Spyre Therapeutics Announces First Participants Dosed in Phase 1 Trial of SPY001, its Novel Half-life Extended anti-α4β7 Antibody, for the Treatment of Inflammatory Bowel Disease

June 18, 2024

Preclinical data for SPY001 demonstrate the potential for improved dosing over standard of care, including the potential for dosing every eight or twelve weeks compared to dosing every two weeks for subcutaneous vedolizumab

Interim subcutaneous pharmacokinetic and safety data from healthy volunteers anticipated by year-end 2024

SPY002, an extended half-life anti-TL1A antibody designed for enhanced potency to both TL1A monomers and trimers, remains on track to begin first-in-human studies in the second half of 2024

All three next-generation antibodies targeting α4β7, TL1A, and IL-23 are on track to be in the clinic within 12 months, each serving as backbones for potential best-in-class combinations

WALTHAM, Mass., June 18, 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 its first clinical trial of SPY001, an investigational novel half-life extended anti-α4β7 monoclonal antibody.

"The Spyre team has executed efficiently to achieve this milestone within a year of our public launch. SPY001 is the first of our programs across three of the most impactful mechanisms in IBD, namely α4β7, TL1A, and IL-23, all of which are expected to enter the clinic within the next twelve months," said Cameron Turtle, D.Phil., Chief Executive Officer of Spyre. "We look forward to highlighting interim data for SPY001 by the end of this year, which we expect will confirm that SPY001 is well tolerated with a half-life that enables a convenient Q8-12W subcutaneous dosing schedule, with interim data for our T1LA program to follow."

The SPY001 Phase 1 trial is a double blind, placebo-controlled study in healthy volunteers and consists of a single-ascending dose (SAD) component and a multi-ascending dose (MAD) component. The study is expected to enroll approximately 48 healthy adult participants into four SAD cohorts and two MAD cohorts. The primary endpoint is safety, with pharmacokinetics (PK) serving as a secondary endpoint. We expect interim safety and PK data from this trial by year-end 2024. Pending data from the Phase 1 trial, the company anticipates progressing into Phase 2 development with SPY001 in 2025.

"α4β7 inhibition is a preferred first-line treatment option among gastroenterologists given its favorable safety profile with a gut-selective mechanism of action and demonstrated efficacy superiority over TNF inhibition in the VARSITY study," said Deanna Nguyen, M.D., SVP of Clinical Development at Spyre. "We believe this unique safety and efficacy profile, combined with a more convenient dosing frequency, could make SPY001 an ideal backbone for combination therapy for IBD with the inhibition of other highly active mechanisms including T1LA and IL-23."

About SPY001

SPY001 is an investigational novel, subcutaneous extended half-life monoclonal antibody targeting α4β7 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, SPY001 demonstrated equivalent potency to vedolizumab in blocking MadCAM-1 adhesion and exhibited significantly longer half-life with the potential to deliver dosing as infrequently as once every two or three months. A Phase 1 trial of SPY001 in healthy volunteers is ongoing, and the Company expects interim safety and pharmacokinetic data by year-end 2024. Pending data from the Phase 1 trial, the company anticipates progressing into Phase 2 development with SPY001 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. 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 of its pipeline and business including, without limitation, Spyre's ability to achieve the expected benefits or opportunities with respect to SPY001 including obtaining interim data supporting target safety profile and dosing schedule by end of year, the timing of commencing clinical studies for Spyre's two other programs and obtaining interim data for SPY002, patient enrollment results for the SPY001 Phase 1 trial and the potential of SPY001, SPY002 and SPY003 to become backbones for potential best-in-class combinations for IBD. 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 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.

Follow Spyre Therapeutics on social media: @spyretx and LinkedIn

SOURCE Spyre Therapeutics, Inc.