Seres Therapeutics Presents Data Across its Broad Microbiome Pipeline Including New 24-Week Data from SER-109 Phase 3 ECOSPOR III Study in Recurrent C. Difficile Infection at Digestive Disease Week 2021

May 21, 2021

– Data validates strength of Seres' investigational microbiome therapeutics pipeline in potentially addressing unmet treatment needs in recurrent C. difficile infection and ulcerative colitis –

– In Phase 3 ECOSPOR III study, SER-109 significantly reduced recurrence rates of C. difficile infection at 24 weeks with an observed safety profile comparable to placebo –

– Preclinical data support the potential of SER-301 as a therapeutic modality for mild-to-moderate ulcerative colitis through microbiome restoration –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 21, 2021-- Seres Therapeutics, Inc. (Nasdaq: MCRB), a leading microbiome therapeutics company, announced the presentation of its final 24-week data from the pivotal Phase 3 ECOSPOR III study evaluating SER-109, an investigational oral microbiome therapy for recurrent *C. difficile* infection (rCDI). The data presented today in a poster of distinction at Digestive Disease Week® 2021 demonstrated that SER-109 significantly reduced recurrence rates compared to placebo over 24 weeks (21.3% vs. 47.3%, respectively).

"This landmark study of SER-109, culminating in the full set of 24-week data, reinforces the potential of its first-in-class clinical profile. In the Phase 3 ECOSPOR III study, SER-109 was observed to rapidly restore the microbiome and significantly reduce the risk of recurrence over time for patients with recurrent *C. difficile* infection—all with a safety profile comparable to placebo," saidLisa von Moltke, M.D., Chief Medical Officer at Seres. "These data, along with Seres' other mechanistic and preclinical data at DDW, continue to provide evidence that our microbiome therapeutics have the potential to target multiple disease pathways and offer new, potentially transformative treatment options."

On Sunday, Seres will also present SER-109 data comparing the modulation of primary and secondary bile acids (BAs) in ECOSPOR III study participants in an oral presentation. The shift in bile acids is believed to be an important mechanism by which SER-109 exerts its clinical benefits.

Additionally, Seres will present preclinical data from SER-287 and SER-301, investigational microbiome therapeutics that are being evaluated for the treatment of mild-to-moderate ulcerative colitis in poster and oral presentations at the meeting.

ECOSPOR-III Phase 3 Trial of SER-109 (Poster Fr572)

Final 24-week efficacy and safety results from the SER-109 ECOSPOR III Phase 3 study (ClinicalTrials.gov identifier: NCT03183128), a multicenter, randomized, placebo-controlled study that enrolled 182 patients with multiple rCDI, indicate that SER-109 was observed to maintain durable efficacy at 24 weeks following dosing, resulting in reducing the risk of rCDI compared with placebo. The safety profile observed to date has been comparable to placebo.

Significantly fewer patients administered SER-109 experienced rCDI compared to the placebo arm at Week 24 (21.3% vs. 47.3%, p-value <0.001), a relative risk reduction of 54%. SER-109 resulted in a 26% absolute reduction of recurrence of CDI compared to placebo at 24 weeks post-treatment. This is comparable to the 27% absolute reduction of recurrence observed in the trial at Week 8.

"As a clinician treating people living with recurrent *C. difficile* infection, I recognize the serious and often debilitating impact it has on their lives. The SER-109 Phase 3 data provide hope that an orally administered microbiome therapeutic, with an entirely new treatment modality, has the potential to alter the devastating cycle of recurrence that these people face," said Louis Korman, M.D., Director, Chevy Chase Clinical Research, Principal Investigator of the SER-109 Phase 3 trial. "Recognizing the potential for SER-109 to modulate the microbiome with the chance of fewer possible risks than currently available treatment options, I believe that SER-109 shows promise in shifting how we may treat recurrent *C. difficile* infection in the future."

In the Phase 3 study, SER-109 was observed to be well tolerated, with the overall incidence of adverse events at Week 24 comparable between the SER-109 and placebo arms. Treatment-emergent serious adverse events (SAEs) were observed in the active arm at a rate lower than in the placebo arm (n=15, 16.7%; n=19, 20.7%).

Previously reported topline data from ECOSPOR III indicated that the study achieved its primary endpoint at eight weeks post-treatment and a sustained clinical response rate of approximately 88% was observed. Seres is currently conducting an ongoing open-label study of SER-109 in patients with rCDI (ClinicalTrials.gov identifier: NCT03183141), with full enrollment anticipated in Q3 2021. Additional information can be found at serescdiffstudy.com.

CDI is one of the top three most urgent bacterial threats in the U.S., according to the Centers for Disease Control and Prevention, and is a leading cause of hospital-acquired infection. It is associated with significant morbidity and mortality, with one study showing the annual cost to the U.S. healthcare system is approximately $6.3 billion.

In addition, in an oral presentation on Sunday, May 23 at DDW, Seres will present an exploratory sub-analysis from the Phase 3 study, which highlights data on changes in bile acid profiles after SER-109, which are known to inhibit *C. difficile* spore germination.

Ulcerative Colitis Preclinical Data

***In Vivo* Characterization of SER-301 (Abstract #3521981)**

Seres will also present preclinical data for SER-301, a rationally-designed, cultivated microbiome therapeutic candidate for the treatment of ulcerative colitis (UC).

"Despite the availability of treatment options for patients with ulcerative colitis, there are still significant gaps—particularly for those living with mild-to-moderate disease who have limited options. When these few options fail, the recourse is mainly treatments that are used in moderate-to-severe disease, many of which have significant adverse events including immune suppression and risk of infections," said Matthew Henn, Ph.D., Chief Scientific Officer at Seres and senior author of the poster.

SER-301 is being evaluated in a Phase 1b study in adults with mild-to-moderate UC to evaluate safety and tolerability and to test the hypothesis that engraftment of drug product species modulates microbe-associated metabolites to reduce intestinal inflammation and improve epithelial barrier integrity.

Preclinical assessments of SER-301 used *in vitro* and i*n vivo* models of colitis to evaluate the ability of SER-301 to promote immune homeostasis in the colon and to counterbalance inflammatory stimuli to prevent the development of colitis. *In vivo* animal model studies demonstrated that SER-301 is capable of reversing established intestinal inflammation and the development of colitis in an animal model. Further *in vitro* human cell-based assays confirm the bacteria in SER-301 can reduce induction of pro-inflammatory activity in intestinal epithelium cells and improve epithelial barrier integrity.

UC is a serious chronic condition affecting more than 700,000 patients in the U.S. and only one third achieve remission. It is marked by persistent inflammation in the gastrointestinal tract and can greatly reduce an individual's quality of life.

An oral presentation of SER-301 design and *in vitro* properties will be presented at DDW on Sunday, May 23. The presentation highlights the SER-301 design using Seres' reverse translation discovery and development platforms, incorporating learnings from the Phase 1b trial of SER-287, an oral microbiome therapeutic candidate consisting of a consortium of highly purified Firmicutes spores being investigated in a Phase 2b study for the treatment of UC.

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 the healthy microbiome. SER-109 is designed to prevent further recurrences of CDI in patients with a history of multiple infections 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. Food and Drug Administration (FDA) has granted SER-109 Breakthrough Therapy designation and Orphan Drug designation for the treatment of rCDI.

About SER-287
SER-287, an investigational oral microbiome therapeutic candidate consisting of a consortium of highly purified Firmicutes spores, is designed to normalize the gastrointestinal microbiome of individuals with UC. Preclinical colitis animal models and *in vitro* screens provide evidence that SER-287 administration has the potential to reduce pathology and modulate inflammatory and immunological functional pathways. SER-287 has been granted Fast Track Designation by the FDA for the induction and maintenance of clinical remission in adult subjects with active mild-to-moderate UC. SER-287 has been designated an Orphan Drug for pediatric UC by the FDA.

About SER-301
SER-301 is a consortium of cultivated bacteria designed using our reverse translational discovery platform that incorporates analysis of microbiome biomarkers from human clinical data and preclinical assessments using human cell-based assays and *in vitro/ex vivo* and *in vivo* disease models. SER-301 is designed to reduce induction of pro-inflammatory activity, improve epithelial barrier integrity and TNF-α driven inflammation in intestinal epithelial cells, or IECs, and modulate UC-relevant anti-inflammatory, innate and adaptive immune pathways. SER-301 is being produced using our advanced fermentation, formulation and delivery platforms. It includes strains delivered in spore form, as well as strains cultivated in non-spore (vegetative) form and delivered using enterically-protected technology designed to release in the colon.

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 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 evaluating SER-301 in a Phase 1b study in patients with ulcerative colitis, and plans to initiate a clinical program with 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 of microbiome therapeutics to treat and prevent disease, the timing and results of our clinical studies, the potential approval of any of our products, the ultimate safety and efficacy data for our products, 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 May 4, 2021, 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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