Spyre Therapeutics Doses First Patient in Pioneering Phase 2 SKYWAY Basket Trial of SPY072, the First Anti-TL1A Antibody Studied in Rheumatic Diseases

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SPY072 is a potential first- and best-in-class anti-TL1A antibody for rheumatic diseases targeting quarterly or twice-yearly subcutaneous dosing

SKYWAY study is evaluating SPY072 in patients with moderate-to-severely active rheumatoid arthritis (RA), psoriatic arthritis (PsA), and axial spondyloarthritis (axSpA)

Proof-of-concept data for all three indications are expected in 2026

SKYLINE and SKYWAY trials are expected to provide 9 proof-of-concept readouts in 2026-27

WALTHAM, Mass., Sept. 15, 2025 (GLOBE NEWSWIRE) -- Spyre Therapeutics, Inc. (NASDAQ: SYRE), a clinical-stage biotechnology company advancing best-in-class antibody engineering, dose optimization, and rational therapeutic combinations for the treatment of Inflammatory Bowel Disease (“IBD”) and other immune-mediated diseases, today announced that the first patient has been dosed in its Phase 2 SKYWAY basket trial evaluating SPY072 in RA, PsA, and axSpA.

SPY072 is an extended half-life investigational antibody targeting TL1A, a cytokine central to T-cell-driven inflammation. Designed for superior potency, convenience, and durability, SPY072 may set a new standard in the treatment of rheumatic diseases with its potential for quarterly or twice-yearly subcutaneous maintenance dosing.

“RA, PsA, and axSpA collectively affect millions of patients globally, including more than three million in the U.S., yet the vast majority do not achieve durable remission with today’s therapies and require frequent injections or infusions,” said Josh Friedman, M.D., Ph.D., SVP of Clinical Development at Spyre. “The evidence for TL1A inhibition in these conditions spans human genetics, in vitro studies, and animal models, suggesting that SPY072 has the potential to match or exceed the efficacy of current therapeutics. With a target dosing profile superior to any existing therapy in these indications, SPY072 has the potential to become a first- and best-in-class therapy for rheumatic diseases.”

The SKYWAY Phase 2 trial is a randomized and placebo-controlled study evaluating SPY072 in patients with moderately to severely active RA, PsA, or axSpA with inadequate response to conventional or advanced therapies. Topline 12-week (RA) and 16-week (PsA, axSpA) proof-of-concept data are expected in 2026.

“We are excited that Spyre is pioneering a potential new therapeutic class for rheumatic diseases. SKYWAY is our second Phase 2 trial launch this year alongside the SKYLINE study evaluating three monotherapies and three combinations in IBD patients,” said Cameron Turtle, DPhil, Chief Executive Officer of Spyre. “Together, we expect these two trials to deliver nine placebo-controlled proof-of-concept readouts over the next two years. These trials aim to efficiently identify multiple products with indication-leading profiles in commercial markets totaling over $60B in annual revenue.”

About SPY072

SPY072 is an investigational, extended half-life monoclonal antibody targeting TL1A for the potential treatment of rheumatic diseases including rheumatoid arthritis, psoriatic arthritis, and axial spondyloarthritis. Together, these conditions affect more than 3 million individuals in the United States. In head-to-head preclinical studies, SPY072 demonstrated potency equivalent to or better than first-generation anti-TL1As. Interim data from a Phase 1 trial demonstrated that SPY072 was well tolerated, exhibited prolonged pharmacokinetics, and rapidly and durably suppressed free TL1A. Based on Phase 1 clinical data, the Company is evaluating SPY072 in its SKYWAY-RD Phase 2 basket study (NCT07148414).

About Spyre Therapeutics

Spyre Therapeutics is a clinical-stage biotechnology company that aims to create next-generation inflammatory bowel disease (IBD) and other immune-mediated disease products by combining best-in-class antibody engineering, dose optimization, and rational therapeutic combinations. 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 SPY072 in humans, including the potential for a quarterly or twice yearly dosing profile that may set a new standard of care for rheumatic diseases; the potential for SPY072 to become a first- and best-in-class therapy for rheumatic diseases; expectations regarding the drug delivery of SPY072, 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 and 2027; the potential consistency of the SPY072 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 and convenience compared to today's standard of care; and estimated market sizes and potential growth opportunities. 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-UC 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; 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.

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