Spero Therapeutics Announces Fourth Quarter and Full Year 2021 Operating Results and Provides Business Update

March 31, 2022

Provides update on ongoing FDA review of Tebipenem HBr NDA

Phase 2 trial of SPR720 in nontuberculous mycobacterial-pulmonary disease on track for initiation in 2H 2022 following lifting of FDA clinical hold

Topline results from Phase 1 bronchoalveolar lavage trial support further development of SPR206 in the setting of hospital-acquired pneumonia and ventilator-associated pneumonia

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

CAMBRIDGE, Mass., March 31, 2022 (GLOBE NEWSWIRE) -- Spero Therapeutics, Inc. (Nasdaq: SPRO) today announced financial results for the fourth quarter and full-year ended December 31, 2021 and provided a business update.

The U.S. Food and Drug Administration (FDA) has notified Spero that, as part of its ongoing review of Spero's New Drug Application (NDA) for tebipenem HBr, it has identified deficiencies that preclude discussion of labeling and post-marketing requirements/commitments at this time. The FDA stated that the notification does not reflect a final decision on the information under review. Spero intends to work with the FDA to seek to resolve the deficiencies expeditiously.

The FDA previously assigned a Prescription Drug User Fee Act (PDUFA) goal action date of June 27, 2022, for completion of its review of the NDA, and initially targeted the midpoint of that review period to communicate proposed labeling and, if necessary, any post-marketing requirement and/or commitment requests to Spero. The Company noted that there are three months remaining before the PDUFA goal action date. Spero also has a late cycle review meeting scheduled with the FDA and expects to provide an update on or before its next earnings call in May 2022.

"We continue to have an active dialogue with the FDA," said Ankit Mahadevia, M.D., Chief Executive Officer of Spero. "We are focused on doing everything we can to address the deficiencies and, given how early in the review period the labeling discussions were originally scheduled, we believe there would be sufficient time to progress to labeling discussions within the existing PDUFA timeframe. However, we do not yet know the effect of this notification, if any, on our anticipated timelines or on the ultimate approval prospects of tebipenem HBr. We continue to prepare for an anticipated commercial launch of tebipenem HBr in the second half of 2022, as we work with the FDA. If approved by the FDA, we believe tebipenem HBr may offer healthcare providers, payers and patients an important oral antibiotic alternative to IV treatment for cUTI for patients with limited oral treatment options."

"With respect to Spero's other clinical programs," Dr. Mahadevia continued, "we also recently announced the FDA's lifting of SPR720's clinical hold and Phase 1 data of SPR206 that support its continued development as a treatment for life-threatening lung infections. Looking forward, we expect the continued advancement of these clinical programs to provide additional opportunities for value-creation and to serve as an important complement to our research efforts."

Program Highlights and Upcoming Milestones

Tebipenem HBr:

- On January 3, 2022, Spero announced that the United States Food and Drug Administration (FDA) had accepted for filing its NDA seeking approval for tebipenem HBr oral tablets for treatment in adult patients with certain bacterial microorganisms that cause complicated urinary tract infections (cUTI), including pyelonephritis, for substantive review. The NDA was granted Priority Review designation and a Prescription Drug User Fee Act (PDUFA) goal action date was set for June 27, 2022. The FDA informed us that, upon further review of the NDA, it determined that an Advisory Committee meeting is not needed to discuss the application. As described above, in late March 2022, the FDA notified Spero that, as part of its ongoing review of the NDA for tebipenem HBr, it has identified deficiencies that preclude discussion of labeling and post-marketing requirements/commitments at this time. Currently, Spero's late cycle review meeting with the FDA is

scheduled for the coming weeks. If approved, tebipenem HBr would be the only oral carbapenem antibiotic available for use in cUTI.

- In January 2022, Spero was awarded up to an additional $12.9 million by the Biomedical Advanced Research and Development Authority (BARDA) to support the development of orally administered tebipenem pivoxil in pediatric patients. By adding and exercising a new option to a contract originally awarded to Spero in 2018, BARDA increased the total amount of committed funding to $46.9 million, and the total potential contract value to $59.7 million. The additional $12.9 million option is expected to provide support for a clinical trial and related activities that are designed to advance orally administered tebipenem HBr's development as a treatment for pediatric patients with cUTI, including acute pyelonephritis.

- In January 2021, Spero announced that the U.S. Patent and Trademark Office issued U.S. Patent No. 10,889,587, which covers a crystalline formulation of tebipenem HBr. This patent expires in February 2038. Tebipenem HBr has also been granted Qualified Infectious Disease Product (QIDP) and Fast Track designations by the FDA for the treatment of cUTI.

SPR720:

- On January 4, 2022, Spero announced that the FDA had lifted the clinical hold previously placed on the Phase 2 trial of SPR720, Spero's investigational oral product candidate being developed for nontuberculous mycobacterial (NTM) disease. Spero engaged with the FDA in the first quarter of 2022 to discuss the re-initiation and planned protocol of the SPR720 Phase 2 trial in NTM-pulmonary disease (NTM-PD) patients, with the study expected to begin in the second half of 2022.

SPR206:

- In February 2022, Spero announced topline results from a Phase 1 bronchoalveolar lavage (BAL) trial of SPR206, the Company's novel IV-administered next generation polymyxin antibiotic being developed to treat multi-drug resistant (MDR) Gram-negative bacterial infections. These results showed that SPR206 was generally well tolerated and achieved mean lung epithelial lining fluid exposures above its MIC (minimum inhibitory concentration) for targeted gram-negative pathogens for the entirety of its 8-hour dosing period when administered three times daily at 100 mg. These data are consistent with prior Phase 1 results showing SPR206's lack of nephrotoxicity at predicted therapeutic dose levels.

- The Phase 1 renal impairment trial for SPR206 has been completed, annotating final safety and PK data, providing data-driven guidance on how to adjust for renally impaired patients in future clinical trials. Funding for the BAL and renal impairment clinical trials is provided by the United States Department of Defense (DoD) under Award Number W81XWH-1910295.

- The SPR206 program is also supported by funding from the National Institute of Allergy and Infectious Diseases and is the subject of a license agreement with Pfizer Inc., which was made alongside Pfizer's previously announced $40 million equity investment in Spero. Pursuant to the licensing agreement between the parties, Spero granted Pfizer the rights 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 $80 million in development and sales milestones, and high single digit to low double-digit royalties on net sales of SPR206 in these territories.

  or more information on the BAL and renal impairment trials and their design see ***ClinicalTrials.gov*** identifiers ***NCT04868292*** (BAL trial) and ***NCT04865393*** (renal impairment trial).

Full Year 2021 Corporate and Leadership Highlights:

- As previously disclosed, in September 2021, Spero entered into a non-dilutive revenue interest financing agreement with HealthCare Royalty Partners® for up to $125 million. Per the agreement, Spero received a $50 million upfront payment in October 2021. The Company is also entitled to receive an additional $50 million upon FDA approval of tebipenem HBr for a cUTI indication, and an additional $25 million upon the attainment of a prespecified commercial milestone and mutual agreement between Spero and HealthCare Royalty Partners®.

- Kathleen Tregoning joined Spero's Board of Directors on October 12, 2021. Ms. Tregoning is currently the Chief Corporate Affairs Officer at Cerevel Therapeutics, with previous service at Sanofi, Biogen, and as a professional staff member for multiple committees in the United States Congress. She brings more than two decades of experience in biotechnology and public policy to Spero's Board.

- Jamie Brady joined Spero as Chief Human Resource Officer (CHRO) on September 20, 2021. Mr. Brady brings nearly 30 years of senior human resources experience to Spero, including extensive experience with companies building towards commercialization. Mr. Brady most recently served as CHRO of uniQure, with previous service at Intarcia

Therapeutics and Genzyme.

- David Musselman joined Spero as Senior Vice President, Sales and Market Access on October 6, 2021, bringing over 23 years of pharmaceutical and biotech experience to the Company. Mr. Musselman also has extensive urology and commercial launch experience, and most recently served as Vice President of Specialty Sales at Urovant, where he was responsible for building and executing on Urovant's first product launch.

Fourth Quarter and Full Year 2021 Financial Results

Spero reported a net loss for the fourth quarter and year ended December 31, 2021, of $29.2 million and $89.8 million, or $0.90 and $2.91 per common share, respectively. Net loss for the fourth quarter and full-year ended December 31, 2020, was $18.6 million and $78.8 million, or $0.68 and $3.52 per common share, respectively.

Total revenue for the fourth quarter of 2021 of $2.7 million increased from $1.9 million for the same period a year ago. Revenue mix was composed of reimbursement for pipeline candidates under collaboration agreements with third parties, and grants from various government agencies. Total revenue for the year ended December 31, 2021, was $18.3 million compared to $9.3 million for the year ended December 31, 2020. Revenue growth was driven by increased grant revenue received from Spero's contracts with DoD relating to SPR206 and with BARDA relating to tebipenem HBr, and collaboration revenue from the Company's license agreements with Pfizer and Everest Medicines.

Research and development expenses for the fourth quarter of 2021 of $17.2 million were higher than the $13.2 million for the same period of 2020 primarily due to increased direct costs related to SPR206 and an increase in research and development headcount. Research and development expenses for the year ended December 31, 2021, were $64.5 million compared to $67.0 million for the year ended December 31, 2020, with decreased expenses due to the completion of significant activities and related costs of the Phase 3 clinical trial for tebipenem HBr, offset by increased direct costs related to SPR206 and an increase in research and development headcount. Spero expects to continue to incur research and development expenses in 2022, similar to 2021, in support of its pipeline candidates.

General and administrative expenses for the fourth quarter of 2021 of $13.0 million were higher than the $7.5 million for the same period of 2020 primarily due to increased headcount and professional fees to support pre-commercial activities and growth of the business. General and administrative expenses for the year ended December 31, 2021, were $41.7 million compared to $21.4 million for the year ended December 31, 2020, with increased expenses in 2021 compared to 2020 due to increased headcount and professional fees to support pre-commercial activities and growth of the business. Spero expects that its general and administrative expenses will increase in 2022 relative to 2021 as it continues to build its commercial capabilities and expand its infrastructure ahead of a potential tebipenem HBr commercial launch in 2022, subject to FDA approval.

As of December 31, 2021, Spero had cash, cash equivalents, and marketable securities of $146.4 million. Based on current projections, Spero believes that its existing cash, cash equivalents and marketable securities, together with committed funding from its BARDA contract and other non-dilutive funding commitments, will be sufficient to fund its operating expenses and capital expenditure requirements into the second half of 2023. This forecast includes the $50 million in upfront proceeds received under the revenue interest financing agreement with HealthCare Royalty Partners® and the additional $50 million milestone payment payable under such financing agreement upon approval of tebipenem HBr in 2022. If the upfront proceeds from HealthCare Royalty Partners® and the additional $50 million milestone payment payable under such financing agreement are excluded, Spero should have sufficient funding into the fourth quarter of 2022.

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 1-877-705-6003 (domestic) or 1-201-493-6725 (international) and refer to conference ID 13727002. The conference call will also be webcast live and a link to the webcast can be accessed ***here*** and also 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, Inc. is a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing and commercializing novel treatments for bacterial infections and rare diseases.

Spero's lead product candidate, tebipenem HBr (tebipenem pivoxil hydrobromide; formerly SPR994), is being developed as the first oral carbapenem antibiotic for use in cUTI, including pyelonephritis caused by certain microorganisms, in adult patients who have limited oral treatment options. On January 3, 2022, Spero announced that the FDA has accepted its NDA for tebipenem HBr tablets.

Tebipenem HBr is an investigational drug in the United States being developed for the treatment of cUTI, including pyelonephritis. Tebipenem HBr is currently not FDA-approved.

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

Spero also has an IV-administered next generation polymyxin product candidate, SPR206, developed from its potentiator platform, which is being developed to treat MDR 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, potential approval of tebipenem HBr by the FDA and the timing thereof; Spero's anticipated commercial launch of tebipenem HBr following FDA approval and the timing thereof; the sufficiency of Spero's cash resources and Spero's anticipated expenses; potential payments under Spero's agreement with BARDA; the ability of the Company to receive payments under the HCR financing facility; future clinical trials for pediatric use of tebipenem HBr; future use of tebipenem HBr for pediatric patients; the potential number of patients who could be treated by tebipenem HBr and market demand for tebipenem HBr generally; the effectiveness of tebipenem HBr and its potential impact on healthcare resource utilizations;; and the availability of additional non-dilutive funding from governmental agencies beyond any initially funded awards . 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 Spero's NDA for tebipenem HBr, for which Spero is currently engaged in discussions with the FDA, is sufficient for approval of tebipenem HBr; whether any additional information we provide to the FDA during the NDA review process may cause delays or extend the PDUFA goal action date; whether the FDA will require any additional clinical data or place labeling restrictions on the use of tebipenem HBr that would add costs for us, delay approval and/or reduce the commercial prospects of tebipenem HBr; Spero's readiness for an anticipated launch of tebipenem HBr if approval is obtained; if the NDA for tebipenem HBr is not approved by December 31, 2022, Spero's obligation to repay $50 million in upfront proceeds received under its revenue interest financing agreement; the COVID-19 pandemic; Spero's need for additional funding; the lengthy, expensive, and uncertain process of clinical drug development; 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; the ability to commercialize Spero's product candidates, if approved; Spero's ability to retain key personnel and to manage its growth; 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,	
	2021	**2020**	**2021**	**2020**
Revenues:				
Grant revenue	$ 2,488	$ 1,907	$ 15,186	$ 9,072
Collaboration revenue	256	—	3,070	258
Total revenues	2,744	1,907	18,256	9,330
Operating expenses:				
Research and development	17,225	13,205	64,526	67,003
General and administrative	13,021	7,498	41,701	21,440
Total operating expenses	30,246	20,703	106,227	88,443
Loss from operations	(27,502)	(18,796)	(87,971)	(79,113)
Other income (expense)	(1,738)	211	(1,785)	833
Net loss	$ (29,240)	$ (18,585)	$ (89,756)	$ (78,280)
Deemed dividend	$ —	$ —	$ —	$ (549)
Net loss attributable to common shareholders of Spero Therapeutics, Inc.	$ (29,240)	$ (18,585)	$ (89,756)	$ (78,829)
Net loss per share attributable to common shareholders per share, basic and diluted	$ (0.90)	$ (0.68)	$ (2.91)	$ (3.52)
Weighted average shares outstanding, basic and diluted:	32,315,521	27,369,943	30,895,756	22,386,122

Spero Therapeutics, Inc.
Condensed Consolidated Balance Sheet Data
(in thousands)
(Unaudited)

	December 31, 2021	**December 31, 2020**	**Change**
Cash, cash equivalents and marketable securities	$ 146,402	$ 126,906	$ 19,496
Other assets	24,670	26,545	(1,875)
Total assets	**$ 171,072**	**$ 153,451**	**$ 17,621**

Total liabilities	$ 82,783	$ 21,411	$ 61,372
Total stockholder's equity	88,289	132,040	(43,751)
Total liabilities and stockholders' equity	**$ 171,072**	**$ 153,451**	**$ 17,621**

Source: Spero Therapeutics, Inc.