Spyre Therapeutics Announces First Participant Dosed in Phase 1 Trial of SPY003, its Novel Half-life Extended IL-23 Antibody

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Preclinical data demonstrates that SPY003 is highly potent and has potential for quarterly or biannual dosing, suggesting opportunity for improved efficacy and convenience over first-generation anti-IL-23 monoclonal antibodies

Interim pharmacokinetic and safety data from healthy volunteers for SPY003 anticipated in the second half of 2025

Subject to interim results, Spyre expects to incorporate SPY003 into its planned Phase 2 study in ulcerative colitis exploring six investigational monotherapies and combinations

WALTHAM, Mass., March 27, 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 that it has initiated dosing in a healthy volunteer, Phase 1 clinical trial of its investigational half-life extended anti-IL-23 monoclonal antibody, SPY003. This milestone marks our fourth on-time clinical trial initiation in nine months.

"Recent third-party clinical data demonstrate that combination therapies that include an IL-23 antibody can produce superior results for IBD patients. We believe SPY003 has the potential to be a best-in-class IL-23 antibody and a compelling combination partner with our α4β7 and TL1A antibodies that can be delivered on a quarterly or bi-annual treatment schedule." said Deanna Nguyen, M.D., SVP of Clinical Development at Spyre. "We look forward to presenting the interim Phase 1 data in the second half of this year before adding SPY003 as the final monotherapy component of our planned Phase 2 platform trial in ulcerative colitis which will evaluate three investigational monotherapies and three investigational combination therapies."

The SPY003 Phase 1 Trial (NCT06873724) is a double-blind, placebo-controlled single-ascending dose study in healthy volunteers. The study is 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 ADA data from this trial are expected in the second half of 2025.

About SPY003

SPY003 is an investigational, novel, extended half-life monoclonal antibody targeting IL-23, being developed for the potential 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. In head-to-head preclinical studies, SPY003 demonstrated equivalent potency to risankizumab in inhibiting pSTAT signaling and IL-17 production and exhibited significantly longer half-life in non-human primates with the potential to deliver dosing in humans as infrequently as once every six months. A Phase 1 trial of SPY003 in healthy volunteers is ongoing, and the Company expects interim safety and pharmacokinetic data in the second half of 2025. Pending data from the Phase 1 trial, the company anticipates progressing into Phase 2 development.

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 dosing regimen; the potential for SPY003 potential to be a best-in-class IL-23 antibody and a compelling combination partner with our anti-α4β7 and anti-TL1A antibodies that can be delivered on a quarterly or bi-annual treatment schedule; the expected participant enrolment of the SPY003 Phase 1 trial; Spyre's future clinical development activities, including its planned Phase 2 trial in ulcerative colitis and timing and design

thereof; the potential therapeutic benefits of Spyre's product candidates as monotherapies and or in combination, including the efficacy and convenience of SPY003 compared to the current standard of care in IBD; and the timing and results of clinical trials, including timing of interim safety and PK data readouts for the SPY003 Phase 1 trial. 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," "pipeline," "can," "aim," "strategy," "target," "anticipate," "achieve," "believe," "contemplate," "could," "estimate," "expect," "intends," "may," "might," "plan," "possible," "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 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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