Spyre Therapeutics Announces Expected Acceleration of SPY003 (IL-23p19) Clinical Timelines and Presentations at UEGW supporting Spyre's Portfolio of Potentially Best-in-Class Antibodies and Combinations

October 14, 2024

SPY003, a novel half-life extended IL-23p19 monoclonal antibody (mAb), with first-in-human dosing now expected first quarter 2025

New data on SPY003 presented at UEGW demonstrating robust preclinical activity including comparable potency and a greater than three-fold extension in half-life in NHPs relative to risankizumab[1]. Spyre portfolio now uniquely includes extended half-life molecules targeting α4β7, TL1A, and IL-23 with potential Q8W-Q12W maintenance dosing.

Additional preclinical data on SPY003 in combination with SPY001 or SPY002 presented at UEGW showing enhanced preclinical efficacy and pharmacodynamics

WALTHAM, Mass., Oct. 14, 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 updated pipeline progress and timelines, as well as scientific presentations at the United European Gastroenterology Week ("UEGW") Congress.

- **First-in-human dosing of SPY003 (anti-IL-23) in healthy volunteers is now expected to start during the first quarter of 2025.** SPY003 is a novel, half-life extended mAb targeting IL-23p19 ("IL-23"). Approved inhibitors of IL-23 are effective and well tolerated treatments of moderate-to-severe IBD, with commercially available therapies dosed six times per year. SPY003 has the potential to be dosed quarterly or twice a year as a monotherapy in maintenance. The company expects to share interim data from the accelerated first-in-human trial in the second half of 2025.

- **Spyre presented preclinical data on SPY003 for the first time at UEGW, expanding its portfolio of half-life extended antibodies to three validated targets in IBD.** The presentation illustrated *in vitro* potency comparable to risankizumab[1] and pharmacokinetics indicating that SPY003 has a half-life of ~30 days in non-human primates ("NHPs"), a greater than three-fold increase relative to risankizumab[1]. These data demonstrate that SPY003 exhibits high selectivity and affinity for IL-23 and potently inhibits downstream cellular signaling. With an extended half-life in NHPs, SPY003 demonstrates therapeutic potential for effective and well-tolerated treatment of Crohn's disease ("CD") and Ulcerative Colitis ("UC") with less frequent dosing than approved therapies. In conjunction with its previously disclosed SPY001 (anti-α4β7) and SPY002 (anti-TL1A) programs, the company has a unique portfolio of antibodies that have the potential to be delivered in combination on a unified, Q8W-Q12W dosing frequency in maintenance.

- **Spyre presented preclinical data combining anti-IL-23 with either anti-α4β7 or anti-TL1A for the first time at UEGW.** The presentation included *in vitro* studies and *in vivo murine colitis model* on anti-IL-23 combined with anti-TL1A and anti-α4β7, respectively. The models showed that IL-23 and TL1A have a synergistic effect on promoting IL-17 secretion from human and mouse immune cells, and that the combination of anti-IL-23 and anti-TL1A suppresses IL-17 secretion more effectively than either agent alone. In a T-cell transfer model of IBD, combination therapy with anti-IL-23 and anti-β7 improved body weight and reduced colonic CD4+ infiltration and IL-17 levels relative to monotherapy.

- **Additional preclinical data for SPY001 (anti-α4β7) and SPY002 (anti-TL1A) presented at UEGW.** These presentations included *in vitro* potency compared to benchmark antibodies, nonclinical safety data, and pharmacokinetics demonstrating extended half-life in NHPs. For SPY002, characterization of the two development candidates planned for first-in-human studies in Q4 2024 is further described. Human pharmacokinetic simulations for SPY001 and both SPY002 candidates support potential Q8-12W dosing regimens in IBD.

"The Spyre team has made significant progress in advancing its potentially best-in-class molecules into first-in-human studies within an expected nine-month window," said Cameron Turtle, DPhil, chief executive officer of Spyre. "With these promising molecules against the top three validated targets in IBD, we believe that Spyre is uniquely positioned to develop monotherapy and combination products with the potential to meaningfully improve both efficacy and convenience compared to today's standard of care."

The posters were presented at the UEGW Congress on Saturday, October 12, 2024, and details are as follows:

Title: A Novel Monoclonal Antibody Drug Candidate SPY001 Targeting Integrin α4β7 for the Treatment of IBD: In Vitro Properties and Non-Human Primate Pharmacokinetics and Safety

Poster #PP1103

Title: Characterization of Two Novel Extended Half-life Monoclonal Antibody Drug Candidates Targeting TL1A for the Treatment of IBD
Poster #MP450

Title: Development and Characterization of SPY003, a Novel Extended Half-life Monoclonal Antibody Drug Candidate Targeting IL-23 for the Treatment of IBD
Poster #MP118

Title: Combining IL-23 Blockade with Anti-α4β7 or Anti-TL1A for the Treatment of IBD is Supported by In Vitro and Mouse IBD Model Experiments
Poster #PP1111

Full session details can be accessed via the UEGW program. New data disclosures are also available in Spyre's updated corporate presentation.

[1]Synthesized comparator antibody

About Spyre Therapeutics

Spyre Therapeutics is a clinical-stage biotechnology company that aims to create next-generation of inflammatory bowel disease (IBD) products by combining best-in-class antibody engineering, rational therapeutic combinations, and precision medicine approaches. 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
This press release contains "forward-looking" statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. All statements contained in this press release, other than statements of historical fact are forward-looking statements. These forward-looking statements include statements regarding the Company's business strategy, including the Company's potential success of developing best-in-class therapeutics for IBD with the potential to meaningfully improve both efficacy and convenience compared to today's standard of care, the potential efficacy, safety and dosing profile of its product candidates, the potential therapeutic benefits of its product candidates as monotherapies or in combinations and their potential extended half-life, and the timing of clinical trials and interim data release, including first-in-human studies for SPY002 and SPY003. The words "believe," "may," "will," "potentially," "estimate," "continue," "anticipate," "predict," "target," "intend," "could," "would," "should," "project," "plan," "expect," the negatives of these terms, and similar expressions that convey uncertainty of future events or outcomes are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. 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 Quarterly Report on Form 10-Q 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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