Spyre Therapeutics Announces Poster Presentations at Digestive Disease Week (DDW) 2025 Including Up to Eight months of Follow-up from an Ongoing Phase 1 Trial of SPY001

May 5, 2025

SPY001 is a novel, half-life extended α4β7 antibody in development for the treatment of Inflammatory Bowel Disease (IBD)

SPY001 pharmacokinetic (PK) data up to eight months continues to support a potential best-in-class profile, including a half-life more than three times that of vedolizumab

SPY001 pharmacodynamic (PD) data up to eight months showed that a single dose of SPY001 resulted in rapid and sustained saturation of α4β7 receptors at expected Phase 2 trough concentrations

Spyre remains on track to initiate its planned platform Phase 2 trial in mid-2025 that includes SPY001, followed by SPY002 (TL1A), SPY003 (IL-23), and combinations thereof, with initial monotherapy data expected in 2026

WALTHAM, Mass., May 5, 2025 /PRNewswire/ -- Spyre Therapeutics, Inc. (NASDAQ: SYRE) (the "Company" or "Spyre"), 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 two poster presentations at Digestive Disease Week (DDW) 2025, being held May 3-6, 2025, in San Diego, California.

- **Spyre presented results out to eight months of follow up from its SPY001 Phase 1 program.** Updated results from our ongoing Phase 1 trial of SPY001, our novel half-life extended α4β7 antibody for the treatment of IBD, continues to show that SPY001 is well tolerated, has a half-life of more than three-fold compared to vedolizumab based on population PK modeling, and sustains target engagement at expected Phase 2 trough concentrations. This longer follow-up data strengthens the potential for SPY001 to demonstrate improved induction responses with greater exposures as well as durable responses with quarterly or biannual maintenance dosing.

- **Spyre presented expanded preclinical data on combined inhibition of α4β7 integrin and TL1A cytokine in murine colitis models**. Data presented demonstrate that combined inhibition of α4β7 integrin and TL1A cytokine is superior to either monotherapy in mouse models of colitis.

"Extended follow-up data continue to show that SPY001 is well tolerated and has a PK and PD profile that supports potential best-in-class quarterly or biannual dosing for patients with IBD," said Deanna Nguyen, MD, SVP of Clinical Development at Spyre. "We look forward to testing SPY001 as a monotherapy and as a backbone for combinations in our Phase 2 platform trial in ulcerative colitis patients, which remains on-track to begin mid-year."

The poster will be available for viewing during the DDW exhibition, and details are as follows:

Title: Interim PK Data for SPY001, a Novel Half-Life Extended Monoclonal Antibody Targeting α4β7, Suggest a Potential for Q3M or Q6M Maintenance Dosing for Inflammatory Bowel Disease
Authors: D Nguyen, L Yan, K Hew, P Patel, R McLean, R Himes, T Das, M Huyghe, B Connolly, J Friedman

Title: Combined inhibition of TL1A and integrin β7 is superior to either monotherapy in mouse models of colitis and coadministration of SPY001 and SPY002 demonstrates no drug-drug effects on exposure in non-human primates
Authors: M Siegel, J Friedman, D Nguyen, J McNally, M Kennedy, O Ballew, M Rose, A Spencer

Full session details can be accessed via the DDW Program.

About SPY001

SPY001 is an investigational novel, extended half-life monoclonal antibody targeting α4β7 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. In the United States, it is estimated that approximately 2.4 million individuals currently have IBD. SPY001 targets the same epitope as vedolizumab and demonstrates equivalent potency and selectivity as vedolizumab in head-to-head preclinical studies. Interim data from a Phase 1 trial demonstrated that SPY001 was well tolerated and exhibited a human half-life of ~80 days, approximately three-fold greater than vedolizumab. This half-life supports potential quarterly or biannual SC maintenance dosing in a single autoinjector compared to vedolizumab's Q2W SC profile. Based on initial Phase 1 clinical data, the company plans to initiate a Phase 2 platform trial in ulcerative colitis in mid-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, dose optimization, and rational therapeutic combinations. Spyre's pipeline includes 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, 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 potential best-in-class dosing regimen and safety profile of SPY001 in humans; expectations regarding the drug delivery of SPY001, including in the form of a single autoinjector; Spyre's future clinical development activities, including the expected design and timing of the planned platform Phase 2 trial of SPY001, SPY002, SPY003 and combinations thereof and timing of each cohort and data readouts; 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 efficacy, durability and exposure of induction responses for SPY001; and the timing and results of clinical trials. 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 those uncertainties and factors described under the heading "Risk Factors" and "Note about Forward-Looking Statements" in Spyre's most recent Annual Report on From 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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