# Spyre Therapeutics Announces First Participants Dosed in Phase 1 Trials of Novel Half-life Extended Anti-TL1A Antibodies

December 2, 2024

*Spyre is concurrently advancing two anti-TL1A molecules into first-in-human studies*

*Preclinical data for both SPY002 molecules demonstrate picomolar potency and potential for quarterly or twice-yearly dosing, suggesting opportunity for improved efficacy and convenience over first-generation anti-TL1As which are dosed every two to four weeks*

*Interim pharmacokinetic, pharmacodynamic, and safety data from healthy volunteers for both SPY002 molecules anticipated in the second quarter of 2025*

*Spyre expects to introduce SPY002 to its planned Phase 2 study in ulcerative colitis exploring quarterly monotherapies and combinations; the Company also intends to initiate a proof-of-concept Phase 2 study outside of IBD in 2025*

*Strong balance sheet with proforma cash, cash equivalents, and marketable securities balance on September 30, 2024 of over $630M following recent oversubscribed $230M financing, providing cash runway into the second half of 2028*

WALTHAM, Mass., Dec. 2, 2024 /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 Inflammatory Bowel Disease ("IBD"), today announced that it has initiated dosing of healthy volunteers in Phase 1 clinical trials of two investigational half-life extended anti-TL1A monoclonal antibodies.

"TL1A inhibition has demonstrated compelling efficacy in ulcerative colitis and Crohn's disease patients and has been shown in pre-clinical IBD models to provide additive benefit when used in combination with other targeted agents. Further, TL1A is implicated in numerous inflammatory and fibrotic diseases beyond IBD," said Josh Friedman, M.D., Ph.D., SVP of Clinical Development at Spyre. "Our SPY002 molecules were engineered to build upon the evidence from first-generation molecules with optimized properties including picomolar potencies, extended half-lives, and high concentration formulations."

The SPY002 Phase 1 Trials (NCT06672718 and NCT06622070) are double blind, placebo-controlled single-ascending dose studies in healthy volunteers. The studies are each expected to enroll approximately 56 healthy adult participants. The primary endpoint is safety, with pharmacokinetics (PK) serving as a secondary endpoint. Interim safety, PK, and pharmacodynamic (PD) data from these trials are expected in the second quarter of 2025. Pending data from the Phase 1 trials, the Company anticipates progressing the SPY002 program into Phase 2 development in 2025.

"Entering the clinic with two optimized anti-TL1A molecules is an exciting next step as we build upon our compelling Phase 1 results for our next-generation anti-α4β7 antibody, SPY001, which exhibited a greater than 90-day half-life enabling quarterly or twice annual dosing in maintenance. Pending Phase 1 success and regulatory feedback, we look forward to introducing one of the SPY002 molecules into our groundbreaking Phase 2 platform study of monotherapies and combination therapies in ulcerative colitis next year, as well as initiating an efficient Phase 2 proof-of-concept study outside of IBD," said Cameron Turtle, D.Phil., Chief Executive Officer of Spyre. "Both of these studies are fully financed following our recent oversubscribed financing. The first-in-human study for SPY003, our extended half-life IL-23 antibody, remains on track to initiate in the first quarter of 2025, which will mark our fourth optimized antibody to initiate clinical trials within nine months."

The Company had a pro forma cash balance of approximately $630.1 million as of September 30, 2024, which includes cash, cash equivalents, and marketable securities as of September 30, 2024 of approximately $414.2 million, plus net proceeds of approximately $215.9 million from the Company's previously announced underwritten public offering, including the full exercise by the underwriters of their option to purchase additional shares of common stock, and assumes no other changes to cash, cash equivalents and marketable securities since September 30, 2024.

**About SPY002-091 and SPY002-072**

SPY002-091 and SPY002-072 are investigational, extended half-life monoclonal antibodies targeting TL1A for the potential treatment of inflammatory and fibrotic diseases including 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. In head-to-head preclinical studies, SPY002 candidates demonstrated equivalent or better potency to first-generation anti-TL1As and exhibited significantly longer half-lives, with the potential for quarterly or twice-yearly dosing. Spyre is advancing two molecules into Phase 1 trials (NCT06672718 and NCT06622070), and the Company expects interim safety, pharmacokinetic, and pharmacodynamic data in the second quarter of 2025. Pending data from the Phase 1 trials, the Company anticipates progressing the SPY002 program into Phase 2 development

in 2025.

**About Spyre Therapeutics**

Spyre Therapeutics is a biotechnology company that aims to create next-generation inflammatory bowel disease (IBD) 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 SPY002 molecules, the potential for efficacy improvement and substantial convenience advantage over first-generation anti-TL1As, the therapeutic benefits of its product candidates as monotherapies or in combinations and their picomolar potencies, extended half-lives, and high concentration formulations, the expected design and timing of the platform Phase 2 trial, including the selection of a SPY002 molecule for the planned Phase 2 trial, 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, its plans to initiate a study of SPY002 in indications outside of IBD, including timing thereof, 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," "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 and clinical trial designs, including the planned Phase 2 trial, 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 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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