Seres Therapeutics Reports SER-155 Phase 1b Placebo-Controlled Cohort 2 Study Safety and Clinical Results in Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplant (allo-HSCT)

September 12, 2024

SER-155 administration was associated with a significant reduction in both bacterial bloodstream infections (BSIs) and systemic antibiotic exposure, as well as lower incidence of febrile neutropenia, as compared to placebo through day 100 post HSCT

Demonstrated generally well tolerated safety profile and confirmed drug bacteria strain engraftment; no treatment-related serious adverse events

Company to seek Breakthrough Therapy designation from the FDA, given the high unmet medical need associated with BSIs, and discuss plans to advance development of SER-155 in allo-HSCT

Results support Seres' strategy to pursue SER-155 and other live biotherapeutics for prevention of a broader range of serious bacterial infections in multiple medically vulnerable patient populations

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

CAMBRIDGE, Mass., Sept. 12, 2024 (GLOBE NEWSWIRE) -- Seres Therapeutics, Inc. (Nasdaq: MCRB), a leading live biotherapeutics company, today reports topline clinical data from Cohort 2 of its SER-155 Phase 1b placebo-controlled study in patients undergoing allo-HSCT. In this patient population, infections are frequent, severe and often life-threatening. BSIs are one of the three leading causes of death in allo-HSCT patients. Additionally, transplant related complications, such as infections, increase the recovery burden for patients as well as increase treatment costs due to readmissions, prolonged hospital stays, and increased time in intensive care units. Seres believes that current options to address infections are not sufficient and that SER-155 has the potential to bring significant value to patients, healthcare providers, and the healthcare system.

SER-155 is an investigational live oral biotherapeutic cultivated from clonal master cell banks designed to prevent GI-derived bacterial bloodstream infections and other pathogen-associated complications. Study results demonstrate that SER-155 was associated with a significant reduction in both bloodstream infections and systemic antibiotic exposure as well as a lower incidence of febrile neutropenia, as compared to placebo through day 100 post HSCT. SER-155 was generally well tolerated, with no observed treatment-related serious adverse events.

The Company believes that the SER-155 Phase 1 study results support Seres' corporate strategy to develop its platform, comprised of a pipeline of designed live biotherapeutics, in multiple medically vulnerable patient populations at high risk of life-threatening bacterial infections and associated negative clinical outcomes. Seres intends to seek Breakthrough Therapy designation, given the high unmet medical need associated with BSIs, and discuss advancing development of SER-155 for allo-HSCT with the U.S. Food and Drug Administration (FDA). The Company also intends to evaluate SER-155 in additional patient populations that have a high risk of serious bacterial infections.

“The placebo-controlled Phase 1b study Cohort 2 results provide further evidence supporting the potential of SER-155 to reduce the risk of bacterial bloodstream infections, a leading cause of mortality and morbidity in patients undergoing allo-HSCT,” said Lisa von Moltke, M.D., Chief Medical Officer of Seres Therapeutics. “Given our encouraging clinical results and the severe consequences of bacterial infections, we will pursue Breakthrough Therapy designation with the FDA. We also look forward to discussing our plans to further develop SER-155 with the Agency.”

“Bacterial infections such as bacteremia (bacteria in blood) are a frequent and often life-threatening complication faced by patients undergoing HSCT as well as other patients with cancer,” said infectious diseases physician David Fredricks, M.D., Professor, Vaccine and Infectious Disease Division, and Professor, Clinical Research Division at the Fred Hutchinson Cancer Center in Seattle. “Many of these infections arise from bacteria in the gastrointestinal tract. Investigational live oral biotherapeutics such as SER-155 hold promise as a novel approach that could protect patients against these serious bacterial infections, resulting in improved patient outcomes, together with reduced use of antibiotics. The data from the SER-155 Phase 1b study, including results showing lower infection rates, less systemic antibiotic exposure, and reduced incidence of febrile neutropenia events, support continued development in allo-HSCT.”

SER-155 Phase 1b Study Design
The SER-155 Phase 1b study (NCT04995653) included two cohorts. Cohort 1 was designed to assess safety and drug pharmacology, specifically the drug strain engraftment in the gastrointestinal tract. Cohort 1 included 13 subjects who received any dosing of the SER-155 regimen, with 11 subjects subsequently receiving an allo-HSCT. Results from this cohort, announced in May 2023, showed SER-155 was generally well tolerated and resulted in successful drug strain engraftment and a reduction in pathogen domination in the GI microbiome relative to a historical control cohort.

Study Cohort 2 utilized a randomized, double-blinded 1:1 placebo-controlled design to further evaluate safety and drug strain engraftment, as well as key secondary and exploratory endpoints such as the incidence of bacterial bloodstream infections and related medical consequences such as febrile neutropenia and antibiotic use. Cohort 2 included 45 patients in the intention-to-treat (ITT) population. Of the ITT population, 20 received SER-155 and 14 received placebo, each of whom subsequently received an allo-HSCT, with data available for clinical evaluation through day 100, the study’s prespecified primary observation point. Exploratory hypothesis testing was conducted at the two-sided α=0.05 level. Ninety-five percent (95%) 2-sided confidence intervals (CIs) were determined, where specified. No adjustment for multiplicity was done. A subset of patient samples was available for drug pharmacology analysis.

The median age in Cohort 2 was 63, and most subjects had acute myeloid leukemia, acute lymphocytic leukemia, myelodysplastic syndrome or

myeloproliferative neoplasia as their primary disease and received reduced-intensity conditioning pre-transplant. Most patients received peripheral blood stem cells from a matched unrelated donor. A majority received post-transplant cyclophosphamide as part of their graft-versus-host disease (GvHD) prophylaxis.

Summary of Cohort 2 Study Results
Consistent with the observations from the Phase 1b study Cohort 1, SER-155 was generally well tolerated, and no treatment-emergent serious adverse events related to drug were observed. SER-155 bacterial strains engrafted into the gastrointestinal tract of patients following the administration of SER-155.

The incidence of BSIs was significantly lower in the SER-155 arm compared with the placebo arm (2/20 (10%) vs. 6/14 (42.9%), respectively; [Odds Ratio: 0.15; 95% CI: 0.01, 1.13, p=0.0423]). In addition, while antibiotic starts were similar in each arm, patients administered SER-155 were treated with antibiotics for a significantly shorter duration compared to patients in the placebo arm (9.2 days vs. 21.1 days, respectively, with a mean difference of -11.9 days [95% CI: -23.85, -0.04; p=0.0494]). The incidence of febrile neutropenia was lower in patients administered SER-155 compared to placebo (65% vs. 78.6%, respectively; [Odds Ratio: 0.51; 95% CI: 0.07, 2.99; p=0.4674]). Six cases of gastrointestinal infections (*C. difficile* infections) were observed in the study, with four cases (20%) in the SER-155 arm and two cases (14.3%) in the placebo arm.

Recent changes in the allo-HSCT standard of care and the increasing use of post-transplant cyclophosphamide as part of prophylactic therapy for GvHD have reduced rates of GvHD overall in this patient population. The rates of GvHD in the study were low, with two cases of grade 2 GvHD observed in each arm, and no cases of grade 3 or 4 GvHD were observed.

In Cohort 2, the ability to detect pathogen domination (i.e., relative abundance in the GI ≥30%) in the placebo arm, and differences between the study arms, was constrained due to the limited number of placebo stool samples and an imbalance in the number of available stool samples between the arms. Observed pathogen domination events were low in the placebo and SER-155 arms with no significant differences identified. In a comparison of the prevalence of pathogen domination versus a larger allo-HSCT historical control cohort, pathogen domination in SER-155 subjects was substantially lower, providing further evidence of SER-155 activity.

“The SER-155 Phase 1b results generate further evidence to support Seres' strategy as SER-155 is our second live biotherapeutic, after VOWST, designed to prevent serious bacterial infections and associated negative clinical outcomes in medically vulnerable populations. An estimated 40,000 patients worldwide undergo allogeneic stem cell transplantation each year. Adding autologous stem cell transplants (auto-HSCT), a natural adjacent patient population, approximately doubles this figure. The potential to contract a bloodstream infection during the allogeneic transplant process is significant, with incidence reports in the literature reaching up to 45%. Allogeneic transplant-related complications, including infections, increase already significant treatment costs by approximately $180,000 per patient. Given this high unmet need, we believe SER-155 could provide meaningful value for patients and the healthcare system,” said Eric Shaff, Chief Executive Officer of Seres Therapeutics.

Mr. Shaff continued, “We are particularly encouraged by the consistency of related efficacy outcomes in this study, especially the significantly lower rates of bloodstream infections and systemic antibiotic exposure as well as fewer instances of febrile neutropenia, as compared to placebo. Supported by these data and our well-established clinical, pharmacological, CMC, and regulatory capabilities, we plan to engage with the FDA to seek Breakthrough Therapy designation and discuss advancing development of SER-155 in allo-HSCT. With SER-155 and additional pipeline programs, we believe we may have the opportunity to address multiple patient groups, including allo-HSCT, auto-HSCT, CAR-T, chronic liver disease, cancer neutropenia, and solid organ transplants, thereby potentially creating significant commercial opportunities.”

Seres fully owns worldwide rights for the commercialization of SER-155.

Conference Call Information
Seres’ management will host a conference call today, September 12, 2024, at 8:30 a.m. ET. The conference call may be accessed by calling 1-800-715-9871 (international callers dial 1-646-307-1963) and referencing the conference ID number 622932. 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 SER-155
SER-155 is an investigational live biotherapeutic designed to prevent GI-derived bloodstream infections, enhance epithelial barrier integrity to reduce the likelihood of bacterial translocation from the gut to the bloodstream, and induce immune tolerance responses to reduce the incidence of GvHD. SER-155 contains 16 bacterial strains selected using Seres’ reverse translation discovery and development platform technologies to optimize SER-155’s functional profile. The design incorporates biomarker data from human clinical data and screening data from nonclinical human cell-based assays and in vivo disease models. SER-155 has been evaluated in a Phase 1b placebo-controlled study in patients undergoing allo-HSCT. SER-155 has received FDA Fast Track designation for reducing the risk of infection and GvHD in patients undergoing HSCT. The early development of the program was supported by Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), a global non-profit partnership accelerating antibacterial products to address drug-resistant bacteria.

About Seres Therapeutics
Seres Therapeutics, Inc. (Nasdaq: MCRB) is a commercial-stage company focused on improving patient outcomes in medically vulnerable populations through novel live biotherapeutics. Seres led the successful development and approval of VOWST™, the first FDA-approved orally administered microbiome therapeutic. The Company is developing SER-155, designed to prevent gastrointestinal-derived bloodstream infections, enhance epithelial barrier integrity, and induce immune tolerance responses to reduce the incidence of graft-versus-host-disease (GvHD). The Company is also advancing additional cultivated oral live biotherapeutics for medically vulnerable populations, including those with chronic liver disease, cancer neutropenia, and solid organ transplants. For more information, please visit www.serestherapeutics.com.

Important Additional Information About the Transaction and Where to Find It
In connection with the proposed transaction involving Seres Therapeutics, Inc. (“Seres”) and Société des Produits Nestlé S.A. (“SPN”), Seres filed a definitive proxy statement with the Securities and Exchange Commission (the “SEC”). Seres may also file other relevant material with the SEC regarding the proposed transaction. Beginning on August 26, 2024, Seres mailed the definitive proxy statement to its stockholders. INVESTORS AND STOCKHOLDERS OF SERES ARE URGED TO READ THE DEFINITIVE PROXY STATEMENT AND OTHER RELEVANT MATERIALS CAREFULLY AND IN THEIR ENTIRETY WHEN THEY BECOME AVAILABLE BECAUSE THEY CONTAIN OR WILL CONTAIN IMPORTANT INFORMATION ABOUT SERES AND THE PROPOSED TRANSACTION. Investors may obtain a free copy of these materials (when they are available) and other

documents filed by Seres with the SEC at the SEC's website at www.sec.gov or from Seres at its website at ir.serestherapeutics.com.

Participants in the Solicitation
Seres and certain of its directors, executive officers and other members of management and employees may be deemed to be participants in soliciting proxies from its stockholders in connection with the proposed transaction. Information regarding the persons who may, under the rules of the SEC, be considered to be participants in the solicitation of Seres' stockholders in connection with the proposed transaction is set forth in Seres' definitive proxy statement for its stockholder meeting, which was filed with the SEC on August 26, 2024, at which the proposed transaction will be submitted for approval by Seres' stockholders. You may also find additional information about Seres' directors and executive officers in Seres' Annual Report on Form 10-K for the fiscal year ended December 31, 2023, which was filed with the SEC on March 5, 2024, Seres' Definitive Proxy Statement for its 2024 annual meeting of stockholders, which was filed with the SEC on March 5, 2024, and in subsequently filed Current Reports on Form 8-K and Quarterly Reports on Form 10-Q.

Forward-Looking Statements
This communication contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this communication that do not relate to matters of historical fact should be considered forward-looking statements, including statements about the potential benefits of any of our products or product candidates; the ultimate safety and efficacy data of SER-155; study results; plans to seek FDA feedback; clinical data and clinical trials; our intentions related to the development of SER-155; our intention to seek Breakthrough Therapy designation; the ability of live biotherapeutics to prevent or reduce infections; or the timing of any of the foregoing 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: (1) we have incurred significant losses, are not currently profitable and may never become profitable; (2) our need for additional funding; (3) our history of operating losses; (4) the restrictions in our debt agreement; (5) our novel approach to therapeutic intervention; (6) our reliance on third parties to conduct our clinical trials and manufacture our product candidates; (7) the competition we will face; (8) risks associated with our clinical trials; (9) whether the FDA grants Breakthrough Therapy designation; (10) our ability to protect our intellectual property; (11) our ability to retain key personnel and to manage our growth; and (12) risks related to the proposed transaction under the Purchase Agreement with Société des Produits Nestlé S.A. for the sale of the VOWST business to SPN. These and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q filed with the SEC, on August 13, 2024, 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 communication. Any such forward-looking statements represent management's estimates as of the date of this communication. 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 communication.

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Source: Seres Therapeutics, Inc.