Seres Therapeutics Presents Phase III Results of SER-109 for Recurrent C. Difficile Infection at the Digestive Disease Week (DDW) Annual Meeting

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– In ECOSPOR lll, Seres' lead therapeutic candidate incorporated itself rapidly and durably into the microbiome to prevent C. difficile infection recurrence –

– Within one week of treatment, SER-109 was observed to diversify the microbiome and support the production of fatty acids that inhibit the growth of C. difficile –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 22, 2022-- Seres Therapeutics, Inc. (Nasdaq: MCRB), a leading microbiome company, today announced the presentation of data from its Phase 3 ECOSPOR III study that suggest investigational microbiome-based therapeutic SER-109 prevents recurrent *C. difficile* infections (rCDI) by rapidly establishing a long-lasting colony of beneficial gut microbes, which can produce fatty acids that disrupt the *C. difficile* lifecycle. These data were shared in oral and poster presentations at the 2022 Digestive Disease Week (DDW) Annual Meeting.

"These results suggest that our investigational microbiome therapeutic, SER-109, is a potentially fast-acting intervention that can provide durable relief from recurrent *C. difficile* infections when administered to vulnerable patients," said Matthew Henn, Ph.D., Chief Scientific Officer at Seres. "Confirming the multiple mechanisms that bacteria in SER-109 utilize to prevent this notoriously challenging infection on the cellular and molecular level not only increases our confidence in this particular therapeutic, but it has the potential to help guide the design of the next generation of microbiome-based therapeutics."

Seres expects to finalize a Biologics License Application (BLA) submission for SER-109 with the U.S. Food and Drug Administration (FDA) in mid-2022, positioning SER-109 up to potentially become the first ever FDA-approved microbiome-based therapeutic for treating recurrent *C. difficile* infections with a potential product launch in the first half of 2023.

Engraftment of SER-109 is Durable through 24 Weeks (Poster # 3701110)

The ECOSPOR III Phase 3 study (NCT03183128), a multicenter, randomized, placebo-controlled clinical trial that enrolled 182 adults with rCDI, previously demonstrated that SER-109 prevented rCDI in 88% of recipients at the eight-week primary endpoint, whereas only 60% in the placebo arm remained recurrence-free over the same time period. The safety profile was similar across both groups.

A pre-planned exploratory analysis from the ECOSPOR III trial shows that approximately two-thirds of CDI recurrences occurred within the first two weeks following antibiotic treatment for CDI – the window of vulnerability – when the microbiome is further decimated and *C. difficile* spores, untouched by antibiotics, are free to germinate into toxin-producing vegetative bacteria.

"These findings suggest that the first two weeks following antibiotic treatment is the time when microbiome therapeutics have the greatest potential benefit, by restoring bacterial diversity and disrupting the cycle of recurrent *C. difficile*," said Lisa von Moltke, M.D., Chief Medical Officer at Seres.

SER-109 introduces a diverse consortium of bacterial species into the gut in the form of spores, which rapidly germinate and incorporate themselves into the microbiome, showing up in the stool as vegetative bacteria. This process is called engraftment.

Within a week of SER-109 treatment, the number of new bacterial species in stool increased and remained significantly higher than the placebo group for the entire 24-week study period. Bacterial diversity rebounded more slowly and to a lesser degree in the placebo group.

The pattern of results was the same regardless of which antibiotic participants received, vancomycin or fidaxomicin.

Impact of SER-109 on Fatty Acid Production (Abstract # 3700066)

To better understand how SER-109 prevents rCDI on the molecular level in a post-hoc analysis, stool samples collected from ECOSPOR III participants were analyzed for changes in their microbial makeup and fatty acid concentrations across the eight weeks following SER-109 treatment. Fatty acids with long and medium carbon chain lengths, such as butyrate, valerate and hexanoate, have been shown to inhibit the growth of *C. difficile.*

For participants who received SER-109, butyrate, valerate and hexanoate levels rapidly increased, starting within the two-week window of vulnerability, and remained significantly higher than the placebo group for the eight-week data analysis period.

Among members of the placebo group who experienced a CDI recurrence, valerate levels tended to be lower compared to members of the placebo group who did not experience a recurrence, further suggesting that valerate plays a protective role against rCDI.

These data and data published previously in the *New England Journal of Medicine* suggest that a two-pronged approach for the treatment of rCDI, with standard-of-care antibiotics to kill vegetative *C. difficile* bacteria followed by investigational agent SER-109 to repair the disrupted microbiome through engraftment of Firmicutes bacteria and the modulation of multiple metabolic pathways in the gut, may be effective.

Posters and presentations will be available for 90 days on the DDW conference website.

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 FDA has granted SER-109 Breakthrough Therapy designation and Orphan Drug designation for the treatment 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 the recurrence 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 mechanism of action of SER-109; the timing of a BLA filing and potential product launch of SER-109; the ultimate safety and efficacy profile; and the possibility of SER-109 being a first in class therapeutic.

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 May 4, 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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