Acquisition, we received the Option to license certain intellectual property rights related to certain research programs. The exercise of the Option allows for us to enter into an exclusive license agreement with Paragon for the respective research program. Thus far we have exercised the Option and entered into license agreements with respect to SPY001, SPY002, SPY072 and SPY003. Under the terms of each License Agreement, we are obligated to pay Paragon up to \$22.0 million based on specific development, regulatory and clinical milestones for the first product under each agreement. As of June 30, 2025, we have

incurred a total of \$12.0 million of milestone fees out of a total maximum of \$66.0 million in potential milestone fees across all License Agreements. As of June 30, 2025 no milestone fees remain outstanding and payable. With respect to the SPY002 and SPY072 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 June 30, 2025 we have incurred \$0.7 million of sublicensing fees of which nil remain outstanding and payable.

### **Recently Adopted Accounting Pronouncements**

There were no recent adopted accounting pronouncements that have had a material effect on our financial position or results of operations.

### **Item 3. Quantitative and Qualitative Disclosures About Market Risk.**

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities related to our interest-earning investments, foreign currency exchange rates and inflation risk affecting labor costs and clinical trial costs.

#### *Interest Rate Risk*

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. As of June 30, 2025, we held \$526.6 million in cash, cash equivalents, and marketable securities, all of which were denominated in U.S. dollars, and consisted primarily of investments in money market funds, commercial paper, U.S. government obligations, and corporate bonds. 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 during any of the periods presented would not have had a material effect on the total market value of our cash equivalents and marketable securities as of June 30, 2025. To date, we have not experienced a loss of principal on any of our investments and as of June 30, 2025, we did not record any allowance for credit loss from our investments.

#### *Foreign Currency Risk*

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. Volatile market conditions arising from the macroeconomic environment (including financial conditions affecting the banking system and financial institutions), inflation, tariff/trade policy, or global political instability may result in significant changes in exchange rates, and in particular, a weakening of the U.S. dollar relative to foreign currencies may negatively affect our expenses and net income as expressed in U.S. dollars. An adverse movement in foreign exchange rates could have a material effect on payments made to foreign suppliers. For the six months ended June 30, 2025, a majority of our expenditures were denominated in U.S. dollars. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

#### *Inflation Fluctuation Risk*

Inflation generally affects us by increasing our costs, such as the cost of labor and research and development contract costs. We do not believe inflation has had a material adverse effect on the results of our operations during the six months ended June 30, 2025.

#### **Item 4. Controls and Procedures.**

##### **Evaluation of Disclosure Controls and Procedures**

Our management, with the participation of our principal executive officer and principal financial officer, evaluated, as of the end of the period covered by this Quarterly Report, the effectiveness of our disclosure controls and procedures. Based on the foregoing evaluation of our disclosure controls and procedures, as of June 30, 2025, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level. 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 are 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.

##### **Changes in Internal Control over Financial Reporting**

There were no changes in our internal control over financial reporting during the quarter ended June 30, 2025, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

## **PART II. – Other Information**

### **Item 1. 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 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. Some of the factors, events and contingencies discussed below may have occurred in the past, but the disclosures below are not representations as to whether or not the factors, events or contingencies have occurred in the past, and instead reflect our beliefs and opinions as to the factors, events or contingencies that could materially and adversely affect us in the future. 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 Quarterly Report 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, participant recruitment or other clinical trial challenges, or unanticipated drug supply disruptions.
- We are substantially dependent on the success of the SPY001, SPY002, SPY072 and SPY003 programs, alone or in combination, and may fail to achieve our 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.
- Regulatory authorities may not accept data from clinical trials we conduct at sites outside the United States or other jurisdiction.

##### ***Risks Related to Government Regulation***

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

#### ***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.
- Our failure to maintain proper and effective internal controls may adversely affect our ability to report our financial condition and results of operations in a timely and accurate manner, decrease investor confidence

in us, and reduce the value of our common stock. For example, in the fourth quarter of 2024, we identified a material weakness in our internal control over financial reporting which resulted in restatements of our previously-issued financial statements to amend certain net loss per share disclosures.

- Our business could be adversely affected by macroeconomic conditions, including geopolitical unrest.

### **Risks Related to Our Financial Condition and Capital Requirements**

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

As of June 30, 2025, we had \$526.6 million of cash, cash equivalents, and marketable securities. We will need to raise additional capital to continue to fund our operations in the future. If we are unable to raise additional capital when needed, we will not be able to continue as a going concern.

Developing our product candidates requires a substantial amount of capital. We expect our research and development expenses to increase in connection with our ongoing activities, particularly as we advance our product candidates through clinical trials. We will need to raise additional capital to fund our operations and such funding may not be available to us on acceptable terms, or at all, and such funding may become even more difficult to obtain due to macroeconomic conditions, including rising interest rates, tariffs and trade restrictions, global conflicts, and other conditions that could result in volatility in the U.S. capital markets and the biotechnology sector in general. Competition for additional capital among biotechnology companies may be particularly intense during economic uncertainty. We may be unable to raise capital through public offerings of our common stock and may need to turn to alternative financing arrangements. Such arrangements, if we pursue them, could involve 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 political, financial, economic and market conditions, many of which are beyond our control. There can be no assurances that sufficient funds will be available to us when required or on acceptable terms, if at all.

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

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

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

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

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

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

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

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by regulatory authorities to perform clinical and other studies in addition to those that we are currently conducting or anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. Portions of our research programs may be in-licensed from third parties, which make the commercial sale of such in-licensed products potentially subject to additional royalty and milestone payments to such third parties. We will also have to develop or acquire manufacturing capabilities or continue to contract with contract manufacturers in order to continue development and potential commercialization of our product candidates. For instance, if the costs of manufacturing our 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 ongoing or planned studies or trials, additional major studies or trials, or supportive trials necessary to support marketing approval.

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

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

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

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

To the extent that we raise additional capital through the sale of equity, including pursuant to any sales under convertible debt or other securities convertible into equity, the ownership interest of our stockholders will be diluted, and the terms of these new securities may include liquidation or other preferences that adversely affect the rights of our stockholders. For instance, in December 2023, we sold an aggregate of 6,000,000 shares of our common stock and 150,000 shares of our Series B Preferred Stock pursuant to a private placement to certain investors for gross proceeds of approximately \$180 million 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 due to beneficial ownership limitations and remain outstanding as of June 30, 2025.

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

**Risks Related to Discovery, Development and Commercialization**

***We face competition from entities that have developed or may develop programs for the diseases 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 competitive safety, efficacy, dosing and/or presentation profiles. Our commercial opportunity and success will be reduced or eliminated if competing products are safer, more effective, have a more attractive dosing profile or presentation or are less expensive than the products we develop, or if our competitors develop competing products or if biosimilars enter the market more quickly than we do and are able to gain market acceptance. See the section titled "Business – Competition" in our Annual Report 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, 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 U.S. Food and Drug Administration ("FDA"), or ethics committees ("ECs")/institutional review boards ("IRBs") may not authorize us or our investigators to commence a clinical trial 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 clinical 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 investigational new drug ("IND") application 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 or otherwise modify our planned clinical trials, the FDA or other regulatory authorities could determine that the data from our nonclinical studies or clinical trials are insufficient to support the safety and efficacy of our product candidates. There are equivalent processes and risks applicable to clinical trial applications in other countries outside of the United States, which may require us to complete additional nonclinical studies or clinical trials, delay the enrollment of our clinical trials or otherwise modify our planned clinical trials or impose stricter approval conditions than we currently expect.

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

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

Our future success is substantially dependent on our ability to timely obtain marketing approval for, and then successfully commercialize, our SPY001, SPY002, SPY072 and SPY003 programs, alone or in combination. We are investing a majority of our efforts and financial resources into the research and development of these programs. We initiated a Phase 1 clinical trial in healthy volunteers of SPY001 in June 2024, a Phase 1 clinical trial in healthy volunteers of SPY002 in the fourth quarter of 2024, a Phase 1 clinical trial in healthy volunteers of SPY003 in the first quarter of 2025 and a Phase 2 platform trial of our product candidates in IBD beginning with SPY001 in May 2025. We also plan to initiate subsequent additions of monotherapy and combination arms for our Phase 2 UC platform trial during 2025 and 2026 as well as a Phase 2 basket trial of SPY072 in RD, including RA, PsA and axSpA, in mid-2025, each subject to regulatory feedback and approval. The FDA and other regulatory authorities may not agree with our clinical trial designs for our SKYWAY-RD trial or with our proposed timing for enrollment or study design of the combination arms of our SKYLINE-UC Phase 2 platform trial. Alignment with regulatory authorities on issues that arise before clinical trials are commenced, during clinical trials or after our clinical trials are completed could result in additional capital expenditures or delays in development that could have a material adverse impact on our business. The success of our programs is dependent on observing longer half-lives of our product candidates in humans and comparable or better safety and efficacy profiles than other mAbs currently marketed or in development. We believe these longer half-lives have the potential to result in more favorable dosing schedules for our product candidates, assuming they successfully complete clinical development and obtain marketing approval. 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, SPY072 or SPY003, alone or in combination, or are significantly delayed in doing so, our business will be materially harmed.

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

From time to time, we estimate the timing of the anticipated accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of nonclinical studies and clinical trials, such as the expected timing for the anticipated completion of our Phase 1 clinical trials in healthy volunteers and topline data from our ongoing and planned Phase 2 clinical trials in IBD and RD, as well as the submission of

regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are and will be based on numerous assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control, including positions that may be taken by or requirements of regulatory authorities. If we do not meet these milestones as publicly announced, or at all, the commercialization of our product candidates may be delayed or never achieved and, as a result, our stock price may decline. Additionally, delays relative to our projected timelines are likely to cause overall expenses to increase, which may require us to raise additional capital sooner than expected and prior to achieving targeted development milestones.

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

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

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

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

In addition, we may in the future seek to discover and develop programs that are based on novel targets and technologies that are unproven. If our discovery activities fail to identify novel targets or technologies for drug discovery, or such targets prove to be unsuitable for treating human disease, we may not

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

***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 stage 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 Phase 1 trials of our SPY001, SPY002, SPY072 and SPY003 programs in healthy volunteers to support Phase 2 trials in IBD, RD and/or 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, clinical trial application or similar application will result in the FDA or comparable foreign regulatory authorities, as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could cause regulatory authorities to suspend or terminate them. 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 ("GCP") requirements 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 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 an ongoing or planned clinical trial is required to be materially modified or suspended or terminated by us, by the ECs/IRBs of the institutions in which such clinical trials are being conducted, by the external Data Monitoring Committee or equivalent body, if any, for such clinical trial or by the FDA or comparable foreign regulatory authorities. Such authorities may suspend, put on clinical hold or terminate a clinical trial due to a number of factors, including not aligning with or supporting our clinical trial designs or our failure to conduct the clinical trial in accordance with regulatory requirements or our clinical trial protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from the programs, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates, if the results of these trials are not positive or are only moderately positive or if there are safety concerns, our business and results of operations may be adversely affected and we may incur significant additional costs.

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

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

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

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

We plan to pursue development of our investigational products in combination with one or more additional products or investigational products. The development of combination therapies may be more complex than the development of monotherapies and generally requires that sponsors demonstrate the contribution of each investigational product to the claimed effect and the safety and efficacy of the combination as a whole. Regulatory authority requirements for the development of combination therapies may make the design and conduct of clinical trials more complex and/or burdensome, requiring more clinical trial participants and additional time and cost to complete than we plan or anticipate. We also may not be able to meet the FDA's

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

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

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

We may experience difficulties in participant enrollment in our current and future clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of participants who remain in the trial until its conclusion. The enrollment of participants will depend on many factors, including 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. In addition, safety findings associated with competing products or product candidates that target similar pathways could result in the FDA or comparable foreign regulatory authorities imposing restrictions on our clinical trials or product labeling or denying approval of our products. Any of these occurrences could harm our business, financial condition, results of operations and prospects significantly.

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

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

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

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

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

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

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

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

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

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

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

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

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

#### **Risks Related to Government Regulation**

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

The process of obtaining regulatory approvals, both in the United States and abroad, is unpredictable, expensive and typically takes many years following commencement of clinical trials, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. We cannot commercialize product candidates in the United States without first

obtaining regulatory approval from the FDA. Similarly, we cannot commercialize product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of our product candidates, including SPY001, SPY002, SPY072 and SPY003, alone or in combination, we must demonstrate through lengthy, complex and expensive nonclinical studies and clinical trials that our product candidates are both safe and effective for each targeted indication. Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Further, our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval. The FDA and comparable foreign regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional nonclinical, clinical or other data. Our product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including: the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials; we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication; the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval; serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates; we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks; the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical trials; the data collected from clinical trials of our product candidates may not be acceptable or sufficient to support the submission of a Biologics License Application ("BLA") or other submission or to obtain regulatory approval in the United States or elsewhere, and we may be required to conduct additional clinical trials; the FDA or the applicable foreign regulatory authority may disagree regarding the formulation, labeling and/or the specifications of our product candidates; the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval. In addition, the FDA and comparable foreign regulatory authorities may undergo leadership changes, change their policies, issue additional regulations or revise existing regulations, or take other actions, such as those implemented by the Department of Government Efficiency, which may impact our clinical development plans or prevent or delay approval of our programs under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals and increase the costs of compliance.

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

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

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

In order to receive approval of our products by the FDA and comparable foreign regulatory authorities, we must show that we and our contract manufacturing partners are able to characterize, control and manufacture our drug products and drug delivery devices safely and in accordance with regulatory

requirements. This includes manufacturing the active ingredient, developing an acceptable formulation and drug delivery device, manufacturing the drug product and drug delivery device, performing tests to adequately characterize the formulated product, documenting a repeatable manufacturing process, meeting facility, process, testing validation and commercialization requirements, and demonstrating that our drug products meet standards for parenteral administration as well as stability and quality requirements. Meeting these chemistry, manufacturing and control requirements is a complex task that requires specialized expertise. If we are not able to meet the chemistry, manufacturing and control requirements, we may not be successful in getting our products approved.

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

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

We believe that any of our product candidates approved as biologics under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not accord our product candidates reference product exclusivity relative to biosimilar products, potentially creating the opportunity for competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any reference products in a way that is similar to traditional generic substitution for non-biological products 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 good manufacturing practices ("cGMPs"), good pharmacovigilance practices ("GVPs") and GCPs for any post-approval trials that we conduct following approval. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMPs. Following approval, sponsors are also subject to continual review and periodic, unannounced inspections for compliance with GVPs.

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

***We may be negatively impacted by 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 and/or increase our manufacturing costs, general operating costs or other costs. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we fail to adequately prepare for the impacts of or are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, our product candidates may be delayed in obtaining regulatory approval or may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability. In addition, the impact of legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the current presidential administration on us and the pharmaceutical industry as a whole is unclear. These government actions could cause delays in our business plans, increase the cost of execution of our business plans or otherwise have a material adverse effect on our business. For example, the federal government recently announced tariffs on goods imported from China and other countries, which have been followed by threatened or enacted counter-measures by certain countries. These measures could impact the cost of manufacturing our product candidates for our ongoing and planned clinical trials and may increase other costs such as import and export costs across different jurisdictions, costs of drug product and clinical trial supplies, and other costs of running our trials and executing on our business plans, which could negatively impact our financial position. We may seek alternative or additional sources for our drug substance or drug product for our clinical trials, clinical trial sites, or service providers, which could negatively impact our expected timelines and business plan. Additionally, 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 or if we undertake such actions to mitigate the effects of such legislation prior to its enactment, 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 our Annual Report for a more detailed description of healthcare reform measures that may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates.

***Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations 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 our Annual Report 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 our Annual Report for a more detailed description of the government regulations and third-party payor practices that may affect our ability to commercialize our product candidates.

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

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

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

In some countries, particularly member states of the EU, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a therapeutic. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing

used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. To obtain coverage and reimbursement or pricing approvals in some countries, we or current or future collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any product candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be materially and adversely affected. If the UK or certain EU member states were to significantly alter their regulations affecting the pricing of prescription pharmaceuticals, we could face significant new costs.

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

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

***Disruptions at the FDA and other government agencies could negatively affect the review of our regulatory submissions, which could negatively impact our business.***

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

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

development or manufacturing of our product candidates, which could have a material adverse effect on our business.

## **Risks Related to Our Intellectual Property**

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

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

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

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

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

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

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

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

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

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

Disputes may arise between us and our current and future licensors regarding intellectual property subject to a license agreement, including: the scope of rights granted under the license agreement and other interpretation-related issues; whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; our right to sublicense patents and other rights to third parties; our right to transfer or assign the license; the inventorship and ownership of

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

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

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

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

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

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

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

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

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

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

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

Changes in either the patent laws or interpretation of patent laws in the United States, including patent reform legislation such as the Leahy-Smith America Invents Act (the "Leahy-Smith Act") could increase the uncertainties and costs surrounding the prosecution of our owned and in-licensed patent applications and the maintenance, enforcement or defense of our owned and in-licensed issued patents. The Leahy-Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO-administered post-grant proceedings, including post-grant review, inter partes review and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first-to-file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. U.S. Supreme Court and U.S. Court of Appeals for the Federal Circuit rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations, including in the antibody arts. For example, the United States Supreme Court in *Amgen, Inc. v. Sanofi (Amgen)* recently held that Amgen's patent claims to a class of antibodies functionally defined by their ability to bind a particular antigen were invalid for lack of enablement where the patent specification provided twenty-six exemplary antibodies, but the claimed class of antibodies covered a "vast number" of additional antibodies not disclosed in the specification. The Court stated that if patent claims are directed to an entire class of compositions of matter, then the patent specification must enable

a person skilled in the art to make and use the entire class of compositions. This decision makes it unlikely that we will be granted U.S. patents with composition of matter claims directed to antibodies functionally defined by their ability to bind a particular antigen. Even if we are granted claims directed to functionally defined antibodies, it is possible that a third party may challenge our patents, when issued, relying on the reasoning in *Amgen* or other recent precedential court decisions. Additionally, there have been proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to enforce our proprietary technology. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in ways that could have a material adverse effect on our patent rights and weaken our ability to protect, defend and enforce our patent rights in the future.

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

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

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

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

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

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

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

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

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

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

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest United States non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the

development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

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

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

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

have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market.

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

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

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

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

In addition, we currently rely on foreign CROs and CMOs, including WuXi Biologics, and will likely continue to rely on foreign CROs and CMOs in the future. We or the foreign CROs or CMOs we work with may

be subject to U.S. legislation, including the 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. For example, in April 2025, the United States government imposed significant tariffs on imports from China and other countries and may impose more restrictions on goods, including biologically derived substances, manufactured in or imported from China or impose other restrictions on companies' ability to work with Chinese biotechnology companies. To the extent these or future tariffs are applicable to the material we import from China and other countries or if we are not able to secure supply of our product candidates as a result of applicable legislation, our business and financial condition could be adversely affected.

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

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

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

Moreover, our CMOs may experience manufacturing difficulties due to resource constraints, supply chain issues, proposed or actual legislative changes or requirements, or as a result of labor disputes or unstable political environments, including tariffs and restrictions imposed by the United States or other foreign

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

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

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

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

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

We are a clinical stage biotechnology company with a limited operating history, and, as of June 30, 2025, we had 87 employees. We have been and will continue to be highly dependent on the research and development, clinical and business development expertise of our executive officers, as well as the other principal members of our management, scientific and clinical team. Any such officers and other principal members may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees.

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

In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our discovery and nonclinical and clinical development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under

consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

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

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

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

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

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

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

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

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

***Our internal information technology systems, 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. The growing use of artificial intelligence ("AI") by malicious actors is expected to further escalate cybersecurity threats. For example, AI may be used to develop adaptive malware, generate highly convincing phishing or impersonation attacks (such as deepfakes), or automate the discovery and exploitation of software vulnerabilities, thereby increasing the likelihood and sophistication of future attacks.

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

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

Our fully-remote workforce may create additional risks for our information technology systems and data because our employees work remotely and utilize network connections, computers, and devices working at home, while in transit and in public locations. 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. Certain third-party platforms or vendors may incorporate AI-driven automation or analytics into their offerings, which may expose us to new categories of risk, such as data being repurposed for AI training, unexplainable outputs generated by machine learning models, or unintended reliance on automated decision-making systems that lack transparency or auditability. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If our third-party service providers experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third-party partners' supply chains have not been compromised.

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

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

Our contracts may not 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, 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 ("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 our Annual Report for a more detailed description of the laws that may affect our ability to operate.

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

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

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

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

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

We may acquire additional businesses or products, form strategic alliances, or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we

are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new product candidates or products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. There is no assurance that, following any such acquisition, we will achieve the synergies expected in order to justify the transaction, which could result in a material adverse effect on our business and prospects.

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

Our cash held in non-interest-bearing and interest-bearing accounts exceeds the Federal Deposit Insurance Corporation ("FDIC") insurance limits. If such banking institutions were to fail, we could lose all or a portion of those amounts held in excess of such insurance limitations. 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 tariff/trade and monetary policies, instability in financial institutions and the prospect of a shutdown of the U.S. federal government;
- geopolitical instability and government actions, including the ongoing military conflict in Ukraine, conflicts in the Middle East, geopolitical tensions between the United States and other countries, including China, and the implementation of measures that restrict international trade by the United States, China or other governments;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- announcements by commercial partners or competitors of new commercial products, clinical progress or the lack thereof, significant contracts, commercial relationships, or capital commitments;
- the introduction of technological innovations or new therapies that compete with our potential products;
- changes in the structure of health care payment systems; and
- period-to-period fluctuations in our financial results.

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

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

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

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

In addition, the Certificate of Designation of Preferences, Rights and Limitations of the Series A Preferred Stock (the "Series A Certificate of Designation") relating to our Series A Preferred Stock may delay or prevent a change in control of our company. At any time while at least 30% of the originally issued Series A Preferred Stock remains issued and outstanding, we may not consummate a Fundamental Transaction (as defined in the Series A Certificate of Designation) or any merger or consolidation of the Company with or into another entity or any stock sale to, or other business combination in which our stockholders immediately before such transaction do not hold at least a majority of our capital stock immediately after such transaction, without

the affirmative vote of the holders of a majority of the then outstanding shares of the Series A Preferred Stock. This provision of the Series A Certificate of Designation may make it more difficult for us to enter into any of the aforementioned transactions as it would require the separate consent of a majority of the holders of the Series A Preferred Stock.

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

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

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

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

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

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

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

If our stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after legal restrictions on resale lapse, the trading price of our common stock could decline. In addition, shares of our common stock that are subject to our outstanding options and restricted stock units will

become eligible for sale in the public market to the extent permitted by the provisions of various vesting agreements and Rules 144 and 701 under the Securities Act.

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

We expect that we will need significant additional capital to fund our current and future operations, including to complete 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.

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

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

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

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

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

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

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

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

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

The global economy, including credit and financial markets, has experienced extreme volatility and disruptions, including, among other things, diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, supply chain shortages, increases in inflation rates, higher interest rates, and uncertainty about economic stability. Adverse macroeconomic conditions, including inflation, slower growth or recession, new or increased tariffs and other barriers to trade, especially in light of recent comments and executive orders made by the Trump administration, changes to fiscal and monetary policy or government budget dynamics (particularly in the pharmaceutical and biotechnology areas), tighter credit, higher interest rates, volatility in financial markets, high unemployment, labor availability constraints, currency fluctuations and other challenges in the global economy have in the past adversely affected, and may in the future adversely affect, us and our business partners and suppliers. In recent months, the United States has announced tariffs on imports from most countries, including significant tariffs on imports from Canada, Mexico and China. Historically, tariffs have led to increased trade and political tensions. In response to tariffs, other countries have implemented retaliatory tariffs on U.S. goods. Political tensions as a result of trade policies could reduce trade volume, investment, technological exchange and other economic activities between major international economies, resulting in a material adverse effect on global economic conditions and the stability of global financial markets. There is substantial uncertainty about the duration of existing tariffs and whether additional tariffs may be imposed, modified or suspended. The Federal Reserve has raised interest rates multiple times in response to concerns about inflation and it may raise them again. Higher interest rates, coupled with reduced government spending and volatility in financial markets, may increase economic uncertainty and affect consumer spending. Similarly, geopolitical uncertainties, international conflicts and government actions, including the ongoing military conflicts between Russia and Ukraine, and conflicts in the Middle East involving Israel and various other parties, including Iran, Hamas and Hezbollah, as well as other conflicts in the region, rising tensions with China and the implementation of tariffs, sanctions, export or import controls, and other measures that restrict international trade by the United States, China or other governments, have created extreme volatility in the global capital markets and may have further global economic consequences, including disruptions of the global supply chain. Any such volatility and disruptions may adversely affect our business or the third parties on whom we rely. If the equity and credit markets deteriorate, including as a result of political unrest or war, it may make any necessary debt or equity financing more costly, more dilutive, or more difficult to obtain in a timely manner or on favorable terms, if at all. Increased inflation rates can adversely affect us by increasing our costs, including labor and employee benefit costs.

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

**Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.**

None.

**Item 3. Defaults Upon Senior Securities.**

None.

**Item 4. Mine Safety Disclosures.**

Not applicable.

**Item 5. Other Information.**

*Trading Plans*

During the fiscal quarter ended June 30, 2025, no director or Section 16 officer adopted or terminated any Rule 10b5-1 trading arrangement or non-Rule 10b5-1 trading arrangement (in each case, as defined in Item 408(a) of Regulation S-K), except as described below.

On June 20, 2025, Cameron Turtle, our Chief Executive Officer, terminated a trading plan dated April 12, 2024 intended to satisfy Rule 10b5-1(c) to sell up to 300,000 shares of our common stock over a period ending November 19, 2026, subject to certain conditions, and adopted a trading plan intended to satisfy Rule 10b5-1(c) to sell up to 360,000 shares of our common stock over a period ending August 4, 2027, subject to certain conditions.

On June 20, 2025, Sheldon Sloan, our Chief Medical Officer, adopted a trading plan intended to satisfy Rule 10b5-1(c) to sell up to 102,958 shares of our common stock over a period ending September 3, 2026, subject to certain conditions, all of which shares are to be acquired upon the exercise of employee stock options.

**Item 6. Exhibits.**

The exhibits filed or furnished as part of this Quarterly Report on Form 10-Q are set forth below.

<u>Exhibit Number</u>	<u>Description</u>	<u>Form</u>	<u>File No</u>	<u>Date of Filing</u>	<u>Exhibit No.</u>	<u>Filed Herewith</u>
2.1	<a href="#">Agreement and Plan of Merger, dated June 22, 2023, by and among Aeglea BioTherapeutics, Inc. Aspen Merger Sub I, Inc., Sequoia Merger Sub II, LLC and Spyre Therapeutics, Inc.</a>	S-1	333-276251	12/22/2023	2.1	
3.1	<a href="#">Second Amended and Restated Certificate of Incorporation of the Company, effective as of May 14, 2024</a>	8-K	001-37722	05/15/2024	3.2	
3.2	<a href="#">Amended and Restated Bylaws</a>	S-1/A	333-276251	02/05/2024	3.2	
3.3	<a href="#">Certificate of Designation of Series A Non-Voting Convertible Preferred Stock</a>	S-1	333-276251	12/22/2023	3.3	
3.4	<a href="#">Certificate of Designation of Series B Non-Voting Convertible Preferred Stock</a>	S-1	333-276251	12/22/2023	3.4	
3.5	<a href="#">Certificate of Amendment to Certificate of Designation of Series B Non-Voting Convertible Preferred Stock</a>	8-K	001-37722	03/18/2024	3.2	
4.1	<a href="#">Form of Warrant to Purchase Common Stock (Parapyre Warrant 2023)</a>					X
4.2	<a href="#">Form of Warrant to Purchase Common Stock (Parapyre Warrant 2024)</a>					X
10.1+	<a href="#">Spyre Therapeutics, Inc. 2018 Equity Inducement Plan and the First Amendment, Second Amendment, Third Amendment, Fourth Amendment, Fifth Amendment and Sixth Amendment thereto</a>					X
31.1	<a href="#">Certification of the Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934</a>					X
31.2	<a href="#">Certification of the Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934</a>					X
32.1(1)	<a href="#">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</a>					X
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

<b>Exhibit Number</b>	<b>Description</b>	<b>Form</b>	<b>File No</b>	<b>Date of Filing</b>	<b>Exhibit No.</b>	<b>Filed Herewi</b>
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 Label Linkbase Document					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					X
104	The cover page from this Quarterly Report formatted in Inline XBRL and contained in Exhibit 101					

+ Indicates management contract or compensatory plan.

# Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

(1) The certifications on Exhibit 32 hereto are deemed furnished and 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.

**Signatures**

Pursuant to the requirements 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: August 5, 2025

Spyre Therapeutics, Inc.

By: /s/ Scott Burrows

Scott Burrows

*Chief Financial Officer*

*(Principal Financial Officer and Principal Accounting Officer)*

**SPYRE THERAPEUTICS, INC.**  
**WARRANT TO PURCHASE COMMON STOCK**

Number of Warrant Shares: 684,407  
(subject to adjustment)

Warrant No. SYRE-001R

Original Issue Date: December 29, 2023

THIS **WARRANT TO PURCHASE COMMON STOCK** (the "Warrant") certifies that, for value received, Parapyre Holding LLC or its assigns (the "Holder") is entitled, upon the terms and subject to the limitations on exercise and the conditions hereinafter set forth, at any time on or after the date hereof (the "Original Issue Date") and on or prior to 5:00 p.m. (New York City time) on December 29, 2033, (the "Termination Date") but not thereafter, to subscribe for and purchase from Spyre Therapeutics, Inc., a Delaware corporation (the "Company"), up to 684,407 shares (as subject to adjustment hereunder, the "Warrant Shares") of common stock, \$0.0001 par value per share, of the Company ("Common Stock"). The purchase price of one share of Common Stock under this Warrant shall be equal to the Exercise Price, as defined in Section 2(b).

Section 1. Definitions. Capitalized terms used and not otherwise defined herein shall have the meanings set forth in that certain Amended and Restated Antibody Discovery and Option Agreement (the "Paragon Agreement"), dated September 29, 2023, among the Company, Paragon Therapeutics, Inc. and Parapyre Holding LLC.

a) "Closing Sale Price" means, for any security as of any date, the last trade price for such security on the Principal Trading Market for such security, as reported by Bloomberg L.P., or, if such Principal Trading Market begins to operate on an extended hours basis and does not designate the last trade price, then the last trade price of such security prior to 4:00 P.M., New York City time, as reported by Bloomberg L.P., or if the security is not listed for trading on a national securities exchange or other trading market on the relevant date, the last quoted bid price for the security in the over-the-counter market on the relevant date as reported by OTC Markets Group Inc. (or a similar organization or agency succeeding to its functions of reporting prices). If the Closing Sale Price cannot be calculated for a security on a particular date on any of the foregoing bases, the Closing Sale Price of such security on such date shall be the fair market value as mutually determined by the Company and the Holder. If the Company and the Holder are unable to agree upon the fair market value of such security, then the board of directors of the Company shall use its good faith judgment to determine the fair market value. The board of directors' determination shall be binding upon all parties absent demonstrable error. All such determinations shall be appropriately adjusted for any stock dividend, stock split, stock combination or other similar transaction during the applicable calculation period.

b) "Commission" means the U.S. Securities and Exchange Commission.

c) "Person" means any natural person or legal entity.

d) "Principal Trading Market" means the national securities exchange or other trading market on which the Common Stock is primarily listed on and quoted for trading, which, as of the Original Issue Date was the Nasdaq Capital Market.

e) "Trading Day" means any weekday on which the Principal Trading Market is open for trading. If the Common Stock is not listed or admitted for trading, "Trading Day" means any day except any Saturday, any Sunday, any day which is a federal legal holiday in the United States or any day on which banking institutions in New York City are authorized or required by law or other governmental action to close.

f) "Transfer Agent" means Equity Trust Company, LLC, the Company's transfer agent and registrar for the Common Stock, and any successor appointed in such capacity.

Section 2. Exercise.

a) Exercise of Warrant. Exercise of the purchase rights represented by this Warrant may be made, in whole or in part, at any time or times on or after the Original Issue Date and on or before the Termination Date, including by means of a "cashless exercise" as described in Section 2(c) below, by

delivery to the Company of a duly executed facsimile copy or PDF copy submitted by e-mail (or e-mail attachment) of the Notice of Exercise in the form annexed hereto (the "Notice of Exercise"). Within the earlier of (i) two (2) Trading Days and (ii) the number of Trading Days comprising the Standard Settlement Period following the date of exercise (the "Exercise Date") as aforesaid, the Holder shall deliver the aggregate Exercise Price for the Warrant Shares specified in the applicable Notice of Exercise by wire transfer or cashier's check drawn on a United States bank unless the cashless exercise procedure specified in Section 2(c) below is specified in the applicable Notice of Exercise. No ink-original Notice of Exercise shall be required, nor shall any medallion guarantee (or other type of guarantee or notarization) of any Notice of Exercise be required. Notwithstanding anything herein to the contrary, the Holder shall not be required to physically surrender this Warrant to the Company until the Holder has purchased all of the Warrant Shares available hereunder and the Warrant has been exercised in full, in which case, the Holder shall surrender this Warrant to the Company for cancellation within three (3) Trading Days of the date on which the final Notice of Exercise is delivered to the Company. Partial exercises of this Warrant resulting in purchases of a portion of the total number of Warrant Shares available hereunder shall have the effect of lowering the outstanding number of Warrant Shares purchasable hereunder in an amount equal to the applicable number of Warrant Shares purchased. The Holder and the Company shall maintain records showing the number of Warrant Shares purchased and the date of such purchases. The Company shall deliver any objection to any Notice of Exercise within one (1) Trading Day of its receipt of such notice. **The Holder and any assignee, by acceptance of this Warrant, acknowledge and agree that, by reason of the provisions of this paragraph, following the purchase of a portion of the Warrant Shares hereunder, the number of Warrant Shares available for purchase hereunder at any given time may be less than the amount stated on the face hereof.** As used herein, "Standard Settlement Period" means the standard settlement period, expressed in a number of Trading Days, on the Principal Trading Market with respect to the Common Stock as in effect on the date of delivery of the Notice of Exercise to the Company.

b) Exercise Price. The exercise price per share of Common Stock under this Warrant shall be \$21.52, subject to adjustment hereunder (the "Exercise Price").

c) Cashless Exercise. This Warrant may be exercised, in whole or in part, by means of a "cashless exercise" in which the Holder shall be entitled to receive a number of Warrant Shares as determined as follows:

$$X = Y [(A-B)/A]$$

where:

"X" equals the number of Warrant Shares to be issued to the Holder;

"Y" equals the total number of Warrant Shares with respect to which this Warrant is then being exercised;

"A" equals the Closing Sale Price per share of Common Stock as of the Trading Day on the date immediately preceding the Exercise Date; and

"B" equals the Exercise Price per Warrant Share then in effect on the Exercise Date.

d) Mechanics of Exercise.

i. Delivery of Warrant Shares Upon Exercise. Within a reasonable time after Holder exercises this Warrant in the manner set forth in Section 2(a) or 2(c) above, the Company shall deliver to Holder a certificate (which certificate may be in the form of an electronic certificate or DTC entry, to the extent used by the Company at the time of such exercise) or evidence of book entry representing the Warrant Shares issued to such Holder upon such exercise. As used herein, "Standard Settlement Period" means

the standard settlement period, expressed in a number of Trading Days, on the Principal Trading Market with respect to the Common Stock as in effect on the date of delivery of the Notice of Exercise to the Company.

ii. Delivery of New Warrants Upon Exercise. If this Warrant shall have been exercised in part, the Company shall, at the request of a Holder and upon surrender of this Warrant certificate, at the time of delivery of the Warrant Shares, deliver to the Holder a new Warrant evidencing the rights of the Holder to purchase the unpurchased Warrant Shares called for by this Warrant, which new Warrant shall in all other respects be identical with this Warrant.

iii. [RESERVED.]

iv. No Fractional Shares or Scrip. No fractional shares or scrip representing fractional shares shall be issued upon the exercise of this Warrant. As to any fraction of a share which the Holder would otherwise be entitled to purchase upon such exercise, the Company shall, at its election, either pay a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the Exercise Price or round down to the next whole share.

v. Charges, Taxes and Expenses. Issuance of Warrant Shares shall be made without charge to the Holder for any issue or transfer tax or other incidental expense in respect of the issuance of such Warrant Shares, all of which taxes and expenses shall be paid by the Company, and such Warrant Shares shall be issued in the name of the Holder or in such name or names as may be directed by the Holder; *provided, however*, that, in the event that Warrant Shares are to be issued in a name other than the name of the Holder, this Warrant when surrendered for exercise shall be accompanied by the Assignment Form attached hereto duly executed by the Holder and the Company may require, as a condition thereto, the payment of a sum sufficient to reimburse it for any transfer tax incidental thereto.

vi. Closing of Books. The Company will not close its stockholder books or records in any manner which prevents the timely exercise of this Warrant, pursuant to the terms hereof.

e) Holder's Exercise Limitations. The Company shall not effect any exercise of this Warrant, and a Holder shall not have the right to exercise any portion of this Warrant, pursuant to Section 2 or otherwise, to the extent that after giving effect to such issuance after exercise as set forth on the applicable Notice of Exercise, the Holder (together with the Holder's Affiliates, and any other Persons acting as a group together with the Holder or any of the Holder's Affiliates (such Persons, "Attribution Parties")), would beneficially own in excess of the Beneficial Ownership Limitation (as defined below). For purposes of the foregoing sentence, the number of shares of Common Stock beneficially owned by the Holder and its Affiliates and Attribution Parties shall include the number of shares of Common Stock issuable upon exercise of this Warrant with respect to which such determination is being made, but shall exclude the number of shares of Common Stock which would be issuable upon (i) exercise of the remaining, nonexercised portion of this Warrant beneficially owned by the Holder or any of its Affiliates or Attribution Parties and (ii) exercise or conversion of the unexercised or nonconverted portion of any other securities of the Company subject to a limitation on conversion or exercise analogous to the limitation contained herein beneficially owned by the Holder or any of its Affiliates or Attribution Parties. Except as set forth in the preceding sentence, for purposes of this Section 2(e), beneficial ownership shall be calculated in accordance with Section 13(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") and the rules and regulations promulgated thereunder, it being acknowledged by the Holder that the Company is not representing to the Holder that such calculation is in compliance with Section 13(d) of the Exchange Act and the Holder is solely responsible for any schedules required to be filed in accordance therewith. To the extent that the limitation contained in this Section 2(e) applies, the determination of whether this Warrant is exercisable (in relation to other securities owned by the Holder together with any Affiliates and Attribution Parties) and of which portion of this Warrant is exercisable shall be in the sole discretion of the Holder, and the

Holder's submission of a Notice of Exercise to the Company shall be deemed to be the Holder's determination of whether this Warrant is exercisable (in relation to other securities owned by the Holder together with any Affiliates and Attribution Parties) and of which portion of this Warrant is exercisable, in each case subject to the Beneficial Ownership Limitation, and, absent manifest error, the Company shall have no obligation to verify or confirm the accuracy of such determination. In addition, a determination as to any group status as contemplated above shall be determined in accordance with Section 13(d) of the Exchange Act and the rules and regulations promulgated thereunder. For purposes of this Section 2(e), in determining the number of outstanding shares of Common Stock, a Holder may rely on the number of outstanding shares of Common Stock as reflected in (A) the Company's most recent periodic or annual report filed with the Commission, as the case may be, (B) a more recent public announcement by the Company or (C) a more recent written notice by the Company or the Transfer Agent setting forth the number of shares of Common Stock outstanding. Upon the written or oral request of a Holder, the Company shall within one Trading Day confirm orally and in writing to the Holder the number of shares of Common Stock then outstanding. In any case, the number of outstanding shares of Common Stock shall be determined after giving effect to the conversion or exercise of securities of the Company, including this Warrant, by the Holder or its Affiliates or Attribution Parties since the date as of which such number of outstanding shares of Common Stock was reported. As used herein, "Affiliate" shall mean any Person directly or indirectly controlled by, controlling or under common control with, a Holder, as such terms are used in and construed under Rule 405 under the Securities Act, but only for so long as such control shall continue. The "Beneficial Ownership Limitation" shall be 4.99% of the number of shares of the Common Stock outstanding immediately after giving effect to the issuance of shares of Common Stock issuable upon exercise of this Warrant. The provisions of this paragraph shall be construed and implemented in a manner otherwise than in strict conformity with the terms of this Section 2(e) to correct this paragraph (or any portion hereof) which may be defective or inconsistent with the intended Beneficial Ownership Limitation herein contained or to make changes or supplements necessary or desirable to properly give effect to such limitation. The limitations contained in this paragraph shall apply to a successor holder of this Warrant.

### Section 3. Certain Adjustments.

a) Stock Dividends and Splits. If the Company, at any time while this Warrant is outstanding: (i) pays a stock dividend or otherwise makes a distribution or distributions on shares of its Common Stock or any other equity or equity equivalent securities payable in shares of Common Stock (which, for avoidance of doubt, shall not include any shares of Common Stock issued by the Company upon exercise of this Warrant), (ii) subdivides outstanding shares of Common Stock into a larger number of shares, (iii) combines (including by way of reverse stock split) outstanding shares of Common Stock into a smaller number of shares, or (iv) issues by reclassification of shares of the Common Stock any shares of capital stock of the Company, then in each case the Warrant Shares shall be multiplied by a fraction of which the numerator shall be the number of shares of Common Stock (excluding treasury shares, if any) outstanding immediately after such event and of which the denominator shall be the number of shares of Common Stock outstanding immediately before such event, and the Exercise Price shall be proportionately adjusted such that the aggregate Exercise Price of this Warrant shall remain unchanged. Any adjustment made pursuant to this Section 3(a) shall become effective immediately after the record date for the determination of stockholders entitled to receive such dividend or distribution and shall become effective immediately after the effective date in the case of a subdivision, combination or re-classification.

b) Fundamental Transaction. If, at any time while this Warrant is outstanding, (i) the Company, directly or indirectly, in one or more related transactions effects any merger or consolidation of the Company with or into another Person, (ii) the Company (and all of its subsidiaries, taken as a whole), directly or indirectly, effects any sale, lease, license, assignment, transfer, conveyance or other disposition of all or substantially all of its assets in one or a series of related transactions, (iii) any, direct or indirect, purchase offer, tender offer or exchange offer (whether by the Company or another Person) is completed pursuant to which holders of Common Stock are permitted to sell, tender or exchange their shares for other securities, cash or property and has been accepted by the holders of 50% or more of the outstanding Common Stock or 50% or more of the outstanding voting power of the common equity of the Company, (iv) the Company, directly or indirectly, in one or more related transactions effects any reclassification,

reorganization or recapitalization of the Common Stock or any compulsory share exchange pursuant to which the Common Stock is effectively converted into or exchanged for other securities, cash or property, or (v) the Company, directly or indirectly, in one or more related transactions consummates a stock or share purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off, merger or scheme of arrangement) with another Person or group of Persons whereby such other Person or group acquires 50% or more of the outstanding shares of Common Stock or 50% or more of the outstanding voting power of the common equity of the Company (each a "Fundamental Transaction"), then, to the extent the fair market value of one Warrant Share as determined in accordance with Section 1(a) above would be greater than the Exercise Price in effect on such date immediately prior to the occurrence of such Fundamental Transaction, and Holder has not exercised this Warrant pursuant to Section 2 above as to all Warrant Shares, then this Warrant shall automatically be deemed to be cashless exercised pursuant to Section 2(c) above as to all Warrant Shares effective immediately prior to and contingent upon the consummation of a Fundamental Transaction. For the avoidance of doubt, if, immediately prior to the Fundamental Transaction, the fair market value of one Warrant Share as determined in accordance with Section 1(a) above is not greater than the Exercise Price in effect on the Trading Day immediately prior to the closing of such Fundamental Transaction, then this Warrant shall terminate without exercise or conversion immediately prior to, and subject to, the closing of such Fundamental Transaction.

c) Calculations. All calculations under this Section 3 shall be made to the nearest one-hundredth of one cent or the nearest share, as the case may be. For purposes of this Section 3, the number of shares of Common Stock deemed to be issued and outstanding as of a given date shall be the sum of the number of shares of Common Stock (excluding treasury shares, if any) issued and outstanding.

d) Voluntary Adjustment By Company. Subject to the rules and regulations of the Principal Trading Market, the Company may at any time during the term of this Warrant, subject to the prior written consent of the Holder, reduce the then current Exercise Price to any amount and for any period of time deemed appropriate by the board of directors of the Company.

e) Notice of Adjustments. Upon the occurrence of each adjustment pursuant to this Section 3, the Company at its expense will, at the written request of the Holder, promptly compute such adjustment, in good faith, in accordance with the terms of this Warrant and prepare a certificate setting forth such adjustment, including a statement of the adjusted Exercise Price and adjusted number or type of Warrant Shares or other securities issuable upon exercise of this Warrant (as applicable), describing the transactions giving rise to such adjustments and showing in detail the facts upon which such adjustment is based. Upon written request, the Company will promptly deliver a copy of each such certificate to the Holder and to the Transfer Agent.

f) Notice of Corporate Events. If, while this Warrant is outstanding, the Company (i) declares a dividend or any other distribution of cash, securities or other property in respect of its Common Stock, including, without limitation, any granting of rights or warrants to subscribe for or purchase any capital stock of the Company or any subsidiary, (ii) authorizes or approves, enters into any agreement contemplating or solicits stockholder approval for any Fundamental Transaction or (iii) authorizes the voluntary dissolution, liquidation or winding up of the affairs of the Company, then, except if such notice and the contents thereof shall be deemed to constitute material non-public information, the Company shall deliver to the Holder a notice of such transaction at least ten (10) days prior to the applicable record or effective date on which a Person would need to hold Common Stock in order to participate in or vote with respect to such transaction; provided, however, that the failure to deliver such notice or any defect therein shall not affect the validity of the corporate action required to be described in such notice. In addition, if while this Warrant is outstanding, the Company authorizes or approves, enters into any agreement contemplating or solicits stockholder approval for any Fundamental Transaction contemplated by Section 3(b), other than a Fundamental Transaction under clause (iii) of Section 3(b), the Company shall deliver to the Holder a notice of such Fundamental Transaction at least ten (10) days prior to the date such Fundamental Transaction is consummated. Holder agrees to maintain any information disclosed pursuant to this Section 3(f) in confidence until such information is publicly available, and shall comply with

applicable law with respect to trading in the Company's securities following receipt of any such information.

Section 4. Transfer of Warrant.

a) Transferability. This Warrant and all rights hereunder (including, without limitation, any registration rights) are transferable only to employees of Paragon Therapeutics, Inc. that are limited partners of Parapyre Holding LLC at the time of transfer, in whole or in part, upon surrender of this Warrant at the principal office of the Company or its designated agent, together with a written assignment of this Warrant substantially in the form attached hereto duly executed by the Holder or its agent or attorney and funds sufficient to pay any transfer taxes payable upon the making of such transfer. Upon such surrender and, if required, such payment, the Company shall execute and deliver a new Warrant or Warrants in the name of the assignee or assignees, as applicable, and in the denomination or denominations specified in such instrument of assignment, and shall issue to the assignor a new Warrant evidencing the portion of this Warrant not so assigned, if any, and this Warrant shall promptly be cancelled. Notwithstanding anything herein to the contrary, the Holder shall not be required to physically surrender this Warrant to the Company unless the Holder has assigned this Warrant in full, in which case, the Holder shall surrender this Warrant to the Company within three (3) Trading Days of the date on which the Holder delivers an assignment form to the Company assigning this Warrant in full. The Warrant, if properly assigned in accordance herewith, may be exercised by a new holder for the purchase of Warrant Shares without having a new Warrant issued.

b) New Warrants. This Warrant may be divided or combined with other Warrants upon presentation hereof at the aforesaid office of the Company, together with a written notice specifying the names and denominations in which new Warrants are to be issued, signed by the Holder or its agent or attorney. Subject to compliance with Section 4(a), as to any transfer which may be involved in such division or combination, the Company shall execute and deliver a new Warrant or Warrants in exchange for the Warrant or Warrants to be divided or combined in accordance with such notice. All Warrants issued on transfers or exchanges shall be dated the Original Issue Date and shall be identical with this Warrant except as to the number of Warrant Shares issuable pursuant thereto and the Exercise Price.

c) Warrant Register. The Company shall register this Warrant, upon records to be maintained by the Company for that purpose (the "Warrant Register"), in the name of the record Holder hereof from time to time. The Company shall deem and treat the registered Holder of this Warrant as the absolute owner hereof for the purpose of any exercise hereof or any distribution to the Holder, and for all other purposes, absent actual notice to the contrary.

Section 5. Miscellaneous.

a) No Rights as Stockholder Until Exercise; No Settlement in Cash. This Warrant does not entitle the Holder to any voting rights, dividends or other rights as a stockholder of the Company prior to the exercise hereof as set forth in Section 2(d)(i), except as expressly set forth in Section 3.

b) Loss, Theft, Destruction or Mutilation of Warrant. The Company covenants that upon receipt by the Company of evidence reasonably satisfactory to it of the loss, theft, destruction or mutilation of this Warrant or any stock certificate relating to the Warrant Shares, and in case of loss, theft or destruction, of indemnity or security reasonably satisfactory to it (which, in the case of the Warrant, shall not include the posting of any bond), and upon surrender and cancellation of such Warrant or stock certificate, if mutilated, the Company will make and deliver a new Warrant or stock certificate of like tenor and dated as of such cancellation, in lieu of such Warrant or stock certificate.

c) Saturdays, Sundays, Holidays, etc. If the last or appointed day for the taking of any action or the expiration of any right required or granted herein shall not be a Trading Day, then such action may be taken or such right may be exercised on the next succeeding Trading Day.

d) Authorized Shares.

The Company covenants that, during the period the Warrant is outstanding, it will reserve from its authorized and unissued Common Stock a sufficient number of shares to

provide for the issuance of the Warrant Shares upon the exercise of any purchase rights under this Warrant. The Company further covenants that its issuance of this Warrant shall constitute full authority to its officers who are charged with the duty of issuing the necessary Warrant Shares upon the exercise of the purchase rights under this Warrant. The Company will take all such reasonable action as may be necessary to assure that such Warrant Shares may be issued as provided herein without violation of any applicable law or regulation, or of any requirements of the Principal Trading Market. The Company covenants that all Warrant Shares which may be issued upon the exercise of the purchase rights represented by this Warrant will, upon exercise of the purchase rights represented by this Warrant and payment for such Warrant Shares in accordance herewith, be duly authorized, validly issued, fully paid and nonassessable and free from all taxes, liens and charges created by the Company in respect of the issue thereof (other than taxes in respect of any transfer occurring contemporaneously with such issue).

Except and to the extent as waived or consented to by the Holder, the Company shall not by any action, including, without limitation, amending its certificate of incorporation or through any reorganization, transfer of assets, consolidation, merger, dissolution, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms of this Warrant, but will at all times in good faith assist in the carrying out of all such terms and in the taking of all such actions as may be necessary or appropriate to protect the rights of Holder as set forth in this Warrant against impairment. Without limiting the generality of the foregoing, the Company will (i) not increase the par value of any Warrant Shares above the amount payable therefor upon such exercise immediately prior to such increase in par value, (ii) take all such action as may be necessary or appropriate in order that the Company may validly and legally issue fully paid and nonassessable Warrant Shares upon the exercise of this Warrant and (iii) obtain all such authorizations, exemptions or consents from any public regulatory body having jurisdiction thereof, as may be, necessary to enable the Company to perform its obligations under this Warrant.

Before taking any action which would result in an adjustment in the number of Warrant Shares for which this Warrant is exercisable or in the Exercise Price, the Company shall obtain all such authorizations or exemptions thereof, or consents thereto, as may be necessary from any public regulatory body or bodies having jurisdiction thereof.

The Company represents, warrants and covenants that, as of the date hereof, (i) the issued and outstanding Common Stock of the Company is registered pursuant to Section 12(b) of the Exchange Act, and listed for trading on the Nasdaq Capital Market; (ii) there is no suit, action, proceeding or investigation pending or, to the knowledge of the Company, threatened against the Company by the Principal Trading Market, or the Commission with respect to any intention by such entity to deregister the Common Stock or prohibit or terminate the listing of the Common Stock on the Principal Trading Market; and (iii) the Company has taken no action that is designed to terminate the registration of Common Stock under the Exchange Act.

e) Jurisdiction. All questions concerning the construction, validity, enforcement and interpretation of this Warrant shall be determined in accordance with the provisions of the Paragon Agreement.

f) Restrictions. The Holder acknowledges that the Warrant Shares acquired upon the exercise of this Warrant, if not registered, will have restrictions upon resale imposed by state and federal securities laws.

g) Nonwaiver. No course of dealing or any delay or failure to exercise any right hereunder on the part of Holder shall operate as a waiver of such right or otherwise prejudice the Holder's rights, powers or remedies.

h) Notices. Any and all notices or other communications or deliveries hereunder (including, without limitation, any Notice of Exercise) shall be in writing and shall be deemed given and effective on the earliest of (i) the date of transmission, if such notice or communication is delivered via facsimile or confirmed e-mail prior to 5:30 P.M., New York City time, on a Trading Day, (ii) the next Trading Day after

the date of transmission, if such notice or communication is delivered via confirmed e-mail on a day that is not a Trading Day or later than 5:30 P.M., New York City time, on any Trading Day, (iii) the Trading Day following the date of mailing, if sent by nationally recognized overnight courier service specifying next business day delivery, or (iv) upon actual receipt by the Person to whom such notice is required to be given, if by hand delivery. The addresses and e-mail addresses for such communications shall be:

If to the Company:

Spyre Therapeutics, Inc.  
221 Crescent Street  
Building 23, Suite 105  
Waltham, MA 02543  
Attention: Chief Financial Officer  
Email:

With a copy (for informational purposes only) to:

Gibson, Dunn & Crutcher LLP  
One Embarcadero Center, Suite 2600  
San Francisco, CA 94111  
E-mail: rmurr@gibsondunn.com; bberns@gibsondunn.com  
Attention: Ryan A. Murr; Branden C. Berns

If to the Holder, to its address or e-mail address set forth herein or on the books and records of the Company.

Or, in each of the above instances, to such other address or e-mail address as the recipient party has specified by written notice given to each other party at least five (5) days prior to the effectiveness of such change.

i) Limitation of Liability. No provision hereof, in the absence of any affirmative action by the Holder to exercise this Warrant to purchase Warrant Shares, and no enumeration herein of the rights or privileges of the Holder, shall give rise to any liability of the Holder for the purchase price of any Common Stock or as a stockholder of the Company, whether such liability is asserted by the Company or by creditors of the Company.

j) Successors and Assigns. Subject to applicable securities laws, this Warrant and the rights and obligations evidenced hereby shall inure to the benefit of and be binding upon the successors and permitted assigns of the Company and the successors and permitted assigns of Holder. The provisions of this Warrant are intended to be for the benefit of any Holder from time to time of this Warrant and shall be enforceable by the Holder or holder of Warrant Shares.

k) Amendment. This Warrant may be modified or amended or the provisions hereof waived with the written consent of the Company and the Holder.

l) Severability. Wherever possible, each provision of this Warrant shall be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Warrant shall be prohibited by or invalid under applicable law, such provision shall be ineffective to the extent of such prohibition or invalidity, without invalidating the remainder of such provisions or the remaining provisions of this Warrant.

m) Headings. The headings used in this Warrant are for the convenience of reference only and shall not, for any purpose, be deemed a part of this Warrant.

\*\*\*\*\*

*(Signature Page Follows)*

IN WITNESS WHEREOF, the Company has caused this Warrant to be executed by its officer thereunto duly authorized as of the date first above indicated.

**SPYRE THERAPEUTICS, INC.**

By: /s/ Scott Burrows  
Name: Scott Burrows  
Title: Chief Financial Officer

**NOTICE OF EXERCISE**

TO: Spyre Therapeutics, Inc. (the "Company")

(1) The undersigned hereby elects to purchase \_\_\_\_\_ Warrant Shares of the Company pursuant to the terms of the attached Warrant (only if exercised in full), and tenders herewith payment of the exercise price in full, together with all applicable transfer taxes, if any.

(2) Payment shall take the form of (check applicable box):

in lawful money of the United States; or

the cancellation of such number of Warrant Shares as is necessary, in accordance with the formula set forth in subsection 2(c), to exercise this Warrant with respect to the maximum number of Warrant Shares purchasable pursuant to the cashless exercise procedure set forth in subsection 2(c).

(3) Please issue said Warrant Shares in the name of the undersigned or in such other name as is specified below:

\_\_\_\_\_

By its delivery of this Notice of Exercise, the undersigned represents and warrants to the Company that in giving effect to the exercise evidenced hereby the Holders will not beneficially own in excess of the number of shares of Common Stock permitted to be owned under Section 2(e) of the Warrant to which this notice relates.

[SIGNATURE OF HOLDER]

Name of Investing Entity:

*Signature of Authorized Signatory of Investing Entity:*

Name of Authorized Signatory:

Title of Authorized Signatory:

Date:

(Signature must conform in all respects to name of Holder as specified on the face of the Warrant)

**ASSIGNMENT FORM**

*(To assign the foregoing Warrant, execute this form and supply required information. Do not use this form to purchase shares.)*

FOR VALUE RECEIVED, the foregoing Warrant and all rights evidenced thereby are hereby assigned to

Name:

\_\_\_\_\_  
(Please Print)

Address:

\_\_\_\_\_  
(Please Print)

Phone Number:

\_\_\_\_\_

Email Address:

\_\_\_\_\_

Dated: \_\_\_\_\_, \_\_\_\_\_

Holder's Signature:

Holder's Address:

**SPYRE THERAPEUTICS, INC.**  
**WARRANT TO PURCHASE COMMON STOCK**

Number of Warrant Shares: 848,184  
(subject to adjustment)

Warrant No. SYRE-002

Original Issue Date: December 31, 2024

THIS **WARRANT TO PURCHASE COMMON STOCK** (the "Warrant") certifies that, for value received, Parapyre Holding LLC or its assigns (the "Holder") is entitled, upon the terms and subject to the limitations on exercise and the conditions hereinafter set forth, at any time on or after the date hereof (the "Original Issue Date") and on or prior to 5:00 p.m. (New York City time) on December 31, 2034, (the "Termination Date") but not thereafter, to subscribe for and purchase from Spyre Therapeutics, Inc., a Delaware corporation (the "Company"), up to 848,184 shares (as subject to adjustment hereunder, the "Warrant Shares") of common stock, \$0.0001 par value per share, of the Company ("Common Stock"). The purchase price of one share of Common Stock under this Warrant shall be equal to the Exercise Price, as defined in Section 2(b).

Section 1. Definitions. Capitalized terms used and not otherwise defined herein shall have the meanings set forth in that certain Second Amended and Restated Antibody Discovery and Option Agreement (the "Paragon Agreement"), dated May 14, 2024, among the Company, Paragon Therapeutics, Inc. and Parapyre Holding LLC.

a) "Closing Sale Price" means, for any security as of any date, the last trade price for such security on the Principal Trading Market for such security, as reported by Bloomberg L.P., or, if such Principal Trading Market begins to operate on an extended hours basis and does not designate the last trade price, then the last trade price of such security prior to 4:00 P.M., New York City time, as reported by Bloomberg L.P., or if the security is not listed for trading on a national securities exchange or other trading market on the relevant date, the last quoted bid price for the security in the over-the-counter market on the relevant date as reported by OTC Markets Group Inc. (or a similar organization or agency succeeding to its functions of reporting prices). If the Closing Sale Price cannot be calculated for a security on a particular date on any of the foregoing bases, the Closing Sale Price of such security on such date shall be the fair market value as mutually determined by the Company and the Holder. If the Company and the Holder are unable to agree upon the fair market value of such security, then the board of directors of the Company shall use its good faith judgment to determine the fair market value. The board of directors' determination shall be binding upon all parties absent demonstrable error. All such determinations shall be appropriately adjusted for any stock dividend, stock split, stock combination or other similar transaction during the applicable calculation period.

b) "Commission" means the U.S. Securities and Exchange Commission.

c) "Person" means any natural person or legal entity.

d) "Principal Trading Market" means the national securities exchange or other trading market on which the Common Stock is primarily listed on and quoted for trading, which, as of the Original Issue Date was the Nasdaq Capital Market.

e) "Trading Day" means any weekday on which the Principal Trading Market is open for trading. If the Common Stock is not listed or admitted for trading, "Trading Day" means any day except any Saturday, any Sunday, any day which is a federal legal holiday in the United States or any day on which banking institutions in New York City are authorized or required by law or other governmental action to close.

f) "Transfer Agent" means Equity Trust Company, LLC, the Company's transfer agent and registrar for the Common Stock, and any successor appointed in such capacity.

Section 2. Exercise.

a) Exercise of Warrant. Exercise of the purchase rights represented by this Warrant may be made, in whole or in part, at any time or times on or after the Original Issue Date and on or before the Termination Date, including by means of a "cashless exercise" as described in Section 2(c) below, by

delivery to the Company of a duly executed facsimile copy or PDF copy submitted by e-mail (or e-mail attachment) of the Notice of Exercise in the form annexed hereto (the "Notice of Exercise"). Within the earlier of (i) two (2) Trading Days and (ii) the number of Trading Days comprising the Standard Settlement Period following the date of exercise (the "Exercise Date") as aforesaid, the Holder shall deliver the aggregate Exercise Price for the Warrant Shares specified in the applicable Notice of Exercise by wire transfer or cashier's check drawn on a United States bank unless the cashless exercise procedure specified in Section 2(c) below is specified in the applicable Notice of Exercise. No ink-original Notice of Exercise shall be required, nor shall any medallion guarantee (or other type of guarantee or notarization) of any Notice of Exercise be required. Notwithstanding anything herein to the contrary, the Holder shall not be required to physically surrender this Warrant to the Company until the Holder has purchased all of the Warrant Shares available hereunder and the Warrant has been exercised in full, in which case, the Holder shall surrender this Warrant to the Company for cancellation within three (3) Trading Days of the date on which the final Notice of Exercise is delivered to the Company. Partial exercises of this Warrant resulting in purchases of a portion of the total number of Warrant Shares available hereunder shall have the effect of lowering the outstanding number of Warrant Shares purchasable hereunder in an amount equal to the applicable number of Warrant Shares purchased. The Holder and the Company shall maintain records showing the number of Warrant Shares purchased and the date of such purchases. The Company shall deliver any objection to any Notice of Exercise within one (1) Trading Day of its receipt of such notice. **The Holder and any assignee, by acceptance of this Warrant, acknowledge and agree that, by reason of the provisions of this paragraph, following the purchase of a portion of the Warrant Shares hereunder, the number of Warrant Shares available for purchase hereunder at any given time may be less than the amount stated on the face hereof.** As used herein, "Standard Settlement Period" means the standard settlement period, expressed in a number of Trading Days, on the Principal Trading Market with respect to the Common Stock as in effect on the date of delivery of the Notice of Exercise to the Company.

b) Exercise Price. The exercise price per share of Common Stock under this Warrant shall be \$23.28, subject to adjustment hereunder (the "Exercise Price").

c) Cashless Exercise. This Warrant may be exercised, in whole or in part, by means of a "cashless exercise" in which the Holder shall be entitled to receive a number of Warrant Shares as determined as follows:

$$X = Y [(A-B)/A]$$

where:

"X" equals the number of Warrant Shares to be issued to the Holder;

"Y" equals the total number of Warrant Shares with respect to which this Warrant is then being exercised;

"A" equals the Closing Sale Price per share of Common Stock as of the Trading Day on the date immediately preceding the Exercise Date; and

"B" equals the Exercise Price per Warrant Share then in effect on the Exercise Date.

d) Mechanics of Exercise.

i. Delivery of Warrant Shares Upon Exercise. Within a reasonable time after Holder exercises this Warrant in the manner set forth in Section 2(a) or 2(c) above, the Company shall deliver to Holder a certificate (which certificate may be in the form of an electronic certificate or DTC entry, to the extent used by the Company at the time of such exercise) or evidence of book entry representing the Warrant Shares issued to such Holder upon such exercise. As used herein, "Standard Settlement Period" means

the standard settlement period, expressed in a number of Trading Days, on the Principal Trading Market with respect to the Common Stock as in effect on the date of delivery of the Notice of Exercise to the Company.

ii. Delivery of New Warrants Upon Exercise. If this Warrant shall have been exercised in part, the Company shall, at the request of a Holder and upon surrender of this Warrant certificate, at the time of delivery of the Warrant Shares, deliver to the Holder a new Warrant evidencing the rights of the Holder to purchase the unpurchased Warrant Shares called for by this Warrant, which new Warrant shall in all other respects be identical with this Warrant.

iii. [RESERVED.]

iv. No Fractional Shares or Scrip. No fractional shares or scrip representing fractional shares shall be issued upon the exercise of this Warrant. As to any fraction of a share which the Holder would otherwise be entitled to purchase upon such exercise, the Company shall, at its election, either pay a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the Exercise Price or round down to the next whole share.

v. Charges, Taxes and Expenses. Issuance of Warrant Shares shall be made without charge to the Holder for any issue or transfer tax or other incidental expense in respect of the issuance of such Warrant Shares, all of which taxes and expenses shall be paid by the Company, and such Warrant Shares shall be issued in the name of the Holder or in such name or names as may be directed by the Holder; *provided, however*, that, in the event that Warrant Shares are to be issued in a name other than the name of the Holder, this Warrant when surrendered for exercise shall be accompanied by the Assignment Form attached hereto duly executed by the Holder and the Company may require, as a condition thereto, the payment of a sum sufficient to reimburse it for any transfer tax incidental thereto.

vi. Closing of Books. The Company will not close its stockholder books or records in any manner which prevents the timely exercise of this Warrant, pursuant to the terms hereof.

e) Holder's Exercise Limitations. The Company shall not effect any exercise of this Warrant, and a Holder shall not have the right to exercise any portion of this Warrant, pursuant to Section 2 or otherwise, to the extent that after giving effect to such issuance after exercise as set forth on the applicable Notice of Exercise, the Holder (together with the Holder's Affiliates, and any other Persons acting as a group together with the Holder or any of the Holder's Affiliates (such Persons, "Attribution Parties")), would beneficially own in excess of the Beneficial Ownership Limitation (as defined below). For purposes of the foregoing sentence, the number of shares of Common Stock beneficially owned by the Holder and its Affiliates and Attribution Parties shall include the number of shares of Common Stock issuable upon exercise of this Warrant with respect to which such determination is being made, but shall exclude the number of shares of Common Stock which would be issuable upon (i) exercise of the remaining, nonexercised portion of this Warrant beneficially owned by the Holder or any of its Affiliates or Attribution Parties and (ii) exercise or conversion of the unexercised or nonconverted portion of any other securities of the Company subject to a limitation on conversion or exercise analogous to the limitation contained herein beneficially owned by the Holder or any of its Affiliates or Attribution Parties. Except as set forth in the preceding sentence, for purposes of this Section 2(e), beneficial ownership shall be calculated in accordance with Section 13(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") and the rules and regulations promulgated thereunder, it being acknowledged by the Holder that the Company is not representing to the Holder that such calculation is in compliance with Section 13(d) of the Exchange Act and the Holder is solely responsible for any schedules required to be filed in accordance therewith. To the extent that the limitation contained in this Section 2(e) applies, the determination of whether this Warrant is exercisable (in relation to other securities owned by the Holder together with any Affiliates and Attribution Parties) and of which portion of this Warrant is exercisable shall be in the sole discretion of the Holder, and the

Holder's submission of a Notice of Exercise to the Company shall be deemed to be the Holder's determination of whether this Warrant is exercisable (in relation to other securities owned by the Holder together with any Affiliates and Attribution Parties) and of which portion of this Warrant is exercisable, in each case subject to the Beneficial Ownership Limitation, and, absent manifest error, the Company shall have no obligation to verify or confirm the accuracy of such determination. In addition, a determination as to any group status as contemplated above shall be determined in accordance with Section 13(d) of the Exchange Act and the rules and regulations promulgated thereunder. For purposes of this Section 2(e), in determining the number of outstanding shares of Common Stock, a Holder may rely on the number of outstanding shares of Common Stock as reflected in (A) the Company's most recent periodic or annual report filed with the Commission, as the case may be, (B) a more recent public announcement by the Company or (C) a more recent written notice by the Company or the Transfer Agent setting forth the number of shares of Common Stock outstanding. Upon the written or oral request of a Holder, the Company shall within one Trading Day confirm orally and in writing to the Holder the number of shares of Common Stock then outstanding. In any case, the number of outstanding shares of Common Stock shall be determined after giving effect to the conversion or exercise of securities of the Company, including this Warrant, by the Holder or its Affiliates or Attribution Parties since the date as of which such number of outstanding shares of Common Stock was reported. As used herein, "Affiliate" shall mean any Person directly or indirectly controlled by, controlling or under common control with, a Holder, as such terms are used in and construed under Rule 405 under the Securities Act, but only for so long as such control shall continue. The "Beneficial Ownership Limitation" shall be 4.99% of the number of shares of the Common Stock outstanding immediately after giving effect to the issuance of shares of Common Stock issuable upon exercise of this Warrant. The provisions of this paragraph shall be construed and implemented in a manner otherwise than in strict conformity with the terms of this Section 2(e) to correct this paragraph (or any portion hereof) which may be defective or inconsistent with the intended Beneficial Ownership Limitation herein contained or to make changes or supplements necessary or desirable to properly give effect to such limitation. The limitations contained in this paragraph shall apply to a successor holder of this Warrant.

### Section 3. Certain Adjustments.

a) Stock Dividends and Splits. If the Company, at any time while this Warrant is outstanding: (i) pays a stock dividend or otherwise makes a distribution or distributions on shares of its Common Stock or any other equity or equity equivalent securities payable in shares of Common Stock (which, for avoidance of doubt, shall not include any shares of Common Stock issued by the Company upon exercise of this Warrant), (ii) subdivides outstanding shares of Common Stock into a larger number of shares, (iii) combines (including by way of reverse stock split) outstanding shares of Common Stock into a smaller number of shares, or (iv) issues by reclassification of shares of the Common Stock any shares of capital stock of the Company, then in each case the Warrant Shares shall be multiplied by a fraction of which the numerator shall be the number of shares of Common Stock (excluding treasury shares, if any) outstanding immediately after such event and of which the denominator shall be the number of shares of Common Stock outstanding immediately before such event, and the Exercise Price shall be proportionately adjusted such that the aggregate Exercise Price of this Warrant shall remain unchanged. Any adjustment made pursuant to this Section 3(a) shall become effective immediately after the record date for the determination of stockholders entitled to receive such dividend or distribution and shall become effective immediately after the effective date in the case of a subdivision, combination or re-classification.

b) Fundamental Transaction. If, at any time while this Warrant is outstanding, (i) the Company, directly or indirectly, in one or more related transactions effects any merger or consolidation of the Company with or into another Person, (ii) the Company (and all of its subsidiaries, taken as a whole), directly or indirectly, effects any sale, lease, license, assignment, transfer, conveyance or other disposition of all or substantially all of its assets in one or a series of related transactions, (iii) any, direct or indirect, purchase offer, tender offer or exchange offer (whether by the Company or another Person) is completed pursuant to which holders of Common Stock are permitted to sell, tender or exchange their shares for other securities, cash or property and has been accepted by the holders of 50% or more of the outstanding Common Stock or 50% or more of the outstanding voting power of the common equity of the Company, (iv) the Company, directly or indirectly, in one or more related transactions effects any reclassification,

reorganization or recapitalization of the Common Stock or any compulsory share exchange pursuant to which the Common Stock is effectively converted into or exchanged for other securities, cash or property, or (v) the Company, directly or indirectly, in one or more related transactions consummates a stock or share purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off, merger or scheme of arrangement) with another Person or group of Persons whereby such other Person or group acquires 50% or more of the outstanding shares of Common Stock or 50% or more of the outstanding voting power of the common equity of the Company (each a "Fundamental Transaction"), then, to the extent the fair market value of one Warrant Share as determined in accordance with Section 1(a) above would be greater than the Exercise Price in effect on such date immediately prior to the occurrence of such Fundamental Transaction, and Holder has not exercised this Warrant pursuant to Section 2 above as to all Warrant Shares, then this Warrant shall automatically be deemed to be cashless exercised pursuant to Section 2(c) above as to all Warrant Shares effective immediately prior to and contingent upon the consummation of a Fundamental Transaction. For the avoidance of doubt, if, immediately prior to the Fundamental Transaction, the fair market value of one Warrant Share as determined in accordance with Section 1(a) above is not greater than the Exercise Price in effect on the Trading Day immediately prior to the closing of such Fundamental Transaction, then this Warrant shall terminate without exercise or conversion immediately prior to, and subject to, the closing of such Fundamental Transaction.

c) Calculations. All calculations under this Section 3 shall be made to the nearest one-hundredth of one cent or the nearest share, as the case may be. For purposes of this Section 3, the number of shares of Common Stock deemed to be issued and outstanding as of a given date shall be the sum of the number of shares of Common Stock (excluding treasury shares, if any) issued and outstanding.

d) Voluntary Adjustment By Company. Subject to the rules and regulations of the Principal Trading Market, the Company may at any time during the term of this Warrant, subject to the prior written consent of the Holder, reduce the then current Exercise Price to any amount and for any period of time deemed appropriate by the board of directors of the Company.

e) Notice of Adjustments. Upon the occurrence of each adjustment pursuant to this Section 3, the Company at its expense will, at the written request of the Holder, promptly compute such adjustment, in good faith, in accordance with the terms of this Warrant and prepare a certificate setting forth such adjustment, including a statement of the adjusted Exercise Price and adjusted number or type of Warrant Shares or other securities issuable upon exercise of this Warrant (as applicable), describing the transactions giving rise to such adjustments and showing in detail the facts upon which such adjustment is based. Upon written request, the Company will promptly deliver a copy of each such certificate to the Holder and to the Transfer Agent.

f) Notice of Corporate Events. If, while this Warrant is outstanding, the Company (i) declares a dividend or any other distribution of cash, securities or other property in respect of its Common Stock, including, without limitation, any granting of rights or warrants to subscribe for or purchase any capital stock of the Company or any subsidiary, (ii) authorizes or approves, enters into any agreement contemplating or solicits stockholder approval for any Fundamental Transaction or (iii) authorizes the voluntary dissolution, liquidation or winding up of the affairs of the Company, then, except if such notice and the contents thereof shall be deemed to constitute material non-public information, the Company shall deliver to the Holder a notice of such transaction at least ten (10) days prior to the applicable record or effective date on which a Person would need to hold Common Stock in order to participate in or vote with respect to such transaction; provided, however, that the failure to deliver such notice or any defect therein shall not affect the validity of the corporate action required to be described in such notice. In addition, if while this Warrant is outstanding, the Company authorizes or approves, enters into any agreement contemplating or solicits stockholder approval for any Fundamental Transaction contemplated by Section 3(b), other than a Fundamental Transaction under clause (iii) of Section 3(b), the Company shall deliver to the Holder a notice of such Fundamental Transaction at least ten (10) days prior to the date such Fundamental Transaction is consummated. Holder agrees to maintain any information disclosed pursuant to this Section 3(f) in confidence until such information is publicly available, and shall comply with

applicable law with respect to trading in the Company's securities following receipt of any such information.

Section 4. Transfer of Warrant.

a) Transferability. This Warrant and all rights hereunder (including, without limitation, any registration rights) are transferable only to employees of Paragon Therapeutics, Inc. that are limited partners of Parapyre Holding LLC at the time of transfer, in whole or in part, upon surrender of this Warrant at the principal office of the Company or its designated agent, together with a written assignment of this Warrant substantially in the form attached hereto duly executed by the Holder or its agent or attorney and funds sufficient to pay any transfer taxes payable upon the making of such transfer. Upon such surrender and, if required, such payment, the Company shall execute and deliver a new Warrant or Warrants in the name of the assignee or assignees, as applicable, and in the denomination or denominations specified in such instrument of assignment, and shall issue to the assignor a new Warrant evidencing the portion of this Warrant not so assigned, if any, and this Warrant shall promptly be cancelled. Notwithstanding anything herein to the contrary, the Holder shall not be required to physically surrender this Warrant to the Company unless the Holder has assigned this Warrant in full, in which case, the Holder shall surrender this Warrant to the Company within three (3) Trading Days of the date on which the Holder delivers an assignment form to the Company assigning this Warrant in full. The Warrant, if properly assigned in accordance herewith, may be exercised by a new holder for the purchase of Warrant Shares without having a new Warrant issued.

b) New Warrants. This Warrant may be divided or combined with other Warrants upon presentation hereof at the aforesaid office of the Company, together with a written notice specifying the names and denominations in which new Warrants are to be issued, signed by the Holder or its agent or attorney. Subject to compliance with Section 4(a), as to any transfer which may be involved in such division or combination, the Company shall execute and deliver a new Warrant or Warrants in exchange for the Warrant or Warrants to be divided or combined in accordance with such notice. All Warrants issued on transfers or exchanges shall be dated the Original Issue Date and shall be identical with this Warrant except as to the number of Warrant Shares issuable pursuant thereto and the Exercise Price.

c) Warrant Register. The Company shall register this Warrant, upon records to be maintained by the Company for that purpose (the "Warrant Register"), in the name of the record Holder hereof from time to time. The Company shall deem and treat the registered Holder of this Warrant as the absolute owner hereof for the purpose of any exercise hereof or any distribution to the Holder, and for all other purposes, absent actual notice to the contrary.

Section 5. Miscellaneous.

a) No Rights as Stockholder Until Exercise; No Settlement in Cash. This Warrant does not entitle the Holder to any voting rights, dividends or other rights as a stockholder of the Company prior to the exercise hereof as set forth in Section 2(d)(i), except as expressly set forth in Section 3.

b) Loss, Theft, Destruction or Mutilation of Warrant. The Company covenants that upon receipt by the Company of evidence reasonably satisfactory to it of the loss, theft, destruction or mutilation of this Warrant or any stock certificate relating to the Warrant Shares, and in case of loss, theft or destruction, of indemnity or security reasonably satisfactory to it (which, in the case of the Warrant, shall not include the posting of any bond), and upon surrender and cancellation of such Warrant or stock certificate, if mutilated, the Company will make and deliver a new Warrant or stock certificate of like tenor and dated as of such cancellation, in lieu of such Warrant or stock certificate.

c) Saturdays, Sundays, Holidays, etc. If the last or appointed day for the taking of any action or the expiration of any right required or granted herein shall not be a Trading Day, then such action may be taken or such right may be exercised on the next succeeding Trading Day.

d) Authorized Shares.

The Company covenants that, during the period the Warrant is outstanding, it will reserve from its authorized and unissued Common Stock a sufficient number of shares to

provide for the issuance of the Warrant Shares upon the exercise of any purchase rights under this Warrant. The Company further covenants that its issuance of this Warrant shall constitute full authority to its officers who are charged with the duty of issuing the necessary Warrant Shares upon the exercise of the purchase rights under this Warrant. The Company will take all such reasonable action as may be necessary to assure that such Warrant Shares may be issued as provided herein without violation of any applicable law or regulation, or of any requirements of the Principal Trading Market. The Company covenants that all Warrant Shares which may be issued upon the exercise of the purchase rights represented by this Warrant will, upon exercise of the purchase rights represented by this Warrant and payment for such Warrant Shares in accordance herewith, be duly authorized, validly issued, fully paid and nonassessable and free from all taxes, liens and charges created by the Company in respect of the issue thereof (other than taxes in respect of any transfer occurring contemporaneously with such issue).

Except and to the extent as waived or consented to by the Holder, the Company shall not by any action, including, without limitation, amending its certificate of incorporation or through any reorganization, transfer of assets, consolidation, merger, dissolution, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms of this Warrant, but will at all times in good faith assist in the carrying out of all such terms and in the taking of all such actions as may be necessary or appropriate to protect the rights of Holder as set forth in this Warrant against impairment. Without limiting the generality of the foregoing, the Company will (i) not increase the par value of any Warrant Shares above the amount payable therefor upon such exercise immediately prior to such increase in par value, (ii) take all such action as may be necessary or appropriate in order that the Company may validly and legally issue fully paid and nonassessable Warrant Shares upon the exercise of this Warrant and (iii) obtain all such authorizations, exemptions or consents from any public regulatory body having jurisdiction thereof, as may be, necessary to enable the Company to perform its obligations under this Warrant.

Before taking any action which would result in an adjustment in the number of Warrant Shares for which this Warrant is exercisable or in the Exercise Price, the Company shall obtain all such authorizations or exemptions thereof, or consents thereto, as may be necessary from any public regulatory body or bodies having jurisdiction thereof.

The Company represents, warrants and covenants that, as of the date hereof, (i) the issued and outstanding Common Stock of the Company is registered pursuant to Section 12(b) of the Exchange Act, and listed for trading on the Nasdaq Capital Market; (ii) there is no suit, action, proceeding or investigation pending or, to the knowledge of the Company, threatened against the Company by the Principal Trading Market, or the Commission with respect to any intention by such entity to deregister the Common Stock or prohibit or terminate the listing of the Common Stock on the Principal Trading Market; and (iii) the Company has taken no action that is designed to terminate the registration of Common Stock under the Exchange Act.

e) Jurisdiction. All questions concerning the construction, validity, enforcement and interpretation of this Warrant shall be determined in accordance with the provisions of the Paragon Agreement.

f) Restrictions. The Holder acknowledges that the Warrant Shares acquired upon the exercise of this Warrant, if not registered, will have restrictions upon resale imposed by state and federal securities laws.

g) Nonwaiver. No course of dealing or any delay or failure to exercise any right hereunder on the part of Holder shall operate as a waiver of such right or otherwise prejudice the Holder's rights, powers or remedies.

h) Notices. Any and all notices or other communications or deliveries hereunder (including, without limitation, any Notice of Exercise) shall be in writing and shall be deemed given and effective on the earliest of (i) the date of transmission, if such notice or communication is delivered via facsimile or confirmed e-mail prior to 5:30 P.M., New York City time, on a Trading Day, (ii) the next Trading Day after

the date of transmission, if such notice or communication is delivered via confirmed e-mail on a day that is not a Trading Day or later than 5:30 P.M., New York City time, on any Trading Day, (iii) the Trading Day following the date of mailing, if sent by nationally recognized overnight courier service specifying next business day delivery, or (iv) upon actual receipt by the Person to whom such notice is required to be given, if by hand delivery. The addresses and e-mail addresses for such communications shall be:

If to the Company:

Spyre Therapeutics, Inc.  
221 Crescent Street  
Building 23, Suite 105  
Waltham, MA 02543  
Attention: Chief Financial Officer  
Email:

With a copy (for informational purposes only) to:

Gibson, Dunn & Crutcher LLP  
One Embarcadero Center, Suite 2600  
San Francisco, CA 94111  
E-mail: rmurr@gibsondunn.com; bberns@gibsondunn.com  
Attention: Ryan A. Murr; Branden C. Berns

If to the Holder, to its address or e-mail address set forth herein or on the books and records of the Company.

Or, in each of the above instances, to such other address or e-mail address as the recipient party has specified by written notice given to each other party at least five (5) days prior to the effectiveness of such change.

i) Limitation of Liability. No provision hereof, in the absence of any affirmative action by the Holder to exercise this Warrant to purchase Warrant Shares, and no enumeration herein of the rights or privileges of the Holder, shall give rise to any liability of the Holder for the purchase price of any Common Stock or as a stockholder of the Company, whether such liability is asserted by the Company or by creditors of the Company.

j) Successors and Assigns. Subject to applicable securities laws, this Warrant and the rights and obligations evidenced hereby shall inure to the benefit of and be binding upon the successors and permitted assigns of the Company and the successors and permitted assigns of Holder. The provisions of this Warrant are intended to be for the benefit of any Holder from time to time of this Warrant and shall be enforceable by the Holder or holder of Warrant Shares.

k) Amendment. This Warrant may be modified or amended or the provisions hereof waived with the written consent of the Company and the Holder.

l) Severability. Wherever possible, each provision of this Warrant shall be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Warrant shall be prohibited by or invalid under applicable law, such provision shall be ineffective to the extent of such prohibition or invalidity, without invalidating the remainder of such provisions or the remaining provisions of this Warrant.

m) Headings. The headings used in this Warrant are for the convenience of reference only and shall not, for any purpose, be deemed a part of this Warrant.

\*\*\*\*\*

*(Signature Page Follows)*

IN WITNESS WHEREOF, the Company has caused this Warrant to be executed by its officer thereunto duly authorized as of the date first above indicated.

**SPYRE THERAPEUTICS, INC.**

By: /s/ Scott Burrows  
Name: Scott Burrows  
Title: Chief Financial Officer

**NOTICE OF EXERCISE**

TO: Spyre Therapeutics, Inc. (the "Company")

(1) The undersigned hereby elects to purchase \_\_\_\_\_ Warrant Shares of the Company pursuant to the terms of the attached Warrant (only if exercised in full), and tenders herewith payment of the exercise price in full, together with all applicable transfer taxes, if any.

(2) Payment shall take the form of (check applicable box):

in lawful money of the United States; or

the cancellation of such number of Warrant Shares as is necessary, in accordance with the formula set forth in subsection 2(c), to exercise this Warrant with respect to the maximum number of Warrant Shares purchasable pursuant to the cashless exercise procedure set forth in subsection 2(c).

(3) Please issue said Warrant Shares in the name of the undersigned or in such other name as is specified below:

\_\_\_\_\_

By its delivery of this Notice of Exercise, the undersigned represents and warrants to the Company that in giving effect to the exercise evidenced hereby the Holders will not beneficially own in excess of the number of shares of Common Stock permitted to be owned under Section 2(e) of the Warrant to which this notice relates.

[SIGNATURE OF HOLDER]

Name of Investing Entity:

*Signature of Authorized Signatory of Investing Entity:*

Name of Authorized Signatory:

Title of Authorized Signatory:

Date:

(Signature must conform in all respects to name of Holder as specified on the face of the Warrant)

**ASSIGNMENT FORM**

*(To assign the foregoing Warrant, execute this form and supply required information. Do not use this form to purchase shares.)*

FOR VALUE RECEIVED, the foregoing Warrant and all rights evidenced thereby are hereby assigned to

Name:

\_\_\_\_\_  
(Please Print)

Address:

\_\_\_\_\_  
(Please Print)

Phone Number:

\_\_\_\_\_

Email Address:

\_\_\_\_\_

Dated: \_\_\_\_\_, \_\_\_\_\_

Holder's Signature:

Holder's Address:

## AEGLEA BIOTHERAPEUTICS, INC.

## 2018 EQUITY INDUCEMENT PLAN

1. **PURPOSE.** The purpose of this Plan is to provide incentives to attract eligible persons whose potential contributions are important to the success of the Company, and any Parents, Subsidiaries and Affiliates that exist now or in the future, by offering them an opportunity to participate in the Company's future performance through the grant of Awards. Each Award granted under the Plan is intended to qualify as an employment inducement award pursuant to Nasdaq Stock Market Rule 5635(c)(4), and shall be interpreted and administered accordingly. Capitalized terms not defined elsewhere in the text are defined in Section 21.

2. **SHARES SUBJECT TO THE PLAN.**

2.1. **Number of Shares Available.** Subject to Sections 2.4 and 15 and any other applicable provisions hereof, the total number of Shares reserved and available for grant and issuance pursuant to this Plan as of the date of adoption of the Plan by the Board is 1,100,000.

2.2. **Lapsed, Returned Awards.** Shares subject to Awards, and Shares issued under the Plan under any Award, will again be available for grant and issuance in connection with subsequent Awards under this Plan to the extent such Shares: (a) are subject to issuance upon exercise of an Option granted under this Plan but which cease to be subject to the Option for any reason other than exercise of the Option; (b) are subject to Awards granted under this Plan that are forfeited; or (c) are subject to Awards granted under this Plan that otherwise terminate without such Shares being issued. To the extent an Award under the Plan is paid out in cash or other property rather than Shares, such cash payment will not result in reducing the number of Shares available for issuance under the Plan. Shares used to pay the exercise price of an Award or withheld to satisfy the tax withholding obligations related to an Award will become available for future grant or sale under the Plan.

2.3. **Minimum Share Reserve.** At all times the Company shall reserve and keep available a sufficient number of Shares as shall be required to satisfy the requirements of all outstanding Awards granted under this Plan.

2.4. **Adjustment of Shares.** If the number of outstanding shares of Common Stock of the Company is changed by a stock dividend, recapitalization, stock split, reverse stock split, subdivision, combination, reclassification or similar change in the capital structure of the Company, without consideration, then (a) the number of Shares reserved for issuance and future grant under the Plan set forth in Section 2.1, (b) the Exercise Prices of and number of Shares subject to outstanding Options, and (c) the number of Shares subject to other outstanding Awards shall be proportionately adjusted, subject to any required action by the Board or the stockholders of the Company and in compliance with applicable securities laws; provided that fractions of a Share will not be issued.

3. **ELIGIBILITY.** Awards may be granted only to a person who, at the time of grant (a) has not previously been an Employee or Director, or (b) is commencing employment following a bona fide period of non-employment by the Company or any Subsidiary; provided that in each case, the grant of the Award is made as a material inducement to his or her commencement as an employee of the Company or a Subsidiary.

#### 4. ADMINISTRATION.

**4.1. Committee Composition; Authority.** This Plan will be administered by the Committee or by the Board acting as the Committee; provided that any action taken by the Board in connection with the administration of the Plan shall not be deemed approved by the Board unless such actions are approved by a majority of the Non-Employee Directors. Subject to the general purposes, terms and conditions of this Plan, and to the direction of the Board, the Committee will have full power to implement and carry out this Plan. The Committee will have the authority to:

(a) construe and interpret this Plan, any Award Agreement and any other agreement or document executed pursuant to this Plan;

(b) prescribe, amend and rescind rules and regulations relating to this Plan or any Award;

(c) select persons to receive Awards;

(d) determine the form and terms and conditions, not inconsistent with the terms of the Plan, of any Award granted hereunder. Such terms and conditions include, but are not limited to, the exercise price, the time or times when Awards may vest and be exercised (which may be based on performance criteria) or settled, any vesting acceleration or waiver of forfeiture restrictions, the method to satisfy tax withholding obligations or any other tax liability legally due and any restriction or limitation regarding any Award or the Shares relating thereto, based in each case on such factors as the Committee will determine;

(e) determine the number of Shares or other consideration subject to Awards;

(f) determine the Fair Market Value in good faith and interpret the applicable provisions of this Plan and the definition of Fair Market Value in connection with circumstances that impact the Fair Market Value, if necessary;

(g) determine whether Awards will be granted singly, in combination with, in tandem with, or as alternatives to, other Awards under this Plan or any other incentive or compensation plan of the Company or any Parent, Subsidiary or Affiliate;

(h) grant waivers of Plan or Award conditions;

(i) determine the vesting, exercisability and payment of Awards;

(j) correct any defect, supply any omission or reconcile any inconsistency in this Plan, any Award or any Award Agreement;

(k) determine whether an Award has been earned;

(l) reduce or waive any criteria with respect to Performance Factors;

(m) adjust Performance Factors to take into account changes in law and accounting or tax rules as the Committee deems necessary or appropriate to reflect the impact of extraordinary or unusual items, events or circumstances to avoid windfalls or hardships;

(n) adopt rules and/or procedures (including the adoption of any subplan under this Plan) relating to the operation and administration of the Plan to accommodate requirements of local law and procedures outside of the United States;

(o) make all other determinations necessary or advisable for the administration of this Plan; and

(p) to exercise negative discretion on Performance Awards, reducing or eliminating the amount to be paid to Participants.

**4.2. Committee Interpretation and Discretion.** Any determination made by the Committee with respect to any Award shall be made in its sole discretion at the time of grant of the Award or, unless in contravention of any express term of the Plan or Award, at any later time, and such determination shall be final and binding on the Company and all persons having an interest in any Award under the Plan. Any dispute regarding the interpretation of the Plan or any Award Agreement shall be submitted by the Participant or Company to the Committee for review. The resolution of such a dispute by the Committee shall be final and binding on the Company and the Participant. The Committee may delegate to one or more executive officers the authority to review and resolve disputes with respect to Awards held by Participants who are not Insiders, and such resolution shall be final and binding on the Company and the Participant.

**4.3. Section 16 of the Exchange Act.** Awards granted to Participants who are subject to Section 16 of the Exchange Act must be approved by two or more “non-employee directors” (as defined in the regulations promulgated under Section 16 of the Exchange Act).

**4.4. Documentation.** The Award Agreement for a given Award, the Plan and any other documents may be delivered to, and accepted by, a Participant or any other person in any manner (including electronic distribution or posting) that meets applicable legal requirements.

**4.5. Foreign Award Recipients.** Notwithstanding any provision of the Plan to the contrary, in order to comply with the laws in other countries in which the Company and its Subsidiaries and Affiliates operate or have Employees eligible for Awards, the Committee, in its sole discretion, shall have the power and authority to: (a) determine which Subsidiaries and Affiliates shall be covered by the Plan; (b) determine which Employees outside the United States are eligible to participate in the Plan; (c) modify the terms and conditions of any Award granted to individuals outside the United States to comply with applicable foreign laws; (d) establish subplans and modify exercise procedures and other terms and procedures, to the extent the Committee determines such actions to be necessary or advisable (and such subplans and/or modifications shall be attached to this Plan as appendices); provided, however, that no such subplans and/or modifications shall increase the share limitations contained in the Plan; and (e) take any action, before or after an Award is made, that the Committee determines to be necessary or advisable to obtain approval or comply with any local governmental regulatory exemptions or approvals. Notwithstanding the foregoing, the Committee may not take any actions hereunder, and no Awards shall be granted, that would violate the Exchange Act or any other applicable United States securities law, the Code, or any other applicable United States governing statute or law.

**5. OPTIONS.** An Option is the right but not the obligation to purchase a Share, subject to certain conditions, if applicable. The Committee may grant Options to eligible Employees and will determine the

number of Shares subject to the Option, the Exercise Price of the Option, the period during which the Option may vest and be exercised, and all other terms and conditions of the Option, subject to the following terms of this section.

**5.1. Option Grant.** Each Option granted under this Plan will be a nonqualified stock option. An Option may be, but need not be, awarded upon satisfaction of such Performance Factors during any Performance Period as are set out in advance in the Participant's individual Award Agreement. If the Option is being earned upon the satisfaction of Performance Factors, then the Committee will: (a) determine the nature, length and starting date of any Performance Period for each Option; and (b) select from among the Performance Factors to be used to measure the performance, if any. Performance Periods may overlap and Participants may participate simultaneously with respect to Options that are subject to different performance goals and other criteria.

**5.2. Date of Grant.** The date of grant of an Option will be the date on which the Committee makes the determination to grant such Option, or a specified future date. The Award Agreement will be delivered to the Participant within a reasonable time after the granting of the Option.

**5.3. Exercise Period.** Options may be vested and exercisable within the times or upon the conditions as set forth in the Award Agreement governing such Option; provided, however, that no Option will be exercisable after the expiration of ten (10) years from the date the Option is granted. The Committee also may provide for Options to become exercisable at one time or from time to time, periodically or otherwise, in such number of Shares or percentage of Shares as the Committee determines.

**5.4. Exercise Price.** The Exercise Price of an Option will be determined by the Committee when the Option is granted; provided that the Exercise Price of an Option will be not less than one hundred percent (100%) of the Fair Market Value of the Shares on the date of grant. Payment for the Shares purchased may be made in accordance with Section 7 and the Award Agreement and in accordance with any procedures established by the Company.

**5.5. Method of Exercise.** Any Option granted hereunder will be vested and exercisable according to the terms of the Plan and at such times and under such conditions as determined by the Committee and set forth in the Award Agreement. An Option may not be exercised for a fraction of a Share. An Option will be deemed exercised when the Company receives: (a) notice of exercise (in such form as the Committee may specify from time to time) from the person entitled to exercise the Option, and (b) full payment for the Shares with respect to which the Option is exercised (together with applicable withholding taxes). Full payment may consist of any consideration and method of payment authorized by the Committee and permitted by the Award Agreement and the Plan. Shares issued upon exercise of an Option will be issued in the name of the Participant. Until the Shares are issued (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company), no right to vote or receive dividends or any other rights as a stockholder will exist with respect to the Shares, notwithstanding the exercise of the Option. The Company will issue (or cause to be issued) such Shares promptly after the Option is exercised. No adjustment will be made for a dividend or other right for which the record date is prior to the date the Shares are issued, except as provided in Section 2.4 of the Plan. Exercising an Option in any manner will decrease the number of Shares thereafter available, both for purposes of the Plan and for sale under the Option, by the number of Shares as to which the Option is exercised.

**5.6. Termination of Service.** If the Participant's Service terminates for any reason except for Cause or the Participant's death or Disability, then the Participant may exercise such Participant's Options only to the extent that such Options would have been exercisable by the Participant on the date Participant's Service terminates no later than three (3) months after the date Participant's Service terminates (or such shorter or longer time period as may be determined by the Committee), but in any event no later than the expiration date of the Options.

(a) **Death.** If the Participant's Service terminates because of the Participant's death (or the Participant dies within three (3) months after Participant's Service terminates other than for Cause or because of the Participant's Disability), then the Participant's Options may be exercised only to the extent that such Options would have been exercisable by the Participant on the date Participant's Service terminates and must be exercised by the Participant's legal representative, or authorized assignee, no later than twelve (12) months after the date Participant's Service terminates (or such shorter time period not less than six (6) months or longer time period-as may be determined by the Committee), but in any event no later than the expiration date of the Options.

(b) **Disability.** If the Participant's Service terminates because of the Participant's Disability, then the Participant's Options may be exercised only to the extent that such Options would have been exercisable by the Participant on the date Participant's Service terminates and must be exercised by the Participant (or the Participant's legal representative or authorized assignee) no later than twelve (12) months after the date Participant's Service terminates, but in any event no later than the expiration date of the Options.

(c) **Cause.** If the Participant is terminated for Cause, then Participant's Options shall expire on such Participant's date of termination of Service, or at such later time and on such conditions as are determined by the Committee, but in any no event later than the expiration date of the Options. Unless otherwise provided in the Award Agreement, Cause shall have the meaning set forth in the Plan.

**5.7. Limitations on Exercise.** The Committee may specify a minimum number of Shares that may be purchased on any exercise of an Option, provided that such minimum number will not prevent any Participant from exercising the Option for the full number of Shares for which it is then exercisable.

**5.8. Modification, Extension or Renewal.** The Committee may modify, extend or renew outstanding Options and authorize the grant of new Options in substitution therefor, provided that any such action may not, without the written consent of a Participant, impair any of such Participant's rights under any Option previously granted.

**6. RESTRICTED STOCK UNITS.** A Restricted Stock Unit ("**RSU**") is an award to an eligible Employee covering a number of Shares that may be settled in cash, or by issuance of those Shares. All RSUs shall be made pursuant to an Award Agreement.

**6.1. Terms of RSUs.** The Committee will determine the terms of an RSU including, without limitation: (a) the number of Shares subject to the RSU; (b) the time or times during which the RSU may be settled; (c) the consideration to be distributed on settlement; and (d) the effect of the Participant's termination of Service on each RSU; provided that no RSU shall have a term longer than ten (10) years. An RSU may be awarded upon satisfaction of such performance goals based on Performance Factors during any Performance Period as are set out in advance in the Participant's Award Agreement. If the

RSU is being earned upon satisfaction of Performance Factors, then the Committee will: (x) determine the nature, length and starting date of any Performance Period for the RSU; (y) select from among the Performance Factors to be used to measure the performance, if any; and (z) determine the number of Shares deemed subject to the RSU. Performance Periods may overlap and participants may participate simultaneously with respect to RSUs that are subject to different Performance Periods and different performance goals and other criteria.

**6.2. Form and Timing of Settlement.** Payment of earned RSUs shall be made as soon as practicable after the date(s) determined by the Committee and set forth in the Award Agreement. The Committee, in its sole discretion, may settle earned RSUs in cash, Shares, or a combination of both. The Committee may also permit a Participant to defer payment under a RSU to a date or dates after the RSU is earned provided that the terms of the RSU and any deferral satisfy the requirements of Section 409A of the Code.

**6.3. Termination of Service.** Except as may be set forth in the Participant's Award Agreement, vesting ceases on such date Participant's Service terminates (unless determined otherwise by the Committee).

**7. PAYMENT FOR SHARE PURCHASES.** Payment from a Participant for Shares purchased pursuant to this Plan may be made in cash or by check or, where approved for the Participant by the Committee and where permitted by law (and to the extent not otherwise set forth in the applicable Award Agreement):

(a) by cancellation of indebtedness of the Company to the Participant;

(b) by surrender of shares of the Company's common stock by the Participant that have a Fair Market Value on the date of surrender equal to the aggregate exercise price of the Shares as to which said Award will be exercised or settled;

(c) by waiver of compensation due or accrued to the Participant for services rendered or to be rendered to the Company or a Parent or Subsidiary of the Company;

(d) by consideration received by the Company pursuant to a broker-assisted or other form of cashless exercise program implemented by the Company in connection with the Plan;

(e) by any combination of the foregoing; or

(f) by any other method of payment as is permitted by applicable law.

**8. WITHHOLDING TAXES.**

**8.1. Withholding Generally.** Whenever Shares are to be issued in satisfaction of Awards granted under this Plan or a tax event occurs, the Company may require the Participant to remit to the Company, or to the Parent, Subsidiary or applicable Affiliate employing the Participant, an amount sufficient to satisfy applicable U.S. federal, state, local and international withholding tax requirements or any other tax or social insurance liability legally due from the Participant prior to the delivery of Shares pursuant to exercise or settlement of any Award. Whenever payments in satisfaction of Awards granted under this Plan are to be made in cash, such payment will be net of an amount sufficient to satisfy applicable U.S.

federal, state, local and international withholding tax or social insurance requirements or any other tax liability legally due from the Participant. The Fair Market Value of the Shares will be determined as of the date that the taxes are required to be withheld and such Shares shall be valued based on the value of the actual trade or, if there is none, the Fair Market Value of the Shares as of the previous trading day.

**8.2. Stock Withholding.** The Committee, or its delegate(s), as permitted by applicable law, in its sole discretion and pursuant to such procedures as it may specify from time to time and to limitations of local law, may require or permit a Participant to satisfy such tax withholding obligation or any other tax liability legally due from the Participant, in whole or in part by (without limitation) (a) paying cash, (b) electing to have the Company withhold otherwise deliverable cash or Shares having a Fair Market Value equal to the minimum statutory amount required to be withheld, (c) delivering to the Company already-owned shares of the Company's common stock having a Fair Market Value up to the maximum amount permitted to be withheld or (d) withholding from proceeds of the sale of otherwise deliverable Shares acquired pursuant to an Award either through a voluntary sale or through a mandatory sale arranged by the Company for up to the maximum statutory amount permitted to be withheld.

## **9. TRANSFERABILITY.**

**9.1. Transfer Generally.** Unless determined otherwise by the Committee or pursuant to Section 9.2, an Award may not be sold, pledged, assigned, hypothecated, transferred, or disposed of in any manner other than by will or by the laws of descent or distribution. If the Committee makes an Award transferable, including, without limitation, by instrument to an inter vivos or testamentary trust in which the Awards are to be passed to beneficiaries upon the death of the trustor (settlor) or by gift or by domestic relations order to a Permitted Transferee, such Award will contain such additional terms and conditions as the Committee deems appropriate. All Awards shall be exercisable: (a) during the Participant's lifetime only by (i) the Participant, or (ii) the Participant's guardian or legal representative; (b) after the Participant's death, by the legal representative of the Participant's heirs or legatees; and (c) by a Permitted Transferee.

**9.2. Award Transfer Program.** Notwithstanding any contrary provision of the Plan, the Committee shall have all discretion and authority to determine and implement the terms and conditions of any Award Transfer Program instituted pursuant to this Section 9.2 and shall have the authority to amend the terms of any Award participating, or otherwise eligible to participate in, the Award Transfer Program, including (but not limited to) the authority to (a) amend (including to extend) the expiration date, post-termination exercise period and/or forfeiture conditions of any such Award, (b) amend or remove any provisions of the Award relating to the Award holder's continued Service to the Company or its Parent, Subsidiary, or Affiliate, (c) amend the permissible payment methods with respect to the exercise or purchase of any such Award, (d) amend the adjustments to be implemented in the event of changes in the capitalization and other similar events with respect to such Award, and (e) make such other changes to the terms of such Award as the Committee deems necessary or appropriate in its sole discretion. Notwithstanding anything to the contrary in the Plan, in no event will the Committee have the right to determine and implement the terms and conditions of any Award Transfer Program without stockholder approval.

## **10. PRIVILEGES OF STOCK OWNERSHIP; RESTRICTIONS ON SHARES.**

**10.1. Voting and Dividends.** No Participant will have any of the rights of a stockholder with respect to any Shares until the Shares are issued to the Participant, except for any dividend equivalent

rights permitted by an applicable Award Agreement (“*Dividend Equivalent Rights*”). After Shares are issued to the Participant, the Participant will be a stockholder and have all the rights of a stockholder with respect to such Shares, including the right to vote and receive all dividends or other distributions made or paid with respect to such Shares; provided, that if such Shares are Unvested Shares, then any new, additional or different securities the Participant may become entitled to receive with respect to such Shares by virtue of a stock dividend, stock split or any other change in the corporate or capital structure of the Company will be subject to the same restrictions as the Unvested Shares; provided, further, that the Participant will have no right to retain such stock dividends or stock distributions with respect to Shares that are repurchased at the Participant’s Exercise Price pursuant to Section 10.2. However, the Committee, in its discretion, may provide in the Award Agreement evidencing any Award that the Participant shall be entitled to Dividend Equivalent Rights with respect to the payment of cash dividends on Shares underlying an Award during the period beginning on the date the Award is granted and ending, with respect to each Share subject to the Award, on the earlier of the date on which the Award is exercised or settled or the date on which it is forfeited. Such Dividend Equivalent Rights, if any, shall be credited to the Participant in the form of additional whole Shares as of the date of payment of such cash dividends on Shares.

**10.2. Restrictions on Shares.** At the discretion of the Committee, the Company may reserve to itself and/or its assignee(s) a right to repurchase (a “*Right of Repurchase*”) a portion of any or all Unvested Shares held by a Participant following such Participant’s termination of Service at any time within ninety (90) days (or such longer or shorter time determined by the Committee) after the later of the date Participant’s Service terminates and the date the Participant purchases Shares under this Plan, for cash and/or cancellation of purchase money indebtedness, at the Participant’s Exercise Price.

**11. CERTIFICATES.** All Shares or other securities whether or not certificated, delivered under this Plan will be subject to such stock transfer orders, legends and other restrictions as the Committee may deem necessary or advisable, including restrictions under any applicable U.S. federal, state or foreign securities law, or any rules, regulations and other requirements of the SEC or any stock exchange or automated quotation system upon which the Shares may be listed or quoted and any non-U.S. exchange controls or securities law restrictions to which the Shares are subject.

**12. ESCROW; PLEDGE OF SHARES.** To enforce any restrictions on a Participant’s Shares, the Committee may require the Participant to deposit all certificates representing Shares, together with stock powers or other instruments of transfer approved by the Committee, appropriately endorsed in blank, with the Company or an agent designated by the Company to hold in escrow until such restrictions have lapsed or terminated, and the Committee may cause a legend or legends referencing such restrictions to be placed on the certificates. Any Participant who is permitted to execute a promissory note as partial or full consideration for the purchase of Shares under this Plan will be required to pledge and deposit with the Company all or part of the Shares so purchased as collateral to secure the payment of the Participant’s obligation to the Company under the promissory note; provided, however, that the Committee may require or accept other or additional forms of collateral to secure the payment of such obligation and, in any event, the Company will have full recourse against the Participant under the promissory note notwithstanding any pledge of the Participant’s Shares or other collateral. In connection with any pledge of the Shares, the Participant will be required to execute and deliver a written pledge agreement in such form as the Committee will from time to time approve. The Shares purchased with the promissory note may be released from the pledge on a pro rata basis as the promissory note is paid.

**13. SECURITIES LAW AND OTHER REGULATORY COMPLIANCE.** An Award will not be effective unless such Award is in compliance with all applicable U.S. and foreign federal and state securities and exchange control laws, rules and regulations of any governmental body, and the requirements of any stock exchange or automated quotation system upon which the Shares may then be listed or quoted, as they are in effect on the date of grant of the Award and also on the date of exercise or other issuance. Notwithstanding any other provision in this Plan, the Company will have no obligation to issue or deliver certificates for Shares under this Plan prior to: (a) obtaining any approvals from governmental agencies that the Company determines are necessary or advisable; and/or (b) completion of any registration or other qualification of such Shares under any state or federal or foreign law or ruling of any governmental body that the Company determines to be necessary or advisable. The Company will be under no obligation to register the Shares with the SEC or to effect compliance with the registration, qualification or listing requirements of any foreign or state securities laws, exchange control laws, stock exchange or automated quotation system, and the Company will have no liability for any inability or failure to do so.

**14. NO OBLIGATION TO EMPLOY.** Nothing in this Plan or any Award granted under this Plan will confer or be deemed to confer on any Participant any right to continue in the employ of, or to continue any other relationship with, the Company or any Parent, Subsidiary or Affiliate or limit in any way the right of the Company or any Parent, Subsidiary or Affiliate to terminate Participant's employment or other relationship at any time.

**15. CORPORATE TRANSACTIONS.**

**15.1. Assumption or Replacement of Awards by Successor.** In the event that the Company is subject to a Corporate Transaction, outstanding Awards acquired under the Plan shall be subject to the agreement evidencing the Corporate Transaction, which need not treat all outstanding Awards in an identical manner. Such agreement, without the Participant's consent, shall provide for one or more of the following with respect to all outstanding Awards as of the effective date of such Corporate Transaction:

(a) The continuation of an outstanding Award by the Company (if the Company is the successor entity).

(b) The assumption of an outstanding Award by the successor or acquiring entity (if any) of such Corporate Transaction (or by its parents, if any), which assumption, will be binding on all selected Participants; provided that the exercise price and the number and nature of shares issuable upon exercise of any option or any award that is subject to Section 409A of the Code will be adjusted appropriately pursuant to Section 424(a) of the Code.

(c) The substitution by the successor or acquiring entity in such Corporate Transaction (or by its parents, if any) of equivalent awards with substantially the same terms for such outstanding Awards (except that the exercise price and the number and nature of shares issuable upon exercise of any option or any award that is subject to Section 409A of the Code will be adjusted appropriately pursuant to Section 424(a) of the Code).

(d) The full or partial acceleration of exercisability or vesting and accelerated expiration of an outstanding Award and lapse of the Company's right to repurchase or re-acquire shares acquired under an Award or lapse of forfeiture rights with respect to shares acquired under an Award.

(e) The settlement of the full value of such outstanding Award (whether or not then vested or exercisable) in cash, cash equivalents, or securities of the successor entity (or its parent, if any) with a Fair Market Value equal to the required amount, followed by the cancellation of such Awards; provided however, that such Award may be cancelled if such Award has no value, as determined by the Committee, in its discretion. Subject to Section 409A of the Code, such payment may be made in installments and may be deferred until the date or dates the Award would have become exercisable or vested. Such payment may be subject to vesting based on the Participant's continued service, provided that the vesting schedule shall not be less favorable to the Participant than the schedule under which the Award would have become vested or exercisable. For purposes of this Section 15.1(e), the Fair Market Value of any security shall be determined without regard to any vesting conditions that may apply to such security.

(f) The cancellation of outstanding Awards in exchange for no consideration.

The Board shall have full power and authority to assign the Company's right to repurchase or re-acquire or forfeiture rights to such successor or acquiring corporation. In addition, in the event such successor or acquiring corporation refuses to assume, convert, replace or substitute Awards, as provided above, pursuant to a Corporate Transaction, the Committee will notify the Participant in writing or electronically that such Award will be exercisable for a period of time determined by the Committee in its sole discretion, and such Award will terminate upon the expiration of such period. Awards need not be treated similarly in a Corporate Transaction. In addition, following a Corporate Transaction, 100% of the total number of Shares subject to each Award held by an Employee shall become vested if the holder is subject to an Involuntary Termination within 12 months after the Corporate Transaction; it being understood that the vesting acceleration set forth in the preceding clause is in addition to vesting of the Award or Shares that has occurred prior to the Involuntary Termination, subject to the Participant executing a general release (in a form prescribed by the Company) of all known and unknown claims that he or she may then have against the Company or persons affiliated with the Company and such release has become effective and agreeing not to prosecute any legal action or other proceeding based upon any of such claims except to the extent otherwise provided in an individual award agreement.

**16. TERM OF PLAN/GOVERNING LAW.** Unless earlier terminated as provided herein, this Plan will become effective on the Effective Date and will terminate ten (10) years from the date this Plan is adopted by the Board. This Plan and all Awards granted hereunder shall be governed by and construed in accordance with the laws of the State of Delaware (excluding its conflict of law rules).

**17. AMENDMENT OR TERMINATION OF PLAN.** The Board may at any time terminate or amend this Plan in any respect, including, without limitation, amendment of any form of Award Agreement or instrument to be executed pursuant to this Plan; provided, however, that the Board will not, without the approval of the stockholders of the Company, amend this Plan in any manner that requires such stockholder approval; provided further, that a Participant's Award shall be governed by the version of this Plan then in effect at the time such Award was granted.

**18. NONEXCLUSIVITY OF THE PLAN.** Neither the adoption of this Plan by the Board nor any provision of this Plan will be construed as creating any limitations on the power of the Board to adopt such additional compensation arrangements as it may deem desirable, including, without limitation, the granting of stock awards and bonuses otherwise than under this Plan, and such arrangements may be either generally applicable or applicable only in specific cases.

19. **INSIDER TRADING POLICY.** Each Participant who receives an Award shall comply with any policy adopted by the Company from time to time covering transactions in the Company's securities by Employees, officers and/or directors of the Company.

20. **ALL AWARDS SUBJECT TO COMPANY CLAWBACK OR RECOUPMENT POLICY.** All Awards shall be subject to clawback or recoupment pursuant to any compensation clawback or recoupment policy adopted by the Board or required by law during the term of Participant's employment or other service with the Company that is applicable to executive officers, employees, directors or other service providers of the Company, and in addition to any other remedies available under such policy and applicable law, may require the cancelation of outstanding Awards and the recoupment of any gains realized with respect to Awards.

21. **DEFINITIONS.** As used in this Plan, and except as elsewhere defined herein, the following terms will have the following meanings:

21.1. "***Affiliate***" means any person or entity that directly or indirectly through one or more intermediaries controls, or is controlled by, or is under common control with, the Company, including any general partner, managing member, officer or director of the Company, in each case as of the date on which, or at any time during the period for which, the determination of affiliation is being made. For purposes of this definition, the term "control" (including the correlative meanings of the terms "controlled by" and "under common control with"), as used with respect to any person or entity, means the possession, directly or indirectly, of the power to direct or cause the direction of the management policies of such person or entity, whether through the ownership of voting securities or by contract or otherwise.

21.2. "***Award***" means any award under the Plan, including any Option or Restricted Stock Unit.

21.3. "***Award Agreement***" means, with respect to each Award, the written or electronic agreement between the Company and the Participant setting forth the terms and conditions of the Award, and country-specific appendix thereto for grants to non-U.S. Participants, which shall be in substantially a form (which need not be the same for each Participant) that the Committee (or in the case of Award agreements that are not used for Insiders, the Committee's delegate(s)) has from time to time approved, and will comply with and be subject to the terms and conditions of this Plan.

21.4. "***Award Transfer Program***" means any program instituted by the Committee which would permit Participants the opportunity to transfer any outstanding Awards to a financial institution or other person or entity approved by the Committee.

21.5. "***Board***" means the Board of Directors of the Company.

21.6. "***Cause***" means (i) an unauthorized use or disclosure by Participant of the Company's confidential information or trade secrets, which use or disclosure causes material harm to the Company or is reasonably likely to cause material harm to the Company, (ii) a material breach of any agreement between Participant and the Company, (iii) a material failure to comply with the Company's written policies or rules that has caused or is reasonably likely to cause material injury to the Company, its successor, or its affiliates, or any of their business, (iv) conviction of, or plea of "guilty" or "no contest" to, a felony under the laws of the United States or any state thereof, (v) willful misconduct that has caused or is reasonably likely to cause material injury to the Company, its successor, or its affiliates, or any of

their business, (vi) embezzlement, (vii) failure to cooperate with the Company in any investigation or formal proceeding if the Company has requested Participant's reasonable cooperation, (viii) violation of any applicable federal, state or foreign statutes or laws that govern or regulate employment, pharmaceutical drugs or securities, including but not limited to the laws enforced by the federal Equal Employment Opportunity Commission, Department of Labor, Food and Drug Administration, Securities and Exchange Commission and Department of Justice or (ix) a continued failure to perform assigned duties after receiving written notification of such failure from the Company's Chief Executive Officer; *provided that* Participant must be provided with written notice of Participant's termination for "Cause" and Participant must be provided with a thirty (30) day period following Participant's receipt of such notice to cure the event(s) that trigger "Cause," with the Company's Chief Executive Officer making the final determination whether Participant has cured any Cause. The determination as to whether a Participant is being terminated for Cause shall be made in good faith by the Company and shall be final and binding on the Participant. The foregoing definition does not in any way limit the Company's ability to terminate a Participant's employment or service at any time as provided in Section 14 above, and the term "Company" will be interpreted to include any Parent, Subsidiary or Affiliate, as appropriate. Notwithstanding the foregoing, the foregoing definition of "Cause" may, in part or in whole, be modified or replaced in each individual employment agreement or Award Agreement with any Participant, provided that such document supersedes the definition provided in this Section 21.6.

**21.7. "Code"** means the United States Internal Revenue Code of 1986, as amended, and the regulations promulgated thereunder.

**21.8. "Committee"** means the Compensation Committee of the Board or the Board acting in such capacity.

**21.9. "Common Stock"** means the common stock of the Company.

**21.10. "Company"** means Aeglea BioTherapeutics, Inc., or any successor corporation.

**21.11. "Corporate Transaction"** means the occurrence of any of the following events: (a) any "Person" (as such term is used in Sections 13(d) and 14(d) of the Exchange Act) becomes the "beneficial owner" (as defined in Rule 13d-3 of the Exchange Act), directly or indirectly, of securities of the Company representing more than fifty percent (50%) of the total voting power represented by the Company's then-outstanding voting securities; provided, however, that for purposes of this subclause (a) the acquisition of additional securities by any one Person who is considered to own more than fifty percent (50%) of the total voting power of the securities of the Company will not be considered a Corporate Transaction; (b) the consummation of the sale or disposition by the Company of all or substantially all of the Company's assets; (c) the consummation of a merger or consolidation of the Company with any other corporation, other than a merger or consolidation which would result in the voting securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or its parent) at least fifty percent (50%) of the total voting power represented by the voting securities of the Company or such surviving entity or its parent outstanding immediately after such merger or consolidation; (d) any other transaction which qualifies as a "corporate transaction" under Section 424(a) of the Code wherein the stockholders of the Company give up all of their equity interest in the Company (except for the acquisition, sale or transfer of all or substantially all of the outstanding shares of the Company) or (e) a change in the effective control of the Company that occurs on the date that a majority of members of the

Board is replaced during any twelve (12) month period by members of the Board whose appointment or election is not endorsed by a majority of the members of the Board prior to the date of the appointment or election. For purpose of this subclause (e), if any Person is considered to be in effective control of the Company, the acquisition of additional control of the Company by the same Person will not be considered a Corporate Transaction. For purposes of this definition, Persons will be considered to be acting as a group if they are owners of a corporation that enters into a merger, consolidation, purchase or acquisition of stock, or similar business transaction with the Company. Notwithstanding the foregoing, to the extent that any amount constituting deferred compensation (as defined in Section 409A of the Code) would become payable under this Plan by reason of a Corporate Transaction, such amount shall become payable only if the event constituting a Corporate Transaction would also qualify as a change in ownership or effective control of the Company or a change in the ownership of a substantial portion of the assets of the Company, each as defined within the meaning of Code Section 409A, as it has been and may be amended from time to time, and any proposed or final Treasury Regulations and IRS guidance that has been promulgated or may be promulgated thereunder from time to time.

**21.12. “Director”** means a member of the Board.

**21.13. “Disability”** means that the Participant is unable to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment that can be expected to result in death or can be expected to last for a continuous period of not less than 12 months.

**21.14. “Effective Date”** means February 20, 2018.

**21.15. “Employee”** means any person, including Officers, employed by the Company or any Parent, Subsidiary or Affiliate. Neither service as a Director nor payment of a director’s fee by the Company will be sufficient to constitute “employment” by the Company.

**21.16. “Exchange Act”** means the United States Securities Exchange Act of 1934, as amended.

**21.17. “Exercise Price”** means, with respect to an Option, the price at which a holder may purchase the Shares issuable upon exercise of an Option.

**21.18. “Fair Market Value”** means, as of any date, the value of a share of the Company’s Common Stock determined as follows:

(a) if such Common Stock is publicly traded and is then listed on a national securities exchange, its closing price on the date of determination on the principal national securities exchange on which the Common Stock is listed or admitted to trading as reported in *The Wall Street Journal* or such other source as the Committee deems reliable;

(b) if such Common Stock is publicly traded but is neither listed nor admitted to trading on a national securities exchange, the average of the closing bid and asked prices on the date of determination as reported in *The Wall Street Journal* or such other source as the Committee deems reliable; or

(c) if none of the foregoing is applicable, by the Board or the Committee in good faith.

**21.19. “Good Reason”** means, without the Participant’s consent, (i) a material reduction in the Participant’s level of responsibility and/or scope of authority, (ii) a reduction by more than 10% in Participant’s base salary (other than a reduction generally applicable to Participant officers of the Company and in generally the same proportion as for the Participant), or (iii) relocation of the Participant’s principal workplace by more than thirty-five (35) miles from Participant’s then current place of employment. For the purpose of clause (i), a change in responsibility shall not be deemed to occur (A) solely because Participant is part of a larger organization or (B) solely because of a change in title. For the Participant to receive the benefits under this Agreement as a result of a voluntary resignation under this subsection (e), all of the following requirements must be satisfied: (1) the Participant must provide notice to the Company of his or her intent to assert Good Reason within sixty (60) days of the initial existence of one or more of the conditions set forth in subclauses (i) through (iii); (2) the Company will have thirty (30) days (the “*Company Cure Period*”) from the date of such notice to remedy the condition and, if it does so, the Participant may withdraw his or her resignation or may resign with no benefits; and (3) any termination of employment under this provision must occur within ten (10) days of the earlier of expiration of the Company Cure Period or written notice from the Company that it will not undertake to cure the condition set forth in subclauses (i) through (iii). Should the Company remedy the condition as set forth above and then one or more of the conditions arises again within twelve months following the occurrence of a Change in Control, the Participant may assert Good Reason again subject to all of the conditions set forth herein.

**21.20. “Insider”** means an officer or director of the Company or any other person whose transactions in the Company’s Common Stock are subject to Section 16 of the Exchange Act.

**21.21. “Involuntary Termination”** means either (a) termination of Service without Cause or (b) resignation from Service for Good Reason.

**21.22. “IRS”** means the United States Internal Revenue Service.

**21.23. “Non-Employee Director”** means a Director of the Company who is not an Employee of the Company or any Parent, Subsidiary or Affiliate, and who qualifies as “independent” within the meaning of Nasdaq Stock Market Rule 5605(a)(2), or any successor rule, if the Company’s securities are traded on the Nasdaq Stock Market, or if the requirements of any other established stock exchange on which the Company’s securities are traded, as such rules or requirements may be amended from time to time.

**21.24. “Option”** means an award of an option to purchase Shares pursuant to Section 5.

**21.25. “Parent”** means any corporation (other than the Company) in an unbroken chain of corporations ending with the Company if each of such corporations other than the Company owns stock possessing fifty percent (50%) or more of the total combined voting power of all classes of stock in one of the other corporations in such chain.

**21.26. “Participant”** means a person who holds an Award under this Plan.

**21.27. “Performance Factors”** means the factors selected by the Committee and specified in an Award Agreement to determine whether the performance goals established by the Committee applicable to any Awards have been satisfied.

**21.28. “Performance Period”** means one or more periods of time, which may be of varying and overlapping durations, as the Committee may select, over which the attainment of one or more Performance Factors will be measured for the purpose of determining a Participant’s right to, and the payment of, a Performance Award.

**21.29. “Permitted Transferee”** means any child, stepchild, grandchild, parent, stepparent, grandparent, spouse, former spouse, sibling, niece, nephew, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law (including adoptive relationships) of the Employee, any person sharing the Employee’s household (other than a tenant or employee), a trust in which these persons (or the Employee) have more than 50% of the beneficial interest, a foundation in which these persons (or the Employee) control the management of assets, and any other entity in which these persons (or the Employee) own more than 50% of the voting interests.

**21.30. “Plan”** means this Aeglea BioTherapeutics, Inc. 2018 Equity Inducement Plan.

**21.31. “Restricted Stock Unit”** means an Award granted pursuant to Section 6 of the Plan.

**21.32. “SEC”** means the United States Securities and Exchange Commission.

**21.33. “Securities Act”** means the United States Securities Act of 1933, as amended.

**21.34. “Service”** shall mean service as an Employee, Director or consultant to the Company or a Parent or Subsidiary, subject to such further limitations as may be set forth in the Plan or the applicable Award Agreement. An employee will not be deemed to have ceased to provide Service in the case of leave of absence approved by the Company. In the case of any employee on an approved leave of absence or a reduction in hours worked (for illustrative purposes only, a change in schedule from that of full-time to part-time), the Committee may make such provisions respecting suspension of, or modification to, vesting of the Award while on leave from the employ of the Company or a Parent or Subsidiary or during such change in working hours as it may deem appropriate, except that in no event may an Award be exercised after the expiration of the term set forth in the applicable Award Agreement. In the absence of such a determination, vesting of Awards shall be tolled during any unpaid leave of absence (unless otherwise required by applicable law). In the event of military leave, if required by applicable laws, vesting shall continue for the longest period that vesting continues under any other statutory or Company approved leave of absence and, upon a Participant’s returning from military leave (under conditions that would entitle him or her to protection upon such return under the Uniform Services Employment and Reemployment Rights Act), he or she shall be given vesting credit with respect to Awards to the same extent as would have applied had the Participant continued to provide Service throughout the leave on the same terms as he or she was providing Service immediately prior to such leave. Service shall not be considered interrupted or terminated in the case of a transfer between locations of the Company or between the Company, its Parent, Subsidiaries or Affiliates, or their respective successors, or a change in status from an employee to a consultant or from a consultant to an employee. The Committee will have sole discretion to determine whether a Participant has ceased to provide Service and the effective date on which the Participant ceased to provide Service.

**21.35. “Shares”** means shares of Common Stock and the common stock of any successor entity.

**21.36. “*Subsidiary*”** means any corporation (other than the Company) in an unbroken chain of corporations beginning with the Company if each of the corporations other than the last corporation in the unbroken chain owns stock possessing fifty percent (50%) or more of the total combined voting power of all classes of stock in one of the other corporations in such chain.

**21.37. “*Treasury Regulations*”** means regulations promulgated by the United States Treasury Department.

**21.38. “*Unvested Shares*”** means Shares that have not yet vested or are subject to a right of repurchase in favor of the Company (or any successor thereto).

**FIRST AMENDMENT TO THE  
AEGLEA BIOTHERAPEUTICS, INC.  
2018 EQUITY INDUCEMENT PLAN**

**WHEREAS**, Aeglea Biotherapeutics, Inc., a Delaware corporation (the “Company”) maintains the Aeglea Biotherapeutics, Inc. 2018 Equity Inducement Plan (the “Plan”); and

**WHEREAS**, pursuant to Section 17 of the Plan, the Board of Directors (the “Board”) may amend the Plan at any time and for any purpose as permitted by law, including to increase the maximum number of Shares for which awards may be granted under the Plan.

**NOW, THEREFORE**, pursuant to its authority under Section 17 of the Plan, the Board hereby amends the Plan as follows, effective as of June 22, 2023 (the “Amendment Effective Date”):

1. Section 2.1 of the Plan is hereby amended and restated in its entirety to read as follows:

**“2.1 Number of Shares Available.** Subject to Sections 2.4 and 15 and any other applicable provisions hereof, the total number of Shares reserved and available for grant and issuance pursuant to this Plan is 71,100,000.”
2. This First Amendment shall be governed by and construed in accordance with the laws of the State of Delaware (excluding its conflict of law rules).
3. All capitalized terms used but not otherwise defined herein shall have the meaning assigned to them in the Plan. Except as expressly amended hereby, the Plan shall remain in full force and effect in accordance with its terms.

[Signature Page Follows]

**IN WITNESS WHEREOF**, the undersigned has executed this First Amendment to the Aeglea Biotherapeutics, Inc. 2018 Equity Inducement Plan, effective as of the Amendment Effective Date.

**AEGLEA BIOTHERAPEUTICS, INC.**

By: /s/ Jonathan Alspaugh

Name: Jonathan Alspaugh  
Title: President and Chief Financial Officer

Signature Page to  
First Amendment to the  
Aeglea Biotherapeutics, Inc.  
2018 Equity Inducement Plan

**SECOND AMENDMENT TO THE  
AEGLEA BIOTHERAPEUTICS, INC.  
2018 EQUITY INDUCEMENT PLAN**

**WHEREAS**, Aeglea BioTherapeutics, Inc., a Delaware corporation (the “Company”) maintains the Aeglea BioTherapeutics, Inc. 2018 Equity Inducement Plan, as amended on June 22, 2023 (the “Plan”); and

**WHEREAS**, pursuant to Section 17 of the Plan, the Board of Directors (the “Board”) may amend the Plan at any time and for any purpose as permitted by law, including to increase the maximum number of Shares for which awards may be granted under the Plan.

**NOW, THEREFORE**, pursuant to its authority under Section 17 of the Plan, the Board hereby amends the Plan as follows, effective as of August 30, 2023 (the “Amendment Effective Date”):

1. Section 2.1 of the Plan is hereby amended and restated in its entirety to read as follows:

**“2.1 Number of Shares Available.** Subject to Sections 2.4 and 15 and any other applicable provisions hereof, the total number of Shares reserved and available for grant and issuance pursuant to this Plan is 101,100,000.”
2. This Second Amendment shall be governed by and construed in accordance with the laws of the State of Delaware (excluding its conflict of law rules).
3. All capitalized terms used but not otherwise defined herein shall have the meaning assigned to them in the Plan. Except as expressly amended hereby, the Plan shall remain in full force and effect in accordance with its terms.

[Signature Page Follows]

**IN WITNESS WHEREOF**, the undersigned has executed this Second Amendment to the Aeglea BioTherapeutics, Inc. 2018 Equity Inducement Plan, effective as of the Amendment Effective Date.

**AEGLEA BIOTHERAPEUTICS, INC.**

By: /s/ Cameron Turtle

Name: Cameron Turtle  
Title: Chief Operating Officer

Signature Page to  
Second Amendment to the  
Aeglea BioTherapeutics, Inc.  
2018 Equity Inducement Plan

**THIRD AMENDMENT TO THE  
AEGLEA BIOTHERAPEUTICS, INC.  
2018 EQUITY INDUCEMENT PLAN**

**WHEREAS**, Aeglea BioTherapeutics, Inc., a Delaware corporation (the “Company”) maintains the Aeglea BioTherapeutics, Inc. 2018 Equity Inducement Plan, as amended on June 22, 2023 and August 30, 2023 (the “Plan”); and

**WHEREAS**, pursuant to Section 17 of the Plan, the Board of Directors (the “Board”) may amend the Plan at any time and for any purpose as permitted by law, including to increase the maximum number of Shares for which awards may be granted under the Plan.

**NOW, THEREFORE**, pursuant to its authority under Section 17 of the Plan, the Board hereby amends the Plan as follows, effective as of October 30, 2023 (the “Amendment Effective Date”):

1. Section 2.1 of the Plan is hereby amended and restated in its entirety to read as follows:

“**2.1 Number of Shares Available.** Subject to Sections 2.4 and 15 and any other applicable provisions hereof, the total number of Shares reserved and available for grant and issuance pursuant to this Plan is 6,044,000.”
2. This Third Amendment shall be governed by and construed in accordance with the laws of the State of Delaware (excluding its conflict of law rules).
3. All capitalized terms used but not otherwise defined herein shall have the meaning assigned to them in the Plan. Except as expressly amended hereby, the Plan shall remain in full force and effect in accordance with its terms.

[Signature Page Follows]

**IN WITNESS WHEREOF**, the undersigned has executed this Third Amendment to the Aeglea BioTherapeutics, Inc. 2018 Equity Inducement Plan, effective as of the Amendment Effective Date.

**AEGLEA BIOTHERAPEUTICS, INC.**

By: /s/ Cameron Turtle

Name: Cameron Turtle  
Title: Chief Operating Officer

Signature Page to  
Third Amendment to the  
Aeglea BioTherapeutics, Inc.  
2018 Equity Inducement Plan

**FOURTH AMENDMENT TO THE  
AEGLEA BIOTHERAPEUTICS, INC.  
2018 EQUITY INDUCEMENT PLAN**

**WHEREAS**, Spyre Therapeutics, Inc., a Delaware corporation (the “Company”) maintains the Aeglea BioTherapeutics, Inc. 2018 Equity Inducement Plan, as amended on June 22, 2023, August 30, 2023 and October 30, 2023 (the “Plan”); and

**WHEREAS**, pursuant to Section 17 of the Plan, the Board of Directors (the “Board”) may amend the Plan at any time and for any purpose as permitted by law; and

**WHEREAS**, pursuant to an Amended and Restated Certificate of Incorporation, the Company changed its name from “Aeglea BioTherapeutics, Inc.” to “Spyre Therapeutics, Inc.” effective November 28, 2023; and

**WHEREAS**, the Board has authorized an officer of the Company to amend the Plan to incorporate the Company’s name change.

**NOW, THEREFORE**, pursuant to its authority under Section 17 of the Plan, the Board hereby amends the Plan as follows, effective as of November 28, 2023 (the “Amendment Effective Date”):

1. The Plan shall hereby be referred to as the “Spyre Therapeutics, Inc. 2018 Equity Inducement Plan.”

2. Section 21.10 of the Plan is hereby amended and restated in its entirety to read as follows:

**“21.10. “*Company*” means Spyre Therapeutics, Inc., or any successor corporation”**

3. All references in the Plan and in any Award Agreements (as defined in the Plan) to “Aeglea BioTherapeutics Inc.” shall instead refer to “Spyre Therapeutics, Inc.”

4. This Fourth Amendment shall be governed by and construed in accordance with the laws of the State of Delaware (excluding its conflict of law rules).

5. All capitalized terms used but not otherwise defined herein shall have the meaning assigned to them in the Plan. Except as expressly amended hereby, the Plan shall remain in full force and effect in accordance with its terms.

[Signature Page Follows]

**IN WITNESS WHEREOF**, the undersigned has executed this Fourth Amendment to the Aeglea BioTherapeutics, Inc. 2018 Equity Inducement Plan, effective as of the Amendment Effective Date.

**SPYRE THERAPEUTICS, INC.**

By: /s/ Cameron Turtle

Name: Cameron Turtle  
Title: Chief Executive Officer

Signature Page to  
Fourth Amendment to the  
Aeglea BioTherapeutics, Inc.  
2018 Equity Inducement Plan

**FIFTH AMENDMENT TO THE SPYRE THERAPEUTICS, INC. 2018 EQUITY  
INDUCEMENT PLAN**

**WHEREAS**, Spyre Therapeutics, Inc., a Delaware corporation (the “Company”) maintains the Spyre Therapeutics, Inc. 2018 Equity Inducement Plan, as amended on June 22, 2023, August 30, 2023, October 30, 2023 and November 28, 2023 (the “Plan”); and

**WHEREAS**, pursuant to Section 17 of the Plan, the Board of Directors (the “Board”) may amend the Plan at any time and for any purpose as permitted by law, including to increase the maximum number of Shares for which awards may be granted under the Plan.

**NOW, THEREFORE**, pursuant to its authority under Section 17 of the Plan, the Board hereby amends the Plan as follows, effective as of September 20, 2024 (the “Amendment Effective Date”):

1. Section 2.1 of the Plan is hereby amended and restated in its entirety to read as follows:

**“2.1 Number of Shares Available.** Subject to Sections 2.4 and 15 and any other applicable provisions hereof, the total number of Shares reserved and available for grant and issuance pursuant to this Plan is 7,044,000.”

2. This Fifth Amendment shall be governed by and construed in accordance with the laws of the State of Delaware (excluding its conflict of law rules).

3. All capitalized terms used but not otherwise defined herein shall have the meaning assigned to them in the Plan. Except as expressly amended hereby, the Plan shall remain in full force and effect in accordance with its terms.

[Signature Page Follows]

**IN WITNESS WHEREOF**, the undersigned has executed this Fifth Amendment to the Spyre Therapeutics, Inc. 2018 Equity Inducement Plan, effective as of the Amendment Effective Date.

**SPYRE THERAPEUTICS, INC.**

By: /s/ Cameron Turtle

Name: Cameron Turtle  
Title: Chief Executive Officer

Signature Page to  
Fifth Amendment to the Spyre Therapeutics, Inc. 2018 Equity Inducement Plan

**SIXTH AMENDMENT TO THE SPYRE THERAPEUTICS, INC. 2018 EQUITY  
INDUCEMENT PLAN**

**WHEREAS**, Spyre Therapeutics, Inc., a Delaware corporation (the “Company”) maintains the Spyre Therapeutics, Inc. 2018 Equity Inducement Plan, as amended on June 22, 2023, August 30, 2023, October 30, 2023, November 28, 2023 and September 20, 2024 (the “Plan”); and

**WHEREAS**, pursuant to Section 17 of the Plan, the Board of Directors (the “Board”) may amend the Plan at any time and for any purpose as permitted by law, including to increase the maximum number of Shares for which awards may be granted under the Plan.

**NOW, THEREFORE**, pursuant to its authority under Section 17 of the Plan, the Board hereby amends the Plan as follows, effective as of June 11, 2025 (the “Amendment Effective Date”):

1. Section 2.1 of the Plan is hereby amended and restated in its entirety to read as follows:

“**2.1 Number of Shares Available.** Subject to Sections 2.4 and 15 and any other applicable provisions hereof, the total number of Shares reserved and available for grant and issuance pursuant to this Plan is 7,794,000.”

2. This Sixth Amendment shall be governed by and construed in accordance with the laws of the State of Delaware (excluding its conflict of law rules).

3. All capitalized terms used but not otherwise defined herein shall have the meaning assigned to them in the Plan. Except as expressly amended hereby, the Plan shall remain in full force and effect in accordance with its terms.

[Signature Page Follows]

**IN WITNESS WHEREOF**, the undersigned has executed this Sixth Amendment to the Spyre Therapeutics, Inc. 2018 Equity Inducement Plan, effective as of the Amendment Effective Date.

**SPYRE THERAPEUTICS, INC.**

By: /s/ Cameron Turtle

Name: Cameron Turtle  
Title: Chief Executive Officer

Signature Page to  
Sixth Amendment to the Spyre Therapeutics, Inc. 2018 Equity Inducement Plan

**Certification of Principal Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002**

I, Cameron Turtle, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Spyre Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;
  - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 5, 2025

/s/ Cameron Turtle, D.Phil

Cameron Turtle, D.Phil

Chief Executive Officer

(Principal Executive Officer)

**Certification of Principal Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002**

I, Scott Burrows, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Spyre Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;
  - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 5, 2025

*/s/ Scott Burrows*

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Scott Burrows

Chief Financial Officer

(Principal Financial Officer and Principal Accounting Officer)

**Certifications 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**

In connection with the Quarterly Report of Spyre Therapeutics, Inc. (the "Company") on Form 10-Q for the quarterly period ended June 30, 2025, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

- 1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- 2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 5, 2025

/s/ Cameron Turtle, D.Phil

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Cameron Turtle, D.Phil

*Chief Executive Officer*

*(Principal Executive Officer)*

/s/ Scott Burrows

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Scott Burrows

*Chief Financial Officer*

*(Principal Financial Officer and Principal Accounting Officer)*