FDA Grants Breakthrough Therapy Designation to Seres Therapeutics' SER-155 for Reduction of Bloodstream Infections in Adults Undergoing Allogeneic Hematopoietic Stem Cell Transplant (allo-HSCT)

December 9, 2024

Designation based on encouraging Phase 1b clinical data, including that SER-155 resulted in a 77% relative risk reduction in bacterial bloodstream infections versus placebo

Breakthrough Therapy meeting with FDA on next study of SER-155 in allo-HSCT expected in Q1 2025

Seres seeking SER-155 strategic partnership to accelerate next study in allo-HSCT and expand to multiple target populations

CAMBRIDGE, Mass., Dec. 09, 2024 (GLOBE NEWSWIRE) -- Seres Therapeutics, Inc. (Nasdaq: MCRB) (Seres or the Company), a leading live biotherapeutics company, today announced that the US Food and Drug Administration (FDA) has granted Breakthrough Therapy designation to SER-155, the Company's lead investigational program, for the reduction of bloodstream infections (BSIs) in adults undergoing allogeneic hematopoietic stem cell transplant (allo-HSCT) for the treatment of hematological malignancies. In September 2024, Seres reported topline clinical data from Cohort 2 of its SER-155 Phase 1b placebo-controlled study in patients undergoing allo-HSCT, in which SER-155 was associated with a significant reduction in BSIs (77% relative risk reduction), a significant reduction in systemic antibiotic exposure, and lower incidence of febrile neutropenia, in each case as compared to placebo, through day 100 post-HSCT. Additionally, SER-155 was generally well tolerated, with no observed treatment-related serious adverse events.

FDA Breakthrough Therapy designation ensures communication and guidance from FDA to expedite the development of medicines which are intended to treat serious or life-threatening diseases, and in which preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint over available therapies. The receipt of Breakthrough Therapy designation for SER-155, the Company's second program to receive such designation, grants Seres access to FDA senior management and a commitment from FDA to work closely with the Company, facilitating an efficient drug development process. In December 2023, SER-155 received FDA Fast Track designation for reducing the risk of infection and GvHD in this patient population.

"We are thrilled that the FDA has granted Breakthrough Therapy designation to SER-155, underscoring the strength of our Phase 1b clinical data and the potential of this live biotherapeutic candidate to address one of the most significant complications faced by patients undergoing allo-HSCT. We are excited to advance the development of SER-155, working diligently to bring this innovative therapeutic to patients in need, while also exploring its potential use in other high-risk patient populations to maximize its impact," said Eric Shaff, President and Chief Executive Officer of Seres Therapeutics.

Lisa von Moltke, M.D., Chief Medical Officer of Seres Therapeutics continued, "This Breakthrough Therapy designation was supported by compelling clinical data demonstrating the potential of SER-155 to significantly reduce bacterial bloodstream infections and associated complications. We intend to meet with FDA in the first quarter of 2025 to discuss the next clinical study of SER-155 in allo-HSCT, which we believe could be a single registrational study for efficacy. We look forward to working closely with the agency on our development plans for SER-155, aimed at addressing this significant unmet need in patients undergoing allo-HSCT."

The SER-155 Breakthrough Therapy designation was supported by positive data from our recent SER-155 Phase 1b clinical trial (NCT04995653). Patients who received SER-155 experienced a significantly lower incidence of bacterial BSIs as 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]), representing a 77% relative risk reduction. 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]). Further, the incidence of febrile neutropenia was reduced, and gastrointestinal pathogen domination was substantially lower compared to a historical control cohort, providing further evidence of SER-155's activity in modulating the microbiome to address critical post-transplant complications. SER-155 was well tolerated with no treatment related serious adverse events and engrafted as expected in the gastrointestinal tract.

Bloodstream infections in allo-HSCT patients are frequent, serious, and potentially fatal. In clinical practice, HSCT patients who experience a BSI or febrile neutropenia are aggressively treated, often with broad-spectrum antibiotics, as infections are a leading cause of death in these patients in the first 100 days post-transplant. While prophylaxis of BSIs with antibiotics is common, antibiotics do not address the root cause as SER-155 is designed to do.

Recent market research conducted by Seres characterized a significant commercial opportunity for SER-155 in allo-HSCT. Health Care Providers (HCPs) treating allo-HSCT patients indicated a high level of concern regarding BSIs. Additionally, HCPs stated that they would rapidly add a product providing similar efficacy to what we have observed in our SER-155 study to standard treatment protocols. The approximately 40,000 worldwide allo-HSCT patients are treated in a subset of large oncology centers across the globe, enabling rapid and efficient education of HCPs about SER-155, if approved.

In addition to allo-HSCT, bloodstream infections are a common and serious complication in many other medically vulnerable populations, including autologous-HSCT patients, cancer patients with neutropenia, CAR-T recipients, individuals with chronic liver disease, solid organ transplant recipients,

as well as patients in the intensive care unit and long-term acute care facilities. Seres intends to explore development of SER-155 and additional pipeline candidates for these populations. The targeted patient populations for SER-155 and Seres' other pipeline candidates could represent multiple blockbuster commercial opportunities.

Seres is actively seeking a partner to provide financial resources and other capabilities to support the Company's goal to maximize the SER-155 program opportunity, while pursuing a capital-efficient development approach.

About SER-155
SER-155 is an investigational, oral, live biotherapeutic designed to decolonize GI pathogens, improve epithelial barrier integrity, and induce immune tolerance to prevent bacterial bloodstream and antimicrobial resistant (AMR) infections, as well as other pathogen associated negative clinical outcomes, in patients undergoing allo-HSCT for the treatment of hematological malignancies.

SER-155 has been evaluated in a Phase 1b placebo-controlled study in patients undergoing allo-HSCT, which demonstrated a significant reduction in both BSIs and systemic antibiotic exposure, as well as lower incidence of febrile neutropenia. SER-155 has received Breakthrough Therapy designation for the reduction of BSIs and Fast Track designation for reducing the risk of infection and GvHD, in both cases in patients undergoing HSCT.

About Seres Therapeutics
Seres Therapeutics, Inc. (Nasdaq: MCRB) is a clinical-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, which was sold to Nestlé Health Science in September 2024. The Company is developing SER-155, which has demonstrated a significant reduction in bloodstream infections and related complications (as compared to placebo) in a clinical study in patients undergoing allo-HSCT. SER-155 and the Company's other pipeline programs are designed to target multiple disease-relevant pathways and are manufactured from standard clonal cell banks via cultivation, rather than from the donor-sourced production process used for VOWST. In addition to allo-HSCT, the Company intends to evaluate SER-155 and other cultivated live biotherapeutic candidates in other medically vulnerable patient populations including autologous-HSCT patients, cancer patients with neutropenia, CAR-T recipients, individuals with chronic liver disease, solid organ transplant recipients, as well as patients in the intensive care unit and long-term acute care facilities. 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 statements about: the timing and results of our clinical studies and data readouts; our clinical development plans; the anticipated timing of communications with the FDA; the impact of Breakthrough Therapy designation, Fast Track designation or any other FDA designations; our ability to secure a partnership and/or generate additional capital; the market for SER-155 and other product candidates; 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) our novel approach to therapeutic intervention; (5) our reliance on third parties to conduct our clinical trials and manufacture our product candidates; (6) the competition we will face; (7) our ability to protect our intellectual property; (8) our ability to retain key personnel and to manage our growth; (9) the effect of the VOWST sale on our ability to retain and hire key personnel and maintain relationships with our customers, suppliers, advertisers, partners and others with whom we do business, or on our operating results and businesses generally; (10) the risks associated with the disruption of management's attention from ongoing business operations due to the obligation to provide transition services; (11) our failure to receive the installment payments or the milestone payments in the future; (12) the uncertainty of impact of the 50/50 profit and loss sharing arrangement on our reported results and liquidity; and (13) we may not be able to realize the anticipated benefits of the VOWST sale. 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 (SEC), on November 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 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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