Spyre Therapeutics Reports First Quarter 2024 Financial Results and Provides Corporate Update

SPY001, an anti-α4β7 antibody engineered for infrequent, subcutaneous dosing successfully completed a 28-day GLP toxicity study and remains on track to begin first-in-human studies in the second quarter of 2024, with interim proof-of-concept data expected year-end 2024

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

Raised $180 million in a March 2024 private placement equity financing with participation from new and existing investors

$485 million of cash, cash equivalents, marketable securities, and restricted cash as of March 31, 2024, with expected runway well into 2027, through multiple clinical readouts

WALTHAM, Mass., May 9, 2024 /PRNewswire/ -- Spyre Therapeutics, Inc. ("Spyre" or the "Company") (NASDAQ:SYRE), a development-stage biotechnology company advancing best-in-class antibody engineering, rational therapeutic combinations, and precision medicine approaches for the treatment of inflammatory bowel disease ("IBD"), today announced its first quarter 2024 financial results and provided program and corporate updates.

"I am proud of Spyre's continued execution against our corporate strategy this past quarter, further expanding our team and building a strong financial foundation with the support of top-tier investors. With a clean safety profile in SPY001's 28-day GLP toxicity study, we remain on track towards initiating a first-in-human study later this quarter and advancing our mission of creating IBD therapies that provide meaningful improvements in both efficacy and convenience," said Cameron Turtle, DPhil., Chief Executive Officer. "We expect to report interim PK and safety data from our Phase 1 trial of SPY001 by the end of this year, setting up the first of what we expect to be a string of important catalysts from year-end 2024 through 2025 across our lead programs. We also anticipate initiating a Phase 2 evaluation of rational therapeutic combinations in IBD patients in 2025."

Development Pipeline Overview and Update

The Company's approach combines best-in-class antibody engineering, rational therapeutic combinations, and precision immunology with the goal of maximizing efficacy, safety, and convenience of its IBD treatments under development. IBD is a chronic condition characterized by inflammation within the gastrointestinal tract, including two main disorders: ulcerative colitis ("UC") and Crohn's disease ("CD"). In the United States, it is estimated that approximately 2.4 million individuals are diagnosed with IBD.

The Company has four programs in preclinical development, three of which are targets in IBD validated by third parties. The fourth program is a novel, undisclosed target. The Company is also researching rational combinations of its therapeutic antibody product candidates to target IBD. All three validated targets offer the potential for effective and safe treatment of UC and CD as a monotherapy or in combination, with the potential advantage of infrequent subcutaneous dosing.

SPY001 – a highly potent and selective investigational anti-α4β7 monoclonal antibody engineered with half-life extension technology and formulated for high concentration and subcutaneous, infrequent dosing.

- The 28-day GLP toxicity study in non-human primates ("NHPs") has been completed, demonstrating a favorable safety profile with the highest dose level evaluated as the no-observed-adverse-effect-level ("NOAEL"). Chemistry, manufacturing, and controls ("CMC") activities to enable the SPY001 first-in-human ("FIH") study are also complete, and SPY001 remains on track to enter FIH studies in the second quarter of 2024.
- In February 2024, expanded preclinical data for SPY001 was presented at the 19th Annual Congress of the European Crohn's and Colitis Organisation ("ECCO"), including head-to-head non-human primate pharmacokinetic data showing an updated half-life of 22 days, a greater than three-fold increase relative to vedolizumab. This data further supports our target human half-life for SPY001 of more than 35 days, predicted by allometric scaling.
- Interim data from a healthy volunteer study are expected by the end of 2024. The Company expects pharmacokinetic data to demonstrate proof of concept for SPY001 to potentially be dosed subcutaneously in an every-eight-week or every-twelve-week dosing interval.

SPY002 – a highly potent, selective, half-life extended, anti-TL1A investigational monoclonal antibody with potential best-in-class subnanomolar binding affinity for both the monomer and trimer forms of the target. The Company believes TL1A has emerged as one of the most promising targets in IBD and broader immunology indications.

- The Company has nominated two lead SPY002 development candidates and exercised its option to exclusively license related intellectual property rights under its agreement with Paragon Therapeutics. The Company's lead candidates bind both TL1A monomers and trimers and have *in vitro* subnanomolar potency and pharmacokinetic half-lives that potentially exceed all clinical-stage TL1A antibodies.
- In February 2024, preclinical data for a lead SPY002 development candidate was presented at the 19th Annual ECCO Congress demonstrating subnanomolar binding affinity and potency, as well as a pharmacokinetic half-life of 24 days in non-human primates, which represents a two to three-fold increase compared to clinical-stage anti-TL1As.
- The Company expects to begin FIH studies of one or both SPY002 candidates in the second half of 2024 with healthy volunteer interim data expected in the first half of 2025. If successful, one SPY002 candidate would then advance into additional clinical development.

SPY003 – a highly potent and selective investigational monoclonal antibody targeting the p19 subunit of IL-23, engineered with half-life extension technology.

- The Company continues preclinical development efforts on a potential best-in-class IL-23 monoclonal antibody. Data from the Phase 3 SEQUENCE study of risankizumab versus ustekinumab in Crohn's disease validates the Company's targeting of the p19 subunit as it demonstrated superiority to targeting the p40 subunit common to IL-12 and IL-23.
- The Company expects to nominate a development candidate in mid-2024 and move into IND-enabling studies in the second half of 2024. The Company expects to initiate FIH studies in the first half of 2025.

Recent Corporate Updates

- In March 2024, the Company announced $180 million in gross proceeds from a private placement equity financing with broad participation from both new and existing investors, extending cash runway well into 2027.
- In February 2024, the Company announced the appointment of Mark C. McKenna, former Chairman, President and CEO of Prometheus Biosciences, Inc., to its Board of Directors. Mr. McKenna's track record of corporate leadership, product development, and value creation will be instrumental to guide the Company as it advances its potentially best-in-class IBD portfolio.

First Quarter 2024 Financial Results

Cash Position: As of March 31, 2024, Spyre had available cash and cash equivalents, marketable securities, and restricted cash of $485.0 million. Net cash used in operating activities was $28.5 million for the first quarter of 2024. In March 2024, the Company raised $180 million in gross proceeds, before deducting $11.2 million in placement agent fees and other offering costs, from a private placement of equity securities.

Research and Development (R&D) expenses: R&D expenses totaled $34.9 million for the first quarter of 2024 and $13.8 million for the first quarter of 2023. The increase was driven by preclinical development and manufacturing expenses for the Company's IBD pipeline, partially offset by a decrease in expenses associated with the Company's legacy rare disease pipeline.

General and Administrative (G&A) expenses: G&A expenses totaled $12.8 million for the first quarter of 2024 and $5.2 million for the first quarter of 2023. This increase was primarily due to higher stock compensation and professional services expenses.

Other income (expense): Other income for the first quarter totaled $3.9 million primarily driven by interest earned on the Company's cash and marketable securities.

Net Loss: Net loss totaled $43.9 million and $18.4 million for the first quarters of 2024 and 2023, respectively, which includes non-cash stock compensation expense of $13.8 million and $1.7 million for the first quarters of 2024 and 2023, respectively.

About Spyre Therapeutics
Spyre Therapeutics is a biotechnology company that aims to create the 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.

Follow Spyre Therapeutics on social media: @spyretx and LinkedIn.

Safe Harbor / 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 future results of operations and financial position, business strategy, including the Company's potential success of developing therapeutics for IBD, the sufficiency of the Company's funding to support the development of its assets, the length of time that the Company believes its existing cash resources will fund its operations, its market size, its potential growth opportunities, its preclinical and future clinical development activities, including the expected timing of nomination of development candidates, submission of investigational new drug ("IND") applications and Phase 2 evaluation of therapeutic combinations, the efficacy and safety profile of its product candidates, the potential therapeutic benefits and economic value of its product candidates, the timing and results of preclinical studies and clinical trials, including the commencement of FIH studies, the timing of data and whether the data demonstrates proof of concept, and the Company's planned regulatory activities including filing of INDs to support development and potential commercialization of product candidates. 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 are subject to a number of risks, uncertainties and assumptions, including the expected or potential impact of macroeconomic conditions, including inflationary pressures, rising interest rates, general economic slowdown or a recession, changes in monetary policy, the prospect of a shutdown of the U.S. federal government, volatile market conditions, financial institution instability, as well as geopolitical instability, including the ongoing military conflict in Ukraine, conflict in Israel and surrounding areas, and geopolitical tensions in China on the Company's operations, the potential impacts of the BIOSECURE Act bill if passed into law and those risks described in the Company's Quarterly Reports on Form 10-Q, Annual Reports on Form 10-K, as well as in other filings and reports that the Company makes from time to time with the Securities and Exchange Commission. Moreover, the Company operates in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for the Company's management to predict all risks, nor can the Company assess the impact of all factors on the business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements it may make. In light of these risks, uncertainties, and assumptions, the forward-looking events and circumstances discussed in this press release may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although the Company believes that the expectations reflected in the forward-looking statements are reasonable, the Company cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. The Company undertakes no obligation to update publicly any forward-looking statement for any reason after the date of this press release to conform these statements to actual results, to reflect changes in the Company's expectations, or otherwise, except as required by law. You should read press release with the understanding that the Company's actual results, levels of activity, performance, events, outcomes, and the timing of results and outcomes, and other circumstances may be materially different from what the Company expects.

Spyre Therapeutics, Inc.
Consolidated Balance Sheets
(Unaudited, in thousands, except share and per share amounts)

	March 31, 2024	December 31, 2023
ASSETS		
CURRENT ASSETS		

Cash and cash equivalents	$ 227,552	$ 188,893
Marketable securities	257,089	150,384
Prepaid expenses and other current assets	2,632	2,251
Total current assets	487,273	341,528
Restricted cash	319	322
Other non-current assets	10	9
TOTAL ASSETS	$ 487,602	$ 341,859
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES		
Accounts payable	$ 3,106	$ 896
CVR liability	2,590	1,390
Accrued and other current liabilities	21,594	13,108
Related party accounts payable and other current liabilities	15,528	16,584
Total current liabilities	42,818	31,978
Non-current CVR liability	39,110	41,310
TOTAL LIABILITIES	81,928	73,288
Commitments and Contingencies		
Series B non-voting convertible preferred stock, $0.0001 par value; 271,625 and 150,000 shares authorized as of March 31, 2024 and December 31, 2023, respectively; 271,625 and 150,000 shares issued and outstanding as of March 31, 2024 and December 31, 2023, respectively	253,405	84,555
STOCKHOLDERS' (DEFICIT) EQUITY		
Series A non-voting convertible preferred stock, $0.0001 par value; 1,086,341 shares authorized as of both March 31, 2024 and December 31, 2023; 437,037 shares issued and outstanding as of March 31, 2024 and December 31, 2023, respectively	184,927	184,927
Preferred stock, $0.0001 par value; 8,642,034 shares and 8,763,659 authorized as of March 31, 2024 and December 31, 2023; no shares issued and outstanding as of March 31, 2024 and December 31, 2023	—	—
Common stock, $0.0001 par value; 400,000,000 shares authorized as of March 31, 2024 and December 31, 2023; 36,629,680 shares and 36,057,109 shares issued and outstanding as of March 31, 2024 and December 31, 2023, respectively	10	10
Additional paid-in capital	775,966	763,191
Accumulated other comprehensive (loss) income	(363)	302
Accumulated deficit	(808,271)	(764,414)
TOTAL STOCKHOLDERS' EQUITY	152,269	184,016
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY	$ 487,602	$ 341,859

Spyre Therapeutics, Inc.
Consolidated Statements of Operations
(Unaudited, in thousands, except share and per share amounts)

	Three Months Ended March 31,	
	2024	2023
Revenue:		
Development fee and royalty	$ —	$ 198
Total revenue	—	198
Operating expenses:		
Research and development [(1)]	34,928	13,776

General and administrative	12,846	5,228
Total operating expenses	47,774	19,004
Loss from operations	(47,774)	(18,806)
Other income (expense):		
Interest income	4,432	420
Other expense	(483)	(72)
Total other income (expense)	3,949	348
Loss before income tax expense	(43,825)	(18,458)
Income tax (expense) benefit	(32)	36
Net loss	$ (43,857)	$ (18,422)
Net loss per share, basic and diluted	$ (1.20)	$ (4.89)
Weighted-average common shares outstanding, basic and diluted	36,512,662	3,770,506

(1) Includes $17.1 million in related party expenses for the three months ended March 31, 2024, and no related party expenses for the three months ended March 31, 2023.

SOURCE Spyre Therapeutics, Inc.

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