Spero Therapeutics Announces First Quarter 2020 Operating Results and Provides Business Update

May 8, 2020

Tebipenem HBr Phase 3 trial enrollment complete with top-line data expected in the third quarter of 2020

SPR720 Phase 2a NTM trial initiation planned for the second half of 2020

Conference call and live webcast at 10:00 a.m. EDT today

CAMBRIDGE, Mass., May 08, 2020 (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 multi-drug resistant bacterial infections and rare diseases, today announced financial results for the first quarter ended March 31, 2020 and provided a business update.

"We have made significant progress to date in 2020 in advancing our pipeline of drug candidates for serious unmet needs and multi-drug resistant infections," said Ankit Mahadevia, M.D., Chief Executive Officer of Spero Therapeutics. "We completed enrollment in our Phase 3 trial, ADAPT-PO, comparing oral tebipenem HBr to IV ertapenem, and look forward to reporting data from the trial in the third quarter of 2020. We believe that positive results and subsequent approval of tebipenem HBr would provide great benefits to patients, hospitals and payors, as it would enable the treatment of complicated urinary tract infections with an oral agent outside of the hospital, an option that is not currently available given the lack of approved oral treatments."

Recent Clinical Highlights and Upcoming Milestones

Tebipenem HBr:
Spero's lead product candidate, tebipenem HBr, has the potential to be the first oral carbapenem antibiotic approved to treat MDR Gram-negative infections. The pivotal Phase 3 clinical trial of tebipenem HBr for the treatment of complicated urinary tract infection (cUTI), ADAPT-PO, completed enrollment of approximately 1,370 patients and Spero continues to expect to report top-line data in the third quarter of 2020. The ADAPT-PO trial is comparing an all oral regimen of tebipenem HBr with an existing standard of care intravenous (IV) antibiotic treatment, ertapenem, in patients with cUTI or acute pyelonephritis, randomized 1:1 in each arm. In October 2019, pharmacokinetic (PK) data from the first 33 patients dosed with tebipenem HBr in the Phase 3 trial were analyzed by an independent review committee which recommended that the trial continue without modifications to the protocol-defined dose. To support continued clinical development of tebipenem HBr, in February 2020 Spero announced that the Biomedical Advanced Research and Development Authority (BARDA) exercised a $15.9 million option under its existing contract with the Company. BARDA's decision to exercise the option brought the total committed funding under the award to $44.0 million in non-dilutive funding, inclusive of $10.0 million in funding from the Defense Threat Reduction Agency (DTRA).

SPR720:
SPR720 is an orally administered antimicrobial agent being developed by Spero for the treatment of non-tuberculous mycobacterial (NTM) disease, a rare orphan disease, as well as other infections, including *Mycobacterium tuberculosis*. In December 2019, results from a Phase 1 clinical trial of SPR720 in healthy volunteers indicated that SPR720 was generally well-tolerated at doses up to 1000 mg over the maximum studied duration of 14 days, with a PK profile that Spero believes supports the further development of SPR720 as an oral agent for the treatment of NTM pulmonary disease. The Phase 1 clinical trial was designed as a double-blind, placebo-controlled clinical trial to assess the safety, tolerability and pharmacokinetics of SPR720 at single and multiple ascending doses in healthy volunteers. In March 2020, Spero announced that the U.S. Food and Drug Administration (FDA) granted Orphan Drug Designation for SPR720 for the treatment of NTM infection. This designation is given to drugs intended to treat a rare disease or condition that affects fewer than 200,000 persons in the United States and provides certain benefits and incentives to develop the drug candidate. Spero met with the FDA in early March 2020 and plans to submit an investigational new drug (IND) application to the FDA in the second half of 2020. Subject to FDA acceptance of the IND, Spero expects to initiate a dose-ranging Phase 2a clinical trial evaluating SPR720 in patients with NTM disease due to *Mycobacterium avium* complex (MAC) in the second half of 2020.

SPR206:
SPR206 is an IV-administered product candidate being developed as an innovative option to treat MDR Gram-negative bacterial infections. In January 2020, Spero reported positive preliminary Phase 1 clinical trial results for SPR206 in healthy volunteers demonstrating that SPR206 was well-tolerated at doses likely to be within a therapeutic range for MDR Gram-negative bacterial infections. The Phase 1 clinical trial was designed as a double-blind, placebo-controlled, single and multiple ascending dose, multi-cohort study in healthy volunteers. In conjunction with Everest Medicines, and through its grant from the U.S. Department of Defense awarded in July 2019, Spero continues to expect to initiate a Phase 1 bronchoalveolar lavage (BAL) clinical trial assessing the penetration of SPR206 into the pulmonary compartment in the second half of 2020 and initiate a renal impairment study of SPR206.

First Quarter 2020 Financial Results
Spero reported a net loss for the first quarter ended March 31, 2020 of $23.3 million or $1.22 per common share, greater than the net loss of $5.1 million or $0.29 per common share, reported for the same period in 2019.

Total revenue for the first quarter of 2020 was $1.7 million, compared with revenues of $7.7 million in the first quarter 2019. The decrease was due to lower funding for tebipenem HBr received under Spero's BARDA contract due to the timing of qualified tebipenem HBr expenses incurred in the

quarter, and lower collaboration revenue as the first quarter of 2019 included a $3 million upfront fee associated with Spero's License Agreement with Everest Medicines entered into during January 2019.

Research and development expenses for the first quarter of 2020 were $20.4 million, compared with $9.5 million of research and development expenses for the same period of 2019. This increase was due to greater spending on the tebipenem HBr program, partially offset by lower spending on the SPR720 program and on Potentiator Platform product candidates. Spero continues to expect that its research and development expenses will increase in 2020 relative to 2019 due to the greater expense associated with the pivotal ADAPT-PO trial, for which Spero expects to report data in the third quarter of 2020, the initiation of a SPR720 Phase 2a trial in the second half of 2020, and increased research and development personnel to support the ongoing and planned programs.

General and administrative expenses for the first quarter of 2020 of $4.1 million were higher than the $3.9 million reported in the same period of 2019, primarily due to increased headcount. The Company continues to expect general and administrative expenses to increase in 2020 relative to 2019 due to additional headcount and professional fees and infrastructure required to support tebipenem HBr as it advances towards regulatory approval, as well as support for Spero's other product candidates.

As of March 31, 2020, the Company had cash and cash equivalents of $88.8 million. On March 5, 2020, Spero announced the closing of its rights offering, which generated net proceeds of approximately $29.5 million. Consistent with previous guidance, Spero believes that its existing cash, cash equivalents and marketable securities, together with committed funding from the BARDA contract and other non-dilutive funding commitments, will be sufficient to fund its operating expenses and capital expenditure requirements into the first quarter of 2021, including through the filing of an NDA for tebipenem HBr.

Upcoming Investor Presentations

- Corporate presentation at the Bank of America Securities Virtual Health Care Conference 2020 on May 13, 2020 at 1:00 PM Eastern Time
- Corporate presentation at the Jefferies 2020 Virtual Healthcare Conference from June 2 – 4, 2020

Conference Call and Webcast
Spero will host a conference call and webcast today at 10:00 a.m. EDT. To access the call, please dial (855) 327-6837 (domestic) or (631) 891-4304 (international) and refer to conference ID 10009477. 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 the Company's website for 30 days following the presentation.

About Spero
Spero Therapeutics, Inc. is a multi-asset, clinical-stage biopharmaceutical company focused on identifying, developing and commercializing novel treatments for multidrug-resistant (MDR) bacterial infections and rare diseases.

Spero's lead product candidate, tebipenem HBr (tebipenem pivoxil hydrobromide; formerly SPR994), is designed to be the first oral carbapenem-class antibiotic for use in adults to treat MDR Gram-negative infections.

Spero is also advancing SPR720, its novel oral therapy product candidate designed for the treatment of rare, orphan disease caused by pulmonary non-tuberculous mycobacterial (NTM) infections.

Spero also has an IV-administered next generation polymyxin product candidate, SPR206, developed from its potentiator platform that 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, statements about Spero's expectation that positive results from a single pivotal Phase 3 clinical trial of tebipenem HBr and ancillary supportive studies to be conducted in parallel with the Phase 3 trial will support the approval of tebipenem HBr; the design, initiation, timing, progress and results of Spero's preclinical studies and clinical trials and its research and development programs, including the timing of Spero's IND submission with the FDA regarding SPR720, the commencement of Spero's planned Phase 2a clinical trial of SPR720 and the commencement of Spero's planned Phase 1 bronchoalveolar lavage (BAL) clinical trial assessing the penetration of SPR206 into the pulmonary compartment; management's assessment of the results of such preclinical studies and clinical trials; the timing of clinical data from the , including final data from the Phase 3 clinical trial of tebipenem HBr, final data from the Phase 1 clinical trial of SPR720 and final data from the Phase 1 clinical trial of SPR206; and Spero's cash forecast and anticipated expenses, anticipated payments under Spero's agreement with Everest Medicines, potential payments under Spero's agreement with BARDA, the sufficiency of its cash resources 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 the FDA will accept a single pivotal study for approval of tebipenem HBr; whether results obtained in preclinical studies and clinical trials will be indicative of results obtained in future clinical trials; whether Spero's product candidates will advance through the preclinical development and 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 U.S. Food and Drug Administration or equivalent foreign regulatory agencies; whether Spero will satisfy all of the pre-conditions to receipt of the development milestone payment under its agreement with Everest Medicines; whether BARDA elects to exercise its second option under Spero's agreement with BARDA; whether Spero's cash resources will be sufficient to fund its continuing operations for the periods and/or trials anticipated; whether Spero's clinical and preclinical development programs are delayed or disrupted due to the coronavirus; 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
(Unaudited, Amounts in Thousands, Except Share and Per Share Data)

	Three Months Ended March 31,	
	2020	**2019**
Revenues:		
Grant revenue	$ 1,532	$ 3,911
Collaboration revenue	169	3,807
Total revenues	1,701	7,718
Operating expenses:		
Research and development	20,436	9,526
General and administrative	4,086	3,888
Total operating expenses	24,522	13,414
Loss from operations	(22,821)	(5,696)
Other income (expense)	(437)	624
Net loss attributable to common shareholders of Spero Therapeutics, Inc.*	$ (23,258)	$ (5,072)
Net loss per share attributable to common shareholders, basic and diluted	$ (1.22)	$ (0.29)
Weighted average shares outstanding, basic and diluted:	19,557,418	17,221,120

* Net loss attributable to common shareholders for the quarter ended March 31, 2020 does not equal net loss used in the calculation of net loss per share attributable to common shareholders due to the accrection of the beneficial conversion feature of the Series C Preferred Stock in the amount of $549,000

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

	March 31, 2020	**December 31, 2019**
Cash, cash equivalents and marketable securities	$ 88,841	$ 82,045
Other assets	21,053	24,058
Total assets	**$ 109,894**	**$ 106,103**
Total liabilities	27,467	31,529
Total stockholder's equity	82,427	74,574
Total liabilities and stockholders' equity	**$ 109,894**	**$ 106,103**

Source: Spero Therapeutics, Inc.