Seres Therapeutics Announces Completion of Enrollment in SER-109 Phase 3 ECOSPOR III Study for Recurrent Clostridium difficile Infection and Provides Clinical Pipeline Updates

March 30, 2020

– Topline ECOSPOR III Phase 3 study data readout timing as planned for mid-2020 –

– Potential for ECOSPOR III to be a single pivotal study supporting product registration with FDA –

– Company assessing the impact of COVID-19 on SER-287, SER-401 and SER-301 clinical development programs –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 30, 2020-- Seres Therapeutics, Inc., (Nasdaq: MCRB) announced today that the Company has completed enrollment of its SER-109 Phase 3 clinical study, ECOSPOR III. SER-109 is an oral, first-in-field microbiome therapeutic candidate that has been granted Orphan Drug and Breakthrough Therapy designations by the U.S. Food and Drug Administration (FDA), and is being investigated for use in preventing recurrent *Clostridium difficile* infection (CDI).

"We are pleased to have achieved this critically important corporate milestone. SER-109 has the potential to be the first FDA-approved therapy for *C. difficile* infection to treat the underlying cause of this disease, and the first approved microbiome drug for any human condition. We believe SER-109 could fundamentally transform the treatment of patients with recurrent *C. difficile* infection, a life-altering infectious disease, and we eagerly look forward to topline clinical results in the middle of this year. With compelling Phase 3 ECOSPOR III clinical data, we plan to engage in discussions with the FDA regarding a filing for product approval," said Eric Shaff, President and Chief Executive Officer of Seres. "We are also working to advance our other promising clinical development candidates in light of the COVID-19 pandemic. This remains an evolving situation and we are carefully reviewing our development plans to determine how to rapidly advance our pipeline toward high-quality data readouts."

SER-109 Study Updates

The SER-109 Phase 3 ECOSPOR III study (ClinicalTrials.gov identifier: NCT03183128) is a multicenter, randomized, placebo-controlled study which has enrolled 181 patients with multiply recurrent CDI to date. ECOSPOR III had been designed to enroll 188 patients. The Company has decided to halt enrollment as a result of the COVID-19 pandemic. Seres believes that ECOSPOR III remains well-powered to evaluate the efficacy of SER-109. The ECOSPOR III study's primary endpoint is the reduction of CDI recurrence at up to eight weeks following SER-109 administration, and the Company expects to report study results in mid-2020 as had been planned.

Seres is grateful to the patients, principal investigators and clinical research teams who participated in ECOSPOR III, many of whom are now involved in the fight against COVID-19.

The SER-109 Phase 3 ECOSPOR III study includes use of an objective *Clostridium difficile* cytotoxin assay to ensure that all patients entering the study have active CDI, as well as to confirm CDI recurrences during the study (i.e., the ECOSPOR III primary endpoint).

Seres plans to initiate a SER-109 Expanded Access Program at selected clinical sites participating in the ongoing Phase 3 ECOSPOR III study, and the Company may also initiate the program at additional clinical sites for eligible patients to have access to SER-109.

Prior completed clinical studies have demonstrated SER-109 bacterial engraftment into the gastrointestinal microbiome, and that engraftment is associated with reduced recurrence of CDI. In all prior clinical studies, SER-109 was associated with a favorable safety profile.

The FDA has issued several safety alerts related to Fecal Microbiota Transplantation (FMT) and the risk of pathogen transmission including warnings related to Multi-Drug Resistant Organisms and SARS-CoV-2, the virus linked to COVID-19 (June 12, 2019 Alert; March 12, 2020 Alert; and March 23, 2020 Alert). Unapproved FMT is widely used under an FDA Enforcement Discretion policy for the treatment of recurrent CDI that is not responsive to standard therapies.

In contrast to FMT, SER-109 is comprised of a highly purified consortia of spore-based commensal bacteria and is manufactured under Good Manufacturing Practices (GMP) conditions using stringent standards to ensure product quality and consistency. Seres utilizes a unique manufacturing process which has been demonstrated to inactivate numerous potential pathogens, including species of non-spore bacteria, such as *Escherichia coli*, and viruses. The Company's manufacturing process inactivates many emerging potential pathogens where diagnostic assays may not yet be available, such as SARS-CoV-2. Seres has issued a position statement highlighting the criticality of including pathogen inactivation processes in the manufacture of microbiome therapeutics. Recent discussions with the FDA have indicated agency support regarding the fundamental differentiation between FMT and Seres' product candidates.

COVID-19 Impact and Other Clinical Program Updates

Seres continues to monitor the impact of the COVID-19 pandemic on Company operations and ongoing clinical development activity, including the SER-287 Phase 2b study in ulcerative colitis, the SER-401 Phase 1b study in metastatic melanoma, and SER-301, a rationally designed, fermented development candidate for ulcerative colitis. Mitigation activities to minimize COVID-19-related operation disruptions are ongoing; however, given the severity and evolving nature of the situation, the timing of SER-287 Phase 2b and SER-401 Phase 1b clinical readouts is uncertain. Seres does not anticipate disruptions to the availability of its drug product candidates for ongoing studies.

The SER-287 Phase 2b study is currently approximately 60% enrolled based on the 201-patient target study size. SER-287 development activity has been adversely impacted by multiple clinical sites halting non-essential procedures, including endoscopies, which may make it difficult to achieve the original enrollment target in H2 2020 as planned. Seres is evaluating enrollment mitigation strategies and possible trial design modifications with the goal of obtaining a high-quality, clinically meaningful dataset within a timeframe consistent with Seres' prior guidance for its cash runway extending into the second quarter of 2021. Furthermore, the Company is encouraged by the FDA's indications of flexibility in light of the COVID-19 pandemic, and plans to engage the FDA in discussions regarding any potential trial modifications.

Seres continues to execute on activities to advance SER-301 clinical development and the planned initiation of patient dosing in Australia and New Zealand later this year.

About Seres Therapeutics

Seres Therapeutics, Inc., (Nasdaq: MCRB) is a leading microbiome therapeutics platform company developing a novel class of biological drugs that are designed to treat disease by restoring the function of a dysbiotic microbiome, where the state of bacterial diversity and function is imbalanced. Seres' SER-287 program has obtained Fast Track and Orphan Drug designation from the U.S. Food and Drug Administration and is being evaluated in a Phase 2b study in patients with active mild-to-moderate ulcerative colitis. Seres' SER-109 program has obtained Breakthrough Therapy and Orphan Drug designations from the FDA and is in Phase 3 development for recurrent *C. difficile* infection. Seres is also developing SER-401 in a Phase 1b study in patients with metastatic melanoma and SER-301 for ulcerative colitis. 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 statements relating to FDA approval of Seres' therapeutic candidates, the timing and results of ECOSPOR III and any of our other clinical studies, the promise of microbiome therapeutics generally, the impact of the COVID-19 pandemic, the potential flexibility of the FDA with regard to our clinical trials, the expected minimal impact of the reduced trial size in ECOSPOR III, and the safety and purity of our product candidates. Any forward-looking statements represent management's opinions 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.

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: the unknown impact of COVID-19; we have incurred significant losses, are not currently profitable and may never become profitable; our need for additional funding; our unproven approach to therapeutic intervention; our reliance on third parties and collaborators to conduct our clinical trials, manufacture our product candidates and develop and commercialize our product candidates, if approved; that we have no experience manufacturing products at commercial scale; our products may become subject to unfavorable pricing restrictions; we may face product liability lawsuits; we may face competition from biosimilars; our ability to protect our trade secrets and know-how; potential changes in U.S. patent law; and the risk of third party lawsuits alleging we are infringing on their intellectual property. These and other important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K filed with the Securities and Exchange Commission, or SEC, on March 2, 2020 and our Current Report on Form 8-K filed with the SEC on March 18, 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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