Spero Therapeutics Announces Fourth Quarter and Full Year 2022 Operating Results and Provides Business Update

Initiated proof-of-concept Phase 2 trial of SPR720 in nontuberculous mycobacterial pulmonary disease (NTM-PD); top line data expected in 1H 2024

Exclusive license agreement with GSK for tebipenem HBr provided Spero with $66 million upfront, a $9 million direct equity investment, and eligibility for future milestone payments and tiered royalties

Conference call and live webcast at 4:30 p.m. ET today

CAMBRIDGE, Mass., March 30, 2023 (GLOBE NEWSWIRE) -- Spero Therapeutics, Inc. (Nasdaq: SPRO), a multi-asset clinical-stage biopharmaceutical company, focused on identifying, developing and commercializing treatments in high unmet need areas involving rare diseases and multi-drug resistant (MDR) bacterial infections, today announced financial results for the fourth quarter and full-year ended December 31, 2022, and provided a business update.

"We were pleased to recently initiate our Phase 2 trial of SPR720 in NTM-PD," said Ankit Mahadevia, M.D., Chief Executive Officer of Spero Therapeutics. "A key objective of the trial is to provide clinical proof-of-concept for SPR720 by demonstrating its ability to drive microbiological response against NTM as a single agent versus placebo. We believe achieving clinical proof of concept would substantially de-risk SPR720 and further demonstrate its potential to address the pressing unmet need for an effective, durable, and tolerable first-line therapy for patients with NTM-PD."

Dr. Mahadevia continued, "We were also delighted to close our exclusive license agreement with GSK for tebipenem HBr last quarter, adding strength to our balance sheet and shareholder base with a $66 million upfront payment, a $9 million equity investment, and potentially significant, near and long-term milestones and royalties. We believe our collaboration with GSK will help position tebipenem HBr to be the first potential oral treatment for complicated urinary tract infections. We also remain on track to advance SPR206 into an externally funded Phase 2 trial in patients with either hospital-acquired or ventilator-associated bacterial pneumonia, with an expectation to file the IND, later this year. This further demonstrates our ability to leverage creative partnerships to advance our multi-asset pipeline with a capital-efficient approach."

Full Year 2022 and Recent Program Highlights and Upcoming Milestones

SPR720:

- Spero recently initiated the Phase 2 clinical trial of SPR720, a potential novel first-line oral therapy for nontuberculous mycobacterial (NTM) infections. The trial is expected to enroll up to 35 treatment-naïve or treatment-inexperienced participants with NTM-PD across four cohorts: a blinded placebo cohort; blinded SPR720 cohorts receiving 500 or 1000 mg of study drug daily; and an open-label SPR720 cohort receiving 1000 mg of study drug daily. The primary endpoint of the trial will evaluate changes in bacterial load in sputum samples from baseline to the end of the trial's 56-day treatment period. For more information on the trial and its design, see ***ClinicalTrials.gov*** identifier ***NCT05496374***.

- The ongoing Phase 2 trial of SPR720 is supported by preclinical results demonstrating SPR720's activity against various NTM species, as well as Phase 1 results in healthy volunteers that showed it to be well tolerated at exposures above predicted therapeutic levels. Top line data for the Phase 2 trial of SPR720 are expected in the first half of 2024.

Tebipenem HBr:

- In September 2022, Spero entered into an exclusive license agreement with GSK for tebipenem HBr, an investigational drug being developed as the first potential oral carbapenem antibiotic for the treatment of complicated urinary tract infections (cUTI), including pyelonephritis, caused by certain bacteria. Pursuant to the license agreement, Spero received a $66 million upfront payment from GSK and is eligible to receive up to $525 million in development, sales, and commercial milestones payments, as well as low single-digit to low double-digit tiered royalties on net product sales. In exchange, GSK was granted an exclusive license to develop and commercialize tebipenem pivoxil and tebipenem HBr in all territories, except Japan and certain other Asian countries, territories which were retained by Spero partner Meiji Seika. Per the license agreement, Spero is responsible for the execution and costs of a follow-up Phase 3 clinical trial of tebipenem HBr. GSK is responsible for the execution and costs of additional development, including Phase 3 regulatory filings and commercialization activities for tebipenem pivoxil and tebipenem HBr outside of the Meiji Seika territories.

- In connection with Spero's license agreement with GSK, and pursuant to a stock purchase agreement, Spero received a $9 million equity investment from GSK, in November 2022, with GSK purchasing 7,450,000 shares of Spero's common stock at a purchase price of approximately $1.21 per share.

- Prior to its license agreement with GSK, Spero completed a Type A meeting with the U.S. Food and Drug Administration (FDA). During the meeting, the agency indicated that positive results from a single additional Phase 3 clinical trial supported by

confirmatory nonclinical evidence of efficacy could be sufficient to support the approval of tebipenem HBr for the treatment of cUTI, including pyelonephritis for a limited use indication. Spero and the FDA also achieved alignment on key components of the proposed pivotal Phase 3 trial design, which will be subject to a Special Protocol Assessment (SPA) agreement.

- Spero has engaged with the FDA on the tebipenem HBr clinical program and expects to provide an update in the first half of 2023 on the status of the SPA and detail of the Phase 3 clinical protocol. Initiation of the Phase 3 clinical trial is expected in the second half of 2023.

SPR206:

- In February 2022, Spero announced top line results from a Phase 1 bronchoalveolar lavage (BAL) clinical trial of SPR206, a novel, investigational, intravenously administered next generation polymyxin antibiotic being developed to treat MDR Gram-negative bacterial infections. Results from the BAL trial showed that, when administered three times daily at 100 mg, SPR206 was generally well tolerated with a mean lung epithelial lining fluid exposure that was continuously above its minimum inhibitory concentration (MIC) for targeted Gram-negative pathogens. These results, together with prior Phase 1 results demonstrating SPR206's lack of nephrotoxicity at predicted therapeutic dose levels, support a planned Phase 2 trial designed to evaluate SPR206 in participants with hospital-acquired or ventilator-associated bacterial pneumonia (HABP/VABP). We expect to submit an IND application to the FDA to support this Phase 2 trial in the fourth quarter of this year.

- In the third quarter of 2022, Spero received a $5 million payment from Pfizer Inc. in connection with the achievement of a regulatory milestone specified in a license agreement for SPR206. This license agreement was entered into alongside Pfizer's previously announced $40 million equity investment in Spero. Pursuant to the license agreement between the two parties, Pfizer has the right to develop, manufacture, and commercialize SPR206 in ex-U.S. and ex-Asia territories. In exchange for these rights, Spero is eligible to receive up to a total of $80 million in development and sales milestone payments, and high single-digit to low double-digit royalties on net sales of SPR206 in these territories.

- In October 2022, the U.S. Patent and Trademark Office issued U.S. Patent No. 11,459,357. The patent is assigned to Spero and covers the SPR206 composition of matter, formulations thereof, and methods of treating a bacterial infection with SPR206. The patent has a term extending into at least June 2039, without accounting for potential extensions.

- Multiple external, non-dilutive funding sources have supported, or continue to support, the SPR206 program. These include United States Department of Defense Award Number W81XWH-1910295, and a previously announced award from the National Institute of Allergy and Infectious Diseases.

Full Year 2022 Corporate Highlights

- Kamal Hamed, MD, MPH, MBA joined Spero as Chief Medical Officer (CMO) in September 2022. Dr. Hamed has over two decades of experience leading various anti-infective clinical development programs, and previously maintained stewardship over ten regulatory approvals. Before joining Spero, Dr. Hamed was the CMO of Lysovant Sciences and held senior positions in clinical development and medical affairs at Novartis (including Therapeutic Area Head for Anti-infectives), Bristol-Myers Squibb, and Bayer.
- In October 2022, Spero hosted a virtual R&D event on NTM-PD and the SPR720 program. The event featured Kevin L. Winthrop, MD, MPH, from the Division of Infectious Disease, OHSU Medical School, a patient with NTM-PD, affiliated with a local chapter of NTMir, the national NTM patient advocacy organization, and Kamal Hamed, Spero's CMO, who detailed the various attributes and pharmacological profile of SPR720. To view a replay of the event, please click ***here***.

Fourth Quarter and Full Year 2022 Financial Results

Spero reported net income of $26.8 million for the fourth quarter and an overall net loss of $46.4 million, for the year ended December 31, 2022, or a net income of $0.55 and net loss of $1.23 per share of common stock, respectively. Net loss for the fourth quarter and year ended December 31, 2021, was $29.2 million and $89.8 million, or $0.90 and $2.91 per share of common stock, respectively.

Total revenues for the fourth quarter of 2022 were $47.4 million, compared with revenues of $2.7 million for the fourth quarter of 2021. The revenue increase for the fourth quarter of 2022 was primarily due to $46.1 million in collaboration revenue related to our agreements with GSK and Pfizer. Total revenue for the year ended December 31, 2022, was $53.5 million, compared to $18.3 million for the year ended December 31, 2021. The revenue increase for the year ended December 31 2022, was primarily due to the aforementioned partnership collaboration revenue.

Research and development expenses for the fourth quarter of 2022 were $15.1 million, compared to $17.2 million of research and development expenses for the same period in 2021. This year-over-year decrease was primarily due to a reduction in personnel-related costs following the strategic restructuring announced in May 2022. Research and development expenses for the year ended December 31, 2022 were $47.6 million, compared to $64.5 million for the year ended December 31, 2021, with lower expenses in 2022 compared to 2021 primarily due to reduced program activity for tebipenem HBr as a result of

the strategic restructuring.

General and administrative expenses for the fourth quarter of 2022 were $6.5 million, compared to $13.0 million of general and administrative expenses for the same period in 2021. This year-over-year decrease was primarily due to reduced headcount costs in our commercial, general and administrative functions as a result of the strategic restructuring. General and administrative expenses for the year ended December 31, 2022, were $36.5 million, compared to $41.7 million for the year ended December 31, 2021, with lower expenses in 2022 compared to 2021 primarily as a result of the strategic restructuring.

Restructuring expenses of $11.6 million were incurred during the year ended December 31, 2022. These expenses were primarily comprised of $8.6 million of severance and other employee costs, $2.4 million of discontinuation costs such as contract termination fees, and $0.6 million of lease impairment expenses.

As of December 31, 2022, Spero had cash and cash equivalents of $109.1 million. Based on its current operating plans, Spero believes that its cash and cash equivalents, together with other non-dilutive funding commitments, will be sufficient to fund its operating expenses and capital expenditure requirements beyond 2024.

Conference Call and Webcast

Spero will host a conference call and webcast today at 4:30 p.m. ET. To access the call, please dial 1-877-704-4453 (domestic) or 1-201-389-0920 (international) and refer to conference ID 13736217, or click on this ***link*** and request a return call. The conference call will also be webcast live and a link to the webcast can be accessed ***here*** and on Spero Therapeutics' website at ***www.sperotherapeutics.com*** in the "Investors and Media" section under "Events and Presentations." An archived webcast will be available on Spero's website for 30 days following the presentation.

Tebipenem HBr Research Support

Select tebipenem HBr studies have been funded in part with federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority, under contract number HHSO100201800015C.

Government Agency Research Support

The views expressed in this press release are those of the authors and may not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government.

Department of Defense

Select SPR206 studies are supported by the Office of the Assistant Secretary of Defense for Health Affairs, through the Joint Warfighter Medical Research Program under Award No. W81XWH 19 1 0295. Opinions, interpretations, conclusions and recommendations are those

of the author and are not necessarily endorsed by the Department of Defense.

National Institute of Allergy and Infectious Disease
Select SPR206 studies have been funded in whole or in part with Federal funds from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under Contract No. 75N93021C00022.

About Spero Therapeutics
Spero Therapeutics, headquartered in Cambridge, Massachusetts, is a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing, and commercializing novel treatments for bacterial infections, including multi-drug resistant bacterial infections and rare diseases.

- Spero Therapeutics is developing SPR720 as a novel oral therapy candidate for the treatment of a rare, orphan pulmonary disease caused by non-tuberculous mycobacterial infections.

- Tebipenem HBr is an investigational drug in the United States being developed for the treatment of cUTI, including pyelonephritis, caused by certain bacteria, in adult patients who have limited treatment options; tebipenem HBr is not FDA-approved.

- Spero Therapeutics also has an IV-administered next generation polymyxin product candidate, SPR206, developed from its potentiator platform, which is in development to treat multi-drug resistant Gram-negative infections in the hospital setting.

For more information, visit ***https://sperotherapeutics.com***.

Forward Looking Statements
This press release may contain forward-looking statements. These statements include, but are not limited to, statements about the regulatory path forward for tebipenem HBr and potential FDA approval, the potential commercialization of tebipenem HBr and its future value, the potential receipt of milestone payments or royalties on under Spero's various license and collaboration agreements, the design, initiation, timing, progress and results of Spero's preclinical studies and clinical trials and its research and development programs, and Spero's cash runway. In some cases, forward-looking statements can be identified by terms such as "may," "will," "should," "expect," "plan," "aim," "anticipate," "could," "intent," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms or other similar expressions. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including whether tebipenem HBr will advance through the clinical trial process on a timely basis, or at all, taking into account the effects of possible regulatory delays, slower than anticipated patient enrollment, manufacturing challenges, clinical trial design and clinical outcomes; whether the results of such trials will warrant submission for approval from the FDA or equivalent foreign regulatory agencies; whether the FDA will ultimately approve

tebipenem HBr and, if so, the timing of any such approval; whether the FDA will require any additional clinical data or place labeling restrictions on the use of tebipenem HBr that would delay approval and/or reduce the commercial prospects of tebipenem HBr; whether a successful commercial launch can be achieved and market acceptance of tebipenem HBr can be established; whether the Company will satisfy all of the pre-conditions to receipt of the milestone payments under its various license and collaboration agreements; the lengthy, expensive, and uncertain process of clinical drug development for SPR720 and SPR206; whether results obtained in preclinical studies and clinical trials will be indicative of results obtained in future clinical trials; Spero's reliance on third parties to manufacture, develop, and commercialize its product candidates, if approved; Spero's need for additional funding; the ability to commercialize Spero's product candidates, if approved; Spero's ability to retain key personnel; whether Spero's cash resources will be sufficient to fund its continuing operations for the periods and/or trials anticipated; and other factors discussed in the "Risk Factors" set forth in filings that Spero periodically makes with the U.S. Securities and Exchange Commission. The forward-looking statements included in this press release represent Spero's views as of the date of this press release. Spero anticipates that subsequent events and developments will cause its views to change. However, while Spero may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing Spero's views as of any date subsequent to the date of this press release.

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Spero Therapeutics, Inc.

Condensed Consolidated Statements of Operations

(in thousands, except share and per share data)

(unaudited)

	Three Months Ended December 31,		Year Ended December 31,	
	2022	**2021**	**2022**	**2021**
Revenues:				
Grant revenue	$1,087	$2,488	$4,930	$15,186
Collaboration revenue	46,354	256	48,579	$3,070
Total revenues	47,441	2,744	53,509	18,256
Operating expenses:				
Research and development	15,089	17,225	47,593	64,526
General and administrative	6,495	13,021	36,483	41,701
Restructuring	(67)	-	11,630	-
Total operating expenses	21,517	30,246	95,706	106,227
Loss from operations	25,924	(27,502)	(42,197)	(87,971)
Other income (expense)	847	(1,738)	(4,218)	(1,785)
Net loss	$26,771	$(29,240)	$(46,415)	$(89,756)
Net loss attributable to common shareholders of Spero Therapeutics, Inc.	$26,771	$(29,240)	$(46,415)	$(89,756)
Net loss per share attributable to common shareholders per share, basic and diluted	$0.55	$(0.90)	$(1.23)	$(2.91)
Weighted average shares outstanding, basic and diluted:	48,715,409	32,315,521	37,585,075	30,895,756

Spero Therapeutics, Inc.

Condensed Consolidated Balance Sheet Data

(in thousands)

(Unaudited)

	December 31, 2022	December 31, 2021	Change
Cash, cash equivalents and marketable securities	$109,107	$146,402	$(37,295)
Other assets	15,695	24,670	(8,975)
Total assets	**$124,802**	**$171,072**	**$(46,270)**
Total liabilities	$48,868	$82,783	$(33,915)
Total stockholder's equity	75,934	88,289	(12,355)
Total liabilities and stockholders' equity	**$124,802**	**$171,072**	**$(46,270)**

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