Seres Therapeutics Reports Third Quarter 2020 Financial Results and Provides Business Updates

November 9, 2020

– Reported ECOSPOR III Phase 3 study of SER-109 met primary endpoint, demonstrated statistically significant absolute reduction of 30.2% in rate of C. difficile infection recurrence compared to placebo –

– SER-109 anticipated to be first-ever FDA-approved microbiome therapy –

– First patient dosed in SER-301 Phase 1b study in mild-to-moderate ulcerative colitis –

– Strengthened balance sheet with $264 million financing to support R&D and CMC capabilities expansion, ongoing clinical studies, and pre-commercial launch activities –

– Conference call at 8:30 a.m. ET today –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Nov. 9, 2020-- Seres Therapeutics, Inc., (Nasdaq: MCRB) today reported financial results from the third quarter ended September 30, 2020, and provided business updates.

“Supported by our positive, highly significant SER-109 Phase 3 results, we expect SER-109 to be the first-ever microbiome therapy approved by the U.S. FDA. Following those remarkable SER-109 study data and a significant capital infusion, Seres is in the midst of transformational growth toward becoming a commercial-stage microbiome company, with a broad portfolio of promising therapeutic candidates. We are expanding our field-leading capabilities across R&D, manufacturing, and commercial operations to maximize the multitude of opportunities we see for our approach,” said Eric Shaff, President and Chief Executive Officer of Seres. “Our immediate priorities are to drive enrollment in our SER-109 open-label study to fulfill our safety database requirements and prepare to file a Biologics License Application (BLA), while also preparing the Company for the potential commercialization of SER-109.”

“In tandem, we continue to advance our deep microbiome pipeline, including SER-287, SER-301, SER-401, and SER-155. These therapeutic candidates span infectious diseases, inflammatory disease, and cancer, and we believe all have the potential to fundamentally improve upon the current standard of care. Most recently, we were pleased to dose the first subject in our SER-301 Phase 1b study in patients with ulcerative colitis. Moving forward, we expect to reach a number of value-creating milestones across multiple therapeutic areas,” concluded Mr. Shaff.

Program and Corporate Updates

SER-109 Phase 3 ECOSPOR III study in recurrent *C. difficile* infection: SER-109 is an investigational, oral, biologically-derived microbiome therapeutic that is designed to reduce recurrence of *C. difficile* infection (CDI), enabling patients to achieve a sustained clinical response by breaking the vicious cycle of CDI recurrence and restoring the diversity of the gastrointestinal microbiome.

In August, Seres announced topline results from ECOSPOR III, demonstrating that SER-109 met the study’s primary endpoint, showing a 30.2% absolute reduction of recurrence of CDI compared to placebo at eight weeks post-treatment. The SER-109 treatment arm relative risk was 0.27 (95% CI=0.15 to 0.51) versus placebo. The study results were equally compelling when characterized by the alternative metric of sustained clinical response, where 88.9% of patients in the SER-109 arm achieved this objective. Based on feedback from the FDA and the strength of the SER-109 Phase 3 data, Seres believes that ECOSPOR III will be a single pivotal efficacy study supporting product registration.

In October, Seres presented the Phase 3 study result and additional data from ECOSPOR III at the virtual American College of Gastroenterology (ACG) Annual Scientific Meeting. These new data showed that at 12 weeks post-treatment the rate of recurrence in the SER-109 arm was 16.7%, compared to a rate of 47.8% in the placebo arm, representing an absolute risk reduction of 31.1% (relative risk 0.35; 95% CI=0.21-0.58; p-value <0.001), consistent with the results seen at eight weeks. Additionally, these new findings demonstrate that SER-109 administration resulted in similar efficacy when groups are stratified by age (i.e., ≥ or <65 years) or prior antibiotic received (i.e., vancomycin or fidaxomicin), which is important in this patient population. The number needed to treat (NNT) at 12 weeks is approximately 3, similar to the figure calculated based on eight-week study results.

The SER-109 manufacturing process inactivates vegetative bacteria and other potential pathogens, which have been linked with fecal microbiota transplant (FMT)-associated disease transmission. Seres believes that this unique manufacturing process provides a critically important safety advantage.

Following the topline Phase 3 study results, the FDA reaffirmed its prior guidance regarding the efficacy requirements to support a SER-109 BLA submission, which were exceeded by the positive SER-109 ECOSPOR III study results, and reaffirmed its prior guidance that the safety database prelicensure should be at least 300 subjects.

Seres is conducting an ongoing SER-109 open-label study in patients with recurrent CDI (ClinicalTrials.gov identifier: NCT03183128), which also admits patients with a single recurrence of CDI, to expand the SER-109 safety database. The Company continues to make progress activating new clinical sites and enrolling subjects into the study. Additional information is available at serescdiffstudy.com.

SER-287 Phase 2b ECO-RESET study in ulcerative colitis: SER-287 is an oral, biologically-derived microbiome therapeutic candidate designed to

have pharmacological effects on multiple pathways relevant to ulcerative colitis that can be modulated by the gastrointestinal microbiome. Seres has obtained FDA Fast Track designation for SER-287 in active mild-to-moderate UC.

The SER-287 Phase 2b ECO-RESET induction study in patients with active mild-to-moderate UC is ongoing. Seres has implemented a number of COVID-19-related mitigation strategies and the study continues to enroll patients. The study is over 75% enrolled.

SER-301 Phase 1b study first patient dosed: In November, the Company announced that the first patient has been dosed in its Phase 1b study for SER-301, an oral, rationally-designed, fermented microbiome therapeutic. SER-301 is being evaluated in a Phase 1b study in adults with mild-to-moderate ulcerative colitis. The study is being conducted in Australia and New Zealand and targets the enrollment of approximately 65 subjects.

A first open-label cohort of 15 subjects will evaluate safety and pharmacokinetics (PK), as measured by bacterial engraftment. In the subsequent second cohort, 50 subjects will be randomized to receive either SER-301 or placebo. The objectives for this cohort are to evaluate drug safety and PK, and to evaluate clinical remission and other measures of efficacy as secondary endpoints.

The consortium of bacteria in SER-301 is designed to modify the microbiome and microbe-associated metabolites in the gastrointestinal tract and modulate pathways linked to gastrointestinal inflammation and epithelial barrier integrity in patients with ulcerative colitis. The design of SER-301 has incorporated learnings from the SER-287 Phase 1b study related to the microbiome signatures associated with clinical efficacy.

Seres is entitled to receive a $10 million milestone payment associated with the Phase 1b SER-301 clinical study initiation from Nestlé Health Science, the Company's ex-North American collaborative partner for this program.

SER-401 Phase 1b study in metastatic melanoma: SER-401 is an orally-administered, biologically-derived, live microbiome therapeutic candidate comprising bacteria that reflect the bacterial signature in the gastrointestinal microbiome associated with patient response to checkpoint inhibitor immunotherapy.

The ongoing placebo-controlled Phase 1b study in patients with metastatic melanoma is supported by the Parker Institute for Cancer Immunotherapy and the University of Texas MD Anderson Cancer Center. The trial is examining safety, tolerability, and drug activity via microbiome engraftment and its association with biomarkers of clinical response in tumor biopsies in patients treated with SER-401 in combination with nivolumab, an approved anti-PD-1 checkpoint inhibitor therapy.

SER-155 Phase 1b clinical study activities: Seres continues to advance SER-155, an oral, rationally-designed, fermented microbiome therapeutic, toward a Phase 1b clinical study. SER-155 is designed to prevent mortality due to gastrointestinal infections, bacteremia, and graft versus host disease (GvHD) in immunocompromised patients, including patients receiving allogeneic hematopoietic stem cell transplantation. SER-155 is a consortium of bacterial species designed using microbiome biomarker data from human clinical data, human cell-based assays, and *in vivo* disease models. The composition aims to decrease infection and translocation of antibiotic-resistant bacteria in the gastrointestinal tract and modulate host immune responses to decrease GvHD.

The SER-155 program is supported by a CARB-X grant that provides financial and operational support through Phase 1b clinical development. The Company intends to advance SER-155 into a Phase 1b study early next year in collaboration with Memorial Sloan Kettering Cancer Center.

Strengthened leadership team: In October, Seres announced the appointments of David Ege Ph.D., as Executive Vice President and Chief Technology Officer, and Jayne Gansler as Executive Vice President and Chief People Officer. John Aunins, Seres' prior Chief Technology Officer, will continue to provide support to the Company as a Senior Advisor.

Dr. Ege joins Seres from Merck, where he held a variety of technical and leadership roles in R&D and manufacturing in the U.S. and Switzerland. He has more than 15 years of experience in the pharmaceutical industry, with a focus on vaccine and biologics manufacturing, facility development and process optimization.

Ms. Gansler has more than 20 years of global human resources experience in the biotechnology, pharmaceutical, and medical device industries. Prior to Seres, she was Head of Human Resources of ARIAD Pharmaceuticals. Earlier in her career, she served as Global Head of Human Resources for Genzyme, a Sanofi Company.

Financial Results

Seres reported a net loss of $30.3 million for the third quarter of 2020, as compared with a net loss of $16.4 million for the same period in 2019. The third quarter net loss was driven primarily by clinical and development expenses, personnel expenses and ongoing development of the Company's microbiome therapeutics platform.

Research and development expenses for the third quarter of 2020 were $23.9 million, compared with $18.3 million for the same period in 2019. The research and development expenses were primarily related to Seres' late-stage SER-109 and SER-287 clinical development programs.

General and administrative expenses for the third quarter of 2020 were $7.6 million, compared with $5.9 million for the same period in 2019. General and administrative expenses were primarily due to consulting fees and professional fees and included expenses to support SER-109 commercialization readiness activities.

Seres ended the third quarter with approximately $320.3 million in cash, cash equivalents and short and long-term investments compared with $63.9 million at the end of the second quarter 2020. In August 2020, the Company completed a public equity offering and sold common stock to Nestlé through a private Securities Purchase Agreement, which together provided approximately $264 million in net proceeds.

Conference Call Information

Seres' management will host a conference call today, November 9, 2020, at 8:30 a.m. ET. To access the conference call, please dial 844-277-9450 (domestic) or 336-525-7139 (international) and reference the conference ID number 1038426. To join the live webcast, please visit the "Investors and News" section of the Seres website at www.serestherapeutics.com.

A webcast replay will be available on the Seres website beginning approximately two hours after the event and will be archived for at least 21 days.

About SER-109

SER-109 is an investigational, oral, biologically-sourced microbiome therapeutic that is designed to reduce recurrence of *C. difficile* infection (CDI), enabling patients to achieve a sustained clinical response by breaking the vicious cycle of CDI recurrence and restoring the diversity of the gastrointestinal microbiome. SER-109 is a consortium of purified Firmicute bacteria in spore form, manufactured by fractionating targeted bacteria from the stool of healthy human donors with further steps to inactivate potential pathogens. The FDA has granted SER-109 Breakthrough Therapy designation and Orphan Drug designation for the treatment of recurrent CDI.

SER-109 is fundamentally distinct from fecal microbiota transplantation (FMT) and FMT-like products. SER-109 is comprised of a highly purified consortium of commensal bacteria in spore form, manufactured in accordance with Current Good Manufacturing Practice (cGMP) conditions using stringent standards to ensure product quality and consistency. To support product safety, Seres utilizes a unique manufacturing process designed to inactivate numerous potential pathogens, including species of non-spore bacteria, such as *Escherichia coli*, and viruses such as SARS-CoV-2.

About *C. difficile* Infection (CDI) and Current Treatments

C. difficile infection (CDI) is one of the top three most urgent antibiotic-resistant bacterial threats in the U.S., according to the Centers for Disease Control, and is a leading cause of hospital-acquired infection in the U.S. It is responsible for the deaths of approximately 20,000 Americans each year. CDI is associated with debilitating diarrhea, which significantly impacts quality of life in every functional domain. Since the discovery of *C. difficile* more than four decades ago, vancomycin has been the drug most commonly used for patient management. Current approaches provide only modest improvements in sustained clinical response rates, leaving behind a significant pool of patients with recurrent disease. Unapproved FMT, used in cases that are not responsive to approved drugs, remains poorly characterized clinically and has been associated with serious safety concerns, including the transmission of bacterial pathogens and the potential transmission of viruses such as SARS-CoV-2, the virus that causes COVID-19. The recent quarantine and shipping hold of FMT material from a major stool bank highlights the urgent need for an approved effective and safe treatment for recurrent CDI.

About Seres Therapeutics

Seres Therapeutics, Inc., (Nasdaq: MCRB) is a leading microbiome therapeutics platform company developing a novel class of multifunctional bacterial consortia that are designed to functionally interact with host cells and tissues to treat disease. Seres' SER-109 program achieved the first-ever positive pivotal clinical results for a targeted microbiome drug candidate and has obtained Breakthrough Therapy and Orphan Drug designations from the FDA. The SER-109 program is being advanced for the treatment of recurrent *C. difficile* infection and has potential to become a first-in-class FDA-approved microbiome therapeutic. Seres' SER-287 program has obtained Fast Track and Orphan Drug designations from the FDA and is being evaluated in a Phase 2b study in patients with active mild-to-moderate ulcerative colitis. Seres is evaluating SER-401 in a Phase 1b study in patients with metastatic melanoma, SER-301 in a Phase 1b study in patients with ulcerative colitis and SER-155 to prevent mortality due to gastrointestinal infections, bacteremia and graft versus host disease. For more information, please visit www.serestherapeutics.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including the potential for the Company to file a BLA and/or commercialize SER-109, the promise and potential impact of our microbiome therapeutics platform, the results from ECOSPOR III providing an efficacy basis for a BLA submission, any requirements for additional safety data, the receipt of milestone payments, the timing and results of studies related to the Company's therapeutic candidates, ability of SER-109 to transform the treatment of CDI, inferences related to the currently-observed efficacy and safety profile of SER-109, and other statements that are not historical facts.

These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: We have incurred significant losses, are not currently profitable and may never become profitable; our need for additional funding; our limited operating history; our unproven approach to therapeutic intervention; the lengthy, expensive, and uncertain process of clinical drug development; our reliance on third parties to manufacture, develop, and commercialize our product candidates, if approved; the ability to develop and commercialize our product candidates, if approved; the potential impact of the COVID-19 pandemic; our ability to retain key personnel and to manage our growth; and that our management and principal stockholders have the ability to control or significantly influence our business. These and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission, or SEC, on July 28, 2020 and our other reports filed with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

SERES THERAPEUTICS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(unaudited, in thousands, except share and per share data)

	September 30, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 207,326	$ 65,126
Short term investments	90,588	29,690
Prepaid expenses and other current assets	6,703	3,588

Accounts receivable	3,393	1,785
Total current assets	308,010	100,189
Property and equipment, net	14,729	19,495
Operating lease assets	9,664	11,356
Restricted investments	1,400	1,400
Long term investments	22,398	—
Total assets	$ 356,201	$ 132,440
Liabilities and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 6,201	$ 4,859
Accrued expenses and other current liabilities	11,318	10,884
Operating lease liabilities	4,950	4,456
Deferred revenue - related party	16,517	20,960
Deferred revenue	6,784	4,834
Total current liabilities	45,770	45,993
Note payable, net of discount	24,977	24,648
Operating lease liabilities, net of current portion	11,894	15,676
Deferred revenue, net of current portion - related party	82,826	89,111
Deferred revenue, net of current portion	1,695	4,834
Other long-term liabilities	987	502
Total liabilities	168,149	180,764
Commitments and contingencies		
Stockholders' deficit:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized at September 30, 2020 and December 31, 2019; no shares issued and outstanding at September 30, 2020 and December 31, 2019	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at September 30, 2020 and December 31, 2019; 91,214,536 and 70,143,252 shares issued and outstanding at September 30, 2020 and December 31, 2019, respectively	91	70
Additional paid-in capital	718,483	411,255
Accumulated other comprehensive income	2	—
Accumulated deficit	(530,524)	(459,649)
Total stockholders' equity (deficit)	188,052	(48,324)
Total liabilities and stockholders' equity (deficit)	$ 356,201	$ 132,440

SERES THERAPEUTICS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(unaudited, in thousands, except share and per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Revenue:				
Collaboration revenue - related party	$ 80	$ 4,840	$ 10,728	$ 21,909
Grant revenue	1,337	85	2,907	791
Collaboration revenue	—	2,106	2,016	4,183
Total revenue	1,417	7,031	15,651	26,883
Operating expenses:				
Research and development expenses	23,861	18,317	65,703	59,109
General and administrative expenses	7,551	5,897	20,180	18,966
Restructuring expenses	—	—	—	1,492
Total operating expenses	31,412	24,214	85,883	79,567
Loss from operations	(29,995)	(17,183)	(70,232)	(52,684)
Other (expense) income:				
Interest income	100	335	333	744
Interest expense	(730)	—	(2,165)	—
Other income	345	439	1,189	439
Total other (expense) income, net	(285)	774	(643)	1,183
Net loss	$ (30,280)	$ (16,409)	$ (70,875)	$ (51,501)

Net loss per share attributable to common stockholders, basic and diluted	$ (0.36)	$ (0.23)	$ (0.93)	$ (0.99)
Weighted average common shares outstanding, basic and diluted	83,531,617	69,944,068	75,914,361	52,143,492
Net loss	(30,280)	(16,409)	(70,875)	(51,501)
Other comprehensive loss:				
Unrealized gain on investments, net of tax of $0	1	7	2	7
Total other comprehensive gain	1	7	2	7
Comprehensive loss	$ (30,279)	$ (16,402)	$ (70,873)	$ (51,494)

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