Seres Therapeutics Presents SER-109 ECOSPOR IV Study Data at IDWeek and American College of Gastroenterology (ACG) 2022 Annual Meetings

October 23, 2022

– Investigational oral microbiome therapeutic was observed to reduce recurrent C. difficile infection (rCDI) after just one recurrence and remained low regardless of diagnostic approach –

– Clinical data shows SER-109 is well tolerated, including among people with multiple comorbidities –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 23, 2022-- Seres Therapeutics, Inc. (Nasdaq: MCRB), a leading microbiome therapeutics company, announces the presentation of safety and efficacy data from its open-label Phase 3 ECOSPOR IV extension study evaluating investigational oral microbiome therapeutic SER-109 for the prevention of rCDI at the IDWeek 2022 and American College of Gastroenterology (ACG) 2022 Annual Meetings. Among the ECOSPOR IV study participants, many of whom have multiple comorbidities, SER-109 was well tolerated, with no serious treatment-related adverse events. In addition, a similar degree of reduction in rCDI during the eight weeks following SER-109 administration was observed when compared to the results of the completed placebo controlled ECOSPOR III Phase 3 study.

"We're aiming to strengthen the body's defenses against the return of *C. difficile* infection by repairing the microbiome," said Lisa von Moltke, M.D., Chief Medical Officer at Seres. "The clinical evidence to date from both ECOSPOR III and ECOSPOR IV continues to support the potential use of SER-109 to reduce the suffering and health risks inflicted by repeated occurrences of this incredibly difficult-to-treat disease."

With nearly 170,000 cases in the U.S. each year, rCDI is one of the top three most urgent bacterial threats in the country, according to the Centers for Disease Control and Prevention, and is a leading cause of hospital-acquired infection.

Together with the safety, tolerability and efficacy results observed during the earlier Phase 3 placebo-controlled ECOSPOR III (NCT03183128) study, the ECOSPOR IV safety data completed the U.S. Food and Drug Administration (FDA) predefined requirements for a Biologics License Application (BLA), which were submitted by the company in August. If granted priority review of the BLA, Seres anticipates the potential approval and launch of SER-109 in the first half of 2023, with SER-109 potentially becoming the first ever FDA-approved oral microbiome therapeutic.

Data presented during ACG will consist of the following:
Title: An Open-Label Study (ECOSPOR IV) to Evaluate the Safety, Efficacy and Durability of SER-109, an Investigational Oral Microbiome Therapeutic, in Adults with Recurrent *Clostridioides difficile* Infection (rCDI)
Oral Presentation: #63
Lead Author: Sahil Khanna, MBBS, MS, FACG

ECOSPOR III enrolled participants with a history of two or more recurrences. ECOSPOR IV (NCT03183141) expanded the participant pool to include people with only one prior recurrence to determine whether earlier intervention with SER-109 may be a safe and effective way to reduce the burden of rCDI. ECOSPOR IV replicated the eight-week results of the earlier trial (91% clinical response rate for ECOSPOR IV versus 88% for ECOSPOR III), regardless of the number of prior CDI recurrences (94% following one recurrence versus 90% following two or more).

"When a person experiences recurrent *C. difficile* infection, the likelihood of future recurrence grows," said Sahil Khanna, M.B.B.S, M.S., F.A.C.G., gastroenterologist at Mayo Clinic and poster presenter. "It's promising to see that early microbiome-based intervention, after just one recurrence, may be able to break the cycle."

ECOSPOR IV enrolled participants with multiple comorbidities, including cardiovascular disease, tumors, diabetes, chronic obstructive pulmonary disorder (COPD) and chronic kidney disease. Overall, SER-109 was well tolerated in the study, with the majority of adverse events reported to be mild to moderate and gastrointestinal in nature. There were no serious treatment-related adverse events observed throughout the 24-week study period.

Dr. Khanna will present these findings at ACG 2022 on October 26 at 9:50 am ET. These data are also available to ACG-registered attendees on the ACG Conference Platform through March 31, 2023.

Data presented during IDWeek are the following:
Title: SER-109, an Oral Investigational Microbiome Therapy for the Prevention of Recurrent *Clostridioides difficile* Infection
Oral Presentation: #50
Lead Author: Barbara McGovern, MD

Antibiotics kill many naturally occurring bacterial species in the gut, which opens the door for *C. diff* and other pathogens to colonize and multiply. SER-109 is an oral capsule that contains key protective bacteria, which has the potential to reduce the risk of CDI recurrence and may serve to restore host defenses against potential pathogens through increased gut microbiome diversity.

In a post hoc analysis, engraftment of SER-109 species was associated with reduction of antibiotic resistance genes (ARGs) thought to occur through remodeling of microbial communities. SER-109 engraftment was associated with marked increases in spore-forming Firmicutes and reciprocal declines in Gram-negative bacteria that harbor ARGs.

"SER-109 is thought to restore host defenses against *C. difficile* by increasing the diversity of the gut microbiome, thus reducing the risk of

recurrence," said Barbara McGovern, M.D., Vice President of Medical Affairs at Seres, who presented these data at IDWeek on October 20. "SER-109 was also observed to reduce the abundance of Gram-negative bacteria – which carry ARGs – and these early observations are a promising avenue for further exploration, due to the urgent global need on combating antimicrobial drug resistance."

This presentation is available to IDWeek-registered attendees on the IDWeek Interactive Program until December 31, 2022.

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 reduce the recurrence 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 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 oral 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 potential approval of SER-109 and its status as a first-in-class oral therapeutic; the timing of a BLA acceptance and potential product launch; the potential market for SER-109; the ultimate safety and efficacy data for SER-109; the anticipated indication of SER-109; and other statements which are not historical fact.

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; the impact of the COVID-19 pandemic; our unproven approach to therapeutic intervention; the lengthy, expensive and uncertain process of clinical drug development; 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; and our ability to retain key personnel and to manage our growth. 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 August 3, 2022, 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
Kristin Ainsworth
kainsworth@serestherapeutics.com

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

Source: Seres Therapeutics, Inc.