Spyre Therapeutics Announces Topline Results from the Rheumatoid Arthritis Sub-study of the SKYWAY Phase 2 Trial of SPY072

August 25, 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 (e.g., ACR50)

SPY072 was well tolerated with rates of adverse events comparable to placebo

Magnitude of effect did not meet the Company's target to prioritize monotherapy development of SPY072 in rheumatoid arthritis (RA); results support the broad potential of Spyre's TL1A antibodies in autoimmune disease and as combination components

Topline data for SPY072 in psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) on track for Q4 2026 and for SPY072 in combination with IL17-A/F in hidradenitis suppurativa (HS) in late 2027 or early 2028

WALTHAM, Mass., Aug. 25, 2026 (GLOBE NEWSWIRE) -- Spyre Therapeutics, Inc. (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 topline results from the RA sub-study of its Phase 2 SKYWAY basket trial evaluating SPY072 in rheumatic diseases. 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. The results provide proof-of-mechanism for TL1A in RA and support its potential in other autoimmune diseases and as a combination component, but did not meet the Company's internal bar to prioritize advancement of SPY072 in RA.

"The SKYWAY trial was designed to explore the safety and efficacy of TL1A inhibition in a range of rheumatic diseases to identify opportunities for indication-leading products. The results today do not lead us to prioritize SPY072 as a monotherapy in RA. However, the favorable safety profile of TL1A inhibition alongside demonstrated efficacy across inflammatory bowel disease, HS, and now RA provide increased conviction that our long-acting TL1A antibodies have potential in a range of autoimmune diseases and as optimal combination components," said Cameron Turtle, DPhil, Chief Executive Officer at Spyre. "We want to thank the patients, investigators, and site staff who participated in this study and look forward to results in PsA and axSpA next quarter. Additionally, we are excited to have initiated our SKYLIGHT trial of SPY072 in combination with IL-17A/F in HS, our fourth investigational combination of validated mechanisms in autoimmune indications with high unmet need."

SKYWAY-RA efficacy results

SPY072 Low Dose demonstrated a statistically significant benefit compared to placebo on the primary endpoint (change from baseline in DAS28-CRP) at Week 12. Nominally significant improvements versus placebo were observed on the secondary endpoint (ACR20) with High Dose and on the exploratory endpoint (ACR50) with Low Dose. Results were generally comparable between advanced-therapy-naïve and advanced-therapy-experienced sub-groups.

Endpoint (W12)	**SPY072 High Dose** (N=48)	**SPY072 Low Dose** (N=48)	**Placebo** (N=47)
ΔDAS28-CRP	-1.5	-1.9*	-1.3
ACR20	63%**	58%	43%
ACR50	31%	38%**	19%
ACR70	13%	4%	2%

*p<0.05 for SPY072 versus placebo **nominal p<0.05 for SPY072 versus placebo

Both doses of SPY072 achieved target drug concentrations and provided complete and durable suppression of free TL1A through Week 12, suggesting complete target engagement.

Safety results

SPY072 was well tolerated with a safety profile consistent with the TL1A class. Rates of adverse events were comparable between active (27%) and placebo (36%) and generally mild or moderate. One Serious TEAE occurred on each arm, none deemed drug-related. One death occurred in a participant receiving placebo. The most common TEAEs were infections and infestations, occurring in 14% of SPY072-treated participants and 15% of placebo-treated participants.

Next steps

The Company remains at the forefront of evaluating potential first- and best-in-class monotherapies and combinations in I&I with numerous expected topline readouts over the next 12-18 months to prioritize programs for further development:

Trial	Indication	Asset(s)	Expected timing
SKYLINE Part A	Ulcerative Colitis	SPY003	Sept 2026
SKYWAY	PsA, axSpA	SPY072	4Q 2026
SKYLINE Part B	Ulcerative Colitis	SPY001, SPY002, SPY003 SPY120, SPY130, SPY230	2027
SKYLIGHT	HS	SPY072 + IL-17A/F	Late 2027 or early 2028

About SKYWAY-RA

The SKYWAY-RA sub-study is one of three sub-studies in the SKYWAY basket trial (NCT07148414) and is a randomized and placebo-controlled study evaluating two doses of SPY072 in patients with moderate to severely active RA with inadequate response to conventional or advanced therapies. The primary endpoint is the change from baseline to Week 12 in Disease Activity Score in 28 joints, C-reactive protein (DAS28-CRP) and the secondary endpoint is the proportion of patients achieving an ACR20 response at Week 12.

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, visit Spyre's website at www.spyre.com.

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: Spyre's ability to achieve the expected benefits or opportunities with respect to its product candidates and combinations thereof, 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 efficacy and safety of SPY072/ our TL1A antibodies and their broad potential in autoimmune diseases and as optimal combination components; the Company remaining at the forefront of evaluating potential first and best-in-class monotherapies and combinations in I&I; the expected timing of topline results from the PsA and axSpA SKYWAY sub-studies, SKYLIGHT trial in HS and SKYLINE part A and B in UC and the potential further development of these programs; the timing of and the Company's ongoing development programs in inflammatory bowel disease and HS; and Spyre's ongoing and future pre-clinical and clinical development activities. The words "opportunity," "potential," "milestones," "pipeline," "strategy," "anticipate," "believe," "could," "estimate," "expect," "may," "might," "plan," "possible," "predict," "should," "will," "would," "can, " "likely," "aim," 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 to, 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 topline or 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 Securities and Exchange Commission 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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