Seres Therapeutics Reports SER-155 Phase 1b Cohort 1 Results Showing Successful Drug Bacteria Engraftment and Substantial Reduction in Pathogen Domination in the Gastrointestinal Microbiome

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– Tolerability profile observed supports continued development in Cohort 2, with no treatment attributed serious adverse events –

– Reduction in incidences of microbiome pathogen domination provides support for intended SER-155 clinical activity –

–SER-155 Phase 1b placebo-controlled Cohort 2 data readout anticipated in mid-2024 –

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

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 9, 2023-- Seres Therapeutics, Inc. (Nasdaq: MCRB), a leading microbiome therapeutics company, today reported initial clinical data about SER-155. SER-155 is an oral, cultivated bacterial consortia investigational therapeutic designed to prevent enteric-derived infections and resulting blood stream infections, as well as induce immune tolerance responses to reduce the incidence of graft-versus-host disease (GvHD) in patients undergoing allogeneic hematopoietic stem cell transplantation (allo-HSCT). Gastrointestinal (GI) microbiome data from the first 100 days post HSCT in Cohort 1 of the SER-155 Phase 1b open-label study showed the successful engraftment of SER-155 bacterial strains and a substantial reduction in the cumulative incidence of pathogen domination, a biomarker associated with the risk of serious enteric infections and bloodstream infections, as well as GvHD. The tolerability profile observed was favorable, with no serious adverse events attributed to SER-155 administration. Enrollment in the placebo-controlled Cohort 2 portion of the study is ongoing and topline results are anticipated in mid-2024.

“We are pleased with these initial SER-155 Phase 1b study results from Cohort 1, which provide encouraging evidence to support our clinical objective of reducing enteric-derived infections, resulting bloodstream infections, and graft-versus-host disease in individuals undergoing allo-HSCT for cancers and other serious conditions,” said Lisa von Moltke, M.D., Chief Medical Officer at Seres. “The tolerability profile of SER-155 was favorable, with no serious adverse reactions associated with SER-155 administration. Enrollment in the placebo-controlled Cohort 2 study is proceeding, and we look forward to gaining further insights into the therapeutic potential of SER-155 to benefit this highly medically compromised patient population.”

SER-155 Phase 1b Study Design and Summary of Cohort 1 Results

SER-155 is an investigational, oral, 16 strain, cultivated microbiome therapeutic designed to prevent colonization and reduce the abundance of ESKAPE pathogens (e.g., from families such as *Enterococcaceae, Enterobacteriaceae, Streptococcaceae, Staphylococcaceae*) in the GI tract to reduce the risk of enteric driven bloodstream infections and other downstream consequences, such as GvHD, in patients receiving allo-HSCT. SER-155 has the potential to impact antimicrobial resistance (AMR), including infections caused by carbapenem-resistant *Enterobacteriaceae* (CRE) and vancomycin-resistant *Enterococci* (VRE).

The development of SER-155 is informed by preclinical data that showed that allo-HSCT patients across multiple study sites had disrupted microbiomes and were susceptible to pathogen overgrowth in the GI tract, as well as in vivo studies that demonstrated SER-155's ability to significantly decolonize VRE and CRE, and further modulate epithelial barrier integrity and T cell biology or relevance to GvHD. Previously published exploratory results from the SER-109 ECOSPOR III Phase 3 study showed decolonization of gut pathogens, including bacteria that carry antibiotic resistance genes, providing clinical proof-of-concept for the SER-155 program.

The SER-155 Phase 1b study includes two cohorts, with Cohort 1 designed to assess safety and drug pharmacology, including the engraftment of drug bacteria in the gastrointestinal tract. Cohort 1 included 13 subjects who received any dosing of the SER-155 regimen, with 11 of these subjects subsequently receiving an allo-HSCT. Nine subjects had evaluable samples for microbiome data analyses. The average age in Cohort 1 was 60, and most subjects had acute myeloid leukemia, myelodysplastic syndrome or myeloproliferative neoplasia as their primary disease and received reduced-intensity conditioning pre-transplant. Most subjects received peripheral blood stem cells from a matched unrelated donor. Neutrophil engraftment was observed in all subjects. The majority of subjects received a tacrolimus-based regimen for GvHD prophylaxis.

“The Phase 1b data provide important mechanistic insights that support the potential utility of microbiome therapeutics such as SER-155 to individuals receiving allo-HSCT,” said Matthew Henn, Ph.D., Chief Scientific Officer at Seres. “Study data from Cohort 1 suggest that SER-155 administration results in substantially lower incidence rates of gastrointestinal pathogen domination with ESKAPE pathogens of clinical concern, including *Enterococcaceae, Enterobacteriaceae, Streptococcaceae* and *Staphylococcaceae*. These are bacteria that can include antibiotic resistant strains such as carbapenem-resistant *Enterobacteriaceae* (CRE) and vancomycin-resistant *Enterococci* (VRE).”

Published data have demonstrated an association between the incidence of GI domination with ESKAPE pathogens in allo-HSCT patients and the risk of serious infections, GvHD, and mortality.[1,2,3] Reducing the incidence of domination of ESKAPE pathogens in the GI microbiome through administration of a microbiome therapeutic has the potential to meaningfully reduce enteric infections, enteric driven blood stream infections and GvHD in this medically compromised patient population and more broadly.

“Allogeneic hematopoietic stem cell transplantation can be a highly effective approach to treat serious cancers, however, the process results in a high risk of complications, including infections and graft-versus-host disease,” said Marcel van den Brink, M.D., Ph.D., Head, Division of Hematologic Malignancies at Memorial Sloan Kettering Cancer Center (MSK). “Microbiome therapeutics have the potential to address underlying mechanisms that

may be involved in many of the issues faced during allo-HSCT. These encouraging initial SER-155 results, particularly the very low levels of gastrointestinal pathogen domination observed, provide support for the promise of these approaches to lead to important clinical benefits."

Enrollment of Cohort 2 is ongoing, incorporating a randomized, double-blinded placebo-controlled design to further evaluate safety, drug strain engraftment, and incidence of gastrointestinal ESKAPE pathogen domination, as well as the incidence of enteric infections, enteric driven blood stream infections and GvHD. Cohort 2 will enroll approximately 60 subjects administered either SER-155 or placebo at a 1:1 ratio. The Company anticipates obtaining top-line placebo-controlled day-100 data from study Cohort 2 in mid-2024.

Seres believes that the medical benefit and commercial potential for SER-155 is substantial. Nearly 30,000 allo-HSCT procedures are performed in the U.S. and Europe per year.[4] Complications are frequent and costly, with additional costs for patients with complications averaging approximately $180,000/year.[5,6] Infections and GvHD are estimated to result in nearly half of mortality associated with allo-HSCT.[4] With the exception of an exclusive license from MSK, Seres fully owns worldwide rights for commercialization of SER-155. In addition to SER-155, the Company is evaluating other microbiome therapeutic preclinical programs for additional medically compromised patient populations who are at risk of life-threatening infections.

Conference Call Information

Seres' management will host a conference call today, May 9, 2023, at 8:30 a.m. ET to discuss Q1 2023 financial results and provide a business update, including a discussion of new SER-155 study results. Prior to the conference call, the Company plans to provide slides to accompany the conference call on the 'Investors and News' section of the Seres website at www.serestherapeutics.com.

To access the conference call, please dial 800-715-9871 (domestic) or 646-307-1963 (international) and reference Conference ID 5098595. 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 Seres Therapeutics

Seres Therapeutics, Inc. (Nasdaq: MCRB) is a commercial-stage company developing novel microbiome therapeutics for serious diseases. Seres' lead program, VOWST™, obtained U.S. FDA approval in April 2023 as the first orally administered microbiota-based therapeutic to prevent recurrence of *C. difficile* infection (CDI) in adults following antibacterial treatment for recurrent CDI and is being commercialized in collaboration with Nestlé Health Science. 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.

About SER-155

SER-155 is a consortium of bacterial species selected using Seres' reverse translation discovery and development platform technologies. The design incorporates microbiome biomarker data from human clinical data and nonclinical human cell-based assays and in vivo disease models. The SER-155 composition aims to decrease the colonization and abundance of bacterial pathogens that can harbor antibiotic resistance and to enhance epithelial barrier integrity in the GI tract to both reduce the likelihood of pathogen translocation and decrease the incidence of bloodstream infections. Further, SER-155 is designed to modulate host immune responses to decrease GvHD.

Forward-Looking Statements and Disclosures

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 additional clinical data, the ability of microbiome therapeutics to prevent or reduce infections, the ultimate safety and efficacy data of SER-155, final study results, 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; our reliance on third parties and collaborators to conduct our clinical trials, manufacture our product candidates and develop and commercialize VOWST or any other product candidates, if approved; the unknown degree and competing factors of market acceptance for VOWST; the competition we will face; our ability to protect our intellectual property; 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 Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC), on March 7, 2023, 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.

SER-155 is covered by certain intellectual property exclusively licensed to Seres from MSK. Drs. van den Brink and Peled have financial interests related to Seres. MSK has institutional financial interests related to Seres.

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