Seres Therapeutics Announces Topline Results for SER-287 Phase 2b Study in Mild-to-Moderate Ulcerative Colitis

July 22, 2021

—Primary endpoint of clinical remission compared to placebo was not achieved—

—Both dosing regimens of SER-287 were generally well tolerated—

—Open label and maintenance portions of the SER-287 study will be closed—

— Microbiome endpoints and analyses expected in the second half of 2021—

—Company to host a conference call at 8:30 a.m. ET—

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jul. 22, 2021-- Seres Therapeutics, Inc. (Nasdaq: MCRB), a leading microbiome therapeutics company, today announced topline results from the Phase 2b ECO-RESET study evaluating SER-287 in patients with mild-to-moderate ulcerative colitis (UC). The study did not meet its primary endpoint of improving clinical remission rates compared to placebo. Both dosing regimens of SER-287 were generally well tolerated. Given the lack of a clinical efficacy signal identified in ECO-RESET, the Company has decided to close the open label and maintenance portions of the study.

“While these outcomes were not what we, nor the UC community, were hoping for, we remain committed to leading the creation of a new class of medicines designed to impact how diseases like ulcerative colitis are treated. As with SER-109, we will again follow the science and the data, conduct a rigorous scientific analysis, and determine the optimal path forward for our UC franchise,” said Eric Shaff, Chief Executive Officer at Seres. “We are well resourced and continue to prepare for SER-109 commercialization, in collaboration with Nestlé Health Science, and we are excited about advancing the development of our SER-301 and SER-155 investigational candidates as well as our earlier stage pipeline.”

The primary objective of the induction portion of the Phase 2b study was to evaluate the safety and efficacy of SER-287, after 10 weeks of induction dosing (following vancomycin pre-conditioning) in achieving clinical remission in participants with mild-to-moderate UC. The trial was a randomized, placebo controlled, double blind, parallel group multicenter study which enrolled 203 UC patients in 104 sites throughout the U.S. and Canada. Dosing was explored in two SER-287 cohorts (full induction dose and step-down induction dose) or placebo (randomized 1:1:1). Clinical remission was analyzed and defined by a 3-component modified Mayo Score. No meaningful clinical differences and no statistical significance were observed in absolute clinical remission rates among the three treatment arms (10.3% for the full induction dose, n=68 and 10.6% for the step-down induction dose, n=66 versus 11.6% for placebo, n=69). There were also no meaningful differences observed across the three treatment groups for endoscopic improvement, endoscopic remission or symptomatic remission.

“While the efficacy results in this trial did not meet the pre-defined threshold, we believe this data-rich study, including microbiome analyses expected in the second half of 2021, will provide valuable insights to inform continued development of our pipeline, including SER-301, our next generation investigational candidate for UC,” said Lisa von Moltke, M.D., Chief Medical Officer at Seres. “We are grateful for everyone who made this study possible, including the study investigators, and in particular, the patients and their families."

Treatment emergent adverse events (AEs) were observed in 67.6%, 46.2% and 50.7% of subjects in the induction dose, step-down dose (both of which included six days of oral vancomycin preconditioning) and placebo treatment arms, respectively. The majority of observed AEs were mild or moderate in intensity. The most commonly observed AEs were worsening of UC, diarrhea, nausea and abdominal distension. Four participants on active treatment reported serious treatment emergent adverse events (worsening ulcerative colitis, colonic dysplasia, congestive heart failure with decreased hemoglobin, and appendicitis), as did one on placebo (worsening ulcerative colitis).

The Company continues to advance its SER-301 program currently in a Phase 1b study that is testing the hypothesis that engraftment of drug product species modulates microbe-associated metabolites to reduce intestinal inflammation and improve epithelial barrier integrity in adults with mild-to-moderate UC. The Phase 1b is currently enrolling in Australia and New Zealand.

SER-287 and SER-301 are both consortia of bacteria found in the gastrointestinal tract of healthy individuals. However, important compositional and potential therapeutic differences exist between the investigational drugs. SER-287 is a donor-derived product candidate, whereas SER-301 utilizes Seres’ next generation technology and is based on rationally designed, cultivated consortia of bacteria. The design of SER-301 has leveraged the Company’s reverse translation platforms and capabilities that can evaluate at high resolution how microbes in the gastrointestinal tract are interacting with one another and human cells and tissues to impact disease pathways. The bacteria in SER-301 are targeted at, and specifically selected in, an effort to optimize the reduction of pro-inflammatory activity, improve epithelial barrier integrity and TNF-a driven inflammation in intestinal epithelial cells, and modulate UC-relevant anti-inflammatory, innate and adaptive immune pathways.

Results from the SER-287 ECO-RESET study, including additional efficacy and safety results as well as microbiome analyses, will be submitted for presentation at a future scientific meeting.

As of June 30, 2021, Seres had approximately $229 million in cash, cash equivalents and marketable securities. The June 30, 2021 cash balance does not include the upfront fee of $175 million that has been received by Seres following the SER-109 Co-Commercialization License Agreement

announced on July 1, 2021 with Nestlé Health Science.

About SER-301
SER-301 is a consortium of cultivated bacteria designed using our reverse translational discovery platform that incorporates analysis of microbiome biomarkers from human clinical data and preclinical assessments using human cell-based assays and *in vitro/ex vivo* and *in vivo* disease models. SER-301 is designed to reduce induction of pro-inflammatory activity, improve epithelial barrier integrity and TNF-α driven inflammation in intestinal epithelial cells, or IECs, and modulate UC-relevant anti-inflammatory, innate and adaptive immune pathways. SER-301 is being produced using our advanced fermentation, formulation and delivery platforms. It includes strains delivered in spore form, as well as strains cultivated in non-spore (vegetative) form and delivered using enterically-protected technology designed to release in the colon.

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 is evaluating SER-301 in a Phase 1b study in patients with ulcerative colitis and SER-155 in a Phase 1b study to address 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 without limitation: the potential impact of microbiome therapeutics; the safety, efficacy and regulatory and clinical progress of our product candidates; plans, timing and potential impact of the release of additional preclinical and clinical data, including with respect to the SER-287 microbiome analyses; our development opportunities, including the future of development in UC; 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, 2021, 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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