Exhibit 99.1

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

Reported positive interim Phase 1 results for two next-generation TL1A antibodies, demonstrating both were well-tolerated, exhibited pharmacokinetic ("PK") profiles supporting quarterly or biannual dosing, and full TL1A engagement through up to 20 weeks of follow-up

Initiated Phase 2 SKYLINE-UC platform study, evaluating three optimized monotherapies and three potentially paradigm-changing combinations in ulcerative colitis ("UC")

On track for Q3 initiation of Phase 2 SKYWAY-RD basket study evaluating TL1A inhibition in rheumatoid arthritis ("RA"), psoriatic arthritis ("PsA"), and axial spondyloarthritis ("axSpA")

On track to report interim Phase 1 data for SPY003 in the fourth quarter of 2025, followed by 9 proof-of-concept readouts planned in 2026 & 2027 across IBD and rheumatic diseases

$526.6 million of cash, cash equivalents, and marketable securities as of June 30, 2025, with expected runway into the second half of 2028

Waltham, Mass, August 5, 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 second quarter 2025 financial results and provided program and corporate updates.

“Spyre is entering a new chapter as we begin to explore the potential of our pipeline to reshape the treatment paradigm in chronic immune-mediated diseases,” said Cameron Turtle, DPhil, Chief Executive Officer of Spyre. “The launch of the SKYLINE-UC platform trial and upcoming initiation of the SKYWAY-RD basket trial mark the beginning of our effort to identify products with indication-leading profiles. Between these two efficient studies, we are poised to generate nine proof-of-concept readouts in inflammatory bowel disease and rheumatic conditions over the next two years. Backed by robust science, a committed team, and a strong balance sheet with expected runway into the second half of 2028, we believe Spyre is uniquely positioned to drive meaningful and sustained value for patients and investors alike.”

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, PsA, and axSpA are chronic inflammatory autoimmune conditions primarily characterized by pain, stiffness, and swelling of the joints, as well as impacts on the spine and skin. RA and PsA each affect more than 1.5 million individuals in the United States alone, while axSpA prevalence is closer to 3 million individuals in the U.S., with underdiagnosis and inadequate efficacy persisting as key issues for these individuals.

Each of the Company's monotherapy programs in IBD target validated mechanisms with the potential for safe and effective treatment of UC and CD with infrequent dosing as a monotherapy or in rational combinations. The Company is also planning to study its anti-TL1A program in indications outside IBD, including RA, PsA, and axSpA.

SPY001 – a highly potent and selective investigational monoclonal antibody targeting α4β7, 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 supporting potential Q3M or Q6M maintenance dosing, and rapid and complete saturation of α4β7 receptors beyond six months with a single dose of 600mg.
- Based on these interim results, SPY001 was advanced into the SKYLINE-UC Phase 2 platform trial, which initiated in May 2025.

SPY002 and SPY072 – 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. SPY002 is being developed for the treatment of IBD and SPY072 is being developed for the treatment of rheumatic diseases.

- In June 2025, interim healthy volunteer data from two Phase 1 trials (one for SPY002 and one for SPY072) were presented, demonstrating favorable safety profiles, meaningfully differentiated PK profiles supporting potential Q3M or Q6M maintenance dosing, and complete suppression of free TL1A through up to 20 weeks at single 100mg doses. Longer-term data from these Phase 1 trials are expected to be presented at a future medical meeting.
- Based on these interim results, SPY002 is expected to advance to the SKYLINE-UC Phase 2 platform trial in the third quarter of 2025, and SPY072 is expected to advance to the SKYWAY-RD Phase 2 basket trial, which is expected to initiate in the third quarter as well.

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 first-in-human ("FIH") trial of SPY003, with healthy volunteer interim data expected in the fourth quarter of 2025. If successful, SPY003 will advance to be further evaluated in the SKYLINE-UC Phase 2 platform trial.
- Preclinical data for SPY003 have demonstrated 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 combinations 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 medical meetings, demonstrating that the combined inhibition of TL1A and α4β7 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.
- Preclinical data for SPY130 and SPY230 have demonstrated enhanced efficacy and pharmacodynamics with SPY003 in combination with SPY001 and with SPY002.
- The Company expects to include each of its rational combinations in Part B of the SKYLINE-UC trial.

SKYLINE-UC Phase 2 Platform Trial - in May 2025, the Company initiated a Phase 2 induction and maintenance platform trial of SPY001, SPY002, SPY003, as well as pairwise combinations thereof (six active investigational agents in total) in patients with moderately to severely active UC. The trial consists of two parts:

- Part A: Open-label assessment of the safety and preliminary efficacy of a single dose level of each investigational monotherapy, with induction data expected in 2026.
- Part B: Randomized and placebo-controlled assessment of the safety and efficacy of investigational monotherapies (two dose levels) and combinations, with induction data expected in 2027.

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

SKYWAY-RD Phase 2 Basket Trial in Rheumatic Diseases (RA, PsA, axSpA) - the Company expects to initiate a Phase 2 randomized and placebo-controlled basket trial of SPY072 in patients with moderately to severely active RA, PsA, or axSpA in the third quarter of 2025. The trial consists of three sub-studies, each expected to provide proof-of-concept data in 2026:

- RA sub-study: Double-blind, placebo-controlled safety and efficacy study of two dose levels of SPY072 at Week 12.
- PsA sub-study: Double-blind, placebo-controlled safety and efficacy study of a single dose level of SPY072 at Week 16.
- axSpA sub-study: Double-blind, placebo-controlled safety and efficacy study of a single dose level of SPY072 at Week 16.

Second Quarter 2025 Financial Results

Cash Position: As of June 30, 2025, Spyre had cash, cash equivalents, and marketable securities of $526.6 million. Net cash used in operating activities was $46.6 million for the second quarter of 2025.

Research and Development (R&D) expenses: R&D expenses totaled $40.1 million for the second quarter of 2025 and $32.6 million for the second quarter of 2024. The increase was primarily driven by higher clinical trial expenses and increased compensation costs, offset partially by lower early-stage R&D activities.

General and Administrative (G&A) expenses: G&A expenses totaled $11.8 million for the second quarter of 2025 and $11.5 million for the second quarter of 2024.

Gain on Sale of In-Process Research and Development Asset: During the second quarter of 2025, the Company recognized a gain of $10.0 million for achieved milestones related to the 2023 sale of the global rights of the legacy Aeglea asset pegzilarginase to Immedica, driven by a favorable reimbursement decision for pegzilarginase in Europe.

Other income: Other income totaled $5.2 million for the second quarter of 2025 and $5.3 million for the second quarter of 2024.

Net Loss: Net loss totaled $36.7 million and $38.8 million for the second quarters of 2025 and 2024, respectively, which includes non-cash stock-based compensation expense of $9.4 million and $8.7 million for the second 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 α4β7, 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 therapeutics for immune-mediated diseases that meaningfully improve both efficacy and convenience compared to today's standard of care; the potential consistency of the SPY001, SPY002 and SPY072 Phase 1 trial final data readouts with previously disclosed interim Phase 1 results; 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; 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 the expected design and timing of the planned SKYWAY-RD Phase 2 basket trial, including sub-studies to be conducted and timing of initiation and data readouts, plans for and timing of monotherapy/combination arm enrollment, cohort initiation and data readouts for the ongoing SKYLINE-UC Phase 2 platform trial and further clinical evaluation of therapeutic combinations, enrollment of clinical trials, number of data readouts expected to be delivered in 2026 and 2027, the expected SPY003 Phase 1 trial readout in the fourth quarter of 2025 and advancements of SPY002 and SPY003 to the SKYLINE-UC Phase 2 platform trial and SPY072 to the SKYWAY-RD Phase 2 basket trial, and related regulatory feedback; further clinical evaluation of therapeutic combinations, including expectations regarding efficacy and dosing regime; the potential efficacy, tolerability, convenience, commercial viability and safety profile of its product candidates, including in combinations; the planned dosing regimen for SPY001, SPY002, SPY072 and our other product candidates, including the potential for a Q3M or Q6M dosing profile; and the potential therapeutic benefits and economic value of its product candidates as monotherapies or in combinations and their extended half-life. 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 those arising from regulatory feedback, including potential disagreement by regulatory authorities with our clinical trial design, interpretation of data and our ongoing or planned clinical trials for our product candidates, including our planned SKYWAY-RD Phase 2 clinical trial design and our plans for and timing of cohort initiation for combination arms for the ongoing SKYLINE-UC Phase 2 platform trial across different jurisdictions; the potential for final clinical data not being consistent with or different than the previously disclosed interim data for our programs; the expected or potential impact of macroeconomic conditions, including inflationary pressures, rising interest rates, general economic slowdown or a recession, changes in tariff/trade and monetary policy, volatile market conditions, financial institution instability, as well as geopolitical instability, including the ongoing military conflicts between Ukraine and Russia, conflicts in the Middle East, and geopolitical tensions between the United States and other countries, including China, on the Company's operations; the implementation of changes in law, tariffs, sanctions, export or import controls, and other government measures that could impact our business operations, including restricting international trade by the United States, China or other countries and the BIOSECURE Act or similar act if passed into law; and those 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.

Contact Information:

Media Contact
Josie Butler, 1AB
josie@1abmedia.com

Investor Contact
Eric McIntyre
eric.mcintyre@spyre.com

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

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

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

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

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

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