Spyre Therapeutics Announces Positive Interim Phase 1 Results for SPY003, Its Novel, Half-Life Extended anti-IL-23 Antibody

November 4, 2025

SPY003 was well tolerated and exhibited an ~85-day half-life, supporting potential quarterly or twice annual maintenance dosing

SPY003 positive interim results unlock development of SPY130 (α4β7 + IL-23) and SPY230 (TL1A + IL-23) investigational combination therapies for IBD with potential for indication-leading efficacy, safety, and dosing profiles

SPY003 expected to advance to the ongoing Part A of the SKYLINE Ph2 platform trial

SKYLINE and SKYWAY trials are expected to provide 6 proof-of-concept readouts in 2026

WALTHAM, Mass., Nov. 04, 2025 (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 interim Phase 1 results from its first-in-human trial of SPY003, an investigational, extended half-life antibody targeting the p19 subunit of IL-23.

"These encouraging Phase 1 data for SPY003 mark our fourth successful first-in-human trial in the past year, underscoring the strength of our antibody engineering platform and efficiency of our development organization,” said Deanna Nguyen, M.D., SVP of Clinical Development at Spyre. “Advancing SPY003 into SKYLINE represents a pivotal step in realizing our vision for a comprehensive IBD portfolio that includes three optimized monotherapies and three uniquely differentiated combinations that have the potential to be dosed on a quarterly or twice annual basis.”

Key Phase 1 Interim Findings

The SPY003 Phase 1 trial was a first-in-human, randomized, double-blind, placebo-controlled study designed to evaluate safety and pharmacokinetic (PK) in healthy volunteers. The trial enrolled 59 healthy adult participants into five single-ascending dose (SAD) cohorts, a multiple dose cohort (MD), and a Chinese ethnobridging (Ch Eb) single dose cohort. Doses of SPY003 evaluated included 200 mg IV, 600 mg SC (two formulations), 600 mg IV, and 1200 mg IV (as single and multiple doses). Interim findings from the trial as of September 19th, 2025 data cutoff include:

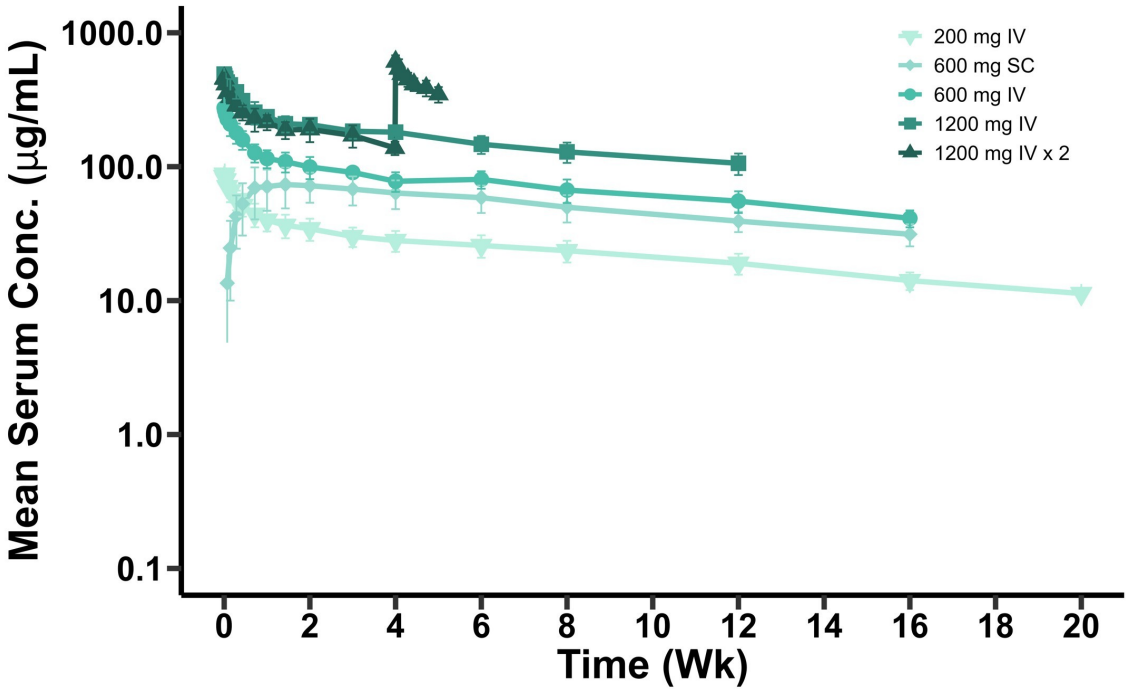
Safety: SPY003 was well tolerated at all dose levels, with a favorable safety profile consistent with the anti-IL-23 class. There were two Grade 2 or above treatment-emergent adverse events (TEAEs), both deemed not treatment-related, and no serious adverse events were observed in the study. The only TEAE to occur in two or more subjects was headache. Blinded safety data are summarized as follows.

Cohort	SAD 1	SAD 2	SAD 3	SAD 4	SAD 5	MD1	Ch Eb 1
Dose	200 mg IV	600 mg SC	600 mg IV	1200 mg IV	600 mg SC[3]	1200 mg IV x 2	1200 mg IV
N=	8	8	9	8	8	8	10
At least one TEAE	5 (63%)	0 (0%)	2 (22%)	2 (25%)	3 (38%)	1 (13%)	0 (0%)
At least one TESAE	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
At least one Treatment-related AE[1]	0 (0%)	0 (0%)	1 (11%)	1 (13%)	0 (0%)	0 (0%)	0 (0%)
At least one ≥Grade 2 TEAE[2]	1 (13%)	0 (0%)	0 (0%)	1 (13%)	0 (0%)	0 (0%)	0 (0%)

[1]One case of infusion reaction and one case of pruritus, both Grade 1 and resolved without medication.
[2]One case of asymptomatic increased lipase, isolated to Day 43 post-dose (Grade 3); One case of bronchitis (Grade 2). Neither deemed treatment related.
[3]High concentration formulation.

PK: SPY003 showed a half-life of approximately 85 days, more than 3-times that of risankizumab's published half-life with dose proportionality and limited intrasubject variability. This differentiated PK profile supports the potential for quarterly or twice annual

maintenance dosing in a single SC injection.



[1]SAD5 (600 mg SC high concentration formulation) and Ch Eb1 (1200 mg SC in volunteers of Chinese descent) not shown for visual clarity, results were consistent with other cohorts at similar doses.

Immunogenicity: No apparent impact of anti-drug-antibodies was observed on PK.

About SPY003

SPY003 is an investigational, extended half-life monoclonal antibody targeting IL-23, being developed for the treatment of IBD. IBD is a chronic condition characterized by inflammation in the gastrointestinal tract and encompasses two main disorders: ulcerative colitis and Crohn's disease. Together, it is estimated that more than 2.4 million individuals currently have IBD in the United States. In head-to-head preclinical studies, SPY003 demonstrated equivalent potency to risankizumab in inhibiting pSTAT signaling and IL-17 production. Interim data from a Phase 1 trial demonstrated that SPY003 was well tolerated and exhibited prolonged pharmacokinetics. Based on Phase 1 clinical data, the company plans to evaluate SPY003 in its SKYLINE Phase 2 platform study (NCT07012395).

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, please visit http://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, concerning Spyre and other matters. These forward-looking statements include, but are not limited to, express or implied statements relating to Spyre's management team's expectations, hopes, beliefs, intentions or strategies regarding the future including, without limitation, Spyre's ability to achieve the expected benefits or opportunities with respect to its pipeline of product candidates such as the potential efficacy, tolerability, convenience, commercial viability, dosing regimen and safety profile of SPY003 in humans, including the potential for a quarterly or twice yearly maintenance dosing profile that may set a new standard of care for IBD; the potential for SPY003 to become a best-in-class therapy for IBD; its plans to advance the SPY003 program into the SKYLINE Phase 2 platform study; expectations regarding the drug delivery of SPY003, including in the form of a subcutaneous injection; Spyre's ongoing 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 data readouts and number of data readouts expected to be delivered in 2026; the potential consistency of the SPY003 Phase 2 trial final data readouts with interim Phase 1 results; the potential therapeutic benefits of Spyre's product candidates as monotherapies or in combinations and their extended half-life, including the expected duration of half-life in comparison to competitor products and the potential potency, efficacy, dosing regimen and convenience compared to today's

standard of care; estimated market sizes and potential growth opportunities and that human PK data is not based on head-to-head clinical trials and differences exist between trial design and patient populations which could confound the results. In addition, any statements that refer to projections, forecasts or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking statements. The words "opportunity," "potential," "milestones," "pipeline," "can," "goal," "aim," "strategy," "target," "seek," "anticipate," "achieve," "believe," "contemplate," "continue," "could," "estimate," "expect," "intends," "may," "might," "plan," "possible," "predict," "project," "should," "will," "would," and similar expressions (including the negatives of these terms or variations of them) 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 concerning future developments and their potential effects. There can be no assurance that future developments affecting Spyre will be those that have been anticipated. These forward-looking statements involve a number of risks, uncertainties (some of which are beyond Spyre's control) or 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, including our plans for and timing of cohort initiation for combination therapy arms for the ongoing SKYLINE Phase 2 platform trial across different jurisdictions; the potential for 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; impacts of adverse events or disappointing results in clinical trials of third parties, including our competitors developing product candidates that target similar mechanisms of action and/or indications as our product candidates; and those uncertainties and factors described under the heading "Risk Factors," "Risk Factor Summary" and "Note about Forward-Looking Statements" in Spyre's most recent Annual Report on Form 10-K, as supplemented and updated by subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K that the Company has filed or will file with the SEC, as well as discussions of potential risks, uncertainties, and other important factors included in other filings by Spyre from time to time. Should one or more of these risks or uncertainties materialize, or should any of Spyre's assumptions prove incorrect, actual results may vary in material respects from those projected in these forward-looking statements. Nothing in this press release should be regarded as a representation by any person that the forward-looking statements set forth therein will be achieved or that any of the contemplated results of such forward-looking statements will be achieved. 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. This press release does not purport to summarize all of the conditions, risks and other attributes of an investment in Spyre.

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

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

A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/8abbc573-d59d-4d30-93e4-70a87c801c34