Spyre Announces Potential Best-in-Class SPY003 (anti-IL-23) Part A Induction Results from SKYLINE Trial, Completing Proof-of-Concept for All Three Components of its IBD Combinations

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SPY003 met its primary endpoint with a statistically significant reduction of 10.0 points (p<0.0001) from baseline at Week 12 in Robart's Histopathology Index (RHI) score

Secondary endpoints included clinical remission by modified Mayo Score of 20% and endoscopic improvement of 30%

SPY003 was well tolerated with a safety profile consistent with the IL-23 class

SKYLINE Part A has demonstrated potential best-in-class results for SPY001 (anti-α4β7), SPY002 (anti-TL1A), and SPY003 (anti-IL-23); SKYLINE Part B evaluating pairwise combinations of these components is enrolling with topline induction data expected in 2027

WALTHAM, Mass., Sept. 08, 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 positive 12-week induction data from Part A of the Phase 2 SKYLINE trial of SPY003, a potential best-in-class anti-IL-23 being investigated for the treatment of moderately-to-severely active ulcerative colitis (UC). With these results, Spyre has now reported positive Part A data for all three mechanisms in its IBD portfolio (α4β7, TL1A, and IL-23), achieving clinical proof-of-concept for each component of the pairwise combinations being evaluated in Part B of the SKYLINE trial.

"SPY003 demonstrated a highly statistically significant 10-point reduction in RHI and meaningful clinical remission and endoscopic outcomes in line with the anti-IL-23 class," said Deanna Nguyen, M.D., SVP of Clinical Development and SKYLINE study lead. "Combined with a well-tolerated safety profile and extended pharmacokinetics in alignment with the rest of our portfolio, these results position SPY003 as a potentially best-in-class combination component for patients with moderately-to-severely active UC."

"With today's SPY003 data building upon impressive SPY001 and SPY002 results, we have now delivered three potential best-in-class IBD readouts within a span of five months, demonstrating the quality and efficiency of our development organization and strategy," said Cameron Turtle, DPhil, Chief Executive Officer of Spyre. "We engineered optimized antibodies against the best targets in IBD based on our thesis that better components will lead to better combinations. Each molecule has now demonstrated compelling monotherapy efficacy and safety data, and the combination cohorts are actively enrolling. We believe that these combinations have the potential to deliver an efficacy, safety, and dosing profile that meaningfully surpasses today's standard of care, and we are excited to unveil those data in 2027."

Efficacy: POC Established Across All Three Combination Components

SKYLINE is a two-part induction and maintenance platform trial of SPY001, SPY002, SPY003, as well as pairwise combinations thereof (six investigational agents total) in patients with moderately-to-severely active ulcerative colitis. Part A is an open-label assessment of the safety and efficacy of a single dose level of each investigational monotherapy, and Part B is a randomized and placebo-controlled assessment of the safety and efficacy of investigational monotherapies (two dose levels) and combinations.

SPY003 is an extended half-life investigational antibody targeting IL-23, a cytokine implicated in chronic inflammation in IBD. Initial 12-week findings from SKYLINE Part A demonstrated that SPY003 met all key objectives. The study population consisted of 41% advanced therapy-exposed participants with a mean disease duration of 7.1 years, a mean baseline RHI score of 17.2 ± 8.3 (SD), a mean modified Mayo Score of 6.9 ± 1.2 (SD), and 59% of whom had a baseline endoscopy score of 3. SPY003 achieved the primary endpoint, demonstrating a statistically significant 10.0-point reduction in RHI score (p<0.0001), robust rates of clinical remission and endoscopic improvement, and a meaningful change in mMS. The 10.0-point reduction in RHI observed in participants receiving SPY003 is in line with the 9.2- and 10.7-point reductions observed in participants receiving SPY001 and SPY002, respectively, and all are among the largest improvements observed in UC trials to date.

Endpoint (Week 12)	**SPY003**
Change in RHI from baseline *Primary endpoint*	-10.0 *(p<0.0001)*
Clinical remission rate	20%
Endoscopic improvement rate	30%
Change in modified Mayo Score	-3.5

Safety: Well-Tolerated Profiles Across All Three Monotherapies Support Combination Development

As previously reported, SPY001 and SPY002 were each well tolerated in Part A, with safety profiles consistent with their respective classes, and no drug-related serious adverse events.

SPY003 was well tolerated with a safety profile consistent with the IL-23 class. There were 19 subjects with treatment-emergent adverse events (TEAEs) during the induction treatment period. Three serious adverse events (SAEs) were reported, deemed not drug-related. The most common adverse events (AEs) (occurring in ≥ 2 patients) were arthralgia (n=2), nasopharyngitis (n=2), and urinary tract infection (n=2).

	SPY003
Subjects with any AE (n, %)	19 (43%)
Severe (Grade ≥ 3) AE	5 (11%)[1]
Drug-related AE	1 (2%)[2]
AE leading to drug discontinuation	0
SAE	3 (7%)[3]
Drug-related SAE	0
AEs of special interest	0
Death	0

[1]Ulcerative colitis flare, intervertebral disc protrusion, anaemia, urinary tract infection, and acute cholecystitis, each in one subject; all deemed not drug-related.

[2]Pruritus (Grade 1) that resolved without intervention or treatment interruption.

[3]Hospitalization for ulcerative colitis flare, hemorrhoid thrombosis, and acute cholecystitis, each in one subject; all deemed not drug-related.

Data pertain to SPY003 (N=44) through Week 12 and data cut-off of July 27, 2026.

Next steps

Clinical proof-of-concept across all three IBD programs strengthens the biological rationale for Spyre's combination strategy and sets the stage for Part B of the SKYLINE trial, which is actively enrolling. Part B includes two dose levels of each monotherapy as well as three high-dose combination arms (SPY120, SPY130, and SPY230), which the Company believes have the potential to deliver best-in-disease efficacy, safety, and treatment experience. Topline induction data from Part B are expected in 2027.

The Company remains at the forefront of evaluating potential first- and best-in-class monotherapies and combinations in immunology and inflammation, with multiple expected topline readouts over the next 12-18 months:

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

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, 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 best-in-class results for SPY001, SPY002 and SPY003; the potential for SPY003 to be a best-in-class IL-23 and combination component for patients with moderately-to-severely active UC; the potential for better components leading to better combinations; the potential for Spyre's combinations to deliver an efficacy, safety, and dosing profile that meaningfully surpasses today's standard of care; the potential for Spyre's three high-dose combination arms to deliver best-in-disease efficacy, safety, and treatment experiences; Spyre's ongoing and future clinical development activities, including Spyre's plans for data readouts for the ongoing SKYLINE, SKYWAY and SKYLIGHT trials and timing thereof. 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 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 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.

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

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