

**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 September 30, 2024  
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 type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" 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 November 1, 2024, the registrant had 51,431,220 shares of common stock, \$0.0001 par value per share, outstanding.

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**SPYRE THERAPEUTICS, INC.**  
**QUARTERLY REPORT ON FORM 10-Q**  
**FOR THE QUARTER ENDED SEPTEMBER 30, 2024**  
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## NOTE ABOUT FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q for the quarter ended September 30, 2024 (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, 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; the length of time that we believe our existing cash resources will fund operations; our market size; our potential growth opportunities; our nonclinical and clinical development activities, including clinical trial designs, submission of investigational new drug ("IND") applications and foreign equivalents and further clinical evaluation of therapeutic combinations, and related regulatory feedback; the potential efficacy and safety of our product candidates, including in combinations; the potential therapeutic benefits and economic value of our product candidates; the timing and results of nonclinical studies and clinical trials, including commencement of first-in-human ("FIH") and Phase 2 trials; 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 U.S. elections, inflation, increasing interest rates and volatile market conditions, current or potential bank failures, as well as global events, including the ongoing military conflict in Ukraine, conflict in Israel and surrounding areas, and geopolitical tensions in China on our operations; and the receipt and timing of potential regulatory designations, approvals and commercialization of product candidates, are forward-looking statements. The words "believe," "may," "will," "potentially," "estimate," "continue," "anticipate," "predict," "target," "intend," "could," "would," "should," "project," "plan," "expect," and similar expressions that convey uncertainty of future events or outcomes are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in Item 1A, "Risk Factors" included in this 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 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," "Aeglea BioTherapeutics, Inc.," "the Company," "we," "us," and "our" refer to Spyre Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries taken as a whole. "Spyre" and all product candidate names are our common law trademarks. This 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, exercised the option to acquire intellectual property license rights to or have the option to acquire intellectual property license rights to pursuant to that certain antibody discovery and option agreement, dated May 25, 2023, and subsequently amended and restated on September 29, 2023 and May 14, 2024, by and among us, Paragon Therapeutics, Inc. ("Paragon") and Parapyre Holding LLC ("Parapyre") (the "Paragon Agreement").

Please be advised that on September 8, 2023, we effected a reverse stock split of our common stock, par value \$0.0001 per share ("Common Stock"), at a ratio of 1-for-25 (the "Reverse Split"). Except as indicated otherwise, all share numbers related to our Common Stock disclosed in this Quarterly Report have been adjusted on a post-Reverse Split basis. In addition, on November 28, 2023, we changed our name from "Aeglea BioTherapeutics, Inc." to "Spyre Therapeutics, Inc."

## PART I. – Financial Information

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

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

	September 30, 2024	December 31, 2023
<b>ASSETS</b>		
<b>CURRENT ASSETS</b>		
Cash and cash equivalents	\$ 71,580	\$ 188,893
Marketable securities	342,647	150,384
Prepaid expenses and other current assets	6,852	2,251
Total current assets	421,079	341,528
Restricted cash	—	322
Other non-current assets	10	9
<b>TOTAL ASSETS</b>	<b>\$ 421,089</b>	<b>\$ 341,859</b>
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
<b>CURRENT LIABILITIES</b>		
Accounts payable	\$ 5,165	\$ 896
CVR liability	24,740	1,390
Accrued and other current liabilities	13,153	13,108
Related party accounts payable and other current liabilities	14,481	16,584
Total current liabilities	57,539	31,978
Non-current CVR liability	36,160	41,310
<b>TOTAL LIABILITIES</b>	<b>93,699</b>	<b>73,288</b>
Commitments and Contingencies (Note 7 and 8)		
Series B non-voting convertible preferred stock, \$0.0001 par value; 150,000 shares authorized, issued, and outstanding as of December 31, 2023.	—	84,555
<b>STOCKHOLDERS' EQUITY</b>		
Series A non-voting convertible preferred stock, \$0.0001 par value; 1,086,341 shares authorized as of September 30, 2024 and December 31, 2023; 346,045 and 437,037 shares issued and outstanding as of September 30, 2024 and December 31, 2023, respectively.	146,425	184,927
Series B non-voting convertible preferred stock, \$0.0001 par value; 271,625 shares authorized and 16,667 shares issued and outstanding as of September 30, 2024.	9,395	—
Preferred stock, \$0.0001 par value; 8,642,034 shares and 8,763,659 shares authorized as of September 30, 2024 and December 31, 2023, respectively; no shares issued and outstanding as of September 30, 2024 and December 31, 2023.	—	—
Common stock, \$0.0001 par value; 400,000,000 shares authorized as of September 30, 2024 and December 31, 2023; 51,395,608 shares and 36,057,109 shares issued and outstanding as of September 30, 2024 and December 31, 2023, respectively.	12	10
Additional paid-in capital	1,086,237	763,191
Accumulated other comprehensive income	1,457	302
Accumulated deficit	(916,136)	(764,414)
<b>TOTAL STOCKHOLDERS' EQUITY</b>	<b>327,390</b>	<b>184,016</b>
<b>TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY</b>	<b>\$ 421,089</b>	<b>\$ 341,859</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 September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
<b>Revenue:</b>				
Development fee and royalty	\$ —	\$ —	\$ —	\$ 886
Total revenue	—	—	—	886
<b>Operating expenses:</b>				
Research and development <sup>(1)</sup>	44,744	24,660	112,308	55,822
General and administrative	10,648	8,584	35,005	25,874
Acquired in-process research and development	—	(298)	—	130,188
Gain on sale of in-process research and development asset	—	(14,609)	—	(14,609)
Total operating expenses	55,392	18,337	147,313	197,275
Loss from operations	(55,392)	(18,337)	(147,313)	(196,389)
<b>Other (expense) income:</b>				
Interest income	5,184	1,251	15,536	2,021
Change in fair value of forward contract liability	—	(25,360)	—	(83,530)
Other (expense) income, net	(18,802)	2,342	(19,895)	2,262
Total other (expense) income	(13,618)	(21,767)	(4,359)	(79,247)
Loss before income tax expense	(69,010)	(40,104)	(151,672)	(275,636)
Income tax (expense) benefit	(18)	(3)	(50)	26
Net loss	\$ (69,028)	\$ (40,107)	\$ (151,722)	\$ (275,610)
<b>Net loss per share, basic and diluted</b>				
	\$ (1.36)	\$ (9.34)	\$ (3.43)	\$ (69.57)
<b>Weighted-average common shares outstanding, basic and diluted</b>				
	50,889,433	4,293,812	44,263,746	3,961,546

(1) Includes \$7.7 million and \$34.2 million in related party expenses for the three and nine months ended September 30, 2024, respectively, and \$19.4 million and \$20.8 million related party expenses for the three and nine months ended September 30, 2023, 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 September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Net loss	\$ (69,028)	\$ (40,107)	\$ (151,722)	\$ (275,610)
Other comprehensive (loss) income:				
Foreign currency translation adjustment	17	(29)	37	(1)
Unrealized gain (loss) on marketable securities	1,993	(114)	1,118	(83)
Total comprehensive loss	<u>\$ (67,018)</u>	<u>\$ (40,250)</u>	<u>\$ (150,567)</u>	<u>\$ (275,694)</u>

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 Nine Months Ended September 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
Exchange of Series A non-voting convertible preferred stock for common stock	—	—	(91)	(38,502)	—	—	3,640	1	38,501	—	—	—
Conversion of Series B non-voting convertible preferred stock into common stock	—	—	—	—	(255)	(244,010)	10,198	1	244,009	—	—	—
Issuance of common stock in connection with 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

Issuance of common stock in connection with at-the-market offerings, net of offering costs	—	—	—	—	—	—	426	—	11,750	—	—	11,750
Vesting of restricted stock units	—	—	—	—	—	—	34	—	—	—	—	—
Issuance of common stock in connection with exercise of stock options and employee stock purchase plan	—	—	—	—	—	—	153	—	1,318	—	—	1,318
Stock-based compensation expense	—	—	—	—	—	—	—	—	6,955	—	—	6,955
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	17	—	17
Unrealized gain on marketable securities	—	—	—	—	—	—	—	—	—	1,993	—	1,993
Net loss	—	—	—	—	—	—	—	—	—	—	(69,028)	(69,028)
Balances - September 30, 2024	—	—	346	\$ 146,425	17	\$ 9,395	51,396	\$ 12	\$ 1,086,237	\$ 1,457	\$ (916,136)	\$ 327,390

Three and Nine Months Ended September 30, 2023

	Series A 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				
		\$		\$				
Balances - December 31, 2022	—	\$ —	2,614	\$ 6	\$ 475,971	\$ (48)	\$ (425,624)	\$ 50,305
Issuance of common stock in connection with employee stock purchase plan	—	—	2	—	18	—	—	18
Stock-based compensation expense	—	—	—	—	1,709	—	—	1,709
Foreign currency translation adjustment	—	—	—	—	—	10	—	10
Unrealized gain on marketable securities	—	—	—	—	—	32	—	32
Net loss	—	—	—	—	—	—	(18,422)	(18,422)
Balances - March 31, 2023	—	\$ —	2,616	\$ 6	\$ 477,698	\$ (6)	\$ (444,046)	\$ 33,652
Issuance of Series A non-voting convertible preferred stock in connection with private placement, net of financing costs	721	197,323	—	—	—	—	—	—
Issuance of common stock forward in connection with the asset acquisition of Spyre	—	—	—	—	3,768	—	—	3,768
Issuance of common stock in connection with exercise of pre-funded warrants	—	—	624	—	—	—	—	—
CVR distribution to common stockholders	—	—	—	—	(29,500)	—	—	(29,500)
Stock-based compensation expense	—	—	—	—	1,775	—	—	1,775
Foreign currency translation adjustment	—	—	—	—	—	18	—	18
Unrealized loss on marketable securities	—	—	—	—	—	(1)	—	(1)
Net loss	—	—	—	—	—	—	(217,081)	(217,081)
Balances - June 30, 2023	721	\$ 197,323	3,240	\$ 6	\$ 453,741	\$ 11	\$ (661,127)	\$ (207,369)
Issuance of Series A non-voting convertible preferred stock in connection with the asset acquisition of Spyre and settlement of related forward contract	365	189,741	—	—	—	—	—	—
Settlement of financing costs in connection with private placement of Series A non-voting convertible preferred stock	—	41	—	—	—	—	—	—
Issuance of common stock in connection with the asset acquisition of Spyre and settlement of related forward contract	—	—	518	1	(1)	—	—	—
Issuance of common stock in connection with exercise of pre-funded warrants	—	—	281	—	—	—	—	—
Issuance of common stock in connection with exercise of stock options and employee stock purchase plan	—	—	10	—	105	—	—	105
CVR distribution to common stockholders	—	—	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	2,112	—	—	2,112
Foreign currency translation adjustment	—	—	—	—	—	(29)	—	(29)
Unrealized loss on marketable securities	—	—	—	—	—	(114)	—	(114)
Net loss	—	—	—	—	—	—	(40,107)	(40,107)
Balances - September 30, 2023	1,086	\$ 387,105	4,049	\$ 7	\$ 455,957	\$ (132)	\$ (701,234)	\$ (245,402)

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)**

	Nine Months Ended September 30,	
	2024	2023
<b>CASH FLOWS FROM OPERATING ACTIVITIES</b>		
Net loss	\$ (151,722)	\$ (275,610)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	35,617	8,405
Acquired in-process research and development	—	130,188
Change in fair value of CVR liability	19,630	(1,300)
Change in fair value of forward contract liability	—	83,530
Gain on sale of in-process research and development asset	—	(14,609)
Lease ROU asset and leasehold improvement impairment loss	—	2,580
Loss on disposal of long-lived assets	—	915
Net accretion of discount on marketable securities	(8,985)	(612)
Interest proceeds from maturities of zero coupon US Treasury Bills	581	—
Depreciation and amortization	—	744
Amortization of operating lease assets	—	220
Other	—	18
Changes in operating assets and liabilities:		
Accounts payable	4,268	1,001
Accrued and other liabilities	(257)	(4,000)
Related party accounts payable	(15,138)	(2,115)
Prepaid expenses and other assets	(4,205)	3,310
Deferred revenue	—	575
Development receivables	—	212
Operating lease liabilities	—	(2,326)
Net cash used in operating activities	(120,211)	(68,874)
<b>CASH FLOWS FROM INVESTING ACTIVITIES</b>		
Proceeds from maturities and sales of marketable securities	183,419	21,000
Purchases of marketable securities	(366,160)	(112,631)
Cash assumed from asset acquisition of Spyre	—	3,035
Proceeds from sale of in-process research & development asset	—	15,000
Proceeds from sale of property and equipment	—	475
Net cash used in investing activities	(182,741)	(73,121)
<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	168,850	—
Proceeds from issuance of Series A non-voting convertible preferred stock in connection with private placement, net of placement and other offering costs	—	197,364
Proceeds from issuance of common stock in connection with at-the-market offerings, net of issuance costs	11,760	—
Payment of deferred offering costs in connection with shelf registration	(78)	—
Payments related to contingent value rights liability	(1,430)	—
Proceeds from employee stock option exercises, employee stock plan purchases, and exercise of prefunded warrants	6,203	123
Principal payments on finance lease obligation	—	(16)
Net cash provided by financing activities	185,305	197,471
Effect of exchange rate on cash, cash equivalents, and restricted cash	12	7
<b>NET (DECREASE) INCREASE IN CASH, CASH EQUIVALENTS, AND RESTRICTED CASH</b>	<b>(117,635)</b>	<b>55,483</b>
<b>CASH, CASH EQUIVALENTS, AND RESTRICTED CASH</b>		
Beginning of period	189,215	36,416
End of period	<u>\$ 71,580</u>	<u>\$ 91,899</u>

(Continued on next page)

	Nine Months Ended September 30,	
	2024	2023
<b>Supplemental Disclosure of Non-Cash Investing and 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 common stock in connection with at-the-market offerings, net of offering costs	\$ 329	\$ —
Allocation of deferred offering costs against proceeds of issuance of common stock	\$ 10	\$ —
<b>Reconciliation of Cash, Cash Equivalents, and Restricted Cash Reported in the Statement of Financial Position</b>		
Cash and cash equivalents	\$ 71,580	\$ 90,592
Restricted cash	—	1,307
<b>Total cash, cash equivalents, and restricted cash shown in the statement of cash flows</b>	<u>\$ 71,580</u>	<u>\$ 91,899</u>

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. The Company was formed as a Limited Liability Company ("LLC") in Delaware on December 16, 2013 under the name Aeglea BioTherapeutics Holdings, LLC and was converted from a Delaware LLC to a Delaware corporation on March 10, 2015. On November 27, 2023, the Company completed its corporate rebranding, changing the name of the Company to Spyre Therapeutics, Inc. The Company operates in one segment and has its principal offices in Waltham, Massachusetts.

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

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

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

In connection with the Asset Acquisition, on June 26, 2023, the Company completed a private placement of shares of Series A Preferred Stock (the "June 2023 PIPE") to a group of investors (the "June 2023 Investors"). The Company sold an aggregate of 721,452 shares of Series A Preferred Stock for an aggregate purchase price of approximately \$210.0 million before deducting approximately \$12.7 million in placement agent and other offering expenses (together with the Asset Acquisition, the "Transactions").

In connection with the Asset Acquisition, a non-transferable contingent value right ("CVR") was distributed to stockholders of record of the Company as of the close of business on July 3, 2023 (the "Legacy Stockholders"), but was not distributed to the holders of shares of Common Stock or Series A Preferred Stock issued to the former stockholders of Pre-Merger Spyre or the June 2023 Investors in the Transactions. 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 November 21, 2023, the Company's stockholders approved the issuance of Common Stock upon conversion of the Company's Series A Preferred Stock to Common Stock. A total of 649,302 shares of Series A Preferred Stock automatically converted to 25,972,080 shares of Common Stock; 437,037 shares of Series A Preferred Stock did not automatically convert and remained outstanding after the conversion.

On December 11, 2023, the Company completed a private placement of shares of Common Stock and Series B non-voting convertible preferred stock, par value of \$0.0001 per share ("Series B Preferred Stock") (convertible on a 40 to 1 basis) (the "December 2023 PIPE") to a group of investors. The Company sold an aggregate of 6,000,000 shares of Common Stock and 150,000 shares of Series B Preferred Stock for an aggregate purchase price of approximately \$180.0 million before deducting approximately \$10.9 million of placement agent and other offering expenses.

On March 20, 2024, the Company completed a private placement of Series B Preferred Stock (convertible on a 40 to 1 basis) (the "March 2024 PIPE") to a group of investors. The Company sold 121,625 shares of Series B Preferred Stock for a purchase price of \$180.0 million before deducting approximately \$11.2 million of placement agent and other offering costs.

On April 23, 2024, the Company entered into an exchange agreement with Fairmount Healthcare Fund II L.P. (the "Stockholder"), pursuant to which the Stockholder agreed to exchange an aggregate of 90,992 shares of Series A Preferred Stock for an aggregate of 3,639,680 shares of 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 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 September 30, 2024.

On September 6, 2024, the Company filed a new shelf registration statement on Form S-3 that was declared effective by the SEC for the potential offering, issuance and sale by the Company of up to \$500.0 million of our common stock, preferred stock, debt securities, warrants and/or units consisting of all or some of these securities. Concurrent with the filing of the shelf-registration statement, the Company entered into a sales agreement with TD Securities (USA) LLC ("TD Cowen"), as its sales agent, pursuant to which the Company may issue and sell shares of its common stock for an aggregate offering price of up to \$200.0 million under an at-the-market ("ATM") offering program included in the shelf registration. In September 2024, the Company sold 426,287 shares of common stock under the ATM at a price per share of \$28.15, resulting in net proceeds of \$11.8 million.

### ***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 September 30, 2024, the Company has funded its operations by raising an aggregate of approximately \$1.1 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 September 30, 2024, Spyre had an accumulated deficit of \$916.1 million, and cash, cash equivalents, and marketable securities of \$414.2 million.

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

### ***Basis of Presentation***

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

### ***Reclassification of Prior Year Presentation***

Certain prior year amounts have been reclassified for consistency with the current year presentation. These reclassifications had no effect on the reported results of operations or balance sheets.

### ***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 September 30, 2024, and its results of operations for the three and nine months ended September 30, 2024 and 2023, changes in convertible preferred stock and stockholders’ equity for the three and nine months ended September 30, 2024 and 2023, and cash flows for the nine months ended September 30, 2024 and 2023. The results of operations for the three and nine months ended September 30, 2024, are not necessarily indicative of the results to be expected for the year ending December 31, 2024 or for any other future annual or interim period. The December 31, 2023 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, 2023 (the “Annual Report”) as filed with the SEC on February 29, 2024 and amended on March 1, 2024.

## **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.

Other than policies noted below, 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.

### ***License Agreements Contingent Milestone Payments***

The Company’s license agreements include specific development, regulatory, and clinical milestone payments that are payable upon the resolution of a contingency, such as upon the selection of a development candidate, first dosing of a human patient in clinical trials or receipt of the Food Drug and Administration’s (“FDA”) approval of a Spyre drug. The achievement of these milestone payments involves many factors outside of the Company’s control and therefore the associated likelihood cannot be considered probable until the

related contingency is resolved. Based on the preceding, the Company accrues each milestone payment upon the achievement of the applicable milestone event.

### **Recently Adopted Accounting Pronouncements**

There have been no recent accounting pronouncements or changes in accounting pronouncements during the nine months ended September 30, 2024 that are of significance or potential significance to the Company.

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

In November 2024, the Financial Accounting Standards Board issued ASU 2024-03 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. This ASU 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 or (2) retrospectively to all prior periods presented in the financial statements. The Company is currently evaluating the impact this ASU will have on our 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):

	September 30, 2024			
	Level 1	Level 2	Level 3	Total
<b>Financial Assets:</b>				
Money market funds	\$ 69,900	\$ —	\$ —	\$ 69,900
U.S. government treasury securities	140,072	—	—	140,072
U.S. government agency securities	—	100,328	—	100,328
Commercial paper	—	75,717	—	75,717
Corporate bonds	—	26,530	—	26,530
<b>Total financial assets</b>	<b>\$ 209,972</b>	<b>\$ 202,575</b>	<b>\$ —</b>	<b>\$ 412,547</b>
<b>Liabilities:</b>				
Parapyre Option Obligation	\$ —	\$ 13,035	\$ —	\$ 13,035
CVR liability	—	—	60,900	60,900
<b>Total liabilities</b>	<b>\$ —</b>	<b>\$ 13,035</b>	<b>\$ 60,900</b>	<b>\$ 73,935</b>

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

### ***Parapyre Option Obligation***

Under the Paragon Agreement, the Company is obligated to issue Parapyre Holding LLC ("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"). The Company determined that the 2023 and 2024 grants are two separate grants, as there would be no obligation for the 2024 grant had the Company exercised or terminated all of the options under the Paragon Agreement prior to December 31, 2023. The service inception period for the grant precedes the grant date, with the full award being vested as of the grant date with no post-grant date service requirement. Accordingly, a liability related to the Parapyre Option Obligation is recorded pursuant to the Paragon Agreement during interim periods. On December 31, 2023, the Company settled its 2023 obligation under the Parapyre Option Obligation by issuing Parapyre 684,407 warrants to purchase the Company's Common Stock, with a \$21.52 per share exercise price for each warrant.

The Parapyre Option Obligation is considered a Level 2 liability based on observable market data for substantially the full term of the liability. The Parapyre Option Obligation is measured each period using a Black-Scholes model to estimate the fair value of the option grant. Changes in the fair value of the Parapyre Option Obligation are recorded as stock-based compensation within Research and development expenses for non-employees who provided pre-clinical development services.

### ***CVR Liability***

In connection with the Asset Acquisition, a non-transferable CVR was distributed to the Legacy Stockholders, but was not distributed to holders of shares of Common Stock or Series A Preferred Stock issued to the June 2023 Investors or former stockholders of Pre-Merger Spyre in connection with the Transactions. Holders of the CVR will be entitled to receive certain cash payments from proceeds received by the Company for a three-year period, if any, related to the disposition or monetization of the Company's legacy assets for a period of one year following the closing of the Asset Acquisition.

The fair value of the CVR liability was determined using the probability weighted discounted cash flow method to estimate future cash flows associated with the sale of the legacy assets. Analogous to a dividend being declared/approved in one period and paid out in another, the liability was recorded at the date of approval, June 22, 2023, as a Common Stock dividend, returning capital to the Legacy Stockholders. Changes in fair

value of the liability will be recognized as a component of Other income (expense) in the consolidated statement of operations and comprehensive loss in each reporting period. The liability value is based on significant inputs not observable in the market such as estimated cash flows, estimated probabilities of regulatory success, and discount rates, which represent a Level 3 measurement within the fair value hierarchy.

The significant inputs used to estimate the fair value of the CVR liability were as follows:

	<b>September 30, 2024</b>
Estimated cash flow dates	05/28/25 - 06/22/26
Estimated probability of success	72% - 100%
Estimated reimbursement rate compared to reimbursement target	81% - 100%
Risk-adjusted discount rates	7.76% - 7.82%

The change in fair value between December 31, 2023 and September 30, 2024 was a \$19.6 million increase, primarily driven by changes in the likelihood of achievement of certain milestones and the time value of money, partially offset by an increase in risk-adjusted discount rates.

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

	<b>CVR Liability</b>
Beginning balance as of December 31, 2023	\$ 42,700
Changes in the fair value of the CVR liability	19,630
Payments	(1,430)
Ending Balance as of September 30, 2024	<u>\$ 60,900</u>

### ***Forward Contract Liability***

In connection with the Asset Acquisition, the Company entered into a contract for the issuance of 364,887 shares of Series A Preferred Stock as part of the consideration transferred. This forward contract was classified as a liability because the underlying preferred shares were contingently redeemable. The forward contract was carried at fair value on the balance sheet, with changes in fair value between the acquisition date and June 30, 2023 recorded in earnings. The liability was settled with the issuance of the Series A Preferred Stock on July 7, 2023.

The fair value of the forward contract as of the acquisition date, June 22, 2023, was \$106.2 million. The liability was settled with the issuance of the Series A Preferred Stock on July 7, 2023 for \$189.7 million. For the three and nine months ended September 30, 2023, \$25.4 million and \$83.5 million, respectively, was recorded as Other (expense) income in the consolidated statements of operations in connection with the change in fair value of the forward contract liability.

#### 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):

September 30, 2024				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
<b>Cash equivalents:</b>				
Money market funds	\$ 69,900	\$ —	\$ —	\$ 69,900
<b>Total cash equivalents</b>	<b>\$ 69,900</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ 69,900</b>
<b>Marketable securities:</b>				
Commercial paper	\$ 75,503	\$ 214	\$ —	\$ 75,717
Corporate bonds	26,457	76	(3)	26,530
U.S. government treasury securities	139,313	768	(9)	140,072
U.S. government agency securities	99,973	363	(8)	100,328
<b>Total marketable securities</b>	<b>\$ 341,246</b>	<b>\$ 1,421</b>	<b>\$ (20)</b>	<b>\$ 342,647</b>
December 31, 2023				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
<b>Cash equivalents:</b>				
Money market funds	\$ 150,648	\$ —	\$ —	\$ 150,648
Commercial paper	24,950	5	—	24,955
U.S. government treasury securities	10,965	1	—	10,966
<b>Total cash equivalents</b>	<b>\$ 186,563</b>	<b>\$ 6</b>	<b>\$ —</b>	<b>\$ 186,569</b>
<b>Marketable securities:</b>				
Commercial paper	\$ 79,124	\$ 62	\$ —	\$ 79,186
Corporate bonds	32,984	81	(1)	33,064
U.S. government treasury securities	21,846	31	—	21,877
U.S. government agency securities	16,147	110	—	16,257
<b>Total marketable securities</b>	<b>\$ 150,101</b>	<b>\$ 284</b>	<b>\$ (1)</b>	<b>\$ 150,384</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 September 30, 2024 and December 31, 2023, aggregated by major security type and length of time in a continuous unrealized loss position:

	September 30, 2024					
	Less Than 12 Months		12 Months or Longer		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
Corporate bonds	\$ 1,952	\$ (3)	\$ —	\$ —	\$ 1,952	\$ (3)
U.S. government treasury securities	17,517	(9)	—	—	17,517	(9)
U.S. government agency securities	18,101	(8)	—	—	18,101	(8)
<b>Total marketable securities</b>	<b>\$ 37,570</b>	<b>\$ (20)</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ 37,570</b>	<b>\$ (20)</b>

	December 31, 2023					
	Less Than 12 Months		12 Months or Longer		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
Corporate bonds	\$ 9,907	\$ (1)	\$ —	\$ —	\$ 9,907	\$ (1)
U.S. government treasury securities	4,831	—	—	—	4,831	—
<b>Total marketable securities</b>	<b>\$ 14,738</b>	<b>\$ (1)</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ 14,738</b>	<b>\$ (1)</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 September 30, 2024 and December 31, 2023, an allowance for credit losses had not been recognized. Given the Company's intent and ability to hold such securities until recovery, and the lack of significant change in credit risk of these investments, the Company does not consider these marketable securities to be impaired as of September 30, 2024 and December 31, 2023.

The financial instruments that potentially subject the Company to a concentration of credit risk consist principally of cash deposits. Accounts at each of our two U.S. banking institutions are insured by the Federal Deposit Insurance Corporation ("FDIC") up to \$250,000 per depositor. As of September 30, 2024 and December 31, 2023, cash deposits at the Company's U.S. banking institutions exceeded the FDIC limits. Uninsured foreign cash deposits were immaterial for both periods.

There were no realized gains or losses on marketable securities for the three and nine months ended September 30, 2024 and 2023. Interest on marketable securities is included in interest income. Accrued interest receivable on available-for-sale debt securities as of September 30, 2024 and December 31, 2023, was \$1.7 million and \$0.9 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):

	September 30, 2024	December 31, 2023
Due in one year or less	\$ 253,613	\$ 115,784
Due in 1 - 2 years	89,034	34,600
<b>Total marketable securities</b>	<b>\$ 342,647</b>	<b>\$ 150,384</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):

	September 30, 2024	December 31, 2023
Accrued compensation	\$ 3,966	\$ 4,054
Accrued contracted research and development costs	7,527	7,092
Accrued professional and consulting fees	1,134	1,474
Accrued other	526	488
Total accrued and other current liabilities	<u>\$ 13,153</u>	<u>\$ 13,108</u>

## 6. Asset Acquisition

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

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

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

The Company concluded that the arrangement met the definition of an asset acquisition rather than a business combination, as substantially all of the fair value of the gross assets acquired was concentrated in a single identifiable asset, Pre-Merger Spyre's option to exclusively license certain intellectual property rights (the "Option"). The Company determined that the Option was a single asset as the Company's strategy relied on developing the entire portfolio of individual treatments to create combination treatments that simultaneously address different mechanisms of inflammatory bowel disease with a single treatment. The Company also determined that the pipeline candidates within the portfolio were similar in nature and risk profile. In addition, the Company did not obtain any substantive processes, assembled workforce, or employees capable of producing outputs in connection with the Asset Acquisition.

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

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

	June 22, 2023
Consideration transferred in Series A Preferred Stock and Common Stock	\$ 110.0
Transaction costs incurred by Pre-Merger Spyre	3.2
<b>Total cost to acquire asset</b>	<b>\$ 113.2</b>

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

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

## 7. Licensing Agreements

On July 12, 2023, December 14, 2023, and June 5, 2024, the Company exercised the Option available under the Paragon Agreement with respect to the SPY001, SPY002, and SPY003 research programs, respectively.

On May 14, 2024, the Company and Paragon entered into (i) a license agreement (the "SPY001 License Agreement"), pursuant to which Paragon granted the Company a royalty-bearing, world-wide, exclusive license to develop, manufacture, commercialize or otherwise exploit certain antibodies and products targeting  $\alpha 4\beta 7$  integrin and (ii) a license agreement (the "SPY002 License Agreement"), pursuant to which Paragon granted the Company a royalty-bearing, world-wide, exclusive license to develop, manufacture, commercialize or otherwise exploit certain antibodies and products targeting TL1A, respectively.

On October 11, 2024, the Company and Paragon entered into a license agreement (the "SPY003 License Agreement" and, together with the SPY001 License Agreement and the SPY002 License Agreement, the "License Agreements"), pursuant to which Paragon granted the Company a royalty-bearing, world-wide, exclusive license to develop, manufacture, commercialize or otherwise exploit certain antibodies and products targeting IL-23 in the field of IBD.

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 \$1.5 million fee for nomination of a development candidate, as applicable, and a further milestone payment of \$2.5 million upon the first dosing of a human patient in a Phase 1 trial. 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 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. During the three and nine months ended September 30, 2024, the Company recognized expense of nil and \$5.5 million related to Paragon license milestone payments recorded within Research and development expenses in the accompanying condensed statement of operations. There was no such expense for the three and nine months ended September 30, 2023.

For the three and nine months ended September 30, 2024, the Company made cash milestone payments to Paragon totaling \$2.5 million and \$5.5 million, respectively. As of September 30, 2024, there were no Paragon license milestone payments outstanding and payable to Paragon.

Additionally, the Company recognized \$0.3 million and \$0.4 million related to sublicensing fees and which was recorded as Research and development expenses in the accompanying condensed statement of operations for the three and nine months ended September 30, 2024, respectively. As of September 30, 2024, \$0.3 million in sublicensing fees were outstanding and payable to Paragon.

## 8. Related Party Transactions

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

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 September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Reimbursable costs under the Paragon Agreement	\$ 1.3	\$ 16.7	\$ 15.3	\$ 17.9
License Agreements milestone and sublicensing fees	0.3	—	5.9	—
<b>Total related party expense (excludes stock comp)</b>	<b>\$ 1.6</b>	<b>\$ 16.7</b>	<b>\$ 21.2</b>	<b>\$ 17.9</b>

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

	September 30, 2024	December 31, 2023
Reimbursable costs under the Paragon Agreement	\$ 1.2	\$ 16.6
Parapyre warrants liability	13.0	—
License Agreements development milestone liability (see Note 7)	0.3	—
Total related party accounts payable	<u>\$ 14.5</u>	<u>\$ 16.6</u>

### ***Paragon Agreement***

In connection with the Asset Acquisition, the Company assumed the rights and obligations of Pre-Merger Spyre under the Paragon Agreement. Under the Paragon Agreement, Spyre is obligated to compensate Paragon for its services performed under each research program based on the actual costs incurred with mark-up costs pursuant to the terms of the Paragon Agreement. Spyre is also obligated under the Paragon Agreement to issue Parapyre annual equity grants of warrants in accordance with the Parapyre Option Obligation.

On July 12, 2023, December 14, 2023, and June 5, 2024, the Company exercised the Option available under the Paragon Agreement with respect to the SPY001, SPY002 and SPY003 research programs, respectively. Our Option available under the Paragon Agreement with respect to the SPY004 program remains unexercised. Please refer to Note 7 for additional information on the License Agreements related to the exercised options.

On May 14, 2024, the Company, Paragon and Parapyre entered into a second amended and restated antibody discovery and option agreement that amends and restates that certain amended and restated antibody discovery and option agreement, dated September 29, 2023, by and between Paragon, Parapyre and Spyre Therapeutics, LLC, in order to, among other things, (i) replace the Company's subsidiary with the Company as a party to the agreement and (ii) amend certain terms related to the SPY003 research program, including without limitation, (a) establishing an SPY003 antibody selection process pursuant to which the Company and Paragon shall alternate in turn to select a project antibody to be included and excluded, respectively, from the Company's rights under its option to license certain intellectual property rights related to SPY003 from Paragon until all project antibodies under the SPY003 research program have been selected; (b) reducing the development costs invoiced to the Company for the SPY003 research program incurred from and after April 1, 2024 through completion of the SPY003 antibody selection process by 50%; (c) requiring Paragon to reimburse the Company for 50% of the development costs for the SPY003 research program incurred prior to April 1, 2024; provided, that Paragon receives rights to at least one SPY003 project antibody following completion of the SPY003 antibody selection process; (d) obligating the Company to exercise its option to license the intellectual property rights to SPY003 project antibodies and technology following the completion of the SPY003 antibody selection process; and (e) establishing a license agreement term sheet for the SPY003 research program with substantially similar milestone payment terms and royalty payment terms as the SPY001 License Agreement. Please refer to Note 7 for additional disclosures.

For the three and nine months ended September 30, 2024, the Company recognized expenses related to services provided by Paragon totaling \$7.4 million and \$28.3 million, respectively, which included \$6.1 million and \$13.0 million, respectively, of stock-based compensation expense, and were recorded as Research and development expenses in the consolidated statements of operations. Included within the expenses recognized for services provided by Paragon for the nine months ended September 30, 2024, is a \$5.9 million reduction in Research and development expenses related to the reimbursement of 50% of the development costs for the SPY003 research program by Paragon.

For the three and nine months ended September 30, 2024, the Company made payments totaling \$1.2 million and \$30.7 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. See Note 10 for disclosures related to the Parapyre Option Obligation.

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

See Note 7 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 8) 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 the three and nine months ended September 30, 2024, the Company recognized \$0.3 million and \$0.8 million, respectively, in stock-based compensation expense related to Mr. McKenna's consulting agreement. There was no such expense for the three and nine months ended September 30, 2023.

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

### ***Pre-Funded Warrants***

In February 2019, April 2020 and May 2022, the Company issued pre-funded warrants to purchase the Company's Common Stock in underwritten public offerings at the offering price of the Common Stock, less the \$0.0025 per share exercise price of each warrant. The warrants were recorded as a component of stockholders' (deficit) equity within additional paid-in capital and have no expiration date. Per the terms of the warrant agreements, the outstanding warrants to purchase shares of Common Stock may not be exercised if the holder's ownership of the Company's Common Stock would exceed 4.99% ("Maximum Ownership Percentage"), or 9.99% for certain holders. By written notice to the Company, each holder may increase or decrease the Maximum Ownership Percentage to any other percentage (not in excess of 19.99% for the majority of such warrants). The revised Maximum Ownership Percentage would be effective 61 days after the notice is received by the Company.

As of September 30, 2024, all pre-funded warrants have been exercised and none remain outstanding.

### ***Parapyre Warrants***

The Company settled its 2023 obligations under the Parapyre Option Obligation by issuing Parapyre 684,407 warrants to purchase the Company's Common Stock, with a \$21.52 per share exercise price for each warrant. Pursuant to the terms of the warrant agreement, the outstanding warrants to purchase shares of Common Stock may not be exercised if the holder's ownership of the Company's Common Stock would exceed 4.99%. As of September 30, 2024, none of the warrants issued under the Parapyre Option Obligation have been exercised.

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

On June 22, 2023, the Company filed a Certificate of Designation of Preferences, Rights and Limitations of the Series A Preferred Stock with the Secretary of State of the State of Delaware (the "Series A Certificate of Designation") in connection with the Asset Acquisition and the June 2023 PIPE.

Pursuant to the Series A Certificate of Designation, holders of Series A Preferred Stock are entitled to receive dividends on shares of Series A Preferred Stock equal to, on an as-if-converted-to-Common Stock basis, and in the same form as, dividends actually paid on shares of Common Stock. Except as provided in the Series A Certificate of Designation or as otherwise required by law, the Series A Preferred Stock does not have voting rights. However, as long as any shares of Series A Preferred Stock are outstanding, the Company will not, without the affirmative vote of the holders of a majority of the then outstanding shares of the Series A Preferred Stock: (a) alter or change adversely the powers, preferences or rights given to the Series A Preferred Stock, or alter or amend the Series A Certificate of Designation, amend or repeal any provision of, or add any provision to, the Company's Certificate of Incorporation or its Bylaws, or file any articles of amendment, certificate of designations, preferences, limitations and relative rights of any series of preferred stock, if such action would adversely alter or change the preferences, rights, privileges or powers of, or restrictions provided for the benefit of the Series A Preferred Stock, regardless of whether any of the foregoing actions will be by means of amendment to the Certificate of Incorporation or by merger, consolidation, recapitalization, reclassification, conversion or otherwise, (b) issue further shares of Series A Preferred Stock or increase or decrease (other than by conversion) the number of authorized shares of Series A Preferred Stock, (c) prior to the stockholder approval of the conversion of the Series A Preferred Stock into shares of Common Stock in accordance with Nasdaq Stock Market Rules (the "Series A Conversion Proposal") or at any time while at least 30% of the originally issued Series A Preferred Stock remains issued and outstanding, consummate (x) any Fundamental Transaction (as defined in the Series A Certificate of Designation) or (y) any merger or consolidation of the Company with or into another entity or any stock sale to, or other business combination in which our stockholders immediately before such transaction do not hold at least a majority of our capital stock immediately after such transaction or (d) enter into any agreement with respect to any of the foregoing. The Series A Preferred Stock does not have a preference upon any liquidation, dissolution or winding-up of the Company.

On June 26, 2023, the Company completed a private placement of 721,452 shares of Series A Preferred Stock in exchange for gross proceeds of approximately \$210.0 million, or net proceeds of \$197.3 million, after deducting placement agent and other offering costs.

On July 7, 2023, the Company issued 364,887 shares of Series A Preferred Stock as part of its consideration transferred in connection with the Asset Acquisition that closed on June 22, 2023 which settled the related forward contract liability.

On November 21, 2023, the Company's stockholders approved the Series A Conversion Proposal, among other matters, at a special meeting of stockholders. As a result of the approval of the Series A Conversion Proposal, all conditions that could have required cash redemption of the Series A Preferred Stock were satisfied. Since the Series A Preferred Stock is no longer redeemable, the associated balances of the Series A Preferred Stock were reclassified from mezzanine equity to permanent equity during the fourth quarter of 2023.

Following stockholder approval of the Series A Conversion Proposal, each share of Series A Preferred Stock automatically converted into 40 shares of Common Stock, subject to certain limitations, including that a holder of Series A Preferred Stock is prohibited from converting shares of Series A Preferred Stock into shares of Common Stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (established by the holder between 0.0% and 19.9%) of the total number of shares of Common Stock issued and outstanding immediately after giving effect to such conversion. 649,302 shares of Series A Preferred Stock automatically converted to 25,972,080 shares of Common Stock; 437,037 shares of Series A Preferred Stock did not automatically convert and remained outstanding following the conversion. This conversion was recorded as a reclassification between Series A Preferred Stock and Common Stock based on the historical per-share contributed capital amount of the Series A Preferred Stock.

On April 23, 2024, in connection with the April 2024 Exchange, the Stockholder agreed to exchange an aggregate of 90,992 shares of Series A Preferred Stock for an aggregate of 3,639,680 shares of the Company's Common Stock. This exchange was recorded as a reclassification between Series A Preferred Stock and Common Stock based on the historical per-share contributed capital amount, inclusive of any forward-contract valuation adjustments, of the Series A Preferred Stock. Following the April 2024 Exchange, 346,045 shares of Series A Preferred Stock remained outstanding.

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

On December 8, 2023, the Company filed a Certificate of Designation of Preferences, Rights and Limitations of Series B Non-Voting Convertible Preferred Stock with the Secretary of State of the State of Delaware (the "Series B Certificate of Designation") in connection with the December 2023 PIPE.

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

On December 11, 2023, as part of the December 2023 PIPE, the Company completed a private placement of 150,000 shares of Series B Preferred Stock in exchange for gross proceeds of \$90.0 million.

On March 18, 2024, in connection with the March 2024 PIPE, the Company filed a certificate of amendment to its Series B Certificate of Designation to increase the number of authorized shares of Series B Preferred Stock from 150,000 to 271,625.

On March 20, 2024, as part of the March 2024 PIPE, the Company completed a private placement of 121,625 shares of Series B Preferred Stock in exchange for gross proceeds of approximately \$180.0 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 the Common Stock, subject to certain limitations, including that a holder of Series B Preferred Stock is prohibited from converting shares of Series B Preferred Stock into shares of Common Stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than a specified percentage (established by the holder between 0.0% 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 September 30, 2024 due to beneficial ownership limitations. This conversion was recorded as a reclassification between Series B Preferred Stock and Common Stock based on the historical per-share contributed capital amount of the Series B Preferred Stock.

### **S-3 Shelf & ATM**

On September 6, 2024, the Company filed a new shelf registration statement on Form S-3 that was declared effective by the SEC for the potential offering, issuance and sale by the Company of up to \$500.0 million of our common stock, preferred stock, debt securities, warrants and/or units consisting of all or some of these securities. Concurrent with the filing of the shelf-registration statement, the Company entered into

a sales agreement (the "Sales Agreement") with TD Securities (USA) LLC ("TD Cowen"), as its sales agent, pursuant to which the Company may issue and sell shares of its common stock for an aggregate offering price of up to \$200.0 million under an at-the-market ("ATM") offering program included in the shelf registration. In September 2024, the Company sold 426,287 shares of common stock under the ATM at a price per share of \$28.15 resulting in net proceeds of \$11.8 million. As of November 1, 2024, \$188.0 million remained available for sale under the Sales Agreement.

## **10. Stock-Based Compensation**

### ***2015 Equity Incentive Plan***

In March 2015, the Company adopted the 2015 Equity Incentive Plan ("2015 Plan"), administered by the board of directors, and provides for the Company to sell or issue share of Common Stock or restricted Common Stock, or to grant incentive stock options or nonqualified stock options for the purchase of Common Stock, to employees, members of the board of directors and consultants of the Company. The Company granted options under the 2015 Plan until April 2016 when it was terminated as to future awards, although it continues to govern the terms of options that remain outstanding under the 2015 Plan.

As of September 30, 2024, a total of 952 shares of Common Stock are subject to options outstanding under the 2015 Plan and will become available under the 2016 Equity Incentive Plan ("2016 Plan") to the extent the options are forfeited or lapse unexercised.

### ***2016 Equity Incentive Plan***

The 2016 Plan became effective in April 2016 and serves as the successor to the 2015 Plan. Under the 2016 Plan, the Company may grant stock options, stock appreciation rights, restricted stock awards, restricted stock units, performance awards, and stock bonuses. The 2016 Plan, 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, 2024 and 2023, an additional 3,023,650 and 104,561 shares, respectively, became available for issuance under the 2016 Plan.

As of September 30, 2024, the 2016 Plan had 7,228,113 shares available for future issuance, of which 3,247,677 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 third quarter of 2024, the Company amended the 2018 Plan to increase the number of shares of Common Stock reserved for issuance by 1,000,000. After this amendment and as of September 30, 2024, the 2018 Plan had 6,999,445 shares available for future issuance, of which 5,624,067 shares were subject to outstanding option awards and restricted unit awards.

Service-based awards granted under the 2018 Plan, 2016 Plan, and 2015 Plan generally vest over four years and expire after ten years, although awards have been granted with vesting terms less than four years. Under the 2016 Plan and 2018 Plan, the Company may grant stock-based awards with service conditions ("service-based" awards), performance conditions ("performance-based" awards), and market conditions ("market-based" awards).

### ***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 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.

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 September 30,				Nine Months Ended September 30,			
	2024		2023		2024		2023	
	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	425,500	\$ 25.74	1,044,667	\$ 14.50	1,857,853	\$ 28.40	3,867,366	\$ 9.65

### **Parapyre Option Obligation**

As of September 30, 2024, the pro-rated estimated fair value of the options to be granted on December 31, 2024 related to the Parapyre Option Obligation, was approximately \$13.0 million. For the three and nine months ended September 30, 2024, \$6.1 million and \$13.0 million, respectively, was recognized as stock compensation expense related to the Parapyre Option Obligation. For the three and nine months ended September 30, 2023, \$2.7 million and \$2.9 million, respectively, was recognized as stock compensation expense related to the Parapyre Option Obligation. As of September 30, 2024, the unamortized expense related to the Parapyre Option Obligation was \$4.4 million.

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

Under the Company's 2016 Employee Stock Purchase Plan ("2016 ESPP"), the Company issued and sold 14,053 and 16,383 shares during the three and nine months ended September 30, 2024, respectively, and sold 704 and 2,496 shares during the three and nine months ended September 30, 2023, respectively. The aggregate cash proceeds were not material for all periods.

### **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 September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Research and development <sup>(1)</sup>	\$ 8,555	\$ 2,965	\$ 18,863	\$ 4,136
General and administrative	4,545	1,820	16,754	4,269
Total stock-based compensation expense <sup>(2)</sup>	\$ 13,100	\$ 4,785	\$ 35,617	\$ 8,405

<sup>(1)</sup> For the three and nine months ended September 30, 2024, \$6.1 million and \$13.0 million, respectively, was recognized as stock compensation expense related to the Parapyre Option Obligation. For the three and nine months ended September 30, 2023, \$2.7 million and \$2.9 million, respectively, was recognized as stock compensation expense related to the Parapyre Option Obligation.

<sup>(2)</sup> Of the total \$13.1 million and \$35.6 million of stock-based compensation expense for the three and nine months ended September 30, 2024, \$0.1 million and \$3.6 million, respectively, is related to legacy Aeglea employees and directors who had been terminated as of the end of the respective period. Of the total \$4.8 million and \$8.4 million of stock-based compensation expense for the three and nine months ended September 30, 2023, \$0.8 million and \$4.2 million, respectively, is related to legacy Aeglea employees and directors who had been terminated as of the end of the period.

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 purchasable under the 2016 ESPP during the periods presented:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
<b>Stock Options Granted</b>				
Expected term (in years)	6.08	6.08	6.02	6.04
Expected volatility	105%	101%	105%	111%
Risk-free interest	4.13%	4.28%	4.03%	4.07%
Dividend yield	—	—	—	—
<b>2016 ESPP</b>				
Expected term (in years)	0.50	0.50	0.50	0.49
Expected volatility	71%	222%	83%	181%
Risk-free interest	5.02%	5.29%	5.15%	4.99%
Dividend yield	—	—	—	—

## 11. Legacy Strategic License Agreements

On March 21, 2021, the Company entered into an exclusive license and supply agreement with Immedica (the "Immedica Agreement"). On July 27, 2023, the Company announced that it had entered into an agreement to sell the global rights to pegzilarginase, an investigational treatment for the rare metabolic disease Arginase 1 Deficiency, to Immedica for \$15.0 million in upfront cash proceeds and up to \$100.0 million in contingent milestone payments. The sale of pegzilarginase to Immedica superseded and terminated the Immedica Agreement.

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. In addition to the payment previously made to holders of the Company's CVRs (as defined in Note 1) related to the upfront cash proceeds, any contingent milestone payments under the Immedica Agreement, if paid within the CVR period, will be distributed to holders of the Company's CVRs net of expenses and adjustments pursuant to the contingent value rights agreement we entered into with Equiniti Trust Company LLC (f/k/a American Stock Transfer & Trust Company LLC) as rights agent in connection with the Asset Acquisition.

The Company did not recognize any revenue under the Immedica Agreement for the three and nine months ended September 30, 2024. For the nine months ended September 30, 2023, the Company recognized \$0.9 million of development fee revenue in connection with the Immedica Agreement, which was attributable to the PEACE Phase 3 trial and BLA package for pegzilarginase. There was no such revenue for the three months ended September 30, 2023.

For more details on the Immedica Agreement, which was terminated on July 27, 2023, please refer to the Note under Item 1 of Part I, titled "12. Strategic License Agreements" of the Company's Annual Report.

### **Contract Balances from Customer Contract**

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

The Company did not have any contract assets or liabilities as of September 30, 2024 and December 31, 2023.

## 12. 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, an investigational treatment for the rare metabolic disease Arginase 1 Deficiency, to Immedica for \$15.0 million in upfront cash proceeds and up to \$100.0 million in contingent milestone payments. The sale of pegzilarginase to Immedica superseded and terminated the previous license agreement between the Company and Immedica. On July 27, 2023, the carrying value of the asset was zero as it was internally developed. Accordingly the Company recognized a \$14.6 million gain within operating expenses, which is the full \$15.0 million in upfront cash proceeds, net of transaction costs and the derecognition of pegzilarginase related nonfinancial assets and liabilities.

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

## 13. Net Loss Per Share

The Company computes net loss attributable per common stockholder using the two-class method required for participating securities. The Company considers convertible preferred stock to be participating securities. In the event that the Company paid out distributions, holders of convertible preferred stock would participate in the distribution.

The two-class method is an earnings (loss) allocation method under which earnings (loss) per share is calculated for Common Stock and participating security considering a participating security's rights to undistributed earnings (loss) as if all such earnings (loss) had been distributed during the period. The holders of Series A Preferred Stock and Series B Preferred Stock do not have an obligation to fund losses and therefore the Series A Preferred Stock and the Series B Preferred Stock were excluded from the calculation of basic net loss per share.

Basic and diluted net loss per share is computed by dividing the net loss by the weighted-average number of Common Stock and pre-funded warrants outstanding during the period, without consideration of potential dilutive securities. The pre-funded warrants are included in the computation of basic net loss per share as the exercise price is negligible and they are fully vested and exercisable. For periods in which the Company generated a net loss, the Company does not include the potential impact of dilutive securities in diluted net loss per share, as the impact of these items is anti-dilutive. The Company has generated a net loss for all periods presented, therefore diluted net loss per share is the same as basic net loss per share since the inclusion of potentially dilutive securities would be anti-dilutive.

The following weighted-average equity instruments were excluded from the calculation of diluted net loss per share because their effect would have been anti-dilutive for the periods presented:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Options to purchase common stock	4,733,609	3,135,672	4,583,260	1,426,224
Unvested restricted stock units	65,925	—	69,503	252
Outstanding Parapyre warrants	684,407	—	684,407	—
Series A Preferred Stock <sup>(1)</sup>	13,841,800	—	15,369,403	—
Series B Preferred Stock <sup>(1)</sup>	666,680	—	340,639	—

<sup>(1)</sup> Assumes each share is converted to 40 shares of Common Stock, in accordance with the terms of the respective certificate of designation without regard to any beneficial ownership limitations.

The following is a reconciliation of the shares used as the denominator for the calculation of basic and diluted net loss per share:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Weighted average Common Stock	50,889,433	4,015,661	44,146,958	3,116,434
Weighted average pre-funded warrants	—	278,151	116,788	845,112
Total basic and diluted weighted average shares	50,889,433	4,293,812	44,263,746	3,961,546

## 14. Restructuring Charges

### *Severance and Stock Compensation*

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

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

### *Sale of Assets*

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

### *Lease Right-of-use Asset and Leasehold Improvement Impairment*

Effective June 30, 2023, the Company abandoned its leased office space in Austin, Texas. As a result, the Company recognized an impairment loss of \$0.9 million related to the operating lease right-of-use asset and \$1.7 million related to leasehold improvements. On August 7, 2023, the Company terminated its building lease in Austin, Texas. The negotiated termination agreement obligated the Company to pay the lessor a \$2.0 million termination fee in exchange for releasing the Company of all further obligations under the lease.

All charges related to the restructuring activities were recognized during the second quarter of 2023. No further restructuring charges were incurred under the restructuring plan. A summary of the charges related to the restructuring activities is as follows (in thousands):

	Severance Related Expenses	Stock Compensation Expenses	Loss on Disposal of Long Lived Assets	Lease Asset Impairment	Total Restructuring Costs
Research and development	\$ 3,182	\$ 123	\$ 749	\$ 1,405	\$ 5,459
General and administrative	3,266	870	182	1,175	5,493
Total	\$ 6,448	\$ 993	\$ 931	\$ 2,580	\$ 10,952

As of December 31, 2023, \$1.1 million of restructuring costs remained outstanding and unpaid. As of September 30, 2024, there were no remaining liabilities under the restructuring plan described above.

## **15. Subsequent Events**

On October 1, 2024, the Company appointed Sheldon Sloan, M.D., M. Bioethics, to serve as its Chief Medical Officer.

On October 11, 2024, the Company and Paragon entered into the SPY003 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 IL-23 in the field of IBD.

## 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 on Form 10-Q for the quarterly period ended September 30, 2024 (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, 2023 (the "Annual Report") filed with the Securities and Exchange Commission (the "SEC") on February 29, 2024 and amended on March 1, 2024. 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. Our actual results and outcomes could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section of this Quarterly Report entitled "Risk Factors." As used in this Quarterly Report, unless the context suggests otherwise, "we," "us," "our," "the Company," "Aeglea BioTherapeutics, Inc." or "Spyre" refers to Spyre Therapeutics, Inc. and its consolidated subsidiaries, including Spyre Therapeutics, LLC, taken as a whole.*

### Acquisition of Pre-Merger Spyre

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

Through the Asset Acquisition, we received the option to license certain intellectual property rights related to four research programs (collectively, the "Option"). On July 12, 2023, we exercised the Option with respect to one of these research programs to be granted an exclusive license to all of Paragon's rights, title and interest in and to intellectual property rights, including inventions, patents, sequence information and results, under SPY001, our  $\alpha\beta7$  integrin program, to develop and commercialize antibodies and products worldwide in all therapeutics disorders. If this research program is pursued non-provisionally and matures into issued patents, we would expect those patents to expire no earlier than 2044, subject to any disclaimers or extensions. On December 14, 2023, we exercised the Option under the Paragon Agreement to be granted an exclusive license to all of Paragon's rights, title and interest in and to intellectual property rights, including inventions, patents, sequence information and results, under SPY002, our TL1A program, to develop and commercialize antibodies and products worldwide in all therapeutics disorders. If this research program is pursued non-provisionally and matures into issued patents, we would expect those patents to expire no earlier than 2044, subject to any disclaimers or extensions. On June 5, 2024, we exercised the Option under the Paragon Agreement to be granted an exclusive license to all of Paragon's rights, title and interest in and to intellectual property rights, including inventions, patents, sequence information and results, under SPY003, our IL-23 program, to develop and commercialize antibodies and products worldwide solely in inflammatory bowel disease ("IBD") indications. If this research program is pursued non-provisionally and matures into issued patents, we would expect those patents to expire no earlier than 2045, subject to any disclaimers or extensions. The License Agreements pertaining to SPY001 and SPY002 between the Company and Paragon were executed in the second quarter of 2024, and the License Agreement pertaining to SPY003 was executed in October 2024. Furthermore, as of the date of this Quarterly Report, the Option remains unexercised with respect to the intellectual property rights related to the last remaining research program under the Paragon Agreement, SPY004.

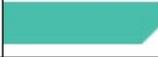
### Overview

Following the Asset Acquisition, we have significantly reshaped the business into a clinical stage biotechnology company focused on developing next generation therapeutics for patients living with IBD, including ulcerative colitis ("UC") and Crohn's disease ("CD"). Our portfolio of novel and proprietary monoclonal

antibody product candidates has the potential to address unmet needs in IBD care by improving efficacy, safety, and/or dosing convenience relative to products currently available or product candidates in development. We have engineered our product candidates with the aim to bind potently and selectively to their target epitopes and to exhibit extended pharmacokinetic half-lives through modifications in the Fc domain, which modifications are designed to increase affinity to human FcRn and increase antibody recycling. We anticipate that half-life extension will enable less frequent administration as compared to marketed or development-stage mAbs that do not incorporate half-life extension modifications. In addition to the development of our product candidates as potential monotherapies, we plan to investigate combinations of our proprietary antibodies in nonclinical studies and clinical trials in order to evaluate whether combination therapy (co-administration or co-formulation of multiple monoclonal antibodies) can lead to greater efficacy, as compared to monotherapies in IBD. We also intend to examine patient selection strategies via complementary diagnostics utilized in our clinical trials to evaluate whether patients may be matched to the optimal therapy based on genetic background and/or other biomarker signatures. We intend to deliver our product candidates through convenient, infrequently self-administered, subcutaneous maintenance injections, although the specific delivery mechanism or technology has not been selected given our early stage.

## Our Portfolio

We are advancing a pipeline of monoclonal antibodies (“mAbs”) for the treatment of IBD (UC and CD) and plan to develop patient selection approaches for each of our programs. The following table summarizes the our programs:

TARGET	PROGRAM	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
$\alpha 4\beta 7$	SPY001				Phase 1 interim data expected YE24
TL1A	SPY002				Phase 1 interim data expected 1H25
IL-23	SPY003				Phase 1 interim data expected 2H25
$\alpha 4\beta 7$ + TL1A	SPY120				
$\alpha 4\beta 7$ + IL-23	SPY130				
TL1A + IL-23	SPY230				

We have one other early-stage program, SPY004, a monoclonal antibody that targets a novel mechanism of action (“MOA”).

We have nominated development candidates for SPY001, SPY002, and SPY003. We executed the License Agreements with Paragon for SPY001 and SPY002 in the second quarter of 2024 and we executed the SPY003 License Agreement in the fourth quarter of 2024. The SPY001 and SPY002 licenses are indication agnostic, and the SPY003 license is restricted to IBD. We additionally have an exclusive option under the agreement for a discovery stage program targeting a novel MOA that also incorporates half-life extension (SPY004). We have sole development responsibility for SPY001, SPY002, and SPY003. We and Paragon have established a Joint Development Committee, comprised of two employees from Spyre and two employees from Paragon, to jointly direct research and development work for SPY004 prior to the execution of a license agreement for such program. We have final decision rights regarding the budget for the SPY004 research program. See the section titled “Paragon Agreement” for more information on the Paragon Agreement, including the Option.

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

For a discussion of the risks associated with our portfolio, see Item 1A, “Risk Factors” included in this Quarterly Report.

#### 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 lymphocytes to the gut, leading to a decrease in inflammation. Since it specifically targets the gut immune system, SPY001 is designed to minimize systemic immunosuppressive effects unrelated to IBD pathology.

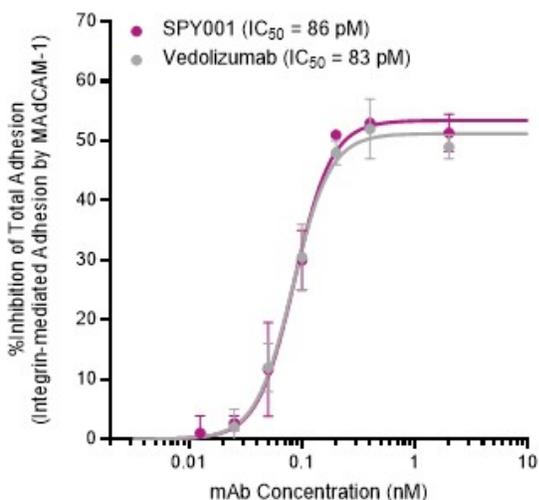
SPY001 preclinical characterization studies were conducted in-house with support from third party vendors. SPY001 demonstrates similar potency and selectivity as synthesized vedolizumab in preclinical *in vitro* models including surface plasmon resonance (n=5 concentrations) and cellular adhesion assays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

The 28-day GLP toxicity study in NHPs (n=42) for SPY001 was completed with the highest dose level tested determined as the no-observed-adverse-effect-level. The Company initiated a FIH Phase 1 trial for SPY001 in June 2024. The SPY001 Phase 1 trial is a double blind, placebo-controlled trial in healthy volunteers and consists of a single-ascending dose (SAD) component and a multi-ascending dose (MAD) component. The trial design includes enrolling 56 healthy adult participants into five SAD cohorts and two MAD cohorts. Additional cohorts may be added to the study to evaluate pharmacokinetics in healthy volunteers of various ethnicities to facilitate subsequent global clinical trials. The primary endpoint is safety, with pharmacokinetics (PK) and Anti-drug Antibodies (ADA) serving as secondary endpoints. We expect interim safety and PK data from this trial by year-end 2024. If successful, SPY001 would then advance to Phase 2 clinical trials and, pending further success, Phase 3 clinical trials to support global regulatory submissions and commercial approval.

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

## Potent and selective inhibition of cellular adhesion

### SPY001 and vedolizumab potently inhibit MAdCAM-1-mediated (gut) cellular adhesion



### No inhibition of unwanted VCAM-1-mediated (CNS) cellular adhesion

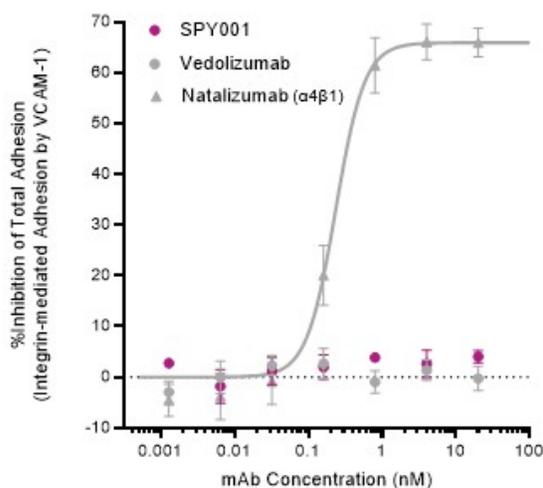
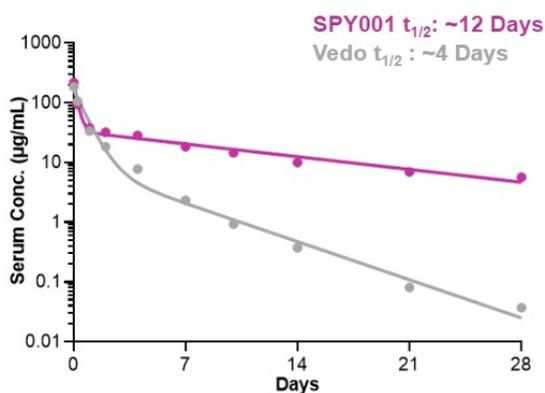
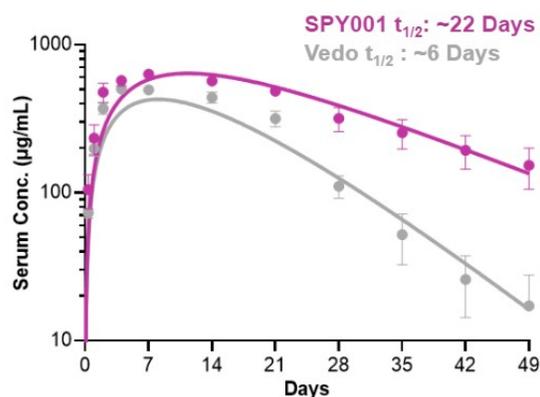


Figure 2. Pharmacokinetic concentration-time curves of SPY001 compared to synthesized vedolizumab in Tg276 transgenic mice and non-human primates (Data on file. Initial group size was n=5 in mouse study (left) and n=6 in NHP study (right). Animals with suspected ADAs were excluded from half-life analysis; this did not impact the mouse study but resulted in n=5/cohort for SPY001 and n=3/cohort for vedolizumab at Day 49 of the NHP study.).

### >3x increased half-life in Tg276 mice



### >3x increased half-life in NHPs



### SPY002 – anti-TL1A mAb

For our co-lead program, SPY002, we have nominated two highly potent, highly selective, and fully human mAb candidates designed to bind to tumor necrosis factor-like ligand 1A (“TL1A”), both of which are in preclinical development for the treatment of IBD (UC and CD). TL1A is a protein that plays a role in regulating

the immune system and is elevated in the gut tissue of individuals with IBD. TL1A interacts with its receptor, death receptor 3 (“DR3”), which is expressed in various immune cells, including T cells. This interaction triggers signaling pathways that contribute to inflammation and immune system activation, leading to IBD symptomology. The SPY002 candidates have been designed to block the interaction between TL1A and DR3, and thereby inhibit the downstream signaling events and dampen the inflammatory response. By neutralizing TL1A, we believe the SPY002 candidates have the potential to modulate the immune response in IBD patients, potentially reducing disease activity and promoting mucosal healing.

SPY002 preclinical characterization studies were conducted in-house with support from third party vendors. Our extensive discovery campaign has identified two lead candidates which bind TL1A monomers and trimers and have subnanomolar potency in cellular assays (see Figure 3, n=4 replicates per group per study). The candidates also exhibited extended pharmacokinetic half-lives of greater than two to three-fold relative to synthesized competitor molecules in clinical development that do not incorporate half-life extending modifications, based on head-to-head preclinical studies in NHPs (see Figure 4, n=5 per group).

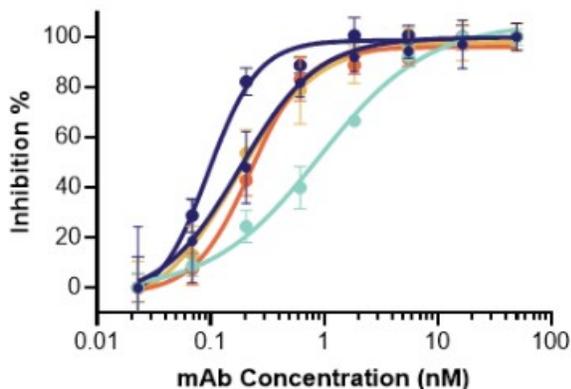
The 42-day GLP toxicity studies in NHPs (n=42) for both SPY002 candidates were completed with the highest dose level tested determined as the no-observed-adverse-effect-level. The Company expects to initiate two FIH trials in healthy volunteers in the fourth quarter of 2024, one for each of our SPY002 candidates, followed by interim safety and PK data from these trials in the first half of 2025. If successful, one SPY002 candidate would then advance to Phase 2 clinical trials and, pending further success, Phase 3 clinical trials to support global regulatory submissions and commercial approval.

Figure 3. Inhibition of TL1-A induced TF-1 cell apoptosis (left) and IFN $\gamma$  secretion in primary human whole blood 1 donor of 4 donors profiled (right) (Data on file. Duvakitug was not benchmarked in IFN $\gamma$  secretion assay; Duvakitug, RO7790121, and tulisokibart are synthesized comparator antibodies).

## Superior or comparable potency in multiple assays

### Superior or comparable inhibition of TF-1 apoptosis

- SPY002 candidates
- RO7790121
- Duvakitug
- Tulisokibart



### Superior or comparable inhibition of IFN $\gamma$ secretion

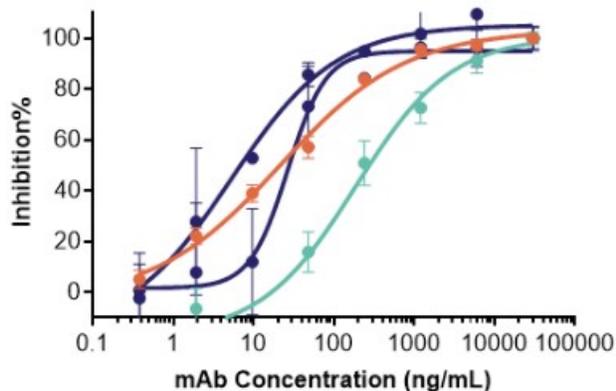
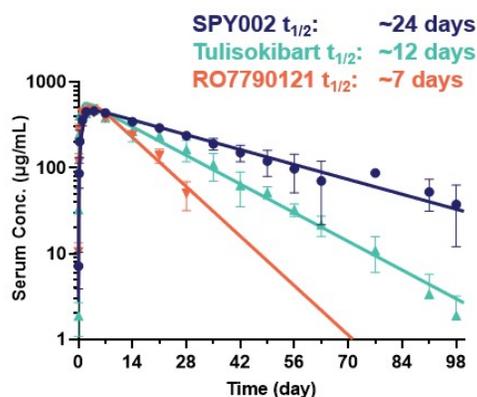
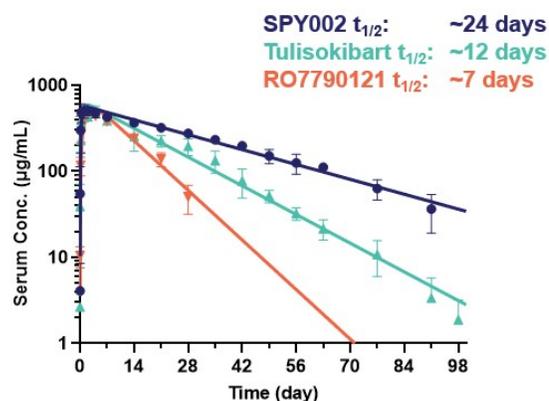


Figure 4. Pharmacokinetic concentration-time curves of SPY002 candidates compared to synthesized competing anti-TL1A molecules in non-human primates (Data on file. Group size was n=5 for SPY002 mAbs and tulisokibart at final endpoints for half-life determination; No RO7790121 detected after day 28. Duvakitug not compared in these models given low human half-life (7-10 days).).

#### SPY002 DC1: >2-3x Increased Half-life in NHPs



#### SPY002 DC2: >2-3x Increased Half-life in NHPs



#### SPY003 – anti-IL-23 mAb

SPY003 is a preclinical-stage program designed to bind to Interleukin 23 (“IL-23”) and incorporates half-life extending modifications. IL-23 is a cytokine that is produced by immune cells and is involved in immune response regulation. IL-23 promotes the survival, expansion, and activity of Th17 cells. Th17 cells produce inflammatory cytokines, such as IL-17, which contribute to the inflammation seen in IBD. IL-23 also helps in the recruitment and activation of other immune cells, such as neutrophils, which further contribute to tissue damage in the gut. We have begun IND-enabling studies for SPY003 and expect to initiate FIH trials in the first quarter of 2025.

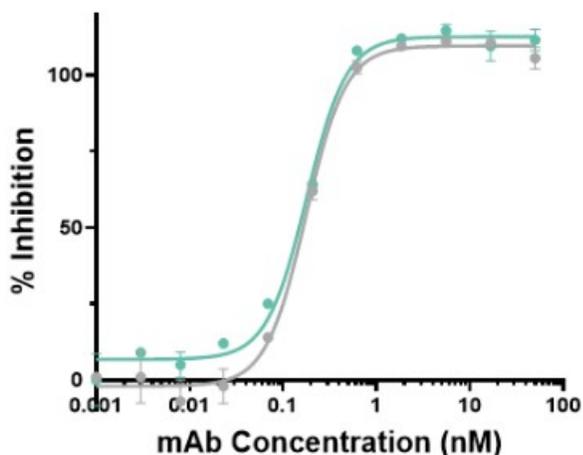
SPY003 preclinical characterization studies were conducted in-house with support from third party vendors. Our extensive discovery campaign has identified a lead candidate which binds to the p19 subunit of IL-23 with subnanomolar potency in cellular assays (see Figure 5, n=2 and n=3 for pSTAT assay and IL-17 assay, respectively). The development candidate also exhibited extended pharmacokinetic half-life of greater than three-fold relative to a synthesized risankizumab comparator that does not incorporate half-life extending modifications, based on head-to-head preclinical studies in NHPs (see Figure 6, n=4 per group with n=4 and n=3 at the final timepoint for half-life determination for SPY003 and risankizumab, respectively).

The 28-day GLP toxicity studies in NHPs is ongoing. The Company expects to initiate a FIH trial in healthy volunteers in the first quarter of 2025, followed by interim safety and PK data from these trials in the second half of 2025. If successful, SPY003 would then advance to Phase 2 clinical trials and, pending further success, Phase 3 clinical trials to support global regulatory submissions and commercial approval.

Figure 5. Inhibition of IL-23 induced STAT3 phosphorylation in a human lymphoma cell line (DB) (left) and IL-23 induced IL-17 secretion in human peripheral blood mononuclear cells (right) by SPY003 and synthesized risankizumab (Data on file).

### Comparable potency in multiple assays

**SPY003 and risankizumab potently inhibit pSTAT signaling**



**SPY003 and risankizumab potently inhibit IL-17 release**

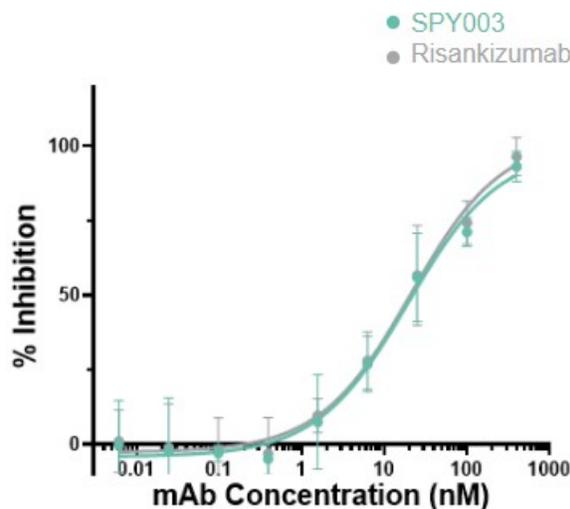
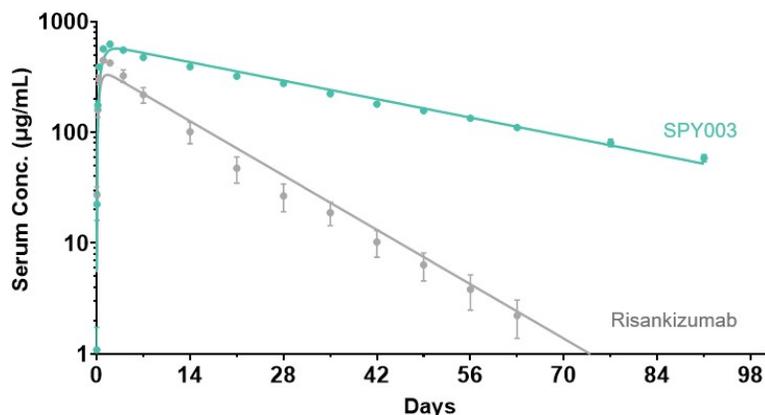
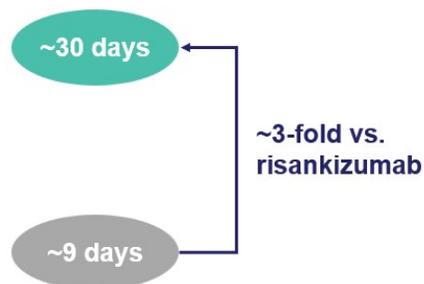


Figure 6. Pharmacokinetic concentration-time curves of SPY003 candidate compared to synthesized risankizumab comparator in non-human primates (Data on file. Group size was n=4 in the NHP studies with n=4 and n=3 at the final timepoint for half-life determination for SPY003 and risankizumab, respectively).

### NHP PK profiles of SPY003 and risankizumab



### Half-life



SPY004 – novel MOA mAb

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

SPY120 - combination, anti- $\alpha$ 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 initiate clinical trials in 2025 that will include SPY120.

In October 2024, the Company presented new preclinical data demonstrating the pharmacokinetics of co-administered SPY001 and SPY002 are comparable to historical monotherapy pharmacokinetics through 28-days in NHPs.

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

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

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 plan to initiate combination toxicology studies in 2024. Subject to regulatory feedback, we intend to initiate clinical trials in 2025 that will include SPY230.

In October 2024, the Company presented new preclinical data, demonstrating that anti-IL-23 and anti-TL1A have a synergistic effect on promoting IL-17 secretion from human and mouse cells, and that the combination of anti-IL-23 and anti-TL1A suppressed IL-17 secretion more effectively than either agent alone.

## **Paragon Agreement**

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

As a result of the Asset Acquisition, we assumed the rights and obligations of Pre-Merger Spyre under the Paragon Agreement, including the obligation 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"). Pursuant to the Paragon Agreement, on a research program-by-research program basis following the finalization of the research plan for each respective research program, we are required to pay Paragon a nonrefundable fee in cash of \$0.8 million.

For the three and nine months ended September 30, 2024, we recognized \$7.7 million and \$34.2 million, respectively, in Research and development expenses that are due to Paragon under the Paragon Agreement. As of September 30, 2024, \$14.5 million was unpaid and owed to Paragon under the Paragon Agreement.

On July 12, 2023, December 14, 2023, and June 5, 2024, we exercised our Option available under the Paragon Agreement with respect to the SPY001, SPY002, and SPY003 research programs, respectively. Our Option available under the Paragon Agreement with respect to the SPY004 program remains unexercised.

On May 14, 2024, we entered into the SPY001 License Agreement and the SPY002 License Agreement, and, on October 11, 2024, we entered into the SPY003 License Agreement.

Following the execution of each of the License Agreements, we became 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. During the three and nine ended September 30, 2024, we recognized nil and \$5.5 million of expense related to license milestones inclusive of milestones related to the nomination of a development candidate for each of SPY001 and SPY002 and the first dosing of a human subject in a Phase 1 trial for SPY001. As of September 30, 2024, there were no amounts due related to development, regulatory and clinical milestones in connection with the License Agreements.

Subject to the execution of the Option with respect to the SPY004 research program, we expect to be obligated to make similar payments upon and following the execution of a license agreement with respect to such research program. With respect to the SPY002 License Agreement only, on a product by product basis, we are obligated to pay sublicensing fees of up to approximately \$20 million upon the achievement of mostly commercial milestones.

## **Corporate Developments**

### *March 2024 Private Placement*

On March 18, 2024, the Company entered into a securities purchase agreement with certain accredited investors, pursuant to which the Company agreed to issue and sell, in a private placement, 121,625 shares of Series B Preferred Stock (convertible on a 40 to 1 basis), par value \$0.0001 per share, for \$1,480 per share for an aggregate purchase price of \$180.0 million (collectively, the "March 2024 PIPE").

### *April 2024 Exchange*

On April 23, 2024, the Company entered into an exchange agreement with Fairmount Healthcare Fund II L.P. (the "Stockholder"), pursuant to which the Stockholder agreed to exchange an aggregate of 90,992 shares of Series A Preferred Stock for an aggregate of 3,639,680 shares of 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.

### *Stockholder Approval of Series B Conversion*

On May 14, 2024, the Company's stockholders approved the conversion of the Company's Series B Preferred Stock to Common Stock and such shares of Series B Preferred Stock were subsequently converted to Common Stock, subject to beneficial ownership limitations, in accordance with the Series B Certificate of Designation. 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 September 30, 2024 due to beneficial ownership limitations.

### *Shelf S-3*

In September 2024, we 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 us of up to \$500.0 million of our common stock, preferred stock, debt securities, warrants and/or units consisting of all or some of these securities. Concurrent with the filing of the shelf-registration statement, we entered into a sales agreement (the "Sales Agreement") with TD Securities (USA) LLC ("TD Cowen"), as its sales agent, pursuant to which we may issue and sell shares of our common stock for an aggregate offering price of up to \$200.0 million under an at-the-market ("ATM")

offering program. In September 2024, we sold 426,287 shares of common stock under the ATM at a price per share of \$28.15 resulting in net proceeds of \$11.8 million. As of November 1, 2024, \$188.0 million remained available for sale under the Sales Agreement.

## **Critical Accounting Policies and Estimates**

Our condensed consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States. The preparation of our 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 condensed consolidated financial statements. The most significant estimates and assumptions that management considers in the preparation of our financial statements relate to accrued research and development costs; the valuation of consideration transferred in acquiring IPR&D; the discount rate, probabilities of success, and timing of estimated cash flows in the valuation of the CVR liability; inputs used in the Black-Scholes model for stock-based compensation expense; estimated future cash flows used in calculating the impairment of right-of-use lease assets; and estimated cost to complete performance obligations related to revenue recognition. The consideration transferred in acquiring IPR&D in connection with the acquisition of Pre-Merger Spyre was comprised of shares of our Common Stock and shares of our Series A non-voting convertible preferred stock, par value \$0.0001 per share ("Series A Preferred Stock"). To determine the fair value of the equity transferred, we considered the per share value of the private placement we closed in June 2023, which was an over-subscribed financing event involving a group of accredited investors. Our significant accounting policies are more fully described in Note 2 to our condensed consolidated financial statements appearing elsewhere in this Quarterly Report.

Other than the policy noted below, 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.

### *License Agreements Contingent Milestone Payments*

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

## Results of Operations

### Comparison of the Three Months Ended September 30, 2024 and 2023

The following table summarizes our results of operations for the three months ended September 30, 2024 and 2023, together with the changes in those items in dollars and as a percentage:

	Three Months Ended September 30,		Dollar Change	% Change
	2024	2023		
(in thousands)				
Revenue:				
Development fee and royalty	\$ —	\$ —	\$ —	*
Total revenue	—	—	—	
Operating expenses:				
Research and development	44,744	24,660	20,084	81 %
General and administrative	10,648	8,584	2,064	24 %
Acquired in-process research and development	—	(298)	298	*
Gain on sale of in-process research and development asset	—	(14,609)	14,609	*
Total operating expenses	55,392	18,337	37,055	*
Loss from operations	(55,392)	(18,337)	37,055	*
Other (expense) income:				
Interest income	5,184	1,251	3,933	*
Change in fair value of forward contract liability	—	(25,360)	(25,360)	*
Other (expense) income, net	(18,802)	2,342	21,144	*
Total other (expense) income	(13,618)	(21,767)	(8,149)	
Loss before income tax expense	(69,010)	(40,104)	28,906	*
Income tax expense	(18)	(3)	15	*
Net loss	\$ (69,028)	\$ (40,107)	\$ 28,921	*

\* Percentage not meaningful

*Research and Development Expenses.* Research and development expenses increased by \$20.1 million, or 81%, to \$44.7 million for the three months ended September 30, 2024, from \$24.7 million for the three months ended September 30, 2023. The increase was primarily driven by a \$20.8 million increase in preclinical and clinical development activities, a \$8.1 million increase in manufacturing costs, and a \$5.0 million increase in compensation costs driven by the build-out of our research and development organization, partially offset by a \$12.0 million decrease in antibody discovery costs and a \$1.8 million decrease in costs related to the Company's legacy rare disease pipeline.

External research and development expenses include costs associated with third parties contracted to conduct research and development activities on behalf of the Company, including through Paragon, CROs, CMOs, and third-party laboratories. For the three months ended September 30, 2024 and 2023, external research and development costs were \$38.9 million and \$24.0 million, respectively. The increase was primarily due to increased costs associated with our IBD pipeline candidates, partially offset by decreased costs related to the Company's legacy rare disease pipeline.

Internal research and development expenses include compensation and related costs associated with our research and development employees, as well as costs associated with the Company's on-premises research laboratory. For the three months ended September 30, 2024 and 2023, internal research and

development costs accounted for \$5.8 million and \$0.6 million, respectively. The increase was primarily due to increased compensation costs driven by the build-out of our research and development organization.

*General and Administrative Expenses.* General and administrative expenses increased by \$2.1 million, or 24%, to \$10.6 million for the three months ended September 30, 2024, from \$8.6 million for the three months ended September 30, 2023. The increase was primarily attributable to a \$2.7 million increase in share-based compensation, partially offset by a \$0.8 million decrease in professional services fees.

*Gain on Sale of In-Process Research and Development Asset.* Gain on sale of in-process research and development asset during the three months ended September 30, 2023 was due to the gain recognized on the sale of pegzilarginase to Immedica. There was no similar gain or loss during the three months ended September 30, 2024.

*Interest Income.* Interest income was \$5.2 million and \$1.3 million for the three months ended September 30, 2024 and 2023, respectively. The increase was primarily due to higher investment balances.

*Change in Fair Value of Forward Contract Liability.* Non-cash expense associated with the change in fair value of the forward contract liability was \$25.4 million for the three months ended September 30, 2023. This expense was due to the change in fair value of the underlying Series A Preferred Stock between June 30, 2023 and the forward contract's settlement on July 7, 2023. There was no similar expense during the three months ended September 30, 2024.

*Other (expense) income, net.* Other (expense) income, net for the three months ended September 30, 2024 increased by \$21.1 million versus the three months ended September 30, 2023 primarily driven by a \$18.7 million change in fair value of the contingent value right liability during the current period compared to a \$1.3 million decrease in fair value of the contingent right liability during the prior period.

## Comparison of the Nine Months Ended September 30, 2024 and 2023

The following table summarizes our results of operations for the nine months ended September 30, 2024 and 2023, together with the changes in those items in dollars and as a percentage:

	Nine Months Ended September 30,		Dollar Change	% Change
	2024	2023		
(dollars in thousands)				
Revenue:				
Development fee and royalty	\$ —	\$ 886	\$ (886)	(100)%
Total revenue	—	886	(886)	(100)%
Operating expenses (income):				
Research and development	112,308	55,822	56,486	101 %
General and administrative	35,005	25,874	9,131	35 %
Acquired in-process research and development	—	130,188	(130,188)	*
Gain on sale of in-process research and development asset	—	(14,609)	14,609	*
Total operating expenses	147,313	197,275	(49,962)	*
Loss from operations	(147,313)	(196,389)	(49,076)	*
Other (expense) income:				
Interest income	15,536	2,021	13,515	*
Change in fair value of forward contract liability	—	(83,530)	(83,530)	*
Other (expense) income, net	(19,895)	2,262	22,157	*
Total other (expense) income	(4,359)	(79,247)	(74,888)	*
Loss before income tax expense	(151,672)	(275,636)	(123,964)	*
Income tax (expense) benefit	(50)	26	76	*
Net loss	<u>\$ (151,722)</u>	<u>\$ (275,610)</u>	<u>\$ (123,888)</u>	*

\* Percentage not meaningful

*Development Fee and Royalty Revenue.* For the nine months ended September 30, 2024, we did not recognize any revenue in connection with the Immedica Agreement. For the nine months ended September 30, 2023, we recognized \$0.9 million of development fee revenue in connection with the Immedica Agreement, which was attributable to the PEACE Phase 3 trial and drug supply and royalties from an early access program in France.

*Research and Development Expenses.* Research and development expenses increased by \$56.5 million, or 101%, to \$112.3 million for the nine months ended September 30, 2024, from \$55.8 million for the nine months ended September 30, 2023. The increase was primarily driven by a \$33.0 million increase in preclinical and clinical development, a \$28.5 million increase in manufacturing costs, a \$7.6 million increase in antibody discovery activities, a \$5.9 million increase in intellectual property license milestone-based fees, and a \$3.5 million increase in compensation costs primarily associated with an increase in research and development headcount, partially offset by a \$20.1 million decrease in costs related to the Company's legacy rare disease pipeline and \$2.9 million decrease in legacy wind-down costs.

External research and development expenses include costs associated with third parties contracted to conduct research and development activities on behalf of the Company, including through Paragon, CROs, CMOs, and third-party laboratories. For the nine months ended September 30, 2024 and 2023, external research and development costs accounted for \$98.0 million and \$42.5 million, respectively. The increase was primarily due to increased costs associated with our IBD pipeline candidates and stock compensation expense

related to the Parapyre Option Obligation, partially offset by decreased costs related to the Company's legacy rare disease pipeline.

Internal research and development expenses include compensation and related costs associated with our research and development employees, as well as costs associated with the Company's on-premises research laboratory. For the nine months ended September 30, 2024 and 2023, internal research and development costs accounted for \$14.3 million and \$13.3 million, respectively. The increase was primarily driven by an increase in compensation costs associated with an increase in research and development headcount, partially offset by a decrease in costs associated with our on-premises research laboratory that was decommissioned, including the elimination of related internal roles, in the first half of 2023.

*General and Administrative Expenses.* General and administrative expenses increased by \$9.1 million, or 35%, to \$35.0 million for the nine months ended September 30, 2024, from \$25.9 million for the nine months ended September 30, 2023. The increase was primarily due to a \$12.5 million increase in stock-based compensation expense, inclusive of a \$2.4 million acceleration expense related to legacy Aeglea officers and directors, partially offset by a \$2.6 million reduction in compensation costs primarily associated with lower legacy severance costs, and \$1.4 million reduction in lease termination costs that were incurred in the prior year.

*Acquired In-process Research and Development Expenses.* Acquired in-process research and development expenses were \$130.2 million for the nine months ended September 30, 2023, as the acquisition of Pre-Merger Spyre was determined by management to be an asset acquisition, in accordance with U.S. GAAP as the product candidates were determined to have no alternative future use. There was no similar expense during the nine months ended September 30, 2024.

*Gain on Sale of In-Process Research and Development Asset.* Gain on sale of in-process research and development asset during the nine months ended September 30, 2023 was due to the gain recognized on the sale of pegzilarginase to Immedica. There was no similar gain or loss during the nine months ended September 30, 2024.

*Interest Income.* Interest income was \$15.5 million and \$2.0 million for the nine months ended September 30, 2024 and 2023, respectively. The increase was primarily due to higher investment balances.

*Change in Fair Value of Forward Contract Liability.* Non-cash expense associated with the change in fair value of the forward contract liability was \$83.5 million for the nine months ended September 30, 2023. This expense was due to the change in fair value of the underlying Series A Preferred Stock between June 22, 2023 and the forward contract's settlement on July 7, 2023. There was no similar expense during the nine months ended September 30, 2024.

*Other (expense) income, net.* Other (expense) income, net for the nine months ended September 30, 2024 increased by \$22.2 million versus the nine months ended September 30, 2023 primarily driven by a \$19.6 million increase in fair value of the contingent value right liability during the current period compared to a \$1.3 million decrease in fair value of the contingent right liability during the prior period.

## **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 September 30, 2024, we have funded our operations by raising an aggregate of approximately \$1.1 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 September 30, 2024, we had an accumulated deficit of \$916.1 million.

Our primary use of cash is to fund the development of our product candidates, and advance our pipeline. This includes both the research and development costs and the general and administrative expenses required to support those operations. Since we are a 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 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.

### ***Recent sources of liquidity***

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

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

In March 2024, we sold 121,625 shares of convertible Series B Preferred Stock for gross proceeds of \$180.0 million before deducting approximately \$11.2 million of placement agent and other offering expenses.

In September 2024, we sold 426,287 shares of common stock under an at-the-market offering program at a price of \$28.15 per share for aggregate gross proceeds of \$12.0 million before deducting \$0.3 million of placement agent and other offering expenses.

### ***Cash Flows***

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

	Nine Months Ended September 30,	
	2024	2023
Net cash, cash equivalents, and restricted cash (used in) provided by:		
Operating activities	\$ (120,211)	\$ (68,874)
Investing activities	(182,741)	(73,121)
Financing activities	185,305	197,471
Effect of exchange rate on cash, cash equivalents, and restricted cash	12	7
Net (decrease) increase in cash, cash equivalents, and restricted cash	<u>\$ (117,635)</u>	<u>\$ 55,483</u>

### ***Cash Used in Operating Activities***

Cash used in operating activities for the nine months ended September 30, 2024 was \$120.2 million and reflected a net loss of \$151.7 million. Our net loss was offset in part by non-cash expenses of \$35.6 million for share-based compensation expense and a \$19.6 million change in fair value of CVR liability, offset by a \$15.3 million net change in operating assets and liabilities and \$9.0 million in net accretion of discount on marketable securities. The net change in operating assets and liabilities was primarily driven by timing of payments to vendors.

Cash used in operating activities for the nine months ended September 30, 2023 was \$68.9 million and reflected a net loss of \$275.6 million. Our net loss was offset in part by non-cash expenses of \$130.2 million for acquired IPR&D, \$83.5 million change in fair value of forward contract liability, \$8.4 million for stock-based compensation, \$2.6 million impairment loss on lease abandonment, \$1.0 million for depreciation and amortization, and \$0.9 million on disposal of long-lived assets. The net change in operating assets and liabilities of \$3.3 million primarily related to the continuing wind down of legacy operations.

#### *Cash Used in Provided by Investing Activities*

Cash used in investing activities for the nine months ended September 30, 2024 was \$182.7 million and primarily consisted of \$366.2 million in purchases of marketable securities, partially offset by \$183.4 million in maturities and sales of marketable securities.

Cash used in investing activities for the nine months ended September 30, 2023, was \$73.1 million and primarily consisted of \$112.6 million in purchases of marketable securities, partially offset by \$21.0 million in maturities and sales of marketable securities, \$15.0 million in proceeds from the sale of in-process research & development asset, and \$3.0 million cash assumed from the Asset Acquisition.

#### *Cash Provided by Financing Activities*

Cash provided by financing activities for the nine months ended September 30, 2024 was \$185.3 million, which primarily consisted of the net proceeds from the issuance of the Series B Preferred Stock in the March 2024 PIPE of \$168.9 million, \$11.8 million in net proceeds from the issuance of common stock in connection with the ATM, and \$6.2 million from proceeds from stock option exercises and sales of Common Stock under our 2016 Employee Stock Purchase Plan and the exercise of pre-funded warrants.

Cash provided by financing activities for the nine months ended September 30, 2023, was \$197.5 million, which primarily consisted of net proceeds from the issuance of the Series A Preferred Stock in the June 2023 PIPE.

#### **Contingent contractual obligations**

Through the Asset Acquisition, we received the Option to license certain intellectual property rights related to four research programs. The exercise of the Option allows for us to enter into an exclusive license agreement with Paragon for the respective research program. Thus far we have exercised the Option and entered into license agreements with respect to SPY001, SPY002, and SPY003. Under the terms of each License Agreement, we are obligated to pay Paragon up to \$22.0 million based on specific development, regulatory and clinical milestones for the first product under each agreement. With respect to the SPY002 License Agreement only, on a product by product basis, we are obligated to pay sublicensing fees of up to approximately \$20 million upon the achievement of mostly commercial milestones.

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

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

There were no recent accounting pronouncements that have had a material effect on the Company's 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. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of United States interest rates, particularly because our investments are in marketable securities. Our marketable securities are subject to interest rate risk and could fall in value if market interest rates increase. However, we believe that our exposure

to interest rate risk is not significant as the majority of our investments are short-term in duration and have a low risk profile. A hypothetical 10% change in interest rates is not expected to have a material effect on the total market value of our investment portfolio. We have the ability to hold our marketable securities until maturity, and therefore, we would not expect our operating results or cash flows to be materially impacted by a change in market interest rates on our investments.

As of September 30, 2024, we held \$414.2 million in cash, cash equivalents, and marketable securities predominately all of which was denominated in U.S. dollars, and consisted primarily of investments in money market funds, commercial paper, U.S. government obligations, and corporate bonds.

We are also exposed to market risk related to changes in foreign currency exchange rates as a result of our entering into transactions denominated in currencies other than U.S. dollars. Due to the uncertain timing of expected payments in foreign currencies, we do not utilize any forward exchange contracts. All foreign transactions settle on the applicable spot exchange basis at the time such payments are made. For the three months ended September 30, 2024, a majority of our expenditures were denominated in U.S. dollars. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

#### **Item 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 on Form 10-Q, the effectiveness of our disclosure controls and procedures. Based on the foregoing evaluation of our disclosure controls and procedures, as of September 30, 2024, 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 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 September 30, 2024, 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**

*Investing in our Common Stock involves a high degree of risk. Before you decide to invest in our common stock, you should consider carefully the risks described below, together with the other information contained in this Quarterly Report, including “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our unaudited condensed financial statements and related notes. We believe the risks described below are the risks that are material to us as of the date of this Quarterly Report. If any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our Common Stock could decline, and you may lose all or part of your investment.*

#### **Risk Factor Summary**

Below is a summary of the material risks to our business, our operations and an investment in our common stock. This summary does not address all of the risks that we face. Risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below and should be carefully considered, together with other information in this Quarterly Report in its entirety before making investment decisions regarding our common stock.

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

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

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

- We face competition from companies that have developed or may develop competing programs.
- Our programs are in clinical and nonclinical stages of development and may fail or suffer delays.
- We are substantially dependent on the success of the SPY001, SPY002 and SPY003 programs.
- We may fail to achieve our projected development goals in the time frames we announce and expect.
- Any drug delivery device used may have its own regulatory development, supply, and other risks.
- We may not be successful in building a pipeline of product candidates with commercial value.
- Our studies and trials may be insufficient to support regulatory approval of any of our product candidates.
- We have limited experience in developing and commercializing diagnostics.
- Additional time may be required to obtain regulatory approval for our product candidates or future product candidates because of their status as combination products.
- If we are not successful in discovering, developing and commercializing our intraportfolio investigational drug combinations to achieve superior outcomes relative to the use of monotherapies or other combination therapies, our ability to achieve our strategic objectives would likely be impaired.
- Development of combination therapies may present more or different challenges than other therapies.
- We may encounter difficulties enrolling participants in our future clinical trials.
- Preliminary or “topline” data from our clinical trials may change as more data becomes available.

- Our 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 current or future products may not achieve regulatory approval, market acceptance or commercial success.
- Some of our programs may compete with our other programs.
- The FDA may not accept data from clinical trials we conduct at sites outside the United States.

***Risks Related to Government Regulation***

- FDA and comparable foreign regulatory approval processes are lengthy and time-consuming and we may not be able to obtain or may be delayed in obtaining regulatory approvals for our product candidates.
- We may not be able to meet requirements for chemistry, manufacturing and control of our programs.
- Our product candidates may face competition sooner than anticipated based on rules and regulations that may apply or government decisions with respect to our intellectual property.
- Even if we receive regulatory approval, we will be subject to extensive ongoing regulatory obligations.
- We may face difficulties from healthcare and other legislative reform measures.
- Our operations and arrangements with third-parties are subject to healthcare regulatory laws.
- We may be unable to offer products at competitive prices due to unfavorable regulations and/or policies.
- We may face criminal liability or other consequences if we violate U.S. and foreign trade regulations.
- Foreign governments may impose strict price controls, which may adversely affect our potential revenue.
- Any accelerated review designations we may pursue may not hasten development or regulatory review.

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

- Our ability to obtain and protect our patents and other proprietary rights is uncertain.
- We may fail in obtaining or maintaining necessary rights to our programs.
- We may be subject to patent infringement claims or may need to file such claims.
- We may 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 the execution of nonclinical studies and clinical trials may fail to carry out their 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 and forecasts of market growth may be inaccurate and our business may not grow at similar rates, or at all.
- Our employees or third-parties may engage in misconduct or other improper activities.
- We may be impacted by security or data breaches or other improper access to our data.
- Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.
- We may fail to comply with privacy and data security regulations despite compliance efforts.

- We may fail to comply with environmental, health and safety laws and regulations.
- We may be subject to adverse legislative or regulatory tax changes.
- We may fail to realize the benefits of our business or product acquisitions or our strategic alliances.

#### ***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 of shares by existing stockholders could cause our stock price to decline.
- Future sales and issuances of equity and debt could result in additional dilution to our stockholders.
- Our principal stockholders own a significant percentage of our stock.

#### ***General Risk Factors***

- We may become exposed to costly and damaging liability claims and our product liability insurance may not cover all damages from such claims.
- Litigation costs and the outcome of litigation could have a material adverse effect on our business.
- We may fail to maintain proper and effective internal controls.
- Our business could be adversely affected by macroeconomic conditions.

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

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

As of September 30, 2024, we had \$414.2 million of cash, cash equivalents, marketable securities, and restricted cash. We will need to raise additional capital to continue to fund our operations and service our debt obligations in the future. If we are unable to raise additional capital when needed, we will not be able to continue as a going concern.

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

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

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

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

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

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

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

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

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

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

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

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

We are a biopharmaceutical company with a limited operating history. Since inception, we have incurred significant operating losses. For the years ended December 31, 2023, 2022 and 2021, we reported a net loss of \$338.8 million, \$83.8 million and \$65.8 million, respectively. As of December 31, 2023, we had an accumulated deficit of \$764.4 million. We will need to raise substantial additional capital to continue to fund our operations in the future.

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

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

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

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

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

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

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

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

To the extent that we raise additional capital through the sale of equity, including pursuant to any sales under convertible debt or other securities convertible into equity, the ownership interest of our stockholders will be diluted, and the terms of these new securities may include liquidation or other preferences that adversely affect the rights of our stockholders. For instance, in March 2024, we sold an aggregate of 121,625 shares of our Series B Preferred Stock in the March 2024 PIPE to the March 2024 Investors for gross proceeds of approximately \$180.0 million. Subject to certain beneficial ownership limitations set by each holder of Series B Preferred Stock, each share of Series B Preferred Stock is convertible into an aggregate of 40 shares of our common stock. Following stockholder approval of the Series B Conversion Proposal, 254,958 shares of Series B Preferred Stock automatically converted to 10,198,320 shares of Common Stock; 16,667 shares of Series B

Preferred Stock did not automatically convert and remain outstanding as of September 30, 2024 due to beneficial ownership limitations.

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

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

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

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

Our competitors have developed, are developing or will develop programs and processes competitive with our programs and processes. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments. Our success will depend partially on our ability to develop and commercialize products that have a competitive safety, efficacy, dosing and/or presentation profile. Our commercial opportunity and success will be reduced or eliminated if competing products are safer, more effective, have a more attractive dosing profile or presentation or are less expensive than the products we develop, or if our competitors develop competing products or if biosimilars enter the market more quickly than we do and are able to gain market acceptance. See the section titled "Business – Competition" in our Annual Report on Form 10-K for more discussion about our competitors.

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

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

We have no products on the market, 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 receive marketing approval or commercialize our current product candidates or any future product candidates, including:

- regulators, such as the FDA, or ethics committees (“ECs”)/institutional review boards (“IRBs”) may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations (“CROs”), the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trial sites may deviate from trial protocol or drop out of a trial;
- clinical trials of any product candidates may fail to show 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 subjects 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 subjects may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, ECs/IRBs may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants in our trials are being exposed to unacceptable health risks;
- the cost of clinical trials of any of our programs may be greater than we anticipate;
- the quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be inadequate to initiate or complete a given clinical trial;
- 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;
- we may fail to establish an appropriate safety profile for a product candidate based on clinical or nonclinical data for such product candidates as well as data emerging from other therapies in the same class as our product candidates; and
- the FDA or other regulatory authorities may require us to submit additional data such as long-term toxicology studies, additional clinical data or additional manufacturing data or impose other requirements before permitting us to initiate clinical trials or approving marketing/commercial sales.

Commencing clinical trials in the United States is subject to acceptance by the FDA of an IND or similar application and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA requires us to complete additional nonclinical studies or we are required to satisfy other FDA requests prior to commencing future clinical trials, the start of such clinical trials may be delayed. Even

after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any 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. There are equivalent processes and risks applicable to clinical trial applications in other countries outside of the United States.

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

***We are substantially dependent on the success of our three most advanced programs, SPY001, SPY002 and SPY003 and our current and planned clinical trials of such programs may not be successful.***

Our future success is substantially dependent on our ability to timely obtain marketing approval for, and then successfully commercialize, our three most advanced programs, SPY001, SPY002 and SPY003. We exercised our Option with respect to the SPY001, SPY002 and SPY003 programs on July 12, 2023, December 14, 2023, and June 5, 2024, respectively. Additionally, in May 2024, we signed license agreements with Paragon for rights to royalty-bearing, world-wide, exclusive licenses to develop, manufacture, commercialize or otherwise exploit certain antibodies and products targeting  $\alpha 4\beta 7$  integrin (SPY001 program) and TL1A (SPY002 program) and, in October 2024, we signed a license agreement for rights to a royalty-bearing, world-wide, exclusive license to develop, manufacture, commercialize or otherwise exploit certain antibodies and products targeting IL-23 (SPY003 program) in the field of IBD. We are investing a majority of our efforts and financial resources into the research and development of these programs. We initiated a Phase 1 clinical trial in healthy volunteers of SPY001 and announced the dosing of our first participant in June 2024. We anticipate initiating Phase 1 clinical trials in healthy volunteers of SPY002 in the fourth quarter of 2024 and a Phase 1 clinical trial in healthy volunteers of SPY003 in the first quarter of 2025, each subject to the filing of an IND or foreign equivalent and regulatory feedback and approval. The success of our programs is dependent on observing longer half-lives of our product candidates in humans and comparable or better safety and efficacy profiles than other mAbs currently marketed or in development. We believe these longer half-lives have the potential to result in more favorable dosing schedules for our product candidates, assuming they successfully complete clinical development and obtain marketing approval. This is based in part on the assumption that the longer half-lives observed in non-human primates ("NHPs") will translate into extended half-lives of our product candidates in humans. To the extent we do not observe these extended half-lives with favorable safety and efficacy profiles when we dose humans with our product candidates, it would significantly and adversely affect the clinical and commercial potential of our product candidates.

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

The success of our product candidates will depend on a variety of factors. We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any current or future collaborator. Accordingly, we cannot assure you that we will ever be able to generate revenue through the sale of these product candidates, even if approved. If we are not successful in commercializing SPY001, SPY002 or SPY003, 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 expected first participant dosing and topline data from our planned Phase 2 clinical trial(s) in IBD, as well as the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are and will be based on numerous assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control, 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. Our product candidates may not be approved or may be substantially delayed in receiving approval if the devices that we choose to develop do not gain and/or maintain their own regulatory approvals or clearances. Where approval of the drug product and device is sought under a single application, the increased complexity of the review process may delay approval. In addition, some drug delivery devices are provided by single-source unaffiliated third-party companies. We may be dependent on the sustained cooperation and effort of those third-party companies both to supply the devices and, in some cases, to conduct the studies required for approval or other regulatory clearance of the devices. Even if approval is obtained, we may also be dependent on those third-party companies continuing to maintain such approvals or clearances once they have been received. Failure of third-party companies to supply the devices, to successfully complete studies on the devices in a timely manner, or to obtain or maintain required approvals or clearances of the devices could result in increased development costs, delays in or failure to obtain regulatory approval and delays in product candidates reaching the market or in gaining approval or clearance for expanded labels for new indications.

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

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

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

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

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

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

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

We cannot be sure that the FDA, or comparable foreign regulatory authority, as applicable, will agree with our clinical development plans. We plan to use the data from our ongoing and planned Phase 1 trials of our SPY001, SPY002 and SPY003 programs in healthy volunteers to support Phase 2 trials in IBD and other I&I indications. If the FDA and/or comparable foreign regulatory authority requires us to materially modify our proposed trial designs, conduct additional trials or enroll additional participants, our development timelines may be delayed. We cannot be sure that submission of an IND, CTA or similar application will result in the FDA or comparable foreign regulatory authorities, as applicable, allowing clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could cause regulatory authorities to suspend or terminate them. Events that may prevent successful or timely initiation or completion of clinical trials include: inability to generate sufficient nonclinical, toxicology or other in vivo or in vitro data; delays in reaching a consensus with regulatory authorities on trial design or implementation of the clinical trials; delays or failure in obtaining regulatory authorization to commence a trial; delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites; CRO personnel changes which could lead to operational delays or complications; delays in identifying, recruiting and training suitable clinical investigators and their study teams; delays in obtaining required EC/IRB approval at each clinical trial site; delays in manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of our product

candidates or other supplies for use in clinical trials or the inability to do any of the foregoing; failure by our CROs, other third-parties or us to adhere to clinical trial protocols; failure to perform in accordance with the FDA's or any other regulatory authority's good clinical practice requirements ("GCPs") or applicable regulatory guidelines in other countries; changes to the clinical trial protocols; clinical sites deviating from trial protocol or dropping out of a trial; changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data; transfer of manufacturing processes to facilities operated by a contract manufacturing organization ("CMO") and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process; and third-parties being unwilling or unable to satisfy their contractual obligations to us.

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

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

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

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

To be successful in developing, validating, obtaining approval of and commercializing a complementary diagnostic, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. We have limited prior experience with medical device or diagnostic test development. If we choose to develop and seek FDA or comparable foreign regulatory authority approval for complementary diagnostic tests on our own, we may require additional personnel. We may rely on third-parties for the design, development, testing, validation and manufacture of complementary diagnostic tests for our therapeutic product candidates that may benefit from such tests, the application for and receipt of any required regulatory approvals, and the commercial supply of these complementary diagnostics.

Although we currently plan to focus our complementary diagnostic development program on diagnostics that may help to identify patients with higher likelihood of response or better response to our product candidates, we do not believe such complementary diagnostics will be required by regulatory authorities in connection with granting regulatory approval for our product candidates but may aid in clinical trial recruitment, post-approval treatment decisions and maximizing the commercial success of our product candidates. If we or

third-parties we engage are unable to successfully develop complementary diagnostics for our product candidates, or experience delays in doing so:

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

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

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

To be successful in developing and commercializing therapeutic product candidates in combination with diagnostic candidates, we will need to address a number of scientific, technical, regulatory and logistical challenges. If we choose or are required to develop a companion diagnostic (i.e. a diagnostic test that is essential for the safe and effective use of one or more of our products), we or a collaborator may need to obtain marketing authorization from the FDA in order to legally market such diagnostics in the United States. As a company, we have little experience in the development of diagnostic tests, including companion diagnostics, and may not be successful in developing appropriate companion diagnostics to pair with any of our therapeutic product candidates that receive marketing approval, and have never applied for or obtained regulatory clearance or approval of any such diagnostic tests. Given our limited experience in developing diagnostic tests, we may rely in part or in whole on third-parties for their design, development and manufacture of such tests.

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

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

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

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

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

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

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

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

In the event that one of our investigational products were to fail to demonstrate sufficient safety and efficacy data or establish its contribution to the claimed effects of a combination therapy or if we are unable to meet the FDA's current or future approval standards required for combination therapies or combination products in a timely manner, we would need to identify and research alternative monotherapy or combination treatments or run additional trials to produce supportive data. 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 clinical trials could reveal a high and unacceptable severity and prevalence of side effects, adverse events or unexpected characteristics. While our nonclinical studies in NHPs have not shown any such characteristics to date, we cannot assure you that the results of our clinical trials will not reveal such characteristics. If significant adverse events or undesirable side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting participants to such trials, participants may drop out of our trials, or we may be required to cease our development efforts of one or more programs. We, the FDA or other applicable regulatory authorities, or an EC/IRB, may suspend any clinical trials of any program at any time for various reasons, including a belief that participants in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential products developed in the biotechnology industry that initially showed therapeutic promise in early-stage studies and trials have later been found to cause side effects that prevented their further development. Other potential products have shown side effects in nonclinical studies, which side effects do not present themselves in clinical trials in humans. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market

acceptance of the approved product due to its tolerability versus other therapies. In addition, an extended half-life could prolong the duration of undesirable side effects, which could also inhibit market acceptance. Treatment-emergent adverse events could also affect participant recruitment or the ability of enrolled participants to complete our clinical trials or could result in potential product liability claims. Potential side effects associated with our product candidates may not be appropriately recognized or managed by the treating medical staff, as toxicities resulting from our product candidates may not be normally encountered in the general patient population and by medical personnel. Any of these occurrences could harm our business, financial condition, results of operations and prospects significantly.

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

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

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

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

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

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

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

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

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

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

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

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

## **Risks Related to Government Regulation**

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

The process of obtaining regulatory approvals, both in the United States and abroad, is unpredictable, expensive and typically takes many years following commencement of clinical trials, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. We cannot commercialize product candidates in the United States without first obtaining regulatory approval from the FDA. Similarly, we cannot commercialize product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of our product candidates, including our most advanced product candidates, SPY001, SPY002 and SPY003, we must demonstrate through lengthy, complex and expensive nonclinical studies and clinical trials that our product candidates are both safe and effective for each targeted indication. Securing regulatory approval also requires the submission of information about the drug

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

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

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

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

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

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

The Patient Protection and Affordable Care Act, as amended by the Healthcare and Education Reconciliation Act (the "ACA"), includes a subtitle called the Biologics Price Competition and Innovation Act of

2009 (“BPCIA”), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a highly similar or “biosimilar” product may not be submitted to the FDA until four years following the date that the reference product was first approved by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first approved. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor’s own nonclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product.

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

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

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

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

***We may face difficulties from healthcare legislative reform measures.***

Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in

the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability. Additionally, if the BIOSECURE Act is passed with terms that require us to switch or move development of our product candidates from one CMO to another, we may incur additional development costs or delays in manufacturing product for clinical trials or commercialization. See the section titled “Business – Government Regulation – Healthcare Reform” in our Annual Report on Form 10-K for a more detailed description of healthcare reform measures that may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates.

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

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

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

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

We intend to seek approval to market our product candidates in both the United States and in selected foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions for our product candidates, we will be subject to rules and regulations in those jurisdictions. Our ability to successfully commercialize any product candidates that we may develop will depend in part on the extent to which reimbursement for these product candidates and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. These entities may create preferential access policies for a competitor’s product, including a branded or generic/biosimilar product, over our products in an attempt to reduce their costs, which may reduce our commercial opportunity. Additionally, if any of our product candidates are approved and we are found to have improperly promoted off-label uses of those product candidates, we may become subject to significant liability, which would materially adversely affect our business and financial condition. See the sections titled “Business – Government Regulation – Coverage and Reimbursement” and “Business – Other Government Regulation Outside of the United States – Regulation in the European Union” in our Annual Report on Form 10-K for a more detailed description of the government regulations and third-party payor practices that may affect our ability to commercialize our product candidates.

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

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

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

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

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

We may seek a breakthrough therapy, fast track, or other designation for appropriate product candidates. Designations such as these are within the discretion of the FDA, or other comparable regulatory authorities. The receipt of a designation for a product candidate may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify under one of FDA's designation programs, the FDA may later decide that the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. See the section titled "Business – Government Regulation – Expedited Development and Review Programs" in our Annual Report on Form 10-K for a more detailed description of the process for seeking expedited designations such as fast track or breakthrough therapy designations.

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

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

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

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

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

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

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

Because our development programs currently do and may in the future require the use of proprietary rights held by third-parties, the growth of our business may depend in part on our ability to acquire, in-license, or use these third-party proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third-parties that we identify as necessary

for our programs. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

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

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

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

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

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

Because the intellectual property landscape in the biotechnology industry is rapidly evolving and interdisciplinary, it is difficult to conclusively assess our freedom to operate and guarantee that we can operate

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

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

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

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

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

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

As is common in the biotechnology industry, in addition to our employees, we engage the services of consultants to assist us in the development of our programs. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology or pharmaceutical companies including our competitors or potential competitors. Despite our training and compliance efforts, we could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other confidential information of former employers or competitors. Although we try to ensure that our employees and consultants

do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may become subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor.

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

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

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

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

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

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

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

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

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

with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

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

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

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

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

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

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

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

Our current or future licensors may retain certain rights under the relevant agreements with us, including the right to use the underlying technology for noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and

scholarly disclosures of information relating to the technology. It is difficult to monitor whether our licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse.

### **Risks Related to Our Reliance on Third-Parties**

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

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

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

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

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

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

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

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

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

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

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

***unable to use third-party manufacturing suites or if the third-party manufacturers encounter difficulties in production.***

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

Moreover, our CMOs may experience manufacturing difficulties due to resource constraints, supply chain issues, proposed or actual legislative changes or requirements, or as a result of labor disputes or unstable political environments. If any CMOs on which we will rely fail to manufacture quantities of our product candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a cost that allows us to achieve profitability, our business, financial condition and prospects could be materially and adversely affected. In addition, our CMOs and other third-parties are responsible for transporting temperature-controlled materials that can be inadvertently degraded during transport due to several factors, rendering certain batches unsuitable for trial use for failure to meet, among others, our integrity and purity specifications. We and any of our CMOs may also face product seizure or detention or refusal to permit the import or export of products. Our business could be materially adversely affected by business disruptions to our third-party providers that could materially adversely affect our anticipated timelines, potential future revenue and financial condition and increase our costs and expenses. Each of these risks could delay or prevent the completion of our nonclinical studies and clinical trials or the approval of any of our product candidates by the FDA, resulting in higher costs or adversely impact commercialization of our product candidates. See the section titled “Business – Manufacturing” in our Annual Report on Form 10-K for a more detailed description of our manufacturing plans and assumptions and the factors that may affect the success of our programs.

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

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

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

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

We are a clinical stage biotechnology company with a limited operating history, and, as of September 30, 2024, we had 60 employees. We have been and will continue to be highly dependent on the research and development, clinical and business development expertise of our executive officers, as well as the other principal members of our management, scientific and clinical team. Any such officers and other principal members may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

systems or third-party systems where information important to our business operations or commercial development is stored.

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

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

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

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

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

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

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

corporation in 2015 also may be limited by the Separate Return Limitation Year rule, which could increase our U.S. federal tax liability. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

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

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

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

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

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

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

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

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

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

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

#### **Risks Related to Our Common Stock**

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

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

- our ability to obtain regulatory approvals for our product candidates, and delays or failures to obtain such approvals;
- failure of any of our product candidates, if approved, to achieve commercial success;
- failure to maintain our existing third-party license and supply agreements;
- changes in laws or regulations applicable to our product candidates;
- any inability to obtain adequate supply of our product candidates or the inability to do so at acceptable prices;
- adverse regulatory authority decisions;
- introduction of new products, services, or technologies by our competitors;
- failure to meet or exceed financial and development projections we may provide to the public and the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators, and the investment community;
- announcements of significant acquisitions, strategic collaborations, joint ventures, or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- additions or departures of key personnel;
- significant lawsuits, including patent or stockholder litigation;

- if securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our business and stock;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions, including global inflationary pressures, rising interest rates, general economic slowdown or a recession, changes in monetary policy, instability in financial institutions and the prospect of a shutdown of the U.S. federal government;
- geopolitical instability, including the ongoing military conflict in Ukraine, conflict in Israel and surrounding areas, and geopolitical tensions in China;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- announcements by commercial partners or competitors of new commercial products, clinical progress or the lack thereof, significant contracts, commercial relationships, or capital commitments;
- the introduction of technological innovations or new therapies that compete with our potential products;
- changes in the structure of health care payment systems; and
- period-to-period fluctuations in our financial results.

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

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

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

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

In addition, the Series A Certificate of Designation relating to our Series A Preferred Stock may delay or prevent a change in control of our company. At any time while at least 30% of the originally issued Series A Preferred Stock remains issued and outstanding, we may not consummate a Fundamental Transaction (as defined in the Series 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.

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

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

We expect that we will need significant additional capital to fund our current and future operations, including to complete potential clinical trials for our product candidates. To raise capital, we may sell common stock, convertible securities, or other equity securities in one or more transactions at prices and in a manner we

determine from time to time. As a result, our stockholders may experience additional dilution, which could cause our stock price to fall.

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

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

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

### **General Risk Factors**

***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 we are no longer a “smaller reporting company,” we will continue to incur significant legal, accounting and other expenses. We incur significant legal, accounting, and other expenses associated with public company reporting requirements. We also incur costs associated with corporate governance requirements, including requirements under the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, as well as rules implemented by the SEC and Nasdaq. 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.

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

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

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

We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, and the rules and regulations of Nasdaq. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. When we lose our status as a "smaller reporting company" and become an "accelerated filer" or a "large accelerated filer," we will be required to have an audit of the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing, and possible remediation. We must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our annual report filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. This requires that we incur substantial professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. We may experience difficulty in meeting these reporting requirements in a timely manner for each period.

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

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

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

***Our business could be adversely affected by economic downturns, inflation, increases in interest rates, natural disasters, public health crises such as the COVID-19 pandemic, political crises, U.S. elections, international or geopolitical events, such as the conflict between Russia and Ukraine, and Israel and Hamas or other macroeconomic conditions, which could have a material and adverse effect on our results of operations and financial condition.***

The global economy, including credit and financial markets, has experienced extreme volatility and disruptions, including, among other things, diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, supply chain shortages, increases in inflation rates, higher interest rates, and uncertainty about economic stability. For example, the COVID-19 pandemic resulted in widespread unemployment, economic slowdown and extreme volatility in the capital markets. The Federal Reserve has raised interest rates multiple times in response to concerns about inflation and it may raise them again. Higher interest rates, coupled with reduced government spending and volatility in financial markets, may increase economic uncertainty and affect consumer spending. Similarly, geopolitical uncertainties and international conflicts, including the ongoing military conflicts between Russia and Ukraine, and Israel and Hamas, and rising tensions with China, have created extreme volatility in the global capital markets and may have further global economic consequences, including disruptions of the global supply chain. Any such volatility and disruptions may adversely affect our business or the third-parties on whom we rely. If the equity and credit markets deteriorate, including as a result of political unrest or war, it may make any necessary debt or equity financing more costly, more dilutive, or more difficult to obtain in a timely manner or on favorable terms, if at all. Increased inflation rates can adversely affect us by increasing our costs, including labor and employee benefit costs.

We may in the future experience disruptions as a result of such macroeconomic conditions, including delays or difficulties in initiating or expanding clinical trials and manufacturing sufficient quantities of materials. Any one or a combination of these events could have a material and adverse effect on our results of operations and financial condition.

## **Item 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 September 30, 2024, 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).

## 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	
10.1#	<a href="#">IL-23 (SPY003) License Agreement, dated October 11, 2024, by and between the Company and Paragon Therapeutics, Inc.</a>	8-K	001-37722	10/15/2024	10.1	
10.2#	<a href="#">Amended and Restated Biologics Master Services Agreement, dated October 14, 2024, by and between the Company and WuXi Biologics (Hong Kong) Limited.</a>	8-K	001-37722	10/15/2024	10.2	
10.3#	<a href="#">Amended and Restated Cell Line License Agreement, dated October 14, 2024, by and between the Company and WuXi Biologics (Hong Kong) Limited.</a>	8-K	001-37722	10/15/2024	10.3	
10.4+	<a href="#">Fifth Amendment to the Spyre Therapeutics, Inc. 2018 Equity Inducement Plan</a>					X
10.5+	<a href="#">Offer Letter, dated September 20, 2024, by and between the Company and Sheldon Sloan</a>					X
10.6	<a href="#">Sales Agreement, dated September 6, 2024, between Spyre Therapeutics, Inc. and TD Securities (USA) LLC</a>	S-3	333-281975	9/6/2024	1.2	
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

<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>
32.1(1)	<a href="#"><u>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</u></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
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: November 7, 2024

Spyre Therapeutics, Inc.

By: /s/ Scott Burrows

Scott Burrows

*Chief Financial Officer*

*(Principal Financial Officer and Principal Accounting Officer)*