Spyre Therapeutics Reports Third Quarter 2026 Financial Results and Provides Corporate Update

Announced positive topline induction data for SPY003 from Part A of the Phase 2 SKYLINE trial ("SKYLINE"), completing proof-of-concept for all three monotherapies in inflammatory bowel disease ("IBD"). SKYLINE Part B is enrolling ahead of schedule, enabling the Company to increase enrollment and provide topline induction results for three potential best-in-indication combinations, which are expected in Q3 2027

Reported positive topline results for SPY072 in rheumatoid arthritis ("RA") sub-study of the Phase 2 SKYWAY basket trial ("SKYWAY"), though with a magnitude of benefit insufficient to prioritize advancement. SPY072 was well-tolerated but did not meet its primary endpoint in the psoriatic arthritis ("PsA") or axial spondyloarthritis ("axSpA") SKYWAY sub-studies. SPY072 will not be advanced in rheumatic disease

Initiated a new Phase 2 trial ("SKYLIGHT") designed to provide clinical proof-of-concept for dual TL1A and IL-17A/F inhibition in hidradenitis suppurativa ("HS"). Raised over $400 million in gross proceeds from an underwritten public offering in October to fund a pivotal program in HS with SPY072, our potential best-in-class TL1A monotherapy

$1.5 billion in pro forma cash, cash equivalents, and marketable securities as of September 30, 2026, with expected runway into the second half of 2029

Waltham, Mass, November 3, 2026 (GLOBE NEWSWIRE) - Spyre Therapeutics, Inc. ("Spyre" or the "Company") (NASDAQ:SYRE), a clinical-stage biotechnology company committed to developing next-generation therapies that elevate the standard in immunology by delivering more complete disease control, greater durability, and a simpler treatment experience for patients, today announced its third quarter 2026 financial results and provided program and corporate updates.

"We are increasingly well-positioned to deliver on our ambition of elevating the standard of care across immunology. In IBD, our three compelling Phase 2 monotherapy readouts and a growing body of supportive clinical evidence strengthen our conviction that our combination products have the potential to transform the treatment paradigm. The combination portion of our SKYLINE trial is enrolling faster than expected enabling an increased enrollment target, and we plan to deliver topline data in Q3 2027 with the potential for efficacy, safety, and convenience that meaningfully surpasses today's standard of care," said Cameron Turtle, DPhil, Chief Executive Officer of Spyre. "Beyond IBD, we were thrilled to see excellent external proof-of-concept data for TL1A in hidradenitis suppurativa, supporting the expansion of our pipeline to include a pivotal monotherapy program as well as a combination study with the current standard of care, IL17-A/F. Collectively, we believe the breadth of our pipeline, strength of our clinical data, and continued execution position Spyre to potentially deliver meaningful advances for patients across multiple large markets and substantial long-term value for shareholders."

Development Pipeline Overview and Update

The Company is committed to developing next-generation therapies that elevate the standard in immunology by delivering more complete disease control, greater durability, and a simpler treatment experience for patients. The Company's pipeline includes extended half-life antibodies targeting α4β7, TL1A, IL-23 and IL-17A/F (each as defined below), as well as rational combination programs, in large therapeutic areas of focus, each with high unmet need.

- In Gastroenterology, the Company is advancing three potential first- and best-in-class combination programs in inflammatory bowel disease ("IBD"). 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 and the global market is forecasted to exceed $40 billion by 2030.

- In Dermatology, the Company is advancing a potential first- and best-in-class anti-TL1A + IL-17A/F combination program in hidradenitis suppurativa ("HS"). Additionally, the Company plans to advance a potential best-in-class anti-TL1A monotherapy agent into pivotal studies for HS in 2027. HS is a chronic inflammatory skin condition characterized by recurrent, painful nodules and abscesses, primarily in areas such as the underarms and groin. The disease can progress to draining tunnels and permanent scarring, substantially impacting patients' quality of life. It is estimated that the disease affects approximately 3.0 million patients in the United States, with the global market forecasted to exceed $10 billion by 2035.

The Company has three ongoing Phase 2 clinical trials with meaningful proof-of-concept data readouts in 2026 and 2027:

SKYLINE Phase 2 Platform Trial in IBD - in May 2025, the Company initiated a Phase 2 induction and maintenance platform trial of SPY001 (long-acting anti-α4β7), SPY002 (long-acting anti-TL1A) and SPY003 (long-acting anti-IL-23), 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. Enrollment for Part A has completed, with initial SPY001, SPY002 and SPY003 Part A topline induction data announced in April 2026, June 2026, and September 2026, respectively.
    - SPY001, SPY002, and SPY003 were well-tolerated with a safety profile consistent with in-class comparators. SPY001, SPY002, and SPY003 all achieved their respective primary endpoints, demonstrating a statistically significant reduction in the Robart's Histopathology Index ("RHI") score of 9.2 points, 10.7 points, and 10.0 points, respectively. Rates of key secondary endpoints of clinical remission and endoscopic improvement were clinically meaningful at 40% and 51%, respectively, for SPY001, 33% and 42%, respectively, for SPY002, and 20% and 30%, respectively, for SPY003. The change in the modified Mayo Score from baseline at Week 12 for both SPY001 and SPY002 was -3.7, and for SPY003 was -3.5, reflecting consistency across secondary endpoints.
- Part B: Randomized and placebo-controlled assessment of the safety and efficacy of monotherapies and combinations, designed to provide dose-ranging data on monotherapies, proof-of-concept, and contribution of components for combinations, with induction data expected in the third quarter of 2027. Study is enrolling ahead of schedule enabling an increased enrollment target.

SKYLIGHT Phase 2 Trial in HS - in September 2026, the Company initiated its SKYLIGHT Phase 2 trial of SPY072 in subjects with moderately to severely active HS who are initiating bimekizumab. The trial serves as a surrogate proof-of-concept study for the Company's internal SPY772 combination program combining SPY072 (long-acting anti-TL1A) and SPY007 (long-acting anti-IL-17A/F). Topline Week 16 results are planned in late 2027 or early 2028.

SKYWAY Phase 2 Basket Trial in Rheumatic Diseases - 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:

- RA sub-study: Double-blind, placebo-controlled safety and efficacy study of two dose levels of SPY072 at Week 12 with open-label follow-up through Week 36. Topline proof-of-concept data were released in August 2026. Both doses of SPY072 demonstrated statistically significant benefits compared to placebo on one or more of the primary (change from baseline in DAS28-CRP), key secondary (ACR20), and

exploratory endpoints (ACR50). SPY072 was well tolerated, with a safety profile consistent with the TL1A class. While SPY072 demonstrated clinical activity in RA, the results did not meet the Company's internal bar to prioritize advancement of SPY072 in RA.

- PsA and axSpA sub-studies: Double-blind, placebo-controlled safety and efficacy studies of a single dose level of SPY072 at Week 16 with open-label follow-up through Week 40. The Company announced that SPY072 was well-tolerated, but neither sub-study met its primary endpoint of ACR20 response in PsA or change from baseline in ASDAS in axSpA.

The Company does not plan to advance SPY072 in rheumatic diseases.

The investigational therapies being studied in the Company's clinical trials include:

SPY001 – a highly potent and selective investigational monoclonal antibody targeting the α4β7 integrin ("α4β7"), engineered with half-life extension technology and formulated at high concentration with the goal of maximizing efficacy and enabling infrequent, subcutaneous maintenance dosing. SPY001 is being evaluated for the treatment of IBD in the SKYLINE study.

SPY002 and SPY072 – two highly potent and selective, investigational anti-tumor necrosis factor-like ligand 1A ("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 developed for the treatment of HS, both as a monotherapy and as part of a combination.

SPY003 – a highly potent and selective investigational monoclonal antibody targeting the p19 subunit of interleukin 23 ("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. SPY003 is being evaluated for the treatment of IBD in the SKYLINE study.

SPY007 – a preclinical-stage program designed to bind to interleukin 17A ("IL-17A") and interleukin 17F ("IL-17F"), while incorporating half-life extending modifications. SPY007 is being developed for the treatment of HS in combination with SPY072.

Rational Combinations (SPY120, SPY130, SPY230, and SPY772) – the Company is investigating combinations of its proprietary antibodies in clinical trials in order to evaluate whether combinations can potentially lead to best-in-class efficacy in several inflammatory diseases, with less frequent dosing.

- The Company is currently enrolling its SPY120, SPY130, and SPY230 combinations in Part B of the SKYLINE trial, with an expected induction read-out in 2027.
- The Company's SPY772 combination program aims to target multiple inflammatory pathways involved in HS, pairing its novel anti-TL1A (SPY072) with SPY007, its anti-IL-17A/F. The goal is to use this long-acting, co-formulated combination in future advanced clinical development, pending the results from the Company's SKYLIGHT proof-of-concept trial.

Third Quarter 2026 Financial Results

Cash Position: As of September 30, 2026, Spyre had cash, cash equivalents, and marketable securities of $1,071.9 million. Pro forma cash of $1,467.9 million as of September 30, 2026, with expected runway into the second half of 2029, also reflects $378.0 million in net proceeds from the recently closed October 2026 underwritten public offering of common stock and $18.0 million in October 2026 at-the-market (ATM) sales. Net cash used in operating activities was $77.5 million for the third quarter of 2026.

Research and Development (R&D) expenses: R&D expenses totaled $89.2 million for the third quarter of 2026 and $45.2 million for the third quarter of 2025. The increase was primarily driven by higher manufacturing costs and clinical trial expenses.

General and Administrative (G&A) expenses: G&A expenses totaled $16.6 million for the third quarter of 2026 and $11.6 million for the third quarter of 2025. The increase was primarily driven by increased headcount and professional services fees.

Total Other Income (Expense): Other income totaled $9.6 million for the third quarter of 2026 compared to $45.7 million of total other income in the third quarter of 2025. The change was primarily due to changes in the fair value of the contingent value right ("CVR") liability in the prior period.

Net Loss: Net loss totaled $96.1 million and $11.2 million for the third quarters of 2026 and 2025, respectively.

About Spyre Therapeutics

Spyre Therapeutics is a clinical-stage biotechnology company committed to developing next-generation therapies that elevate the standard in immunology by delivering more complete disease control, greater durability, and a simpler treatment experience for patients. Spyre's pipeline includes investigational extended half-life antibodies targeting α4β7, TL1A, IL-23, and IL-17A/F as well as rational combination programs.

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 ability to achieve the expected benefits or opportunities with respect to its product candidates, including its ability to develop next-generation therapies that elevate the standard in immunology by delivering more complete disease control, greater durability, and a simpler treatment experience for patients; the potential continued speed of enrollment in SKYLINE, the ability to reach the increased enrollment target and the Company's plans to deliver topline data in Q3 2027 with the potential for efficacy, safety, and convenience that meaningfully surpasses today's standard of care; its business strategy, including its ability to successfully develop best-in-class therapeutics for IBD and HS and deliver meaningful advances for patients across multiple large markets and substantial long-term value for shareholders; the potential for the Company's combination products to transform the treatment paradigm; the potential for the Company's product candidates in development, including rational combination programs, to be first-in-class and/or best-in-class therapies in IBD and HS; the potential for future clinical readouts from the Company's programs to further establish the utility of TL1A inhibition across autoimmune diseases; expectations regarding the drug delivery of the Company's product candidates, including in the form of a subcutaneous injection; the length of time that the Company believes its existing cash resources will fund its operations, including the expectation of cash runway extending into the second half of 2029; estimated market sizes and potential growth opportunities; its current and future clinical development activities, including the Company's plans for and timing of cohort initiation and data readouts for the ongoing SKYLINE Phase 2 platform trial and SKYLIGHT Phase 2 trial, the advancement of a potential best-in-class anti-TL1A monotherapy agent into pivotal studies for HS in 2027, and the potential of using SPY772 in future advanced clinical development; the potential efficacy, tolerability, convenience, dosing profile, commercial viability and safety profile of its product candidates, including rational combinations; the potential therapeutic benefits and economic value of its product candidates as monotherapies or in combinations, including the potential for efficacy, safety and convenience to meaningfully surpass today's standard of care; 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 the Company's programs; the potential impact of Trump Administration policies and changes in law on the Company's 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.

Contact Information:

For Investors:
Eric McIntyre, Spyre Therapeutics
SVP of Finance and Investor Relations
Eric.mcintyre@spyre.com

For Media:
Josie Butler, 1AB
josie@1abmedia.com

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

	September 30, 2026	December 31, 2025
ASSETS		
CURRENT ASSETS		
Cash and cash equivalents	$ 82,727	$ 85,721
Marketable securities	989,180	670,812
Prepaid expenses and other current assets	27,821	21,248
Total current assets	1,099,728	777,781
TOTAL ASSETS	$ 1,099,728	$ 777,781
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES		
Accounts payable	$ 9,466	$ 8,904
CVR liability	—	22,820
Accrued and other current liabilities	30,595	26,947
Related party accounts payable	82	14
Total current liabilities	40,143	58,685
Non-current CVR liability	6,760	3,860
Other non-current liabilities	1,290	—
TOTAL LIABILITIES	48,193	62,545
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 as of September 30, 2026 and December 31, 2025; 346,045 shares issued and outstanding as of September 30, 2026 and December 31, 2025.	146,425	146,425
Series B non-voting convertible preferred stock, $0.0001 par value; 271,625 shares authorized as of September 30, 2026 and December 31, 2025; nil and 16,667 shares issued and outstanding as of September 30, 2026 and December 31, 2025, respectively.	—	9,395
Preferred stock, $0.0001 par value; 8,642,034 shares authorized as of September 30, 2026 and December 31, 2025; no shares issued and outstanding as of September 30, 2026 and December 31, 2025.	—	—
Common stock, $0.0001 par value; 400,000,000 shares authorized as of September 30, 2026 and December 31, 2025; 89,953,997 shares and 78,189,811 shares issued and outstanding as of September 30, 2026 and December 31, 2025, respectively.	16	15
Additional paid-in capital	2,239,437	1,686,167
Accumulated other comprehensive (loss) income	(5,382)	869
Accumulated deficit	(1,328,961)	(1,127,635)
TOTAL STOCKHOLDERS' EQUITY	1,051,535	715,236
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY	$ 1,099,728	$ 777,781

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2026	2025	2026	2025
Operating expenses:				
Research and development [1]	$ 89,169	$ 45,247	215,083	127,015
General and administrative [2]	16,550	11,641	47,916	35,375
Gain on sale of in-process research and development asset	—	—	(70,000)	(10,000)
Total operating expenses	105,719	56,888	192,999	152,390
Loss from operations	(105,719)	(56,888)	(192,999)	(152,390)
Other income (expense):				
Interest income	10,625	5,379	27,673	17,746
Other (expense) income, net	(1,027)	40,326	(36,000)	41,956
Total other income (expense)	9,598	45,705	(8,327)	59,702
Loss before income tax benefit	(96,121)	(11,183)	(201,326)	(92,688)
Income tax benefit	—	—	—	15
Net loss	$ (96,121)	$ (11,183)	$ (201,326)	$ (92,673)
Net loss per share, basic and diluted, Series A Preferred Stock	$ (37.60)	$ (5.97)	$ (81.74)	$ (49.53)
Weighted-average Series A non-voting convertible preferred stock outstanding, basic and diluted	346,045	346,045	346,045	346,045
Net loss per share, basic and diluted, Series B Preferred Stock	$ —	$ (5.97)	$ (81.74)	$ (49.53)
Weighted-average Series B non-voting convertible preferred stock outstanding, basic and diluted	—	16,667	10,623	16,667
Net loss per share, basic and diluted, common	$ (0.94)	$ (0.15)	$ (2.04)	$ (1.24)
Weighted-average common stock outstanding, basic and diluted	88,410,821	60,414,223	84,255,008	60,338,541

(1) Includes related party expenses of $0.1 million and $7.0 million for the three months ended September 30, 2026 and 2025, respectively. Includes related party expenses of $3.2 million and $9.6 million for the nine months ended September 30, 2026 and 2025, respectively.

(2) Includes related party expenses of $0.3 million for the three months ended September 30, 2026 and 2025, and $0.8 million for the nine months ended September 30, 2026 and 2025.