Seres Therapeutics Reports SER-287 Phase 1b Microbiome Analyses that Provide Mechanistic Support for Clinical Efficacy in Ulcerative Colitis

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- Microbiome analyses demonstrate engraftment of SER-287-derived bacteria; microbiome compositional changes correlate with clinical remission -

- SER-287 engraftment maintained four weeks after completion of dosing -

- Company to discuss proposed SER-287 development plan with FDA and intends to initiate next clinical trial in mid-2018 -

- FDA granted SER-287 Orphan Drug designation for treatment of pediatric UC patients -

- Additional results to be presented at a Webcast 2018 JP Morgan Healthcare conference presentation on Thursday, Jan. 11 at 8:30 a.m. PT -

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jan. 4, 2018-- Seres Therapeutics, Inc., (NASDAQ:MCRB) today announced initial microbiome results from its Phase 1b study of SER-287, a microbiome therapeutic candidate derived from healthy individuals, in patients with mild-to-moderate Ulcerative Colitis (UC) who were failing current therapies. Analyses of study patients' microbiome data, a co-primary study endpoint of the trial, demonstrate that SER-287 induced dose-dependent engraftment of SER-287-derived bacterial species into the colonic microbiome of the patients treated with SER-287. Patients administered vancomycin pre-treatment followed by daily administration of SER-287 had the highest level of SER-287 engraftment, which was statistically significant. This patient cohort corresponded with the study arm where the most significant clinical benefits were observed, including clinical remission and endoscopic improvement. Differences in the composition of the microbiome post treatment were also associated with clinical remission. Bacterial engraftment signatures were durable throughout the dosing period of the trial and were also observed at four weeks post administration of the final SER-287 dose. The SER-287 Phase 1b study microbiome data support the previously reported clinical results.

"These microbiome data provide Seres with important proprietary insights into the mechanisms of action of SER-287 in Ulcerative Colitis and inform the study design of our next SER-287 clinical trial. The SER-287 bacterial signatures identified in humans also provide indispensable clinical insights towards optimizing the composition of SER-301, a rationally designed microbiome therapeutic candidate for UC and other forms of inflammatory bowel disease," said Roger J. Pomerantz, M.D., President, CEO and Chairman of Seres. "We look forward to discussing the SER-287 clinical and microbiome data with the FDA as we move this program forward in clinical development."

SER-287 Phase 1b study design, summary of previously reported clinical results

As reported in October 2017, Seres completed a successful Phase 1b study of SER-287 in patients with mild-to-moderate UC who were failing current therapies. The SER-287 Phase 1b study, a randomized, double-blinded, placebo-controlled, multiple-dose, induction study, enrolled 58 patients with mild-to-moderate UC. Patients were assigned to one of three SER-287 treatment arms or a placebo arm for an eight-week treatment period. SER-287 arms included a daily dosing arm with six days of oral vancomycin pre-treatment, a weekly dosing arm without vancomycin pre-treatment, and a weekly dosing arm with six days of oral vancomycin pre-treatment. Clinical study results demonstrated that SER-287 administration resulted in a dose-dependent improvement of clinical remission rates and endoscopic results. High clinical response placebo rates that were not differentiated from the SER-287 treatment arms were observed. Clinical response is a subjective endpoint and is prone to high variability, as previously observed in several other UC trials of various drug types[1]. In the most recent FDA regulatory guidance, clinical remission, and not clinical response, is recommended as the primary endpoint in UC registrational studies. The SER-287 Phase 1b safety and tolerability profile observed was very favorable.

Seres used stool samples and whole metagenomic sequencing analyses that enable species-level resolution analyses to characterize changes in the gastrointestinal microbiome.

Microbiome study results

Microbiome results demonstrated engraftment of SER-287-derived bacterial species in patients pre-treated with vancomycin who received SER-287. The degree of SER-287 engraftment, as measured by the number of detectable SER-287-derived bacterial species, increased in a dose-dependent manner, with daily dosing providing the most rapid and robust change in patients' microbiome. Engraftment was maintained during the entire dosing period and was observed four weeks after the last dose of SER-287 was administered. Thus, engraftment was durable. Changes in the composition of the gastrointestinal microbiome were associated with clinical remission.

Vancomycin pre-treatment, as compared to placebo pre-treatment, led to an immediate reduction of microbiome diversity followed by rapid and robust engraftment of SER-287-derived bacterial species. These data suggest that vancomycin pre-treatment opens ecological niches for SER-287 engraftment in the human microbiome of patients with UC.

Seres intends to present additional study data in a webcast company presentation at the 2018 JP Morgan Healthcare Conference on Thursday, Jan. 11 at 8:30 a.m. PT. A live audio webcast of the presentation will be available under the "Investors and Media" section of Seres' website. A replay of the presentation will become available approximately one hour after the event and will be archived for 21 days.

About SER-287

SER-287 is a biologically sourced, oral formulation containing a consortium of live bacterial spores that is being developed for Ulcerative Colitis and

other forms of inflammatory bowel disease. The FDA has designated SER-287 as an Orphan Drug for pediatric Ulcerative Colitis. SER-287 is hypothesized to act through a novel mechanism of action by modulating the dysbiotic microbiome, reducing inflammation without immunosuppression effects. A healthy microbiome has been shown to maintain the integrity of the colonic barrier, reduce the signaling by pro-inflammatory molecules produced by certain bacteria, and induce regulatory T cells in the colon to modulate immune responses.[2]

About Ulcerative Colitis

Ulcerative Colitis (UC) is a serious chronic condition affecting approximately 700,000 individuals in the United States. The disease results in inflammation of the colon and rectum and can cause debilitating symptoms, including abdominal pain, bowel urgency, and diarrhea. Severe cases of UC may result in surgical removal of the colon.

About Seres Therapeutics

Seres Therapeutics, Inc., is a leading microbiome therapeutics platform company developing a novel class of biological drugs that are designed to treat disease by restoring the function of a dysbiotic microbiome, where the natural state of bacterial diversity and function is imbalanced. Seres' lead program, SER-109, has obtained Breakthrough Therapy and Orphan Drug designations from the U.S. Food and Drug Administration and is in Phase 3 development for multiply recurrent *C. difficile* infection. Seres' clinical candidate SER-287 has successfully completed a Phase 1b study in patients with mild-to-moderate Ulcerative Colitis and has obtained Orphan Drug designation in pediatric UC. Seres is also developing SER-262, the first-ever synthetic microbiome therapeutic candidate, in a Phase 1b study in patients with primary *C. difficile* infection.

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 statements regarding the release of further data, the potential for SER-287 to treat UC patients, including pediatric UC patients, the timing of discussions with the FDA and the potential approval of SER-287, and the overall development of SER-287.

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; our unproven approach to therapeutic intervention; the lengthy, expensive, and uncertain process of clinical drug development, including potential delays in regulatory approval; 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; our lack of experience in manufacturing, selling, marketing, and distributing our product candidates; orphan drug designation may not lead to faster development; failure to compete successfully against other drug companies; protection of our proprietary technology and the confidentiality of our trade secrets; potential lawsuits for, or claims of, infringement of third-party intellectual property or challenges to the ownership of our intellectual property; our patents being found invalid or unenforceable; risks associated with international operations; our ability to retain key personnel and to manage our growth; the potential volatility of our common stock; our management and principal stockholders have the ability to control or significantly influence our business; and we are currently subject to securities class action litigation. 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 November 8, 2017 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.

References

1. Jairath V. et al., Systematic review and meta-analysis: placebo rates in induction and maintenance trials in ulcerative colitis; Journal of Crohn's and Colitis, 2016
2. Blander JM et al., Regulation of inflammation by microbiota interactions with the host, Nature Immunology, 2017; Lynch S and Pedersen O, The Human Intestinal Microbiome in Health and Disease, The New England Journal of Medicine, 2016.

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