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 March 31, 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	**46-4312787**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

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

(Address of principal executive offices 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	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☐

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

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

As of May 1, 2024, the registrant had 40,283,414 shares of common stock, $0.0001 par value per share, outstanding.

SPYRE THERAPEUTICS, INC.

QUARTERLY REPORT ON FORM 10-Q
FOR THE QUARTER ENDED MARCH 31, 2024

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NOTE ABOUT FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q for the quarter ended March 31, 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, including statements regarding stockholder approval of the conversion rights of our Series B preferred stock, par value $0.0001 (the "Series B Preferred Stock"); 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 ability to achieve the expected benefits or opportunities and related timing with respect to the Asset Acquisition or to monetize our legacy assets, our future results of operations and financial position, business strategy, the length of time that we believe our existing cash resources will fund operations, market size, potential growth opportunities, preclinical and future clinical development activities, efficacy and safety profile of our product candidates, potential therapeutic benefits and economic value of our product candidates, use of net proceeds from our public offerings, the timing and results of preclinical studies and clinical trials, the expected impact of macroeconomic conditions, including inflation, increasing interest rates and volatile market conditions, current or potential bank failures, as well as global events, including the ongoing military conflict in Ukraine, conflict 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 our Annual Report on Form 10-K for the year ended December 31, 2023 (the "Annual Report") as filed with the Securities Exchange Commission ("SEC") on February 29, 2024 and amended on March 1, 2024 and elsewhere 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 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, by and among Spyre Therapeutics, LLC, 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)

	March 31, 2024	December 31, 2023
ASSETS		
CURRENT ASSETS		
Cash and cash equivalents	$ 227,552	$ 188,893
Marketable securities	257,089	150,384
Prepaid expenses and other current assets	2,632	2,251
Total current assets	487,273	341,528
Restricted cash	319	322
Other non-current assets	10	9
TOTAL ASSETS	$ 487,602	$ 341,859
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES		
Accounts payable	$ 3,106	$ 896
CVR liability	2,590	1,390
Accrued and other current liabilities	21,594	13,108
Related party accounts payable and other current liabilities	15,528	16,584
Total current liabilities	42,818	31,978
Non-current CVR liability	39,110	41,310
TOTAL LIABILITIES	81,928	73,288
Commitments and Contingencies (Note 6)		
Series B non-voting convertible preferred stock, $0.0001 par value; 271,625 and 150,000 shares authorized as of March 31, 2024 and December 31, 2023, respectively; 271,625 and 150,000 shares issued and outstanding as of March 31, 2024 and December 31, 2023, respectively	253,405	84,555
STOCKHOLDERS' EQUITY		
Series A non-voting convertible preferred stock, $0.0001 par value; 1,086,341 shares authorized as of March 31, 2024 and December 31, 2023; 437,037 shares issued and outstanding as of March 31, 2024 and December 31, 2023, respectively	184,927	184,927
Preferred stock, $0.0001 par value; 8,642,034 shares and 8,763,659 shares authorized as of March 31, 2024 and December 31, 2023, respectively; no shares issued and outstanding as of March 31, 2024 and December 31, 2023	—	—
Common stock, $0.0001 par value; 400,000,000 shares authorized as of March 31, 2024 and December 31, 2023; 36,629,680 shares and 36,057,109 shares issued and outstanding as of March 31, 2024 and December 31, 2023, respectively	10	10
Additional paid-in capital	775,966	763,191
Accumulated other comprehensive (loss) income	(363)	302
Accumulated deficit	(808,271)	(764,414)
TOTAL STOCKHOLDERS' EQUITY	152,269	184,016
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY	$ 487,602	$ 341,859

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 March 31,	
	2024	2023
Revenue:		
Development fee and royalty	$ —	$ 198
Total revenue	—	198
Operating expenses:		
Research and development [1]	34,928	13,776
General and administrative	12,846	5,228
Total operating expenses	47,774	19,004
Loss from operations	(47,774)	(18,806)
Other income (expense):		
Interest income	4,432	420
Other expense	(483)	(72)
Total other income (expense)	3,949	348
Loss before income tax expense	(43,825)	(18,458)
Income tax (expense) benefit	(32)	36
Net loss	$ (43,857)	$ (18,422)
Net loss per share, basic and diluted	$ (1.20)	$ (4.89)
Weighted-average common shares outstanding, basic and diluted	36,512,662	3,770,506

(1) Includes $17.1 million in related party expenses for the three months ended March 31, 2024 and no related party expenses for the three months ended March 31, 2023.

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 March 31,	
	2024	2023
Net loss	$ (43,857)	$ (18,422)
Other comprehensive (loss) income:		
Foreign currency translation adjustment	16	10
Unrealized (loss) gain on marketable securities	(681)	32
Total comprehensive loss	$ (44,522)	$ (18,380)

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 Months Ended March 31, 2024									
	Series B Non-Voting Convertible Preferred Stock		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	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 gain 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

	Three Months Ended March 31, 2023									
	Series B Non-Voting Convertible Preferred Stock		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	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

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)

	Three Months Ended March 31,	
	2024	2023
CASH FLOWS FROM OPERATING ACTIVITIES		
Net loss	$ (43,857)	$ (18,422)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	13,835	1,709
Change in fair value of CVR liability	430	—
Net accretion of discount on marketable securities	(2,423)	(107)
Depreciation and amortization	—	384
Amortization of operating lease assets	—	164
Other	—	2
Changes in operating assets and liabilities:		
Accounts payable	2,210	1,384
Accrued and other liabilities	8,151	(3,164)
Related party payable	(6,507)	—
Prepaid expenses and other assets	(381)	622
Deferred revenue	—	(53)
Development receivables	—	45
Operating lease liabilities	—	(198)
Net cash used in operating activities	(28,542)	(17,634)
CASH FLOWS FROM INVESTING ACTIVITIES		
Purchases of marketable securities	(152,713)	—
Proceeds from maturities and sales of marketable securities	47,750	17,750
Net cash (used in) and provided by investing activities	(104,963)	17,750
CASH FLOWS FROM FINANCING ACTIVITIES		
Proceeds from issuance of Series B non-voting convertible preferred stock in connection with private placement, net of placement and other offering costs	169,205	—
Payments related to contingent value rights liability	(1,430)	—
Proceeds from employee stock plan purchases and stock option exercises	4,390	18
Principal payments on finance lease obligation	—	(8)
Net cash provided by financing activities	172,165	10
Effect of exchange rate on cash, cash equivalents, and restricted cash	(4)	11
NET INCREASE IN CASH, CASH EQUIVALENTS, AND RESTRICTED CASH	38,656	137
CASH, CASH EQUIVALENTS, AND RESTRICTED CASH		
Beginning of period	189,215	36,416
End of period	$ 227,871	$ 36,553
Supplemental Disclosure of Non-Cash Investing and Financing Information:		
Unpaid amounts related to issuance of Series B non-voting convertible preferred stock in connection with private placement	$ 355	$ —

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

1. The Company and Basis of Presentation

Spyre Therapeutics, Inc., formerly Aeglea BioTherapeutics, Inc. (“Spyre” or the “Company”), is a preclinical 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 ("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, 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 an into a second wholly 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 conversion of the Company's Series A Preferred Stock to Common Stock.

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.

Liquidity

The Company is a preclinical 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 March 31, 2024, the Company has 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 its product rights for commercialization of pegzilarginase in Europe and certain countries in the Middle East. As of March 31, 2024, Spyre had an accumulated deficit of $808.3 million, and cash, cash equivalents, marketable securities and restricted cash of $485.0 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 (“FASB”) and include the accounts of the Company and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Unaudited Interim Financial Information

The interim condensed consolidated financial statements included in this Quarterly Report on Form 10-Q are unaudited. The unaudited interim financial statements have been prepared on the same basis as the annual financial statements and reflect, in the opinion of management, all adjustments of a normal and recurring nature that are necessary for a fair statement of the Company’s financial position as of March 31, 2024, and its results of operations for the three months ended March 31, 2024 and 2023, changes in convertible preferred stock and stockholders’ equity for the three months ended March 31, 2024 and 2023, and cash flows for the three months ended March 31, 2024 and 2023. The results of operations for the three months ended March 31, 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. 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

Spyre Therapeutics' significant accounting policies are detailed in the Notes titled “1. The Company and Basis of Presentation” and "2. Summary of Significant Accounting Policies” of the Company's Annual Report.

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.

Recently Adopted Accounting Pronouncement

There have been no recent accounting pronouncements or changes in accounting pronouncements during the three months ended March 31, 2024 that are of significance or potential significance to the Company.

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):

	March 31, 2024			
	Level 1	Level 2	Level 3	Total
Financial Assets:				
Money market funds	$ 225,797	$ —	$ —	$ 225,797
U.S. government treasury securities	85,045	—	—	85,045
U.S. government agency securities	—	55,818	—	55,818
Commercial paper	—	74,792	—	74,792
Corporate bonds	—	41,434	—	41,434
Total financial assets	$ 310,842	$ 172,044	$ —	$ 482,886
Liabilities:				
Parapyre Option Obligation	$ —	$ 5,449	$ —	$ 5,449
CVR liability	—	—	41,700	41,700
Total liabilities	$ —	$ 5,449	$ 41,700	$ 47,149

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

The Company measures the fair value of money market funds on quoted prices in active markets for identical 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 and Level 2 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 CVR liability value is based on significant inputs not observable in the market such as estimated cash flows, estimated probabilities of success, and risk-adjusted discount rates, which represent a Level 3 liability.

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:

	March 31, 2024
Estimated cash flow dates	02/28/25 - 06/22/26
Estimated probability of success	39% - 100%
Estimated reimbursement rate compared to reimbursement agent	81% - 100%
Risk-adjusted discount rates	6.32% - 6.65%

The change in fair value between December 31, 2023 and March 31, 2024 was a $0.4 million increase, and was primarily driven by changes in the risk-adjusted discount rates and the time value of money.

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

	CVR Liability
Beginning balance as of December 31, 2023	$ 42,700
Changes in the fair value of the CVR liability	430
Payments	(1,430)
Ending Balance as of March 31, 2024	$ 41,700

4. Cash Equivalents and Marketable Securities

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

	March 31, 2024			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Cash equivalents:				
Money market funds	$ 225,797	$ —	$ —	$ 225,797
Total cash equivalents	$ 225,797	$ —	$ —	$ 225,797
Marketable securities:				
Commercial paper	$ 74,803	$ 12	$ (23)	$ 74,792
Corporate bonds	41,497	11	(74)	41,434
U.S. government treasury securities	85,250	4	(209)	85,045
U.S. government agency securities	55,937	26	(145)	55,818
Total marketable securities	$ 257,487	$ 53	$ (451)	$ 257,089

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

The following table summarizes the available-for-sale securities in an unrealized loss position for which an allowance for credit losses has not been recorded as of March 31, 2024 and December 31, 2023, aggregated by major security type and length of time in a continuous unrealized loss position:

	March 31, 2024					
	Less Than 12 Months		12 Months or Longer		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
Commercial paper	$ 30,027	$ (23)	$ —	$ —	$ 30,027	$ (23)
Corporate bonds	30,737	(74)	—	—	30,737	(74)
U.S. government treasury securities	77,707	(209)	—	—	77,707	(209)
U.S. government agency securities	44,742	(145)	—	—	44,742	(145)
Total marketable securities	$ 183,213	$ (451)	$ —	$ —	$ 183,213	$ (451)

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

The Company evaluated its securities for credit losses and considered the decline in market value to be primarily attributable to current economic and market conditions and not to a credit loss or other factors. Additionally, the Company does not intend to sell the securities in an unrealized loss position and does not expect it will be required to sell the securities before recovery of the unamortized cost basis. As of March 31, 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 March 31, 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 March 31, 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 months ended March 31, 2024 and 2023. Interest on marketable securities is included in interest income. Accrued interest receivable on available-for-sale debt securities as of March 31, 2024 and December 31, 2023, was $1.3 million and $0.9 million, respectively.

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

	March 31, 2024	December 31, 2023
Due in one year or less	$ 191,090	$ 115,784
Due in 1 - 2 years	65,999	34,600
Total marketable securities	$ 257,089	$ 150,384

The Company may sell investments at any time for use in current operations even if they have not yet reached maturity. As a result, the Company classifies marketable securities, including securities with maturities beyond twelve months as current assets.

5. Accrued and Other Current Liabilities

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

	March 31, 2024	December 31, 2023
Accrued compensation	$ 2,506	$ 4,054
Accrued contracted research and development costs	18,149	7,092
Accrued professional and consulting fees	720	1,474
Accrued other	219	488
Total accrued and other current liabilities	$ 21,594	$ 13,108

6. Related Party Transactions

Paragon Agreement

Paragon and Parapyre each beneficially owns 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.

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.

For the three months ended March 31, 2024, the Company recognized expenses related to services provided by Paragon subsequent to the Asset Acquisition totaling $17.1 million, which included $5.4 million of stock-based compensation expense, and were recorded as Research and development expenses in the consolidated statements of operations. As of March 31, 2024 and December 31, 2023, $15.5 million and $16.6 million, respectively, was unpaid and was included in Related party accounts payable and other current liabilities on the Company's consolidated balance sheets.

For the three months ended March 31, 2024, the Company made payments totaling $18.2 million to Paragon.

On July 12, 2023 and December 14, 2023, the Company exercised the option to license certain intellectual property rights (collectively, the "Option") available under the Paragon Agreement with respect to the SPY001 and SPY002 research programs, respectively, and expects to enter into a SPY001 license agreement (the "SPY001 License Agreement") and a SPY002 license agreement (the "SPY002 License Agreement"). Our Option available under the Paragon Agreement with respect to the SPY003 and SPY004 programs remains unexercised.

Following the execution of each of the SPY001 License Agreement and SPY002 License Agreement, the Company will be 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. Upon execution of each of the SPY001 License Agreement and the SPY002 License Agreement, we expect to pay Paragon a $1.5 million fee for nomination of a development candidate, as applicable, and the Company expects to be obligated to make a further milestone payment of $2.5 million upon the first dosing of a human subject in a Phase 1 trial. With respect to the SPY002 License Agreement only, on a product by product basis, the Company expects to pay Paragon sublicensing fees of up to approximately $20.0 million upon the achievement of mostly commercial milestones.

The following is the summary of expenses related to the Paragon Agreement, which were ultimately settled in cash (in millions):

	Three Months Ended March 31,		
	2024	2023	Financial Statement Line Item
Reimbursable costs under the Paragon Agreement	$ 11.7	$ —	Research and development

Parapyre Option Obligation

Pursuant to the Paragon Agreement, the Company agreed to issue Parapyre an annual equity grant of warrants, on the last business day of each of the years ended December 31, 2023 and December 31, 2024, to purchase 1% of the then outstanding shares of the Company's Common Stock, on a fully diluted basis, during the term of the Paragon Agreement

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

	March 31, 2024	December 31, 2023
Reimbursable costs under the Paragon Agreement	$ 10.1	$ 16.6
Parapyre warrants liability	5.4	—
Total related party accounts payable	$ 15.5	$ 16.6

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 months ended March 31, 2024, the Company recognized $0.3 million in stock-based compensation expense related to Mr. McKenna's consulting agreement. There was no such expense for the three months ended March 31, 2023.

7. 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 March 31, 2024, the following pre-funded warrants for Common Stock were issued and outstanding:

Issue Date	Expiration Date	Exercise Price	Number of Warrants Outstanding
May 20, 2022	None	$ 0.0025	250,000
Total pre-funded warrants			250,000

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 March 31, 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.

The Company held a stockholders' meeting to submit the following matters to its stockholders for their consideration: (i) the approval of the Series A Conversion Proposal, and (ii) if deemed necessary or appropriate by the Company or as otherwise required by law or contract, the approval of an amendment to the Certificate of Incorporation to authorize sufficient shares of Common Stock for the conversion of the Series A Preferred Stock issued pursuant to the Acquisition Agreement. In connection with these matters, the Company filed with the SEC a definitive proxy statement and other relevant materials.

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.

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. In addition, 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 remain outstanding as of March 31, 2024 due to beneficial ownership limitations. This conversion 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.

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.

The Company has agreed to use its best efforts to obtain stockholder approval of 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") at its 2024 annual meeting of stockholders (the "2024 Annual Meeting"), which the Company expects to hold on May 13, 2024. The Series B Preferred Stock is recorded outside of stockholders' equity because, if conversion to Common Stock is not approved by the stockholders, the Series B Preferred Stock will be redeemable at the option of the holders for cash equal to the closing price of the Common Stock per share of Common Stock underlying the Series B Preferred Stock, on the last trading day prior to the holder's redemption request. As of March 31, 2024, the redemption value of the Company's outstanding Series B Preferred Stock was $412.1 million based on the closing stock price of the Company's Common Stock on March 31, 2024 of $37.93 per share. The Company has determined that the Series B Preferred Stock did not contain any embedded derivatives and therefore the conversion and redemption features did not require bifurcation.

Following stockholder approval of the Series B Conversion Proposal, each share of Series B Preferred Stock will automatically convert 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.

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 April 1, 2024, the Company filed a definitive proxy statement with the SEC to solicit approval of the Series B Conversion Proposal, among other matters, at the 2024 Annual Meeting.

8. 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 March 31, 2024, a total of 3,029 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 March 31, 2024, the 2016 Plan had 7,393,885 shares available for future issuance, of which 2,996,404 shares were subject to outstanding option awards.

2018 Equity Inducement Plan

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

As of March 31, 2024, the 2018 Plan had 6,029,000 shares available for future issuance, of which 5,384,241 shares were subject to outstanding option awards and restricted unit 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.

Parapyre Option Obligation

As of March 31, 2024, the pro-rated estimated fair value of the options to be granted on December 31, 2024, was approximately $21.9 million. For the three months ended March 31, 2024, $5.4 million was recognized as stock compensation expense related to the Parapyre Option Obligation. There was no similar expense for the three months ended March 31, 2023. As of March 31, 2024, the unamortized expense related to the Parapyre Option Obligation was $16.5 million.

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

	Three Months Ended March 31,			
	2024		2023	
	Grants	Weighted Average Grant Date Fair Value	Grants	Weighted Average Grant Date Fair Value
Stock options	1,044,658	$ 26.50	177,620	$ 11.00

2016 Employee Stock Purchase Plan

Under the Company's 2016 Employee Stock Purchase Plan ("2016 ESPP"), the Company issued and sold 2,330 and 1,793 shares during the three months ended March 31, 2024 and March 31, 2023, respectively. The aggregate cash proceeds were di minimis for both 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 March 31,	
	2024	2023
Research and development [1]	$ 6,857	$ 777
General and administrative	6,978	932
Total stock-based compensation expense	$ 13,835	$ 1,709

[1] For the three months ended March 31, 2024, $5.4 million, was recognized as stock compensation expense related to the Parapyre Option Obligation. There were no such expenses for the three months ended March 31, 2023.

[2] Of the total $13.8 million and $1.7 million of stock-based compensation expense for the three months ended March 31, 2024 and 2023, respectively, $2.9 million and $0.5 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 March 31,	
	2024	2023
Stock Options Granted		
Expected term (in years)	6.03	6.02
Expected volatility	105%	99%
Risk-free interest	3.88%	4.06%
Dividend yield	—	—
2016 ESPP		
Expected term (in years)	0.50	0.49
Expected volatility	98%	181%
Risk-free interest	5.31	4.99
Dividend yield	—	—

9. 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. The upfront payment and contingent milestone payments if paid, net of expenses and adjustments, will be distributed to holders of the Company's CVRs (as defined in Note 1) 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 months ended March 31, 2024. For the three months ended March 31, 2023, the Company recognized $0.2 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.

For more details on the now terminated Immedica Agreement, 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 March 31, 2024 and December 31, 2023.

10. 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 March 31,	
	2024	2023
Options to purchase common stock	3,200,918	459,425
Unvested restricted stock units	61,253	766
Outstanding Parapyre warrants	684,407	—

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 March 31,	
	2024	2023
Weighted average Common Stock	36,262,662	2,614,843
Weighted average pre-funded warrants	250,000	1,155,663
Total basic and diluted weighted average shares	36,512,662	3,770,506

11. Subsequent Events

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.

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 March 31, 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 filed with the SEC on February 29, 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 the in-process research and development ("IPR&D") 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 exclusively license intellectual property rights related to such research program directed to antibodies that selectively bind to α4β7 integrin and methods of using these antibodies, including methods of treating inflammatory bowel disease ("IBD") using SPY001. 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. The license agreements pertaining to such research programs are currently being finalized on previously agreed terms. Furthermore, as of the date of this Quarterly Report, the Option remains unexercised with respect to the IPR&D rights related to the two remaining research programs under the Paragon Agreement.

Overview

Following the Asset Acquisition, we have significantly reshaped the business into a preclinical stage biotechnology company focused on developing next generation therapeutics for patients living with IBD, including ulcerative colitis ("UC") and Crohn's disease ("CD"). Through the Paragon Agreement, 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 preclinical and clinical studies 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 studies 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 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) in connection with the research programs with respect to which we have exercised the Option to exclusively license all of Paragon's right, title, and interest in, including all intellectual property license rights to, or have the Option to acquire such intellectual property and other rights to pursuant to the Paragon Agreement and plan to develop patient selection approaches for each program. The following table summarizes the programs that have been exercised to date pursuant to the Paragon Agreement:

Other early-stage programs:

- SPY003 – anti-IL-23 mAb
- SPY004 – novel MOA mAb
- SPY130 – combination anti-α4ß7 and anti-IL-23 mAbs
- SPY230 – combination anti-TL1A and anti-IL-23 mAbs

We have nominated development candidates for SPY001 and SPY002. We have exercised our Option to license worldwide rights from Paragon for the SPY001 and SPY002 programs and a SPY001 license agreement (the "SPY001 License Agreement") and a SPY002 license agreement (the "SPY002 License Agreement") are currently being finalized with execution expected to occur in the second quarter of 2024. We continue to hold the Option to license similar rights from Paragon for certain other programs. We expect the SPY003 license to be restricted to IBD, and we expect other potential program licenses related to the Option to be indication agnostic. 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). See the section titled "Paragon Agreement" for more information on the Paragon Agreement, including the Option.

Although we hold the Option to acquire intellectual property license rights related to the SPY003 and SPY004 programs, such Option remains unexercised.

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 tested 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 our Annual Report.

SPY001 – anti-α4β7 mAb

Our most advanced product candidate, SPY001, is a highly potent, highly selective, and humanized monoclonal immunoglobulin G1 antibody designed to bind selectively to the α4β7 integrin being developed for the treatment of IBD (UC and CD). The α4β7 integrin is a protein found on the surface of immune cells known as lymphocytes. This integrin regulates the migration of lymphocytes to the gut where they contribute to the inflammatory process in IBD. By selectively binding to the α4β7 integrin, SPY001 is designed to prevent the interaction of these lymphocytes with MAdCAM-1, a molecule expressed on endothelial cells lining the blood vessels in the gut. This interaction is responsible for guiding lymphocytes from the bloodstream into the gut tissue, where they cause inflammation. By blocking the interaction between α4β7 integrin and MAdCAM-1, SPY001 aims to reduce the recruitment of 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 is being developed by us and our research partners at Paragon. Prior to the closing of the Asset Acquisition, Paragon had sole leadership in conducting *in vitro* and *in vivo* studies for SPY001 clones, including the potency, selectivity, and non-human primate ("NHP") PK data supporting development candidate nomination for the SPY001 program. Following the closing of the Asset Acquisition and the exercise of the Option with respect to the SPY001 program, Spyre and Paragon established a Joint Development Committee (“JDC”) comprised of two employees from Spyre and two employees from Paragon and jointly directed research and development work, with Spyre having final decision rights on the budget for any research program. The JDC is the decision-making body for SPY001 and our other pipeline programs prior to the execution of the SPY001 License Agreement and, in addition to SPY001, we will also control and lead the development process for each of SPY002, non-optioned programs SPY003 and SPY004, and each of the combination programs once the respective license agreements are executed.

SPY001 preclinical characterization studies were conducted in-house with support from third party vendors. SPY001 demonstrates similar potency and selectivity as vedolizumab in preclinical *in vitro* models including surface plasmon residence (n=5 concentrations, study completed September 2023) and cellular adhesion assays (see Figure 1, n=6 replicates per group, study completed in August 2023). It also incorporates a half-life extending modification resulting in an increase in half-life of >three-fold in Tg276 transgenic mice that express human FcRn (n=5 per group, studies completed in August 2023) and an increase in half-life of >three-fold in NHPs (n=6 per group, studies completed in December 2023), compared to vedolizumab (see Figure 2).

The 28-day GLP toxicity study in NHPs (n=42) for SPY001 has been completed with the highest dose level tested determined as the no-observed-adverse-effect-level ("NOAEL"). Chemistry, manufacturing, and control ("CMC") activities to enable the SPY001 first-in-human (“FIH”) study are also complete. Initiation of the FIH study in the second quarter of 2024 remains on track, pending health agency approval. Interim data from the Phase 1 healthy volunteer study are expected by the end of 2024. If successful, SPY001 would then advance to Phase 2 clinical studies and, pending further success, Phase 3 clinical studies to support global regulatory submissions and commercial approval.

Figure 1. Potency and selectivity of SPY001 relative to vedolizumab in cellular assays.

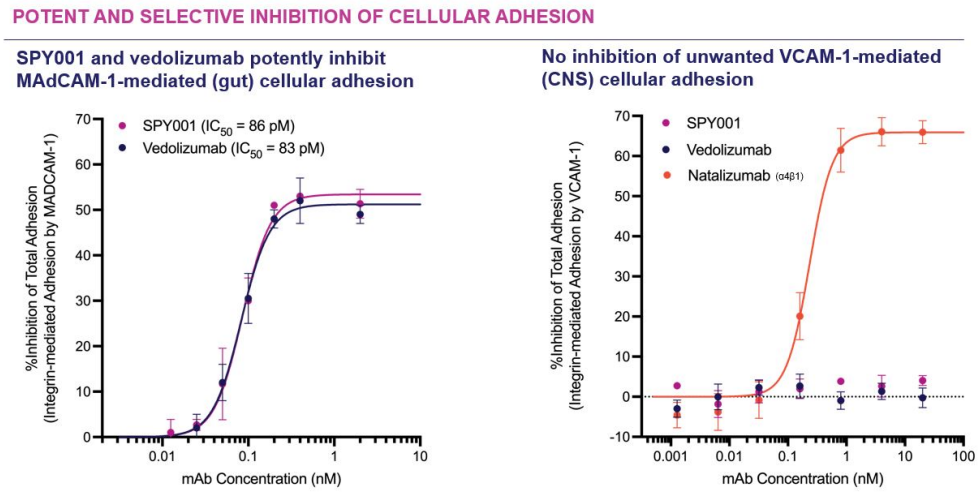
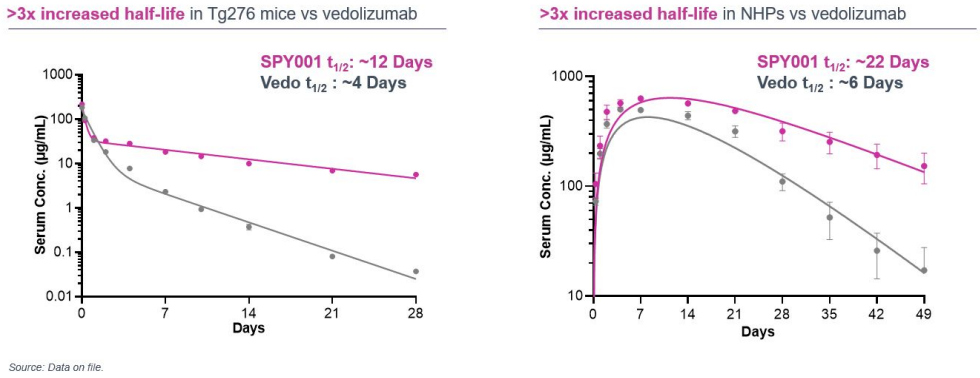


Figure 2. Pharmacokinetic concentration-time curves of SPY001 compared to vedolizumab in Tg276 transgenic mice and non-human primates (n=3-5 per group shown, removing primates that developed anti-drug antibodies).



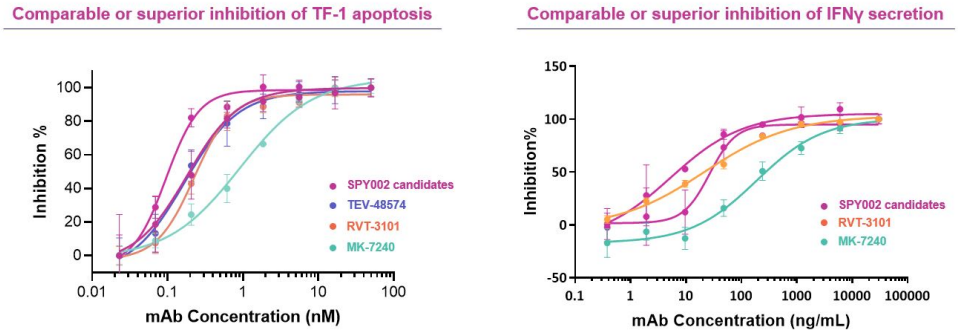
SPY002 – anti-TL1A mAb

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 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, studies completed in Q42023 and Q12024). The candidates also exhibited extended pharmacokinetic half-lives of greater than two to three-fold relative to 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, studies completed in Q42023 and Q12024). SPY002 candidates are currently progressing through IND-enabling studies (CMC scale-up ongoing) and we expect to submit an IND or equivalent foreign regulatory submission and enter a Phase 1 FIH study in healthy volunteers in the second half of 2024, with one or both of our SPY002 candidates pending additional preclinical data and pending health agency approval. Interim data from the Phase 1 healthy volunteer study are expected in the first half of 2025. If successful, one SPY002 candidate would then advance to Phase 2 clinical studies and, pending further success, Phase 3 clinical studies to support global regulatory submissions and commercial approval.

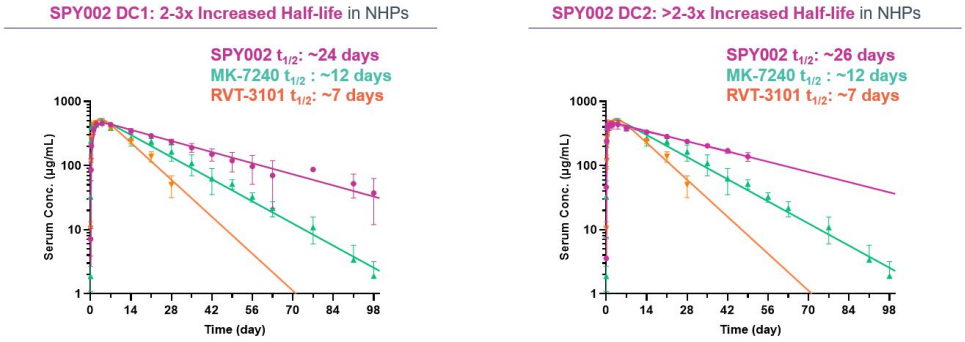
Figure 3. Inhibition of TL1-A induced TF-1 cell apoptosis (left) and IFNγ secretion in primary human whole blood 1 donor of 4 donors profiled (right).



Note: Inhibition of TL1A-induced TF-1 cell apoptosis (left) and IFNg secretion in primary human whole blood 1 donor of 4 donor profiled (right).

Source: Data on file

Figure 4. Pharmacokinetic concentration-time curves of SPY002 candidates compared to competing anti-TL1A molecules in non-human primates.



Source: Data on file.

SPY003 – anti-IL-23 mAb

SPY003 is a discovery-stage program focused on designing antibodies 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. To date, we have identified several promising clones that meet our target product profile, and we are in the process of narrowing down the potential clones to select a development candidate based on pharmacokinetic performance and CMC developability. We are continuing our preclinical development efforts with the SPY003 program and expect to nominate a development candidate in mid-2024, move into IND-enabling studies in the second half of 2024 and initiate FIH studies in the first half of 2025. Upon development candidate nomination, we intend to exercise our Option to acquire intellectual property rights for the SPY003 program pursuant to the Paragon Agreement. We expect the license to be restricted to IBD.

SPY004 – novel MOA mAb

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

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

SPY120 combines SPY001 (anti-α4β7) and SPY002 (anti-TL1A) antibodies, pairing two mechanisms studied in third-party clinical trials targeting non-overlapping sites of action. We are currently evaluating SPY120 in preclinical studies, and plan to initiate combination toxicology studies in 2024. We expect to initiate clinical studies for SPY120 in 2025, pending approval of an IND or equivalent foreign regulatory submission anticipated in 2025.

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

SPY130 combines SPY001 (anti-α4ß7) and SPY003 (anti-IL-23) antibodies, pairing two commercially validated mechanisms targeting non-overlapping sites of action. We are currently evaluating SPY130 in preclinical studies and potentially initiate combination toxicology studies in 2025.

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 preclinical studies and potentially initiate combination toxicology studies in 2025.

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 Fair Journey 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 months ended March 31, 2024, we recognized $17.1 million, in Research and development expenses that are due to Paragon under the Paragon Agreement. As of March 31, 2024, $15.5 million was unpaid and owed to Paragon under the Paragon Agreement.

On July 12, 2023 and December 14, 2023, we exercised our Option available under the Paragon Agreement with respect to the SPY001 and SPY002 research programs, respectively, and expect to enter into the SPY001 License Agreement and the SPY002 License Agreement. Our Option available under the Paragon Agreement with respect to the SPY003 and SPY004 programs remains unexercised.

Following the execution of each of the SPY001 License Agreement and SPY002 License Agreement, we will be 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. Upon execution of each of the SPY001 License Agreement and the SPY002 License Agreement, we expect to pay Paragon a $1.5 million fee for nomination of a development candidate, as applicable, and we expect to be obligated to make a further milestone payment of $2.5 million upon the first dosing of a human subject in a Phase 1 trial. With respect to the SPY002 License Agreement only, on a product by product basis, the Company will pay Paragon sublicensing fees of up to approximately $20.0 million upon the achievement of mostly commercial milestones. Subject to the execution of the Option with respect to the SPY003 or SPY004 research programs, we expect to be obligated to make similar payments upon and following the execution of license agreements with respect to these research programs, respectively.

Corporate Developments

Board Changes

On February 1, 2024, Alison Lawton resigned from the Board and the Board appointed Mark McKenna as a Class I director. Mr. McKenna and the Company are parties to a consulting agreement, pursuant to which Mr. McKenna agreed to continue to provide consulting services as an independent contractor to the Company, with an effective date of August 1, 2023 (the “Vesting Commencement Date”). As compensation for Mr. McKenna’s consulting services, on November 22, 2023, he was granted non-qualified stock options to purchase 477,000 shares of the Company’s Common Stock under the Company's equity incentive plan with an exercise price of $10.39 per share, which vest as to 25% on the one year anniversary of the Vesting Commencement

Date and thereafter vest and become exercisable in 36 equal monthly installments, subject to Mr. McKenna's continued service to the Company through each applicable vesting date.

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").

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 these condensed consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue, costs and expenses, and related disclosures. These estimates form the basis for judgments we make about the carrying values of our assets, liabilities and equity and the amount of revenues and expenses, which are not readily apparent from other sources. We base our estimates on historical experience and on various other assumptions that we believe are reasonable under the circumstances. On an ongoing basis, we evaluate our estimates and assumptions. Our actual results may differ materially from these estimates under different assumptions or conditions.

Our critical accounting policies are those policies which require the most significant judgments and estimates in the preparation of our 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.

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

Results of Operations

Comparison of the Three Months Ended March 31, 2024 and 2023

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

	Three Months Ended March 31,		Dollar Change	% Change
	2024	2023		
	(in thousands)			
Revenue:				
Development fee and royalty	$ —	$ 198	$ (198)	(100)%
Total revenue	—	198	(198)	(100)%
Operating expenses:				
Research and development	34,928	13,776	21,152	154 %
General and administrative	12,846	5,228	7,618	146 %
Total operating expenses	47,774	19,004	28,770	*
Loss from operations	(47,774)	(18,806)	(28,968)	*
Other income (expense):				
Interest income	4,432	420	4,012	*
Other expense	(483)	(72)	(411)	*
Total other income (expense)	3,949	348	3,601	
Loss before income tax expense	(43,825)	(18,458)	(25,367)	*
Income tax (expense) benefit	(32)	36	(68)	*
Net loss	$ (43,857)	$ (18,422)	$ (25,435)	*

* Percentage not meaningful

Development Fee and Royalty Revenue. For the three months ended March 31, 2024, we did not recognize any revenue in connection with our now terminated exclusive license and supply agreement with Immedica Pharma AB, dated March 21, 2021 (the "Immedica Agreement"). For the three months ended March 31, 2023, we recognized $0.2 million of development fee revenue in connection with the Immedica Agreement, which was attributable to the PEACE Phase 3 trial and BLA package.

Research and Development Expenses. Research and development expenses increased by $21.2 million, or 154%, to $34.9 million for the three months ended March 31, 2024, from $13.8 million for the three months ended March 31, 2023. Our Research and development expenses incurred during the three months ended March 31, 2024 primarily related to $26.9 million in costs associated with preclinical development and manufacturing costs associated with advancing our IBD pipeline, and $5.4 million in stock-based compensation expenses associated with the Parapyre Option Obligation, partially offset by a $9.7 million decrease in costs related to the Company's legacy rare disease pipeline and a $1.5 million decrease related to lower research and development headcount.

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 March 31, 2024 and 2023, external research and development costs accounted for $31.3 million and $7.9 million, respectively. The increase in external research and development expenses is primarily due to increases in costs associated with our IBD pipeline candidates and stock compensation expense related to the Parapyre Option Obligation, partially offset by a decrease in activities associated with the Legacy Assets.

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 March 31, 2024 and 2023, internal research and development

costs accounted for $3.6 million and $5.9 million, respectively. The decrease in internal research and development expenses is primarily due to 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 $7.6 million, or 146%, to $12.8 million for the three months ended March 31, 2024, from $5.2 million for the three months ended March 31, 2023. The increase in general and administrative expenses was primarily due to a $6.0 million increase in stock-based compensation expense and a $1.5 million increase in professional services and legal fees.

Other income (expense). Other income for the three months ended March 31, 2024, totaled $3.9 million primarily driven by $4.4 million of interest earned on the Company's cash and marketable securities, partially offset by a $0.4 million expense related to the change in fair value of the contingent value right liability.

Liquidity and Capital Resources

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

Since our inception and through March 31, 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 March 31, 2024, we had an accumulated deficit of $808.3 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 preclinical 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 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 May 2022, we sold 430,107 shares of common stock and pre-funded warrants to purchase up to 694,892 shares of common stock in a registered direct offering for gross proceeds of $45.0 million, resulting in net proceeds of $42.9 million after deducting placement agent fees and offering costs.

In June 2023, we sold 721,452 shares of convertible Series A Preferred Stock 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.

Cash Flows

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

	Three Months Ended March 31,	
	2024	2023
Net cash, cash equivalents, and restricted cash (used in) provided by:		
Operating activities	$ (28,542)	$ (17,634)
Investing activities	(104,963)	17,750
Financing activities	172,165	10
Effect of exchange rate on cash, cash equivalents, and restricted cash	(4)	11
Net increase in cash, cash equivalents, and restricted cash	$ 38,656	$ 137

Cash Used in Operating Activities

Cash used in operating activities for the three months ended March 31, 2024 was $28.5 million and reflected a net loss of $43.9 million and $2.4 million in net accretion of discount on marketable securities, partially offset by stock-based compensation of $13.8 million and a $3.5 million decrease in net operating assets and liabilities driven by timing of payments.

Cash used in operating activities for the three months ended March 31, 2023 was $17.6 million and reflected a net loss of $18.4 million and a $1.4 million increase in net operating assets and liabilities, partially offset by non-cash expense of $1.7 million for stock-based compensation and $0.6 million for depreciation and amortization.

Cash (Used in) Provided by Investing Activities

Cash used in investing activities for the three months ended March 31, 2024 was $105.0 million and primarily consisted of $152.7 million in purchases of marketable securities, partially offset by $47.8 million in maturities and sales of marketable securities.

Cash provided by investing activities for the three months ended March 31, 2023 was $17.8 million from maturities and sales of marketable securities.

Cash Provided by Financing Activities

Cash provided by financing activities for the three months ended March 31, 2024 was $172.2 million, which primarily consisted of the net proceeds from the issuance of the Series B Preferred Stock in the March 2024 PIPE of $169.2 million and $4.4 million from proceeds from stock option exercises and sales of Common Stock under our Employee Stock Purchase Plan.

Cash provided by financing activities for the three months ended March 31, 2023, was $0.1 million, which primarily consisted of the sale of Common Stock under our 2016 Employee Stock Purchase Plan.

Contingent contractual obligations

Through the Asset Acquisition, we received the Option to license the IPR&D rights related to four research programs. On July 12, 2023 and on December 14, 2023, we exercised the Option with respect to two of these research programs, respectively. The exercise of the Option allows for us to enter into an exclusive license agreement with Paragon for the respective research program. Upon license execution, we expect to be obligated to pay Paragon up to $22.0 million based on specific development, regulatory and clinical milestones for each licensed research program. As of March 31, 2024, none of the $22.0 million obligation was accrued for since the related license agreements are still being negotiated. As of the date of the filing of this Quarterly Report, the Option remains unexercised with respect to the two remaining research programs under the Paragon Agreement. Should the Option for these research programs be exercised and upon entry into license

agreements with respect to such research programs, we expect to be obligated to pay Paragon up to $22.0 million per research program based on certain development, regulatory and clinical milestones.

We expect to enter into the SPY001 License Agreement and the SPY002 License Agreement. Upon execution of each of the SPY001 License Agreement and the SPY002 License Agreement, we expect to pay Paragon a $1.5 million fee for nomination of a development candidate, as applicable, and we expect to be obligated to make a further milestone payment of $2.5 million upon the first dosing of a human subject in a Phase 1 trial. Subject to the execution of the Option with respect to the SPY003 or SPY004 research programs, we expect to be obligated to make similar payments upon and following the execution of license agreements with respect to these research programs.

In addition to the above, although the SPY001 License Agreement and the SPY002 License Agreement have not been entered into as of the date hereof, the following summarizes other key terms that we expect to be included in such agreements:

- Paragon will provide Spyre with an exclusive license to its patents covering the related antibody, the method of use and its method of manufacture.
- Paragon will not conduct any new campaigns that generate anti-α4ß7 or anti-TL1A monospecific antibodies for at least 5 years.
- Spyre 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 Spyre patent directed to a derived antibody or (ii) 12 years from the date of first sale of a Spyre product.
- Agreement may be terminated on 60 days' notice by Spyre; 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, Spyre will pay Paragon sublicensing fees of up to approximately $20.0 million upon the achievement of mostly commercial 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 March 31, 2024, we held $485.0 in cash, cash equivalents, marketable securities, and restricted cash, predominately all of which was denominated in U.S. dollars, and consisted primarily of investments in money market funds, commercial paper, U.S. government obligations, and corporate bonds.

We are also exposed to market risk related to changes in foreign currency exchange rates as a result of our entering into transactions denominated in currencies other than U.S. dollars. Due to the uncertain timing of

expected payments in foreign currencies, we do not utilize any forward exchange contracts. All foreign transactions settle on the applicable spot exchange basis at the time such payments are made. For the three months ended March 31, 2024, a majority of our expenditures were denominated in U.S. dollars. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

Item 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 March 31, 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 and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting during the quarter ended March 31, 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

There have been no material changes to the risk factors disclosed in our Annual Report on Form 10-K for the year ended December 31, 2023 and in our registration statement on Form S-1 filed with the SEC on April 19, 2024 (the "Form S-1"). For a detailed description of our risk factors, refer to Part I, Item IA, "Risk Factors" of our Annual Report and the section titled "Risk Factors" of our Form S-1.

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

On February 22, 2024, in accordance with the Paragon Agreement and to settle the Company's 2023 obligations under the Parapyre Option Obligation, the Company delivered to Paragon a warrant to purchase an aggregate of up to 684,407 shares of Common Stock, with a per share exercise price equal to $21.52, which was the closing price of a share of Common Stock on December 29, 2023 (the "Issue Date"), the last business day of the calendar year-ended December 31, 2023, effective as of the Issue Date and an expiration date of the 10th anniversary of the Issue Date. We have relied on the exemption from registration requirements provided by Section 4(a)(2) under the Securities Act of 1933, as amended, relating to a transaction not involving any public offering to a single accredited investor.

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 March 31, 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.

Exhibit Number	Description	Form	File No	Date of Filing	Exhibit No.	Filed Herewith
2.1	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.	S-1	333-276251	12/22/2023	2.1	
3.1	Amended and Restated Certificate of Incorporation	S-1	333-276251	12/22/2023	3.1	
3.2	Amended and Restated Bylaws	S-1/A	333-276251	02/05/2024	3.2	
3.3	Certificate of Designation of Series A Non-Voting Convertible Preferred Stock	S-1	333-276251	12/22/2023	3.3	
3.4	Certificate of Designation of Series B Non-Voting Convertible Preferred Stock	S-1	333-276251	12/22/2023	3.4	
3.5	Certificate of Amendment to Certificate of Designation of Series B Non-Voting Convertible Preferred Stock	8-K	001-37722	03/18/2024	3.2	
4.1	Form of Registration Rights Agreement (March 2024 PIPE)	8-K	001-37722	03/18/2024	10.2	
4.2	Form of Warrant to Purchase Common Stock (Parapyre Warrant 2023)					X
10.1	2024 Form of Indemnification Agreement	S-1/A	333-276251	02/05/2024	10.19	
10.2+	Amended and Restated Offer Letter, dated November 22, 2023 and as amended on February 1, 2024, by and between the Company and Cameron Turtle	S-1/A	333-276251	02/05/2024	10.4	
10.3	Securities Purchase Agreement, dated as of March 18, 2024, by and among Spyre Therapeutics, Inc. and each purchaser identified on Annex A thereto	8-K	001-37722	03/18/2024	10.1	
10.4	Consulting Agreement by and between the Company and Mark McKenna, effective August 1, 2023	10-K	001-37722	02/29/2024	10.20	
10.5	Exchange Agreement, dated April 23, 2024, by and between the Company and Fairmount Healthcare Fund II L.P.	8-K	001-37722	4/25/2024	10.1	
10.6	Amendment No. 1 to Novation Agreement, dated April 25, 2024, by and between Paragon Therapeutics, Inc., the Company and WuXi Biologics (Hong Kong) Limited					X
31.1	Certification of the Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934					X

Exhibit Number	Description	Form	File No	Date of Filing	Exhibit No.	Filed Herewith
31.2	Certification of the Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934					X
32.1(1)	Certification of the Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
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: May 9, 2024

Spyre Therapeutics, Inc.

By: /s/ Scott Burrows

Scott Burrows

Chief Financial Officer

(Principal Financial Officer and Principal Accounting Officer)

E

Exhibit 4.2
SPYRE THERAPEUTICS, INC.
WARRANT TO PURCHASE COMMON STOCK

Number of Warrant Shares: 684,407
(subject to adjustment)
Original Issue Date: December 29, 2023

Warrant No. SYRE-001R

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

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

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

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

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

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

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

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

Section 2. Exercise.

a) Exercise of Warrant. Exercise of the purchase rights represented by this Warrant may be made, in whole or in part, at any time or times on or after the Original Issue Date and on or before the Termination Date, including by means of a "cashless exercise" as described in Section 2(c) below, by delivery to the Company of a duly executed facsimile copy or PDF copy submitted by e-mail (or e-mail attachment) of the Notice of Exercise in the form annexed hereto (the "Notice of Exercise"). Within the earlier of (i) two (2) Trading Days and (ii) the number of

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

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

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

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

where:

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

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

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

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

d) Mechanics of Exercise.

i. Delivery of Warrant Shares Upon Exercise. Within a reasonable time after Holder exercises this Warrant in the manner set forth in Section 2(a) or 2(c) above, the Company shall deliver to Holder a certificate (which certificate may be in the form of an electronic certificate or DTC entry, to the extent used by the Company at the time of such exercise) or evidence of book entry representing the Warrant Shares issued to such Holder upon such exercise As used herein, "Standard Settlement Period" means the standard settlement period, expressed in a number of Trading Days, on the Principal Trading Market with respect to the Common Stock as in effect on the date of delivery of the Notice of Exercise to the Company.

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

iii. [RESERVED.]

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

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

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

e) Holder's Exercise Limitations. The Company shall not effect any exercise of this Warrant, and a Holder shall not have the right to exercise any portion of this Warrant, pursuant to Section 2 or otherwise, to the extent that after giving effect to such issuance after exercise as set forth on the applicable Notice of Exercise, the Holder (together with the Holder's Affiliates, and any other Persons acting as a group together with the Holder or any of the Holder's Affiliates (such Persons, "Attribution Parties")), would beneficially own in excess of the Beneficial Ownership Limitation (as defined below). For purposes of the foregoing sentence, the number of shares of Common Stock beneficially owned by the Holder and its Affiliates and Attribution Parties shall include the number of shares of Common Stock issuable upon exercise of this Warrant with respect to which such determination is being made, but shall exclude the number of shares of Common Stock which would be issuable upon (i) exercise of the remaining, nonexercised portion of this Warrant beneficially owned by the Holder or any of its Affiliates or Attribution Parties and (ii) exercise or conversion of the unexercised or nonconverted portion of any other securities of the Company subject to a limitation on conversion or exercise analogous to the limitation contained herein beneficially owned by the Holder or any of its Affiliates or Attribution Parties. Except as set forth in the preceding sentence, for purposes of this Section 2(e), beneficial ownership shall be calculated in accordance with Section 13(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") and the rules and regulations promulgated thereunder, it being acknowledged by the Holder that the Company is not representing to the Holder that such calculation is in compliance with Section 13(d) of the Exchange Act and the Holder is solely responsible for any schedules required to be filed in accordance therewith. To the extent that the limitation contained in this Section 2(e) applies, the determination of whether this Warrant is exercisable (in relation to other securities owned by the Holder together with any Affiliates and Attribution Parties) and of which portion of this Warrant is exercisable shall be in the sole discretion of the Holder, and the Holder's submission of a Notice of Exercise to the Company shall be deemed to be the Holder's determination of whether this Warrant is exercisable (in relation to other securities owned by the Holder together with any Affiliates and Attribution Parties) and of which portion of this Warrant is exercisable, in each case subject to the Beneficial Ownership Limitation, and, absent manifest error, the Company shall have no obligation to verify or confirm the accuracy of such determination. In addition, a determination as to any group status as contemplated above shall be determined in accordance with Section 13(d) of the Exchange Act and the rules and regulations promulgated thereunder. For purposes of this Section 2(e), in determining the number of outstanding shares of Common Stock, a Holder may rely on the number of outstanding shares of Common Stock as reflected in (A) the Company's most recent periodic or annual report filed with the Commission, as the case may be, (B) a more recent public announcement by the Company or (C) a more recent written notice by the Company or the Transfer Agent setting forth the number of shares of Common Stock outstanding. Upon the written or oral request of a Holder, the Company shall within one Trading Day confirm orally and in writing to the Holder the number of shares of Common Stock then outstanding. In any case, the number of outstanding shares of Common Stock shall be determined after giving effect to the conversion or exercise of securities of the Company, including this Warrant, by the Holder or its Affiliates or Attribution Parties since the date as of which such number of outstanding shares of Common Stock was reported. As used herein, "Affiliate" shall mean any Person directly or indirectly controlled by, controlling or under common control with, a Holder, as such terms are used in and construed under Rule 405 under the Securities Act, but only for so long as such control shall continue. The "Beneficial Ownership Limitation" shall be 4.99% of the number of shares of the Common Stock

outstanding immediately after giving effect to the issuance of shares of Common Stock issuable upon exercise of this Warrant. The provisions of this paragraph shall be construed and implemented in a manner otherwise than in strict conformity with the terms of this Section 2(e) to correct this paragraph (or any portion hereof) which may be defective or inconsistent with the intended Beneficial Ownership Limitation herein contained or to make changes or supplements necessary or desirable to properly give effect to such limitation. The limitations contained in this paragraph shall apply to a successor holder of this Warrant.

Section 3. Certain Adjustments.

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

b) Subsequent Rights Offerings. In addition to any adjustments pursuant to Section 3(a) above, if at any time the Company grants, issues or sells any rights to purchase stock, warrants, securities or other property pro rata to the record holders of any class of shares of Common Stock (the "Purchase Rights"), then the Holder will be entitled to acquire, upon the terms applicable to such Purchase Rights, the aggregate Purchase Rights which the Holder could have acquired if the Holder had held the number of shares of Common Stock acquirable upon complete exercise of this Warrant (without regard to any limitations on exercise hereof, including without limitation, the Beneficial Ownership Limitation) immediately before the date on which a record is taken for the grant, issuance or sale of such Purchase Rights, or, if no such record is taken, the date as of which the record holders of shares of Common Stock are to be determined for the grant, issue or sale of such Purchase Rights (*provided*, *however*, that, to the extent that the Holder's right to participate in any such Purchase Right would result in the Holder exceeding the Beneficial Ownership Limitation, then the Holder shall not be entitled to participate in such Purchase Right to such extent (or beneficial ownership of such shares of Common Stock as a result of such Purchase Right to such extent) and such Purchase Right to such extent shall be held in abeyance for the Holder until such time, if ever, as its right thereto would not result in the Holder exceeding the Beneficial Ownership Limitation).

c) Pro Rata Distributions. During such time as this Warrant is outstanding, if the Company shall declare or make any dividend or other distribution of its assets (or rights to acquire its assets) to holders of shares of Common Stock, by way of return of capital or otherwise (including, without limitation, any distribution of cash, stock or other securities, property or options by way of a dividend, spin off, reclassification, corporate rearrangement, scheme of arrangement or other similar transaction) (a "Distribution"), at any time after the issuance of this Warrant, then, in each such case, the Holder shall be entitled to participate in such Distribution to the same extent that the Holder would have participated therein if the Holder had held the number of shares of Common Stock acquirable upon complete exercise of this Warrant (without regard to any limitations on exercise hereof, including without limitation, the Beneficial Ownership Limitation) immediately before the date of which a record is taken for such Distribution, or, if no such record is taken, the date as of which the record holders of shares of Common Stock are to be determined for the participation in such Distribution (*provided*, *however*, that, to the extent that the Holder's right to participate in any such Distribution would result in the Holder exceeding the Beneficial Ownership Limitation, then the Holder shall not be entitled to participate in such Distribution to such extent (or in the beneficial ownership of any shares of Common Stock as a result of such Distribution to such extent) and the portion of such Distribution shall be held in abeyance for the benefit of the Holder until such time, if ever, as its right thereto would not result in the Holder exceeding the Beneficial Ownership Limitation).

d) Fundamental Transaction. If, at any time while this Warrant is outstanding, (i) the Company, directly or indirectly, in one or more related transactions effects any merger or consolidation of the Company with or into

another Person, (ii) the Company (and all of its subsidiaries, taken as a whole), directly or indirectly, effects any sale, lease, license, assignment, transfer, conveyance or other disposition of all or substantially all of its assets in one or a series of related transactions, (iii) any, direct or indirect, purchase offer, tender offer or exchange offer (whether by the Company or another Person) is completed pursuant to which holders of Common Stock are permitted to sell, tender or exchange their shares for other securities, cash or property and has been accepted by the holders of 50% or more of the outstanding Common Stock or 50% or more of the outstanding voting power of the common equity of the Company, (iv) the Company, directly or indirectly, in one or more related transactions effects any reclassification, reorganization or recapitalization of the Common Stock or any compulsory share exchange pursuant to which the Common Stock is effectively converted into or exchanged for other securities, cash or property, or (v) the Company, directly or indirectly, in one or more related transactions consummates a stock or share purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off, merger or scheme of arrangement) with another Person or group of Persons whereby such other Person or group acquires 50% or more of the outstanding shares of Common Stock or 50% or more of the outstanding voting power of the common equity of the Company (each a "Fundamental Transaction"), then, upon any subsequent exercise of this Warrant, the Holder shall have the right to receive, for each Warrant Share that would have been issuable upon such exercise immediately prior to the occurrence of such Fundamental Transaction, at the option of the Holder (without regard to any limitation in Section 2(e) on the exercise of this Warrant), the number of shares of Common Stock of the successor or acquiring corporation or of the Company, if it is the surviving corporation, and any additional consideration (the "Alternate Consideration") receivable as a result of such Fundamental Transaction by a holder of the number of shares of Common Stock for which this Warrant is exercisable immediately prior to such Fundamental Transaction (without regard to any limitation in Section 2(e) on the exercise of this Warrant). For purposes of any such exercise, the determination of the Exercise Price shall be appropriately adjusted to apply to such Alternate Consideration based on the amount of Alternate Consideration issuable in respect of one share of Common Stock in such Fundamental Transaction, and the Company shall apportion the Exercise Price among the Alternate Consideration in a reasonable manner reflecting the relative value of any different components of the Alternate Consideration.

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

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

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

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

Transaction at least ten (10) days prior to the date such Fundamental Transaction is consummated. Holder agrees to maintain any information disclosed pursuant to this Section 3(h) in confidence until such information is publicly available, and shall comply with applicable law with respect to trading in the Company's securities following receipt of any such information.

Section 4. Transfer of Warrant.

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

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

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

Section 5. Miscellaneous.

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

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

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

d) Authorized Shares.

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

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

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

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

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

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

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

h) Notices. Any and all notices or other communications or deliveries hereunder (including, without limitation, any Notice of Exercise) shall be in writing and shall be deemed given and effective on the earliest of (i) the date of transmission, if such notice or communication is delivered via facsimile or confirmed e-mail prior to 5:30 P.M., New York City time, on a Trading Day, (ii) the next Trading Day after the date of transmission, if such notice or communication is delivered via confirmed e-mail on a day that is not a Trading Day or later than 5:30 P.M., New York City time, on any Trading Day, (iii) the Trading Day following the date of mailing, if sent by nationally recognized overnight courier service specifying next business day delivery, or (iv) upon actual receipt by the Person to whom such notice is required to be given, if by hand delivery. The addresses and e-mail addresses for such communications shall be:

If to the Company:

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

With a copy (for informational purposes only) to:

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

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

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

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

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

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

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

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

****

(Signature Page Follows)

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

SPYRE THERAPEUTICS, INC.

By: /s/ Scott Burrows

Name: Scott Burrows

Title: Chief Financial Officer

NOTICE OF EXERCISE

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

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

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

[ ] in lawful money of the United States; or

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

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

_____

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

[SIGNATURE OF HOLDER]

Name of Investing Entity:
Signature of Authorized Signatory of Investing Entity:
Name of Authorized Signatory:
Title of Authorized Signatory:
Date:

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

ASSIGNMENT FORM

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

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

Name: _____
(Please Print)

Address: _____
(Please Print)

Phone Number: _____
Email Address: _____

Dated: _____ __, _____
Holder's Signature:
Holder's Address:

Exhibit 10.6

AMENDMENT NO. 1 TO THE NOVATION AGREEMENT

This Amendment No. 1 (the "**Amendment**"), effective as of April 25, 2024 (the "**Amendment Effective Date**") to the Novation Agreement effective as of July 21, 2023 and executed on September 19, 2023 (the "**Novation Agreement**") is entered into by and among (i) Paragon Therapeutics, Inc., a Delaware corporation with an office at 221 Crescent Street, Building 23, Suite 105, Waltham, MA 02453 (the "**Transferor**"), (ii) Spyre Therapeutics, Inc. (f/k/a Aeglea BioTherapeutics, Inc.), a Delaware corporation with an office at 221 Crescent Street Building 23, Suite 105, Waltham, MA 02453 ("**Spyre**"), and (iii) WuXi Biologics (Hong Kong) Limited, a Hong Kong corporation with its registered address at Flat/RM826, 8/F Ocean Centre Harbour City, 5 Canton Road TST, Hong Kong (the "**Counterparty**").

WHEREAS, Spyre, Transferor and Counterparty entered into the Novation Agreement;

WHEREAS, Spyre effected a change of its name from Aeglea Biotherapeutics, Inc. to Spyre Therapeutics, Inc. on November 28, 2023 (the "**Name Change**"); and

WHEREAS, Spyre, Transferor and Counterparty desire to amend the Novation Agreement to reflect (i) the Name Change; (ii) a correction to Spyre's address to 221 Crescent Street Building 23, Suite 105, Waltham, MA 02453; and (iii) the addition of certain additional contracts to be novated in Exhibit A thereto.

NOW, THEREFORE, in consideration of the above provisions and the mutual agreements contained herein and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, Spyre, Transferor, and Counterparty agree as follows:

1. **Amendments**.

    a. *Name Change.* All references to "Aeglea Biotherapeutics, Inc." and the defined term "Aeglea" in the Novation Agreement are hereby deleted and replaced with "Spyre Therapeutics, Inc." and "Spyre", respectively.

    b. *Address*. The address of Spyre referenced in the first paragraph of the Novation Agreement is hereby deleted and replaced with "221 Crescent Street Building 23, Suite 105, Waltham, MA 02453".

    c. *Exhibit A.* Exhibit A of the Novation Agreement is hereby deleted in its entirety and replaced with the revised Exhibit A attached hereto.

2. **No Further Amendments.** Except as expressly provided in this Amendment, the Novation Agreement will remain unchanged and in full force and effect in accordance with its original terms.

3. **Miscellaneous.**

a. This Amendment shall be governed by, and construed in accordance with, the laws of the State of New York, without giving effect to its conflicts of law principles.

b. This Amendment may be executed and delivered in any number of counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Counterparts may be executed and delivered via facsimile, electronic signature, electronic mail (including pdf or any electronic signature complying with the U.S. federal ESIGN Act of 2000, e.g., www.docusign.com) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

c. The invalidity or unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision.

[SIGNATURE PAGE FOLLOWS]

In witness whereof, the parties hereto have executed this Amendment as of the Amendment Effective Date.
Transferor:

PARAGON THERAPEUTICS, INC.

By: /s/ Evan Thompson
Name: Evan Thompson
Title: COO

Spyre:

SPYRE THERAPEUTICS, INC.

By: /s/ Cameron Turtle
Name: Cameron Turtle
Title: Chief Executive Officer

Counterparty:

WUXI BIOLOGICS (HONG KONG) LIMITED

By: /s/ Chris Chen
Name: Chris Chen
Title: Director

EXHIBIT A

Original Contracts

A. Biologics Master Services Agreement effective June 20, 2022, signed in April 2023.
B. Cell Line License Agreement dated June 20, 2022, signed in April 2023.
C. Customer Order: WO.PARAG-20230601 dated June 9, 2023.
D. Customer Order: WO.PARAG-20230606 dated August 11, 2023.
E. Work Order WO. PARAG-20230210 (WuXi Biologics Project ID: PARAG-20230210), dated February 16, 2023.
F. Change Order CO.WBP5055-001.V01 for WuXi Biologics Project Code: WBP5055 (Project ID: PARAG-20230210), effective June 13, 2023.
G. Change Order CO.WBP5055-002.V01 for WuXi Biologics Project Code: WBP5055 (Project ID: PARAG-20230210), effective June 19, 2023.
H. Change Order CO.WBP5055-003.V05 for WuXi Biologics Project Code: WBP5055 (Project ID: PARAG-20230210), effective November 16, 2023.
I. Change Order CO.WBP5055-004.V1 for WuXi Biologics WBP5055 (Project ID: PARAG-20230210), effective January 17, 2024.
J. Change Order CO.WBP5055-005.V01 for WuXi Biologics Project Code: WBP5055 (Project ID: PARAG-20230210), effective January 30, 2024.

Exhibit 31.1

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

I, Cameron Turtle, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Spyre Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures, and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 9, 2024

/s/ Cameron Turtle, D.Phil

Cameron Turtle, D.Phil
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

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

I, Scott Burrows, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Spyre Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures, and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 9, 2024

/s/ Scott Burrows

Scott Burrows

Chief Financial Officer

(Principal Financial Officer and Principal Accounting Officer)

Exhibit 32.1

Certifications of the
Principal Executive Officer and Principal Financial Officer
Pursuant To 18 U.S.C. Section 1350,
As Adopted Pursuant To
Section 906 of The Sarbanes-Oxley Act Of 2002

In connection with the Quarterly Report of Spyre Therapeutics, Inc. (the "Company") on Form 10-Q for the quarterly period ended March 31, 2024, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: May 9, 2024

/s/ Cameron Turtle, D.Phil

Cameron Turtle, D.Phil
Chief Executive Officer
(Principal Executive Officer)

/s/ Scott Burrows

Scott Burrows
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)