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

Initiated dosing in Phase 1 trial of SPY001, an anti-α4β7 antibody engineered for infrequent, subcutaneous maintenance dosing, with interim proof-of-concept data on track for year-end 2024

SPY002, an anti-TL1A antibody program 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 trials in the second half of 2024

Nominated a development candidate for SPY003, a highly potent anti-IL-23 antibody with an extended half-life compared to existing molecules, with expectations to begin a first-in-human trial in the first half of 2025

$426 million of cash, cash equivalents, marketable securities, and restricted cash as of June 30, 2024, with expected runway well into 2027, through multiple clinical readouts

WALTHAM, Mass., Aug. 7, 2024 /PRNewswire/ -- Spyre Therapeutics, Inc. ("Spyre" or the "Company") (NASDAQ:SYRE), 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 its second quarter 2024 financial results and provided program and corporate updates.

"Initiation of our Phase 1 trial of SPY001 represents an important transition of Spyre into a clinical-stage biotechnology company and sets the stage for an important year of catalysts to validate the promise of our portfolio. Specifically, by this time next year, we expect to have reported Phase 1 data from our α4β7 and TL1A programs and have an ongoing Phase 1 trial of our IL-23 program reporting data shortly thereafter," said Cameron Turtle, DPhil., Chief Executive Officer. "We believe each of these agents has the possibility to become a best-in-class monotherapy for the treatment of IBD. As a portfolio, we believe these optimized molecules could become ideal building blocks for rational therapeutic combinations with the potential to meaningfully improve efficacy and convenience compared to today's standard of care."

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 nonclinical and clinical 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 maintenance dosing.

SPY001 – a highly potent and selective investigational anti-α4β7 monoclonal antibody engineered with half-life extension technology and formulated for high concentration to maximize induction exposure and potential remission rates, and to enable infrequent, subcutaneous maintenance dosing.

- In June 2024, the Company announced the initiation of dosing of healthy volunteers in its first-in-human ("FIH") trial of SPY001. The Phase 1 trial is a double blind, placebo-controlled trial expected to enroll approximately 48 healthy volunteers, consisting of at least four single-ascending dose (SAD) cohorts and two multi-ascending dose (MAD) cohorts.
- Interim data from this Phase 1 trial 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 maintenance dosing interval.
- In February 2024, expanded preclinical data for SPY001 were presented at the 19th Annual Congress of the European Crohn's and Colitis Organisation ("ECCO"), including comparable potency and selectivity to the vedolizumab epitope, as well as 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. These data further support our target human half-life for SPY001 of more than 35 days, predicted by allometric scaling.

SPY002 – a program with two highly potent, selective, half-life extended, anti-TL1A investigational monoclonal antibody candidates 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 which bind both TL1A monomers and trimers and have *in vitro* subnanomolar potency and pharmacokinetic half-lives that potentially exceed all clinical-stage TL1A antibodies.
- The Company expects to begin FIH trials of both SPY002 candidates in the second half of 2024 with healthy volunteer interim data expected in the first half of 2025. If successful, the Company expects one SPY002 candidate would then advance into further clinical development.
- In February 2024, preclinical data for a lead SPY002 development candidate were 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.

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

- The Company nominated its potential best-in-class development candidate in June 2024 and expects to initiate IND-enabling studies in the second half of 2024. The Company expects to initiate FIH trials in the first half of 2025.

- Data from the Phase 3 SEQUENCE trial of risankizumab versus ustekinumab in Crohn's disease, as well as recent data from the Phase 3 VIVID-1 trial of mirikizumab versus ustekinumab, validate the Company's targeting of the p19 subunit as it demonstrated superiority to targeting the p40 subunit common to IL-12 and IL-23.

Recent Corporate Updates

- In May 2024, the Company announced the appointment of Sandra Milligan, M.D., J.D. to its Board of Directors. Dr. Milligan's deep expertise in clinical development and regulatory affairs, including within IBD, will be invaluable to guide the Company as it advances its potentially best-in-class IBD portfolio. Jeffrey Albers was also appointed Chairman of the Board of Directors as successor to Russell Cox, whose Board term ended in May.
- In May 2024, the Company's stockholders approved all proposals at the 2024 annual meeting of stockholders, including the conversion of the Company's Series B Preferred Stock to Common Stock.

Second Quarter 2024 Financial Results

Cash Position: As of June 30, 2024, Spyre had available cash and cash equivalents, marketable securities, and restricted cash of $426.3 million. Net cash used in operating activities was $62.4 million for the second quarter of 2024. Net cash used in operating activities exceeded net loss for the second quarter primarily due to the timing of certain vendor payments.

Research and Development (R&D) expenses: R&D expenses totaled $32.6 million for the second quarter of 2024 and $17.4 million for the second quarter of 2023. The increase was driven by preclinical and clinical 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 as well as a non-recurring credit from Paragon Therapeutics related to SPY003 development costs.

General and Administrative (G&A) expenses: G&A expenses totaled $11.5 million for the second quarter of 2024 and $12.1 million for the second quarter of 2023.

Acquired in-process research and development expenses: Acquired in-process research and development totaled $130.5 million for the second quarter of 2023 related to the acquisition of the Company's IBD pipeline assets. There was no similar expense for the second quarter of 2024.

Other income (expense): Other income totaled $5.3 million for the second quarter of 2024 primarily driven by interest earned on the Company's cash and marketable securities. For the second quarter of 2023, other expense totaled $57.8 million, primarily driven by a $58.2 million non-cash forward contract liability expense related to an increase in fair value of the underlying Series A Preferred Stock between June 22, 2023 and June 30, 2023.

Net Loss: Net loss totaled $38.8 million and $217.1 million for the second quarters of 2024 and 2023, respectively, which includes non-cash stock compensation expense of $8.7 million and $1.9 million for the second quarters of 2024 and 2023, respectively.

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.

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 nonclinical and future clinical development activities, including the expected timing of nomination of development candidates, submission of investigational new drug ("IND") applications and further clinical 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 nonclinical studies and clinical trials, including the commencement of FIH trials, the timing of data and whether the data demonstrate 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)

	June 30, 2024	December 31, 2023
ASSETS		
CURRENT ASSETS		
Cash and cash equivalents	$ 45,144	$ 188,893
Marketable securities	380,851	150,384
Prepaid expenses and other current assets	9,741	2,251
Total current assets	435,736	341,528
Restricted cash	321	322
Other non-current assets	10	9
TOTAL ASSETS	$ 436,067	$ 341,859
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES		
Accounts payable	$ 3,231	$ 896
CVR liability	2,640	1,390
Accrued and other current liabilities	5,683	13,108
Related party accounts payable and other current liabilities	10,568	16,584
Total current liabilities	22,122	31,978
Non-current CVR liability	39,560	41,310
TOTAL LIABILITIES	61,682	73,288
Commitments and Contingencies		

Series B non-voting convertible preferred stock, $0.0001 par value; 150,000 shares authorized, issued, and outstanding as of December 31, 2023.	—	84,555
STOCKHOLDERS' EQUITY		
Series A non-voting convertible preferred stock, $0.0001 par value; 1,086,341 shares authorized as of June 30, 2024 and December 31, 2023; 346,045 and 437,037 shares issued and outstanding as of June 30, 2024 and December 31, 2023, respectively.	146,425	184,927
Series B non-voting convertible preferred stock, $0.0001 par value; 271,625 shares authorized and 16,667 shares issued and outstanding as of June 30, 2024.	9,395	—
Preferred stock, $0.0001 par value; 8,642,034 shares and 8,763,659 shares authorized as of June 30, 2024 and December 31, 2023, respectively; no shares issued and outstanding as of June 30, 2024 and December 31, 2023.	—	—
Common stock, $0.0001 par value; 400,000,000 shares authorized as of June 30, 2024 and December 31, 2023; 50,783,384 shares and 36,057,109 shares issued and outstanding as of June 30, 2024 and December 31, 2023, respectively.	12	10
Additional paid-in capital	1,066,214	763,191
Accumulated other comprehensive (loss) income	(553)	302
Accumulated deficit	(847,108)	(764,414)
TOTAL STOCKHOLDERS' EQUITY	374,385	184,016
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY	$ 436,067	$ 341,859

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2024	2023	June 30, 2024	June 30, 2023
Revenue:				
Development fee and royalty	$ —	$ 688	$ —	$ 886
Total revenue	—	688	—	886
Operating expenses:				
Research and development [1]	32,636	17,386	67,564	31,162

General and administrative	11,511	12,062	24,357	17,290
Acquired in-process research and development	—	130,486	—	130,486
Total operating expenses	44,147	159,934	91,921	178,938
Loss from operations	(44,147)	(159,246)	(91,921)	(178,052)
Other income (expense):				
Interest income	5,920	350	10,352	770
Change in fair value of forward contract liability	—	(58,170)	—	(58,170)
Other expense, net	(610)	(8)	(1,093)	(80)
Total other income (expense)	5,310	(57,828)	9,259	(57,480)
Loss before income tax expense	(38,837)	(217,074)	(82,662)	(235,532)
Income tax (expense) benefit	—	(7)	(32)	29
Net loss	$ (38,837)	$ (217,081)	$ (82,694)	$ (235,503)
Net loss per share, basic and diluted	$ (0.86)	$ (56.79)	$ (2.02)	$ (62.03)
Weighted-average common shares outstanding, basic and diluted	45,316,264	3,822,605	40,914,463	3,796,699

(1) Includes $9.4 million and $26.5 million in related party expenses for the three and six months ended June 30, 2024, respectively, and $1.4 million related party expenses for the three and six months ended June 30, 2023.

SOURCE Spyre Therapeutics, Inc.

For further information: Media Contact: Amanda Sellers, Verge Scientific Communications, amanda.sellers@vergescientific.com, Investor Contact: Eric McIntyre, eric.mcintyre@spyre.com

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https://ir.spyre.com/2024-08-07-Spyre-Therapeutics-Reports-Second-Quarter-2024-Financial-Results-and-Provides-Corporate-Update