Spyre Announces Potential Best-in-Class SPY001 Part A Induction Results from SKYLINE Trial in Moderate-to-Severe Ulcerative Colitis Patients

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SPY001 met its primary endpoint with a statistically significant reduction of 9.2 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 40% and endoscopic improvement of 51%

SPY001 was well tolerated with a safety profile consistent with the α4β7 class

Recruitment for SKYLINE Part A closed, now enrolling Part B monotherapy and combination cohorts

Management will host a conference call today at 8:00 a.m. ET

WALTHAM, Mass., April 13, 2026 (GLOBE NEWSWIRE) -- Spyre Therapeutics, Inc. (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 positive 12-week induction data from Part A of the Phase 2 SKYLINE trial of SPY001, a potential best-in-class anti-α4β7 being investigated for the treatment of moderate-to-severely active ulcerative colitis (UC).

"SPY001 was designed to improve upon vedolizumab's proven activity in IBD by matching its epitope and potency while increasing target coverage through an extended half-life and greater induction dosing. Our data today support the hypothesis that this approach could lead to a best-in-class anti-α4β7 product across safety, efficacy, and convenience," said Deanna Nguyen, M.D., SVP of Clinical Development and SKYLINE study lead. "Beyond SPY001's potential as a monotherapy, we continue to believe that its gut-selective mechanism makes it an ideal backbone for combination therapy alongside our cytokine-targeting investigational antibodies SPY002 (anti-TL1A) or SPY003 (anti-IL23). We have begun enrolling these combinations globally and look forward to unveiling proof-of-concept data next year."

Additionally, Spyre announced today that recruitment for Part A of SKYLINE is now closed and enrollment is open for Part B, which includes three monotherapy cohorts (SPY001, SPY002, and SPY003) and three combination cohorts (SPY120, SPY130, and SPY230) into which participants may be randomized versus a shared placebo. Proof-of-concept induction data for the remaining cohorts of Part A are now expected mid-2026 (SPY002) and Q3 2026 (SPY003). Part B induction data (all cohorts) remain on track for 2027.

"On behalf of the Spyre team, I'd like to thank the patients and investigators whose partnership has made this progress possible as we advance the study with the goal of delivering paradigm-changing combinations for IBD patients," said Sheldon Sloan, M.D. MBE, Chief Medical Officer of Spyre Therapeutics. "Thanks to our team's outstanding execution, we enrolled Part A with exceptional speed and now transition to Part B. We expect heightened investigator enthusiasm given these promising results for SPY001, a low placebo allocation for the remainder of the trial, and a unique opportunity to evaluate perhaps the three most promising combinations in development."

SPY001 SKYLINE Part A Induction Topline Results

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.

SPY001 is an extended half-life investigational antibody targeting α4β7, an integrin central to immune cell trafficking to the gut. Initial 12-week findings from SKYLINE Part A demonstrated that SPY001 met or exceeded all key objectives.

Efficacy: SPY001 achieved the primary endpoint, demonstrating a statistically significant reduction in the RHI score of 9.2 points (p<0.0001). Rates of key secondary endpoints of clinical remission and endoscopic improvement were clinically meaningful and support SPY001's potential best-in-class profile.

Endpoint	**Week 12 Result**
Change in RHI from baseline *Primary endpoint*	-9.2 *(p<0.0001)*
Clinical remission rate	40%
Endoscopic improvement rate	51%

Change in Modified Mayo Score	-3.7

Safety: SPY001 was well tolerated with a safety profile consistent with the α4β7 class. There were six subjects with treatment-emergent adverse events (TEAEs) during the induction treatment period, with one serious adverse event (SAE), deemed not drug-related. The most common AE (occurring in ≥ 2 patients) was back pain (n=2).

	SPY001 (n=43)
Subjects with any AE (n, %)	**6 (14%)**
Severe (Grade ≥ 3) AE	1 (2%)*
Drug-related AE	0
AE leading to study discontinuation	0
SAE	1 (2%)*
Drug-related SAE	0
AEs of special interest	0
Death	0

**Chest pain in a 68-year-old male with history of coronary artery disease and angina pectoris, type 2 diabetes mellitus, hypertension, and hypercholesterolemia who presented with chest pain. ECG and cardiac enzymes did not show signs of a myocardial infarction.*

Webcast Details

Spyre Therapeutics' webcast of the SPY001 Phase 2 SKYLINE Part A data will begin today at 8:00 a.m. ET. The webcast can be accessed via this link or the Investors section of the Company's website at https://ir.spyre.com/news-events/events. A replay of the webcast will be available following the call.

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. Spyre's pipeline includes investigational extended half-life antibodies targeting α4β7, TL1A, and IL-23.

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 their potential commercialization; Spyre's ongoing and future clinical development activities, including Spyre's plans for and timing of cohort initiation and data readouts for the ongoing SKYLINE trial and ongoing SKYWAY trial and enrollment of clinical trials; the inclusion of each rational combination in Part B of the SKYLINE Phase 2 platform trial; expectations regarding investigator enthusiasm and placebo allocation; the potential for SPY001 to be an ideal backbone for combination therapy; the potential therapeutic benefits of Spyre's product candidates as monotherapies or in combinations, including potency, convenience, durability, and dosing profile, and their extended half-life; potential growth opportunities; and Spyre's business plans, milestones, strategy 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 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 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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