Spyre Therapeutics Reports Fourth Quarter and Full Year 2025 Financial Results and Provides Corporate Update

On track for 6 proof-of-concept readouts in 2026 across the SKYLINE and SKYWAY Phase 2 trials

Part A readouts from SKYLINE platform trial in ulcerative colitis ("UC") expected to begin in the second quarter, with enrollment continuing ahead of schedule

Enrollment on track in Phase 2 SKYWAY basket trial evaluating TL1A inhibition in rheumatoid arthritis ("RA"), psoriatic arthritis ("PsA"), and axial spondyloarthritis ("axSpA"), with fourth quarter readouts expected in each sub-study

Strengthened the balance sheet with an underwritten public offering of common stock in October 2025 and announced the appointment of Kate Tansey Chevlen as Chief Commercial Officer (CCO)

$757 million of cash, cash equivalents, and marketable securities as of December 31, 2025, with expected runway into the second half of 2028

Waltham, Mass, February 19, 2026 (GLOBE NEWSWIRE) - Spyre Therapeutics, Inc. ("Spyre" or the "Company") (NASDAQ:SYRE), a clinical-stage biotechnology company pioneering long-acting antibodies and antibody combinations to redefine the standard of care for inflammatory bowel disease ("IBD") and rheumatic diseases, today announced its fourth quarter and full year 2025 financial results and provided program and corporate updates.

"This year is a pivotal period for Spyre as we begin to unveil results from our two groundbreaking Phase 2 trials with the potential to identify multiple products that leapfrog today's standard of care and provide substantially improved therapies for patients suffering from severe autoimmune diseases. In IBD, we plan to reveal initial safety and efficacy data for our optimized antibodies against the most compelling targets in the space. If successful, these results would support our view that our antibodies are the ideal components for combination therapies with the potential to transform the treatment paradigm in this disease," said Cameron Turtle, DPhil, Chief Executive Officer of Spyre. "Beyond IBD, we are moving full speed ahead with a potentially first- and best-in-class anti-TL1A antibody in a basket study of three rheumatic diseases. Numerous sources of evidence support potential efficacy of TL1A inhibition in these indications, and our quarterly or twice-annual subcutaneous dosing profile could be the leading product profile in these large markets. Taken together, we believe our assets, strategy, and execution can deliver meaningful value for patients, physicians, and shareholders alike."

Development Pipeline Overview and Update

The Company is pioneering long-acting antibodies and antibody combinations to redefine the standard of care in IBD and rheumatic diseases. IBD is a chronic condition characterized by inflammation within the gastrointestinal tract, including two main disorders: ulcerative colitis ("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. Together, these rheumatic conditions affect more than three million individuals in the U.S. Existing therapies for these diseases today generally offer incomplete efficacy, meaningful safety warnings, and inconvenient dosing profiles.

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 studying its anti-TL1A program as a monotherapy in indications outside IBD, including RA, PsA, and axSpA.

The Company has two ongoing Phase 2 clinical trials with proof-of-concept data readouts beginning in 2026:

SKYLINE Phase 2 Platform Trial in IBD - 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 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 beginning in the second quarter of 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 is currently enrolling subjects into Part A of the trial, with Part B expected to begin enrolling after all arms in Part A complete enrollment.

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

The investigational therapies being studied in the SKYLINE and SKYWAY clinical trials include:

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 pharmacokinetic ("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 Phase 2 platform trial.

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 evaluated for the treatment of IBD in the SKYLINE study and SPY072 is being evaluated for the treatment of rheumatic diseases in the SKYWAY study.

- 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 were presented at medical meetings in late 2025, providing further support for these potential best-in-class profiles.
- Based on these interim results, SPY002 was advanced to the SKYLINE Phase 2 platform trial, and SPY072 was advanced to the SKYWAY Phase 2 basket trial.

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 November 2025, interim healthy volunteer data from a Phase 1 trial were disclosed, demonstrating that SPY003 exhibited a favorable safety profile and a meaningfully differentiated PK profile supporting potential Q3M or Q6M maintenance dosing. Additional data from this Phase 1 trial were presented at the 21st Congress of the European Crohn's and Colitis Organisation ("ECCO") in February 2026, providing further support for this potential best-in-class profile.
- Based on these interim results, SPY003 was advanced to the SKYLINE Phase 2 platform trial.

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 the PK profiles of SPY001 and SPY002 were similar in non-human primates whether dosed as monotherapy or in combination, while also demonstrating no drug effects on PK.
- 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 trial.

Fourth Quarter 2025 Financial Results

Cash Position: As of December 31, 2025, Spyre had cash, cash equivalents, and marketable securities of $756.5 million*.* In October 2025, the Company raised $316.2 million in gross proceeds, before deducting $19.8 million in underwriting discounts and other offering expenses, from a public offering of common stock. Net cash used in operating activities was $44.6 million for the fourth quarter of 2025.

Research and Development (R&D) expenses: R&D expenses totaled $44.6 million for the fourth quarter of 2025 and $50.5 million for the fourth quarter of 2024. The decrease was primarily driven by lower early-stage R&D activities, partially offset by higher clinical trial expenses.

General and Administrative (G&A) expenses: G&A expenses totaled $12.5 million for the fourth quarter of 2025 and $10.8 million for the fourth quarter of 2024. The increase was primarily driven by higher headcount.

Total Other Expense (Income): For the fourth quarter of 2025, other expense totaled $5.4 million primarily driven by changes in the fair value of the contingent value right (CVR) liability, partially offset by interest earned on the Company's cash and marketable securities. For the fourth quarter of 2024, other income totaled $5.0 million primarily driven by interest earned on the Company's cash and marketable securities.

Net Loss: Net loss totaled $62.5 million and $56.3 million for the fourth quarters of 2025 and 2024, respectively.

About Spyre Therapeutics

Spyre Therapeutics is a clinical-stage biotechnology company pioneering long-acting antibodies and antibody combinations to redefine the standard of care for inflammatory bowel disease (“IBD”) and rheumatic diseases ("RD"). 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

Certain statements in this press release, other than purely historical information, may constitute "forward-looking statements" within the meaning of the federal securities laws, including for purposes of the safe harbor provisions under the United States Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements regarding: the Company's future results of operations and financial position; its business strategy, including the Company's ability to deliver meaningful value for patients, physicians and shareholders through its assets, strategy and execution, including its ability to successfully develop best-in-class therapeutics for IBD or RD that meaningfully improve both efficacy and convenience compared to today's standard of care and the Company's ability to develop first-in-class therapeutics for RD; the potential consistency of the SPY001, SPY002, SPY072 and SPY003 Phase 1 trial final data readouts with previously disclosed data for our programs; 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 timing and results of the ongoing SKYWAY Phase 2 basket trial and SKYLINE phase 2 platform trial, including timing of cohort initiation and data readouts for the ongoing SKYWAY Phase 2 basket trial and SKYLINE Phase 2 platform trial, enrollment of clinical trials, the inclusion of each rational combination in Part B of the SKYLINE Phase 2 platform trial and the number of data readouts expected to be delivered in 2026 and 2027, and related regulatory feedback; the potential efficacy, tolerability, convenience, commercial viability and safety profile of its product candidates, including in combinations; the potential viability of the Company's antibodies as ideal components for combination therapies; the planned dosing regimen for SPY001, SPY002, SPY072 and SPY003, including the potential for a Q3M or Q6M dosing profile and the potential for such dosing profile to be the leading product profile in IBD and RD; the potential therapeutic benefits and economic value of its product candidates as monotherapies or in combinations and their extended half-life; and Spyre’s business plans, milestones, and goals. The words "opportunity," "potential," "milestones," "pipeline," "strategy," "anticipate," "believe," "could," "estimate," "expect," "may," "might," "plan," "possible," "predict," "should," "will," "would," and similar expressions (including the negatives of these terms) may identify forward-looking statements, but the absence of these words does not mean that a statement is not forward-looking. These forward-looking statements are based on current expectations and beliefs and involve a number of risks and uncertainties, many of which are beyond Spyre’s control, and other assumptions that may cause actual results or performance to be materially different from those expressed or implied by these forward-looking statements. These risks and uncertainties include, but are not limited, uncertainties and risks arising from regulatory feedback, including potential disagreement by regulatory authorities with the Company’s interpretation of data and the Company’s clinical trials for its product candidates; the potential for interim data not being delivered within expected time frames or final data not being consistent with or different than the interim data reported for our programs; the potential impact of Trump Administration policies and changes in law on our business; and those uncertainties and factors described in Spyre's most recent Annual Report on Form 10-K, as supplemented and updated by subsequent

Quarterly Reports on Form 10-Q and any other filings that Spyre has made or may make with the SEC from time to time. You should not place undue reliance on forward-looking statements in this press release, which speak only as of the date they are made and are qualified in their entirety by reference to the cautionary statements herein. Spyre does not undertake or accept any duty to make any updates or revisions to any forward-looking statements.

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

	December 31,	
	2025	**2024**
ASSETS		
CURRENT ASSETS		
Cash and cash equivalents	$ 85,721	$ 89,423
Marketable securities	670,812	513,665
Prepaid expenses and other current assets	21,248	5,386
Total current assets	777,781	608,474
Other non-current assets	—	10
TOTAL ASSETS	$ 777,781	$ 608,484
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES		
Accounts payable	$ 8,904	$ 666
CVR liability	22,820	25,080
Accrued and other current liabilities	26,947	27,711
Related party accounts payable	14	603
Total current liabilities	58,685	54,060
Non-current CVR liability	3,860	36,620
TOTAL LIABILITIES	62,545	90,680
Commitments and Contingencies		
CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY		
Series A non-voting convertible preferred stock, $0.0001 par value; 1,086,341 shares authorized and 346,045 shares issued and outstanding as of December 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 December 31, 2025 and December 31, 2024.	9,395	9,395
Preferred stock, $0.0001 par value; 8,642,034 shares authorized and no shares issued and outstanding as of December 31, 2025 and December 31, 2024.	—	—
Common stock, $0.0001 par value; 400,000,000 shares authorized as of December 31, 2025 and December 31, 2024; 78,189,811 shares and 60,257,023 shares issued and outstanding as of December 31, 2025 and December 31, 2024, respectively.	15	13
Additional paid-in capital	1,686,167	1,334,223
Accumulated other comprehensive income	869	180
Accumulated deficit	(1,127,635)	(972,432)
TOTAL CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY	715,236	517,804
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY	$ 777,781	$ 608,484

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

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2025	2024	2025	2024
Operating expenses:				
Research and development [1]	44,638	50,482	171,653	162,790
General and administrative [2]	12,534	10,771	47,909	45,776
Gain on sale of in-process research and development asset	—	—	(10,000)	—
Total operating expenses	57,172	61,253	209,562	208,566
Loss from operations	(57,172)	(61,253)	(209,562)	(208,566)
Other (expense) income:				
Interest income	7,139	5,776	24,885	21,312
Other (expense) income, net	(12,497)	(818)	29,459	(20,713)
Total other (expense) income	(5,358)	4,958	54,344	599
Loss before income tax expense	(62,530)	(56,295)	(155,218)	(207,967)
Income tax (expense) benefit	—	(1)	15	(51)
Net loss	$ (62,530)	$ (56,296)	$ (155,203)	$ (208,018)
Net loss per share, basic and diluted, Series A Preferred Stock	$ (27.92)	$ (32.28)	$ (79.02)	$ (127.21)
Weighted-average Series A non-voting convertible preferred stock outstanding, basic and diluted	346,045	346,045	346,045	374,387
Net loss per share, basic and diluted, Series B Preferred Stock	$ (27.92)	$ (32.28)	$ (79.02)	$ (127.21)
Weighted-average Series B non-voting convertible preferred stock outstanding, basic and diluted	16,667	16,667	16,667	85,208
Net loss per share, basic and diluted, common	$ (0.70)	$ (0.81)	$ (1.98)	$ (3.18)
Weighted-average common stock outstanding, basic and diluted	75,088,910	55,259,227	64,056,442	47,027,638

(1) Includes $1.0 million and $5.8 million in related party expenses for the three months ended December 31, 2025 and 2024, respectively. Includes $10.5 million and $40.1 million in related party expenses for the years ended December 31, 2025 and 2024, respectively.

(2) Includes $0.2 million and $0.3 million in related party expenses for the three months ended December 31, 2025 and 2024, respectively. Includes $1.0 million and $1.1 million in related party expenses for the years ended December 31, 2025 and 2024, respectively.