Seres Therapeutics Announces Confirmatory Results from Investigational Microbiome Therapeutic SER-109 ECOSPOR IV Open-Label Study in Recurrent C. Difficile Infection

June 7, 2022

– ECOSPOR IV study shows favorable safety profile through 24-week follow-up, consistent with the safety profile observed in ECOSPOR III study

– 91.3% sustained clinical response achieved at eight weeks in overall population with consistent results in key subpopulations including first recurrence –

– Rolling Biologics License Application (BLA) submission initiated and on track for mid-2022 completion –

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

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 7, 2022-- Seres Therapeutics, Inc. (Nasdaq: MCRB) today announced confirmatory results from ECOSPOR IV, an open-label study for SER-109, an investigational oral microbiome therapeutic for the prevention of recurrent *C. difficile* infection (rCDI). The overall safety profile observed in ECOSPOR IV through 24 weeks indicated that SER-109 was well tolerated, consistent with the safety profile observed in the prior placebo-controlled ECOSPOR III study. The ECOSPOR III and ECOSPOR IV studies together conclude the SER-109 Phase 3 development program.

In ECOSPOR IV, subjects treated with SER-109 had a recurrence rate of 8.7% at eight weeks, which indicates a 91.3% sustained clinical response, consistent with the 88% rate observed in the ECOSPOR III study. Subjects with a first recurrence of CDI (29% of subjects in the ECOSPOR IV study) had a CDI recurrence rate of 6.5%, and subjects with ≥ two prior CDI episodes (ECOSPOR III inclusion criteria) had a CDI recurrence rate of 9.7% at eight weeks. At 24 weeks, 13.7% of all subjects treated with SER-109 had a recurrence of CDI. The data from this study help complete the U.S. Food and Drug Administration's (FDA's) predefined safety database requirements for SER-109.

"The ECOSPOR IV data confirm the well-tolerated safety profile and clinical benefit observed in the prior ECOSPOR III study," said Eric Shaff, President and Chief Executive Officer at Seres. "These results, along with the start of the rolling BLA submission, significantly advance our ability to deliver what may be the first FDA-approved microbiome therapeutic. We believe that SER-109 has the potential to fundamentally transform the management of rCDI across all 170,000 annual cases in the U.S. and are working closely with Aimmune Therapeutics, a Nestlé Health Science Company, to bring this therapeutic candidate to patients as quickly as possible."

In addition to data from the SER-109 ECOSPOR III study (NCT03183128), the ECOSPOR IV data will be included as part of the rolling submission of the BLA to the FDA. While the ECOSPOR III data alone will serve as the basis for efficacy in Seres' BLA submission, the FDA requested safety data from at least 300 subjects treated with SER-109 at the commercial dose as the basis for safety. Safety data across both ECOSPOR IV and ECOSPOR III are expected to fulfill this requirement and complete Seres' Phase 3 program for SER-109. Seres has initiated the rolling submission of the SER-109 BLA and anticipates completion of the BLA submission by mid-2022. SER-109 has obtained FDA Breakthrough Therapy, which provides the potential for priority review of the application and, as a result, Seres anticipates a potential launch of SER-109 in the first half of 2023.

The open-label ECOSPOR IV (NCT03183141) study consisted of two cohorts of adult subjects with rCDI, providing 24-week data for an additional 263 subjects administered SER-109. The study enrolled subjects with a clinical profile consistent with those commonly evaluated and treated in clinical practice. The overall safety profile through the 24-week follow-up showed that SER-109 was well tolerated, consistent with the safety profile observed in ECOSPOR III. Similarly low recurrence rates were observed in key subpopulations at eight weeks, including subjects with a first recurrence (6.5%), second recurrence (6.1%) and three or more recurrences (13.8%). Furthermore, the study allowed for initial CDI diagnosis to be made with either toxin or PCR, reflecting the variability across local medical practices; on-study recurrences continued to be confirmed by toxin to ensure study data integrity.

"The 91.3% sustained clinical response rate observed at eight weeks in the overall study population with recurrent CDI, including those with first recurrence, reaffirms the superior efficacy and favorable safety profile previously observed in the pivotal placebo-controlled ECOSPOR III trial," said Paul Feuerstadt, MD, FACG, AGAF, Yale University School of Medicine and lead author of the *New England Journal of Medicine* (NEJM) paper. "As a treating physician, I look forward to the potential approval of this meaningful therapeutic option for patients living with this challenging and debilitating disease."

Additional Details on the ECOSPOR III and ECOSPOR IV Studies:

- **ECOSPOR III (SERES-012):** A multicenter, randomized, placebo-controlled study that enrolled 182 adults with rCDI. Results published in the *New England Journal of Medicine* in January showed that 88% of subjects in the SER-109 group were free from *C. difficile* recurrence at eight weeks post-treatment, compared to 60% in the placebo group. At six months post-treatment, 79% of the SER-109 group were still free from *C. difficile* recurrence, compared to 53% in the placebo group, reinforcing the durable relief.
- **ECOSPOR IV (SERES-013):** An open-label extension study of ECOSPOR III and open-label program for evaluating SER-109 in 263 adult subjects with rCDI at the commercial dose to fulfill FDA requirements for the SER-109 safety database. The study duration for both cohorts was approximately 27 weeks, including a three-week screening period, an

eight-week primary efficacy period, and a 16-week follow-up period. Topline results showed favorable safety and 91% sustained clinical response at eight weeks in the overall population. At 24 weeks post-treatment, 86% of subjects treated with SER-109 experienced sustained clinical response. Full results from ECOSPOR IV will be submitted for presentation at a future scientific meeting and publication in a medical journal.

Seres entered into an agreement with Nestlé Health Science in July 2021 to jointly commercialize SER-109 in the U.S. and Canada. Under the terms of the agreement, Nestlé Health Science will use its global pharmaceutical business, Aimmune Therapeutics, and will assume the role of lead commercialization party. Seres has received an upfront license payment of $175 million and will receive an additional $125 million upon FDA approval of SER-109. The agreement also includes sales target milestones which, if achieved, would total up to $225 million. Seres will be responsible for development and pre-commercialization costs in the U.S. Upon commercialization, Seres will be entitled to an amount equal to 50% of the commercial profits.

Conference Call Information

Seres' management will host a conference call today, June 7, 2022, 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 5658565. 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 oral microbiome therapeutic candidate consisting of a consortium of highly purified Firmicutes spores, which normally live in a healthy microbiome. SER-109 is designed to prevent further recurrences of CDI by modulating the disrupted microbiome to a state that resists *C. difficile* colonization and growth. The SER-109 manufacturing purification process is designed to remove unwanted microbes, thereby reducing the risk of pathogen transmission beyond donor screening alone. The U.S. FDA has granted SER-109 Breakthrough Therapy designation and Orphan Drug designation for the prevention of rCDI.

About Seres Therapeutics

Seres Therapeutics, Inc. (Nasdaq: MCRB) is a leading microbiome therapeutics 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 to prevent further recurrences of *C. difficile* infection and has potential to become a first-in-class FDA-approved microbiome therapeutic. Seres is evaluating SER-155 in a Phase 1b study in patients receiving allogeneic hematopoietic stem cell transplantation to reduce incidences of gastrointestinal infections, bloodstream infections and graft-versus-host disease as well as additional preclinical stage programs targeting Infection Protection in medically compromised patients. The Company is also conducting research to inform further development of microbiome therapeutics 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 the ultimate efficacy and safety profile of SER-109; Seres' receipt of potential milestone payments, including the ability to achieve the targets and receive any milestone payments from Nestlé Health Science; the potential market for SER-109; the timing and potential FDA review and approval of SER-109, including the expectation of an expedited review; the potential for SER-109 to become a first-in-class therapeutic; the treatment potential for SER-109; the timing of the launch of SER-109; and the submission for publication or scientific presentation of the final ECOSPOR IV data.

These forward-looking statements are based on Seres' 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 Seres' 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: Seres has incurred significant losses, is not currently profitable and may never become profitable; Seres' need for additional funding; Seres' limited operating history; the impact of the COVID-19 pandemic; Seres' unproven approach to therapeutic intervention; the lengthy, expensive and uncertain process of clinical drug development; Seres' reliance on third parties and collaborators to manufacture their product candidates and develop and commercialize their product candidates, if approved; and their ability to retain key personnel and to manage growth. These and other important factors discussed under the caption "Risk Factors" in Seres Therapeutics, Inc.'s Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission, or SEC, on May 4, 2022, and their 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 Seres' management's estimates as of the date of this press release. While Seres may elect to update such forward-looking statements at some point in the future, Seres disclaims any obligation to do so, even if subsequent events cause their views to change. These forward-looking statements should not be relied upon as representing Seres' views as of any date subsequent to the date of this press release.

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Seres Therapeutics Media
Kristin Ainsworth
kainsworth@serestherapeutics.com

Seres Therapeutics Investor Relations

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

Source: Seres Therapeutics, Inc.