Seres Therapeutics Presents Microbiome Therapeutic Research at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting

June 1, 2022

– Preclinical data suggest efficacy of new investigational microbial consortium, called DE486, to reduce chemotherapy-induced mucositis inflammation –

– A Phase 1b clinical trial to assess whether SER-155 prevents life-threatening complications of stem cell transplant –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 1, 2022-- Seres Therapeutics, Inc. (Nasdaq: MCRB), a leading microbiome therapeutics company, announced the presentation of preclinical data supporting further investigation of a rationally designed microbial consortium candidate (DE486) to prevent or treat gastrointestinal (GI) mucositis – a common and often painful complication of radiation and chemotherapy involving the breakdown of the rapidly-dividing epithelial cells lining the GI tract. These results are available online as part of the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting.

“Microbiome-based therapeutics may offer a potentially novel approach to mitigate debilitating side-effects that can lead to delays or dose reductions of life-saving cancer treatments,” said Matthew Henn, Ph.D., Chief Scientific Officer at Seres. “This microbial consortium builds on our scientific and clinical data, and we are encouraged by these preclinical results that suggest potential areas of investigation and future development opportunities for this new area of medicine.”

In laboratory experiments, chemotherapy caused mice to develop mucositis of the small intestine and rapidly lose weight. Treatment with a defined consortium of microbes from Seres' proprietary strain library was shown to reduce inflammation and restore the mice to their normal weight after about a week. In contrast, treating mice with a different microbial cocktail that was intentionally selected to include pro-inflammatory bacteria that may be found in cancer patients with a disrupted microbiome was observed to have the opposite effect, resulting in continued weight loss.

These data support the potential of specifically designed combinations of microbes to minimize damage done to the lining of the GI tract by cancer treatment as a strategy to prevent or manage GI mucositis.

Seres will also present a poster on June 4 at 8:00-11:00 AM CDT detailing the design of an early Phase 1b trial evaluating the efficacy, safety and pharmacokinetics of SER-155 in adults undergoing allogeneic hematopoietic stem cell transplantation (HSCT). SER-155 is a cultivated investigational microbiome therapeutic rationally designed to improve clinical outcomes in patients undergoing HSCT by restoring colonization resistance to pathobionts, promoting epithelial barrier integrity, and reducing colonic inflammation. In addition to SER-109, SER-155 represents Seres’ second active development program in its Infection Protection franchise.

Another poster presentation on June 4 at 1:15-4:15 PM CDT will reprise Phase III trial results of SER-109, an investigational microbiome therapeutic for recurrent *C. difficile* infection (rCDI). The data showed SER-109 was associated with lower recurrence rate vs. placebo regardless of baseline comorbidity score category. This suggests SER-109 has a side effect profile comparable to placebo and may significantly reduce rCDI rates, which disproportionately affect cancer patients.

Phase 1b Study of SER-155 in Stem Cell Transplant

Hematopoietic stem cell transplant (HSCT) is frequently used to treat lymphoma, leukemia and multiple myeloma or for people who received high doses of chemotherapy or radiation that damaged their bone marrow. While it can be curative, stem cell transplant also carries the risk of life-threatening complications.

A Phase 1b clinical trial (NCT04995653) is now enrolling adults undergoing allogeneic HSCT to test whether the investigational microbiome therapeutic SER-155 is safe and effective at preventing graft-versus-host disease, blood infections and other serious complications.

The trial is designed to enroll 10 participants in an initial open-label cohort to gauge safety. Then, an additional 60 adults will be enrolled into a double-blind, randomized, placebo-controlled arm to assess efficacy. Participants in the second cohort will receive either vancomycin followed by SER-155 or placebo. Adverse events and microbiome samples will be logged for the first year following stem cell transplantation.

Phase 3 ECOSPOR III Study of SER-109 Data Encore

Cancer patients are at greater risk of developing rCDI and tend to have worse outcomes, due to their weakened immune system and frequent antibiotics exposure.[i]

Encore data from the completed double-blind, randomized, placebo-controlled Phase 3 ECOSPOR III trial (NCT03183128) show that the investigational microbiome therapeutic SER-109 significantly reduced rCDI rates. SER-109 was also observed to be well tolerated, with a safety profile comparable to placebo and no serious drug-related adverse events observed. From 4 weeks post-treatment through 24 weeks, adults with a history of rCDI had fewer recurrences after taking SER-109 compared with those who received placebo.

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, with an anticipated launch in the first half of 2023, if approved. SER-109 has obtained FDA Breakthrough Therapy and Orphan Drug

Designations, supporting the expectation of an expedited review timeline.

About SER-155
SER-155, an oral consortium of cultivated bacteria, is a microbiome therapeutic candidate in clinical development. SER-155 is designed using microbiome biomarker data from human clinical data, human cell-based assays, and in vivo disease models, with the aim to decrease infection and translocation of antibiotic-resistant bacteria in the gastrointestinal tract and modulate host immune responses to decrease GvHD. The rationale for this program is based in part on published clinical evidence from Seres' collaborators at Memorial Sloan Kettering Cancer Center showing that allogeneic HSCT patients with decreased diversity of commensal microbes are significantly more likely to die due to infection and/or lethal GvHD. SER-155 was developed using Seres' reverse translational discovery platform to potentially reduce incidences of gastrointestinal infections, bloodstream infections and GvHD in immunocompromised patients, including in patients receiving allogeneic HSCT or solid organ transplants.

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 the recurrence of CDI by restructuring the 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 the recurrence of *C. difficile* infection and has potential to become the first 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 timing of a BLA submission and potential product launch of SER-109; the ultimate safety and efficacy profile of any microbiome therapeutics; the timing and outcome of clinical development; the promise of microbiome therapeutics to treat and prevent disease; 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.

[i] Sahu, K. K., Mishra, A. K., Jindal, V., Siddiqui, A. D., & George, S. V. (2021). To study the contributing factors and outcomes of Clostridioides difficile infection in patients with solid tumors. *Heliyon*, 7(12), e08450. https://doi.org/10.1016/j.heliyon.2021.e08450

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