



Spyre Therapeutics Reports First Quarter 2025 Financial Results and Provides Corporate Update

On track for mid-year initiations of planned Phase 2 studies in ulcerative colitis ("UC") and rheumatoid arthritis ("RA"), providing for 7+ proof-of-concept readouts in 2026 & 2027

Reported extended follow-up Phase 1 data for SPY001, supporting that the molecule is well tolerated, has a pharmacokinetic ("PK") profile enabling quarterly or biannual dosing, and provides complete target engagement at expected Phase 2 trough concentrations

Remain on track to report interim Phase 1 data for SPY002 later this quarter, with the potential to demonstrate a product profile superior to first-generation TL1A antibodies

Announced first participant dosed in Phase 1 trial of SPY003, with interim PK and safety data readout on track for the second half of 2025

\$565 million of cash, cash equivalents, and marketable securities as of March 31, 2025, with expected runway into the second half of 2028

Waltham, Mass, May 8, 2025 - Spyre Therapeutics, Inc. ("Spyre" or the "Company") (NASDAQ:SYRE), a clinical-stage biotechnology company utilizing best-in-class antibody engineering, dose optimization, and rational therapeutic combinations to target improved efficacy and convenience in the treatment of inflammatory bowel disease ("IBD") and other immune-mediated diseases, today announced its first quarter 2025 financial results and provided program and corporate updates.

"We continued to efficiently execute on our ambitious strategy this quarter - presenting longer-term SPY001 Phase 1 data that further supports its potential best-in-class profile, continuing dosing with our SPY002 molecules in parallel Phase 1 trials, and initiating our fourth Phase 1 trial within nine months with SPY003," said Cameron Turtle, DPhil., Chief Executive Officer. "This quarter, we look forward to sharing interim SPY002 Phase 1 data which has the potential to demonstrate a best-in-class profile for the treatment of IBD and other immune-mediated diseases, as well as a second optimized component of our potentially paradigm-changing investigational combination therapies. Following these data, we plan to embark on two fully funded, groundbreaking Phase 2 trials that will provide 7+ proof-of-concept readouts in markets with annual revenues totaling approximately \$50B. With de-risked biology, an experienced team, and a strong balance sheet, we are focused on delivering against our plans to redefine the standard-of-care in IBD and beyond while providing a transformative set of catalysts for our investors."

Development Pipeline Overview and Update

The Company's approach combines best-in-class antibody engineering, dose optimization, and rational therapeutic combinations with the goal of maximizing efficacy, safety, and convenience in the treatment of IBD and other immune-mediated diseases. IBD is a chronic condition characterized by inflammation within the gastrointestinal tract, including two main disorders: UC and Crohn's disease ("CD"). In the United States, it is estimated that approximately 2.4 million individuals are diagnosed with IBD. RA is a chronic inflammatory autoimmune condition that primarily affects the joints but also other parts of the body. It is characterized by pain, stiffness, and swelling of one or more joints and can progress from mild swelling of the joints in early stages

to severe deformations of the feet, ankles, and hands in late/severe stages. RA affects more than 1.5 million individuals in the United States.

The Company has three programs in clinical development, all of which are targets in IBD validated by third parties. All three validated targets offer the potential for safe and effective treatment of UC and CD, with infrequent, subcutaneous maintenance dosing as a monotherapy or in rational combinations. The Company is also planning to study its anti-TL1A program in additional indications outside IBD, beginning with RA.

SPY001 – a highly potent and selective investigational monoclonal antibody targeting $\alpha 4\beta 7$, engineered with half-life extension technology and formulated at high concentration with the goal of maximizing efficacy and enabling infrequent, subcutaneous maintenance dosing.

- In May 2025, extended follow up data were presented at Digestive Disease Week ("DDW") 2025 from the Phase 1 healthy volunteer trial, demonstrating a favorable safety profile across all dose groups, a meaningfully differentiated PK profile with half-life estimate of more than three times that of vedolizumab that remains supportive of potential Q6M maintenance dosing, and rapid and complete saturation of $\alpha 4\beta 7$ receptors beyond six months with a single dose of 600mg.
- Based on these interim results, Spyre plans to advance SPY001 to a Phase 2 clinical trial in UC patients in mid-2025.

SPY002 – a program with two highly potent and selective, investigational anti-TL1A monoclonal antibodies, engineered with half-life extension technology and formulated at high concentration with the goal of maximizing efficacy and enabling infrequent, subcutaneous maintenance dosing. The Company believes TL1A has emerged as one of the most promising targets in IBD and broader immunology indications.

- In January 2025, the Company announced its intent to study one of its anti-TL1A antibodies in RA, with Phase 2 trial initiation expected in mid-2025 and topline results in 2026. With class-leading potency and half-life established in preclinical studies, SPY002 has the potential to become the first-in-class and best-in-class anti-TL1A treatment for RA.
- In December 2024, the Company announced initiation of first-in-human ("FIH") trials of both SPY002 candidates, with healthy volunteer interim data expected in the second quarter of 2025. If successful, the Company expects one or more SPY002 candidates would then advance to Phase 2 clinical trials.
- In October 2024, preclinical data for both SPY002 development candidates were presented at the United European Gastroenterology Week ("UEGW") Congress demonstrating superior or comparable in vitro potency to first-generation anti-TL1As, as well as a pharmacokinetic half-life of 24 days in non-human primates ("NHPs"), which represents a two to three-fold increase compared to these same first-generation anti-TL1As.

SPY003 – a highly potent and selective investigational monoclonal antibody targeting the p19 subunit of IL-23, engineered with half-life extension technology and formulated at high concentration with the goal of maximizing efficacy and enabling infrequent, subcutaneous maintenance dosing.

- In March 2025, the Company initiated a FIH trial of SPY003, with healthy volunteer interim data expected in the second half of 2025.
- In October 2024, preclinical data for SPY003 were presented for the first time at UEGW, demonstrating comparable potency to risankizumab, as well as a pharmacokinetic half-life of 30 days in NHPs, greater than three-fold compared to risankizumab. These data also demonstrated that SPY003 exhibits high selectivity and affinity for IL-23 and potently inhibits downstream cellular signaling.

Rational Combinations – the Company plans to investigate combinations of our proprietary antibodies in nonclinical studies and clinical trials in order to evaluate whether combination therapy can potentially lead to best-in-class efficacy in IBD, with less frequent dosing.

- In February and May 2025, preclinical data for SPY120 were presented at various medical meetings, demonstrating that the combined inhibition of TL1A and $\alpha 4\beta 7$ is superior to either monotherapy in mouse models of colitis and that coadministration of SPY001 and SPY002 demonstrated no drug effects on PK in NHPs.
- In October 2024, preclinical data for SPY130 and SPY230 were presented at UEGW, demonstrating enhanced efficacy and pharmacodynamics with SPY003 in combination with SPY001 and with SPY002.
- The Company expects to initiate a Phase 2 clinical trial in 2025 that is intended to include each of its rational combinations, as well as all three of its lead monotherapy programs.

First Quarter 2025 Financial Results

Cash Position: As of March 31, 2025, Spyre had cash, cash equivalents, and marketable securities of \$564.8 million. Net cash used in operating activities was \$41.0 million for the first quarter of 2025.

Research and Development (R&D) expenses: R&D expenses totaled \$41.6 million for the first quarter of 2025 and \$34.9 million for the first quarter of 2024. The increase was primarily driven by higher clinical and nonclinical development expenses, offset partially by lower antibody discovery costs.

General and Administrative (G&A) expenses: G&A expenses totaled \$11.9 million for the first quarter of 2025 and \$12.8 million for the first quarter of 2024.

Other income (expense): Other income totaled \$8.8 million for the first quarter of 2025 and \$3.9 million for the first quarter of 2024. The increase was primarily driven by higher interest earned on the Company's cash and marketable securities as well as a change in fair value of the contingent value right liability.

Net Loss: Net loss totaled \$44.8 million and \$43.9 million for the first quarters of 2025 and 2024, respectively, which includes non-cash stock-based compensation expense of \$8.9 million and \$13.8 million for the first quarters of 2025 and 2024, respectively.

About Spyre Therapeutics

Spyre Therapeutics is a clinical-stage biotechnology company that aims to create next-generation inflammatory bowel disease (IBD) and other immune-mediated disease products by combining best-in-class antibody engineering, dose optimization, and rational therapeutic combinations. Spyre's pipeline includes investigational extended half-life antibodies targeting $\alpha 4\beta 7$, TL1A, and IL-23.

For more information, please visit <http://spyre.com>.

Safe Harbor / Forward Looking Statements

This press release contains "forward-looking" statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. All statements contained in this press release, other than statements of historical fact, are forward-looking statements. These forward-looking statements include statements regarding the Company's future results of operations and financial position; its business strategy, including the Company's ability to successfully develop best-in-class and/or first-in-class therapeutics for IBD, RA, or other immune-mediated diseases that meaningfully improve both efficacy and convenience compared to today's standard of care; the SPY002 Phase I data potential to demonstrate a product profile superior to first generation TL1As; the SPY001 Phase 1 trial final data readouts not being consistent with or being different than the interim Phase 1 results; the expected timing for receipt of interim data, including interim Phase 1 data for SPY002 and SPY003; the sufficiency of the Company's funding to support the development of its assets, including expectations of cash runway extending into the second half of 2028 and being sufficient to fully fund two planned Phase 2 trials in UC and RA providing for 7+ proof-of-concept readouts in 2026 and 2027; the length of time that the Company believes its existing cash resources will fund its operations; estimated market sizes and potential growth opportunities; its nonclinical and future clinical development activities, including expected timing of each cohort for the platform Phase 2 trial in UC; the expected number of proof-of-concept readouts to be delivered; the expected advancement of one or more SPY002 candidates to Phase 2 trials; clinical trial designs, including the Company's planned platform Phase 2 trial in UC, and related regulatory feedback; further clinical evaluation of therapeutic combinations; the potential efficacy, tolerability, convenience, commercial viability and safety profile of its product candidates, including in combinations; the planned dosing regimen for SPY001 and our other product candidates, including the potential for a Q3M or Q6M dosing profile; the potential therapeutic benefits and economic value of its product candidates as monotherapies or in combinations and their extended half-life; the timing for initiation of nonclinical studies and clinical trials, including the Phase 2 trials in UC and RA; and the planned expansion of SPY002 into RA and other indications, including timing thereof. The words "believe," "may," "will," "potentially," "estimate," "continue," "anticipate," "predict," "target," "intend," "could," "would," "should," "project," "plan," "expect," the negatives of these terms, 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 the expected or potential impact of macroeconomic conditions, including inflationary pressures, rising interest rates, general economic slowdown or a recession, changes in tariff/trade and monetary policy, the prospect of a shutdown of the U.S. federal government, volatile market conditions, financial institution instability, as well as geopolitical instability, including the ongoing military conflict in Ukraine, conflicts in the middle east, and geopolitical tensions between the United States and other countries, including China, on the Company's operations, the implementation of measures that restrict international trade by the United States, China or other governments, the potential impacts of the BIOSECURE Act or similar act if passed into law and those risks described in the Company's Quarterly Reports on Form 10-Q, Annual Reports on Form 10-K, as well as in other filings and reports that the Company makes from time to time with the Securities and Exchange Commission. Moreover, the Company operates in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for the Company's management to predict all risks, nor can the Company assess the impact of all factors on the 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 it may make. In light of these risks, uncertainties, and assumptions, the forward-looking events and circumstances discussed in this press release 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 the Company believes that the expectations reflected in the forward-looking statements are reasonable, the Company 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. The Company undertakes no obligation to update publicly any forward-looking statement for any reason after the date of this press release to conform these statements to actual results, to reflect changes in the Company's expectations, or otherwise, except as required by law. You

should read press release with the understanding that the Company's actual results, levels of activity, performance, events, outcomes, and the timing of results and outcomes, and other circumstances may be materially different from what the Company expects.

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

	March 31, 2025	December 31, 2024
ASSETS		
CURRENT ASSETS		
Cash and cash equivalents	\$ 48,493	\$ 89,423
Marketable securities	516,327	513,665
Prepaid expenses and other current assets	4,948	5,386
Total current assets	569,768	608,474
Other non-current assets	10	10
TOTAL ASSETS	\$ 569,778	\$ 608,484
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES		
Accounts payable	\$ 3,689	\$ 666
CVR liability	42,810	25,080
Accrued and other current liabilities	21,631	27,711
Related party accounts payable	2,548	603
Total current liabilities	70,678	54,060
Non-current CVR liability	16,490	36,620
TOTAL LIABILITIES	87,168	90,680
Commitments and Contingencies		
STOCKHOLDERS' EQUITY		
Series A non-voting convertible preferred stock, \$0.0001 par value; 1,086,341 shares authorized as of March 31, 2025 and December 31, 2024; 346,045 shares issued and outstanding as of March 31, 2025 and December 31, 2024.	146,425	146,425
Series B non-voting convertible preferred stock, \$0.0001 par value; 271,625 shares authorized and 16,667 shares issued and outstanding as of March 31, 2025 and December 31, 2024.	9,395	9,395
Preferred stock, \$0.0001 par value; 8,642,034 shares authorized as of March 31, 2025 and December 31, 2024; no shares issued and outstanding as of March 31, 2025 and December 31, 2024.	—	—
Common stock, \$0.0001 par value; 400,000,000 shares authorized as of March 31, 2025 and December 31, 2024; 60,275,561 shares and 60,257,023 shares issued and outstanding as of March 31, 2025 and December 31, 2024, respectively.	13	13
Additional paid-in capital	1,343,300	1,334,223
Accumulated other comprehensive income	682	180
Accumulated deficit	(1,017,205)	(972,432)
TOTAL STOCKHOLDERS' EQUITY	482,610	517,804
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY	\$ 569,778	\$ 608,484

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

	Three Months Ended March 31,	
	2025	2024
Operating expenses:		
Research and development ⁽¹⁾	41,623	34,928
General and administrative ⁽²⁾	11,944	12,846
Total operating expenses	<u>53,567</u>	<u>47,774</u>
Loss from operations	(53,567)	(47,774)
Other income:		
Interest income	6,493	4,432
Other income (expense), net	<u>2,286</u>	<u>(483)</u>
Total other income	<u>8,779</u>	<u>3,949</u>
Loss before income tax expense	(44,788)	(43,825)
Income tax benefit (expense)	<u>15</u>	<u>(32)</u>
Net loss	<u>\$ (44,773)</u>	<u>\$ (43,857)</u>
Net loss per share, basic and diluted, Series A Preferred Stock	\$ (23.95)	\$ (28.93)
Weighted-average Series A non-voting convertible preferred stock outstanding, basic and diluted	346,045	437,037
Net loss per share, basic and diluted, Series B Preferred Stock	\$ (23.95)	\$ (28.93)
Weighted-average Series B non-voting convertible preferred stock outstanding, basic and diluted	16,667	166,261
Net loss per share, basic and diluted, common	\$ (0.60)	\$ (0.72)
Weighted-average common stock outstanding, basic and diluted	60,265,932	36,512,662

(1) Includes \$2.5 million and \$17.1 million in related party expenses for the three months ended March 31, 2025 and 2024, respectively.

(2) Includes \$0.3 million in related party expenses for the three months ended March 31, 2025 and 2024.