Spyre Therapeutics Highlights 2025 Priorities and Robust Pipeline of Upcoming Clinical Readouts

January 13, 2025

Phase 1 interim results expected for SPY002, two distinct extended half-life TL1A antibodies, in 2Q2025

Phase 1 interim results expected for SPY003, an extended half-life IL-23 antibody, in 2H2025

Phase 2 platform trial in ulcerative colitis (UC) remains on track for initiation in mid-2025 with SPY001 (α4β7), followed by SPY002 (TL1A), SPY003 (IL-23), and combinations thereof, with initial results expected in 2026

Announces indication expansion into rheumatoid arthritis (RA) with SPY002;
Phase 2 RA trial initiation anticipated in mid-2025 with topline results in 2026

Strong balance sheet with preliminary cash, cash equivalents, and marketable securities balance of over $600M as of December 31, 2024, anticipated to provide cash runway into the second half of 2028*

WALTHAM, Mass., Jan. 13, 2025 /PRNewswire/ -- Spyre Therapeutics, Inc. (NASDAQ: SYRE) (the "Company" or "Spyre"), a clinical-stage biotechnology company utilizing best-in-class antibody engineering, rational therapeutic combinations, and precision medicine approaches to target improved efficacy and convenience in the treatment of IBD and other immune-mediated diseases, today highlighted its 2025 priorities, including: upcoming first-in-human clinical data for SPY002 and SPY003, an indication expansion of its SPY002 program into RA, and a plan to deliver four clinical proof-of-concept readouts in 2026.

"Spyre made substantial progress in 2024 including entering first-in-human studies with SPY001 and SPY002. We reported outstanding interim Phase 1 results for SPY001 suggesting the potential for quarterly or twice-annual dosing with a molecule that has the potential to match or exceed the efficacy of the current best-selling product in IBD and look forward to reporting interim Phase 1 results for SPY002 and SPY003 in 2025. This year, we expect to advance all three programs into a groundbreaking Phase 2 platform study in ulcerative colitis patients testing monotherapies and combination therapies under a single master protocol," said Cameron Turtle, DPhil, CEO of Spyre. "We are also announcing the planned expansion of our SPY002 program into RA, a debilitating condition affecting millions of patients worldwide with continued unmet need for effective agents and improved convenience. The potential benefit of anti-TL1A in RA is supported by multiple lines of evidence including human genetics, blood and tissue samples from RA patients, and animal models of disease. With SPY002's class-leading potency and half-life established in pre-clinical studies, it has the potential to become the first-in-class and best-in-class anti-TL1A treatment for RA. Between these planned Phase 2 studies in UC and RA, we expect to deliver four proof-of-concept readouts in 2026."

Anticipated 2025 milestones for Spyre's next-generation monotherapies

- SPY001 – a highly potent and selective, half-life extended, investigational anti-α4β7 monoclonal antibody
    - Initiation of Phase 2 proof-of-concept study in UC patients in mid-2025 with target exposures that have the potential to increase or accelerate efficacy
    - Longer-term Phase 1 data expected to be presented at a medical meeting in 2025, following interim data presented in November 2024 demonstrating SPY001 was well tolerated with a half-life of >90 days, supporting Q3M-Q6M dosing
- SPY002 – a program with two highly potent and selective, half-life extended, investigational anti-TL1A monoclonal antibodies
    - Phase 1 studies initiated in 4Q2024 for both anti-TL1A molecules
    - Phase 1 interim data for both molecules on track for 2Q2025
- SPY003 – a highly potent and selective, half-life extended investigational monoclonal antibody targeting the p19 subunit of IL-23
    - Phase 1 initiation on track for 1Q2025
    - Phase 1 interim data expected in 2H2025

Platform Phase 2 trial in ulcerative colitis evaluating next-generation monotherapies and paradigm-changing combinations

- Spyre plans to advance SPY001, SPY002, SPY003, and combinations thereof into a double-blind, randomized, placebo-controlled, Phase 2 platform trial with a master protocol in patients with moderately-to-severely active ulcerative colitis
    - Platform trial is designed to efficiently evaluate each of Spyre's monotherapy and combination therapies against a common placebo control and to evaluate the contribution of each monotherapy component to the safety and efficacy of Spyre's combination therapies
    - Trial is anticipated to initiate in mid-2025 with SPY001, followed by SPY002, SPY003, and combinations thereof. All

investigational products in the study are expected to be dosed as subcutaneous quarterly injections in the maintenance setting with pharmacokinetic exposures targeting maximal efficacy based on published exposure- or dose- responses for each mechanism of action
- Initial open label monotherapy data from this study are expected beginning in mid-2026, with full placebo-controlled data expected in 2027

Rheumatoid arthritis indication expansion

- SPY002 (anti-TL1A) has first-in-class and best-in-class potential in RA, a chronic autoimmune inflammatory condition that affects millions of individuals worldwide
  - Lack of response, insufficient response, or waning of response to existing mechanisms highlights the need for new treatment options
  - TL1A levels are elevated in the blood and synovial fluid of RA patients and higher TL1A levels are correlated with disease severity
  - TL1A blockade has been shown to be efficacious in murine models of inflammatory arthritis. Blockade using Spyre's anti-TL1A antibodies matched or exceeded the efficacy of anti-TNF treatment in collagen-induced rat models of RA
  - SPY002's projected quarterly to twice-annual subcutaneous dosing in a single autoinjector has the potential to be the most convenient product available for RA
  - Phase 2 clinical trial initiation expected in mid-2025 with topline results in 2026

Strong financial position

The Company had a preliminary cash, cash equivalents, and marketable securities balance of approximately $603 million as of December 31, 2024*. The Company anticipates that this cash balance provides operational runway into the second half of 2028.

** These preliminary selected financial results are unaudited and subject to adjustment. The Company expects to report its final and complete fourth quarter and full-year 2024 financial results in late February 2025.*

About Spyre Therapeutics

Spyre Therapeutics is a 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, rational therapeutic combinations, and precision medicine approaches. Spyre's pipeline includes extended half-life antibodies targeting α4β7, TL1A, and IL-23.

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 of its pipeline and business including, without limitation, the planned dosing regimen for SPY001 and SPY002 molecules, including the potential for quarterly or twice-annual dosing; the potential for its product candidates to have efficacy improvement and convenience advantage over existing products targeting IBD and RA; the therapeutic benefits of its product candidates as monotherapies or in combinations and their picomolar potencies, extended half-lives, and high concentration formulations; the potential of a SPY002 molecule to be best-in-class half-life extended anti-TL1A antibodies and best-in-class and first-in-class anti-TL1A treatment for RA; the expected designs and timing of the platform Phase 2 trials in IBD and RA, including the selection of a SPY002 molecule for each planned Phase 2 trial and the timing of each cohort; its plans to conduct its first-in-human study of SPY003, including expected timing thereof; the expected timing for receipt of interim PK, PD and safety data for its studies in IBD; the expected initiation of proof-of-concept studies, including number of proof-of-concept studies and timing for receipt of readouts; its plans to initiate a study of SPY002 in indications outside of IBD, including timing thereof; potential market opportunities; the Company's expected cash, cash equivalents and short-term investments of approximately $603 million as of December 31, 2024; and the sufficiency of its cash runway into the second half of 2028. 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," "aim," "strategy," "target," "anticipate," "achieve," "believe," "contemplate," "continue," "could," "estimate," "expect," "intends," "may," "might," "plan," "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 and clinical trial designs, including the planned Phase 2 trials, to be materially different from those expressed or implied by these forward-looking statements. These risks and uncertainties include, but are not limited to regulatory feedback including potential disagreement by regulatory authorities with the Company's interpretation of data and the Company's planned clinical trials for its product candidates, including the Company's planned Phase 2 platform clinical trial design, and those uncertainties and factors described under the heading "Risk Factors" and "Note about Forward-Looking Statements" in Spyre's most recent Annual Report on Form 10-K filed 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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