Seres Therapeutics Announces Positive Topline Results from SER-109 Phase 3 ECOSPOR III Study in Recurrent C. difficile Infection

August 10, 2020

– SER-109 met Phase 3 primary endpoint, showing a highly statistically significant 30.2% absolute reduction in the rate of C. difficile infection recurrence compared to placebo –

– SER-109 was well tolerated, with a safety profile comparable to placebo –

– Efficacy results substantially exceeded FDA regulatory guidance to support BLA filing as a single pivotal trial; Company to meet with agency to discuss filing for product approval as soon as possible –

– Positive SER-109 Phase 3 data provide validation for Seres' microbiome therapeutics platform and further development of its pipeline of product candidates –

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

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Aug. 10, 2020-- Seres Therapeutics, Inc. (Nasdaq: MCRB) today reported positive topline results from the pivotal Phase 3 ECOSPOR III study evaluating its investigational oral microbiome therapeutic SER-109 for recurrent *C. difficile* infection (CDI). The study showed that SER-109 administration resulted in a highly statistically significant absolute decrease of 30.2% in the proportion of patients who experienced a recurrence in CDI within eight weeks of administration versus placebo, the study's primary endpoint. 11.1% of patients administered SER-109 experienced a CDI recurrence, versus 41.3% of placebo patients. 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.

The study's efficacy results exceeded the statistical threshold previously provided in consultation with the U.S. Food and Drug Administration (FDA) that could allow this single clinical study to fulfill efficacy requirements for a Biologics License Application (BLA). The SER-109 safety results were favorable, with an adverse event profile comparable to placebo.

"We are extremely pleased with these highly clinically meaningful SER-109 Phase 3 study results, greatly exceeding the statistical threshold provided by the FDA. Based on our prior discussions with the FDA, we believe this trial should provide the efficacy basis for submitting an application for product approval. We look forward to meeting with the FDA as soon as possible to discuss the regulatory path forward with the goal of bringing SER-109 to patients as a first-in-class microbiome therapeutic," said Eric D. Shaff, President and Chief Executive Officer of Seres. "Our results represent the first-ever positive pivotal clinical study results for a targeted microbiome drug candidate. We believe these Phase 3 data provide strong validation for our underlying microbiome therapeutics platform, which has been the scientific basis for the Company, as well as persuasive clinical evidence supporting our other active pipeline programs."

"We would like to thank all those who participated in this landmark study. Based on these highly positive SER-109 ECOSPOR III results, we believe that this novel microbiome therapeutic candidate could potentially provide a much-needed effective oral treatment option for the approximately 170,000 patients in the U.S. that suffer from recurrent CDI annually," said Lisa von Moltke, M.D., FCP, Chief Medical Officer of Seres. "Seres applied a data-driven and scientifically rigorous approach to develop SER-109. The proprietary scientific learnings we have obtained continue to drive our overall R&D efforts and the advancement of our other ongoing microbiome therapeutic programs."

"Recurrent *C. difficile* infection is a serious disease that devastates patients' quality of life, and in many severe cases may result in a patient's death. Today's treatment options have important shortcomings related to efficacy, safety and route of administration, and novel approaches that target the root causes of the disease are urgently needed. The SER-109 Phase 3 results are highly impressive and represent an exceptional advance in the fight against this disease. I believe that SER-109 has the potential to fundamentally transform the treatment of recurrent *C. difficile* infection," said Mark Wilcox, M.D., Professor of Medical Microbiology, University of Leeds.

ECOSPOR III Study Design and Results

The ECOSPOR III study (ClinicalTrials.gov identifier: NCT03183128) is a multicenter, randomized, placebo-controlled study that enrolled 182 patients with multiply recurrent CDI. Patients were randomized 1:1 to receive either SER-109 or placebo, after standard of care antibiotic treatment. SER-109, or placebo, was administered orally for three consecutive days. All patients were required to have a positive *C. difficile* toxin diagnostic test both at study entry and in the case of suspected recurrence to ensure the selection of individuals with active disease and to confirm the accuracy of the primary endpoint.

The primary efficacy endpoint of ECOSPOR III was the proportion of patients with recurrent CDI at up to eight weeks following administration of SER-109 or placebo. As a secondary endpoint, patients are evaluated for CDI recurrence through 24 weeks post-treatment, and the Company plans to present those results at a future date.

SER-109 met the study's primary endpoint with a significantly lower recurrence rate of 11.1% in SER-109 patients versus 41.3% in placebo patients at eight weeks; $p<0.001$ tested at the one-sided 0.25 level. Patients administered SER-109 experienced a 30.2% lower rate of recurrence, on an absolute basis, compared to placebo. The SER-109 treatment arm relative risk was 0.27 (95% CI=0.15 to 0.51) versus placebo. The ECOSPOR III

recurrence rates translate into a sustained clinical response rate of 88.9% versus 58.7% with SER-109 and placebo, respectively. The SER-109 Number Needed to Treat (NNT) was approximately 3.

In prior discussions, the FDA communicated that demonstration of a statistically very persuasive efficacy finding in the ECOSPOR III primary endpoint, defined as demonstrating a 95% upper confidence level of relative risk lower than 0.833, could support a BLA submission on the basis of this single study. The results of ECOSPOR III demonstrated a SER-109 relative risk of 0.27 (95% CI=0.15 to 0.51) compared to placebo. As a result, Seres believes that this study should support the efficacy basis for BLA submission. SER-109 has obtained FDA Breakthrough Therapy and Orphan Drug designations.

SER-109 was well tolerated, with no treatment-related serious adverse events (SAEs) observed in the active arm, and an adverse event profile similar to placebo. The overall incidence of patients who experienced AEs during the eight-week study period was similar between SER-109 and placebo arms. The most commonly observed treatment-related AEs were flatulence, abdominal distention and abdominal pain, which were generally mild to moderate in nature, and these were observed at a similar rate in both the SER-109 and placebo arms.

A SER-109 open-label study is ongoing (ClinicalTrials.gov identifier: NCT03183141) at selected clinical sites that participated in the ECOSPOR III study, and the Company may initiate the program at additional clinical sites. The FDA has previously indicated that SER-109 administration to at least 300 patients, consistent with standard FDA guidance, would be required to support BLA submission. The ongoing SER-109 open-label study is continuing to contribute to the SER-109 safety database.

The Company plans to immediately request a Breakthrough Therapy designation meeting with the FDA to discuss the requirements to submit a BLA seeking regulatory approval of SER-109. Given the favorable efficacy and safety results seen in ECOSPOR III, the safety results observed in prior SER-109 clinical studies, and the critical unmet need for a therapeutic option for recurrent CDI patients, the Company plans to discuss with the FDA the safety data requirements for a BLA filing.

Seres continues to advance its commercial readiness for the potential launch of SER-109. In June 2020, Seres appointed Terri Young, Ph.D., R.Ph., as Chief Commercial and Strategy Officer. The Company has been conducting activities to support successful future potential commercialization. Seres believes that the commercial opportunity for SER-109 could be substantial, given the dire need for an effective, safe, oral therapeutic, and the strength of the SER-109 Phase 3 study results.

Conference Call Information

Seres' management will host a conference call today, August 10, 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 3216859. Accompanying slides will be posted on the Seres website ahead of the conference call. To join the live webcast, and to view the accompanying slides, please visit the "Investors and Media" 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 approximately 21 days.

About SER-109

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. SER-109 is a consortium of purified bacterial spores of multiple Firmicute species, 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 CDI.

SER-109 is fundamentally distinct from fecal microbiota transplantation (FMT). SER-109 is comprised of a highly-purified consortia of spore-based commensal bacteria and designed to be manufactured in accordance with Good Manufacturing Practice conditions using stringent standards to ensure product quality and consistency. To support product safety, Seres utilizes a unique manufacturing process that inactivates 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 most commonly used drug 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 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 developing SER-401 in a Phase 1b study in patients with metastatic melanoma, SER-301 for 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 approval of SER-109 by the FDA, the potential for SER-109 to be a first-in-class therapy, the timing, content and outcome of any meetings with the FDA, the results from ECOSPOR III providing an efficacy basis for a BLA submission, the potential number of patients who could be treated by SER-109, the ability of SER-109 to transform the treatment of CDI or be a much-needed effective oral treatment option for recurrent CDI, the potential requirements by the FDA for additional safety data, initiation of additional clinical sites in the open-label study of SER-109, commercial opportunity of SER-109, the impact of SER-109 data on the Seres pipeline programs and platform overall, the design of SER-109 and its treatment potential, and the presentation of ECOSPOR III 24-week data, 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.

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PR Contact
Lisa Raffensperger
lisa@tenbridgecommunications.com

IR Contact
Carlo Tanzi, Ph.D.
ctanzi@serestherapeutics.com

Source: Seres Therapeutics, Inc.