Seres Therapeutics Presents Research from its Early-Stage Microbiome Therapeutic Oncology Programs at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting

June 4, 2021

- Decreased microbial gastrointestinal diversity in patients undergoing allogeneic HSCT procedures associated with higher mortality and increased incidence of intestinal GvHD -

- Data support a cancer-specific microbiome relationship, with correlation identified between microbiome composition and response to immune checkpoint inhibitor treatment in patients with certain cancers –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 4, 2021-- Seres Therapeutics, Inc. (Nasdaq: MCRB), a leading microbiome therapeutics company, today announced data from their collaboration with the University of Cologne (Köln, Germany) demonstrating that decreased microbiome diversity in allogeneic hematopoietic stem cell transplantation (HSCT) recipients is associated with poor clinical outcomes including mortality and increased incidence of intestinal graft-versus-host disease (GvHD). The data are being presented in an oral presentation at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting, taking place virtually. A separate poster presentation, including data from a collaboration with Memorial Sloan Kettering Cancer Center (New York, NY), established a significant association between microbiome composition and response to immune checkpoint inhibitor (ICI) treatment in patients who have metastatic melanoma, metastatic lung (NSCLC), urothelial, or renal cancer.

Seres is advancing development programs in oncology to evaluate the potential of microbiome therapeutics to modulate host immunity or inflammation to improve response and tolerability of cancer treatments. This includes SER-155, an investigational, oral, rationally-designed, cultivated microbiome therapeutic, which is advancing into a Phase 1b clinical trial to reduce the incidence of antibiotic-resistant bacterial infections and GvHD in patients following transplant procedures.

“Disruption of microbiome-modulated functions can impact clinical outcomes for patients being treated for cancer, including those who are undergoing allogeneic hematopoietic stem cell transplantation and those treated with cancer immunotherapy,” said Lisa von Moltke, M.D., Chief Medical Officer at Seres. “The findings we are presenting at ASCO provide further evidence that our SER-155 program, as well as our earlier stage oncology programs, will help to advance our understanding of the potential of microbiome therapeutics to work with the body’s immune system to improve cancer treatment outcomes.”

Clinical Evidence of Impact of Microbial Diversity on Mortality and GvHD in HSCT Patients

In collaboration with the University of Cologne, a prospective observational study was conducted to evaluate changes in microbial diversity over time in acute myeloid leukemia (AML) and acute lymphocytic leukemia (ALL) patients undergoing allogeneic HSCT and the impact on clinical outcomes. Patients were administered antibiotics as empiric treatment for febrile neutropenia or as targeted treatment and were monitored for incidence of GvHD. Stool was collected on a weekly basis prior to an HSCT procedure and up to 28 days post HSCT, with additional samples collected at days 56, 90, and 365, as well as upon diagnosis of intestinal GvHD. Gut microbiome profiles were generated from 381 stool samples (representing 65 subjects) to evaluate the relationship between gastrointestinal microbial diversity over time and clinical outcome.

“Frequent complications associated with stem cell transplantation include antibiotic-resistant infection and GvHD. Current treatments for the prevention of GvHD rely on increased immunosuppression, leaving the patient susceptible to a host of bacterial infections – and offer limited efficacy. The findings from this prospective study demonstrate a need for continued investigation into the use of microbiome therapeutics to reduce morbidity and mortality among transplant recipients,” said Christopher Ford, Ph.D., Senior Director, Computational Microbiome Sciences at Seres Therapeutics and co-author of the presentation.

Twenty-eight patients (42%) developed intestinal GvHD and 16 (25%) died prior to study completion. Across all subjects, a decline in microbiome diversity was observed immediately following HSCT. Decreased diversity and intestinal domination by two bacterial groups – Enterococcus and Enterobacteriaceae - was significantly associated with mortality across the study time course ($p<0.001$). Further, patients who ultimately developed intestinal GvHD had a significantly lower diversity at the time of stem cell engraftment ($p<0.05$) and that lower diversity was maintained throughout the study period.

Evaluation of Microbiome Composition in Correlation to Cancer-Specific Immune Checkpoint Inhibitor (ICI) Response

A study conducted with Memorial Sloan Kettering explored the relationship between microbiome composition and ICI response in patients with metastatic melanoma, metastatic lung (NSCLC), urothelial, or renal cancer. Fecal microbiome samples were collected from 94 patients (metastatic melanoma, n=17, NSCLC, n=44, urothelial, n=23, renal cancer, n=10) immediately before ICI therapy. Bacterial genomic DNA was isolated and profiled by whole metagenomic sequencing to evaluate bacterial signatures associated with response (R) and nonresponse (NR).

Treatment included anti-PD(L)1 monotherapy (n=51), anti-PD1 + anti-CTLA4 combination therapy (n=17), or a combination of anti-PD1 and chemotherapy (n=26). Clinical response was observed in 58% of patients, including partial or complete response (45%) and on treatment for more than 6 months (55%, with 31% on treatment for more than 1 year). Ordination of microbiome data from all four cancers reveals a small cluster of patients that were NR regardless of cancer type. Although the variance in the composition of pretreatment microbiome samples did not explain response alone (R vs. NR, PERMANOVA, $p=0.273$), a significant portion of the variance in microbiome composition was explained by the interaction of cancer type and outcome (PERMANOVA, $p=0.014$), suggesting a cancer-specific microbiome relationship. Notably, there was some similarity in the

signature of NR across three of the four cancer types. The relationship observed in this study was also identified and corroborated in pre-clinical models of ICI response. In these models, NR was characterized by active tumor growth in mice and a lack of induction of cytotoxic CD8+ T cells after ICI treatment.

About SER-155

SER-155, an investigational oral consortium of cultivated bacteria, is a microbiome therapeutic candidate intended to advance into 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 reduce morbidity and mortality due to gastrointestinal infections, bacteremia and GvHD in immunocompromised patients, including in patients receiving allogeneic HSCT or solid organ transplants.

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 or improve the outcomes of cancer patients, the timing of our clinical studies, the impact of microbiome therapeutics, the ultimate 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, 2020, 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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