# Seres Therapeutics Reports Positive Topline Results from SER-287 Phase 1b Study in Patients with Ulcerative Colitis

October 2, 2017

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*– No clinically significant safety or tolerability findings were observed –*

*– Company intends to rapidly advance SER-287 to further development for Ulcerative Colitis –*

*– Conference call scheduled for 8 a.m. today –*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 2, 2017-- In the table following the sixth paragraph, the difference from placebo under Clinical Response for Vancomycin/SER-287 Daily is 0.0% and the Placebo/SER-287 Weekly is -17.1% (not -17.1% and 0.0%, respectively).

**SERES THERAPEUTICS REPORTS POSITIVE TOPLINE RESULTS FROM SER-287 PHASE 1B STUDY IN PATIENTS WITH ULCERATIVE COLITIS**

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Seres Therapeutics, Inc., (NASDAQ:MCRB) today announced positive topline results from a SER-287 Phase 1b placebo-controlled induction study in 58 patients with mild-to-moderate Ulcerative Colitis (UC), who were failing current therapies. Study data demonstrate that SER-287, a microbiome therapy containing a consortium of live bacterial spores, resulted in a benefit in clinical remission rates, and also an improvement in mucosal appearance by endoscopy. The SER-287 safety and tolerability profile, a co-primary study endpoint, demonstrated no clinically significant safety findings. Microbiome study results, a co-primary endpoint, are expected in the coming months.

“We are extremely pleased with these SER-287 Phase 1b efficacy and safety study results. The clinical data demonstrate the potential for microbiome therapeutics to provide an effective and safer alternative treatment modality for patients suffering from Ulcerative Colitis,” said Roger J. Pomerantz, M.D., President, Chief Executive Officer and Chairman of Seres. “Based on the strength of these data, Seres intends to work expeditiously to advance SER-287 into more advanced development studies. We plan to further evaluate SER-287 in mild, moderate and severe forms of Ulcerative Colitis, in maintenance after induction therapy, and we also intend to assess development in Crohn’s disease, and pediatric forms of inflammatory bowel disease. We expect to discuss these data with the FDA as soon as possible, to determine the most accelerated path to advance SER-287 development.”

“New treatment modalities are urgently needed that both address the inadequate levels of remission with available Ulcerative Colitis therapies, and have a favorable safety profile. The dose dependent and highly positive clinical remission rates and endoscopic scores from this study are very encouraging. SER-287 may represent an important new treatment option for patients,” said Stephen B. Hanauer, M.D., Professor of Medicine, Gastroenterology and Hepatology, Feinberg School of Medicine at Northwestern University, Chicago, Illinois.

**Study Design**

The SER-287 Phase 1b study, a randomized, double-blinded, placebo-controlled, multiple-dose, induction study enrolled patients with mild-to-moderate Ulcerative Colitis, with Mayo scores of 4 to 10. The study enrolled 58 patients at 20 sites across the United States. Twenty-four patients were classified as having mild disease, and 33 patients had moderate disease. Study subjects exhibited pre-study disease activity despite use of current therapies in a majority of subjects, which included 5-amino-salacylic acid, low dose corticosteroids, or immunomodulatory therapy.

Patients were randomly 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 vancomycin pre-treatment, a weekly dosing arm, and a weekly dosing arm with vancomycin pre-treatment. The co-primary study objectives were to evaluate safety and tolerability, and the change in the microbiome at up to 8 weeks after dosing. The secondary efficacy endpoints included clinical remission rates, endoscopic improvement and clinical response, assessed by a total modified Mayo score and endoscopy, which, of importance utilized a central reader. The Mayo score includes measures of stool frequency, rectal bleeding, the physician’s global assessment, and an endoscopic evaluation. Regulatory guidance from both the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for Ulcerative Colitis, both issued in 2016, recommends the use of clinical remission, including endoscopic improvement, as the primary endpoint in all registrational studies.

**Efficacy and Safety Results**

Study efficacy related analysis is based on intent to treat 'observed case' data in 53 patients. Eight-week results demonstrate that SER-287 administration resulted in a dose dependent improvement of clinical remission rates and an improvement in endoscopic scores. Data suggest that the most significant treatment effect occurred in patients treated with the daily dose of SER-287. Vancomycin addition to the regimen did not clearly alter efficacy effects.

Summary of efficacy results:

| **Endpoint** | **Intent to Treat Population, Observed Case: Treatment Group** | | | |
|---|---|---|---|---|
| | **Placebo / Placebo (N = 10) (%)** | **Vancomycin / SER-287 Daily (N = 15) (%)** | **Placebo / SER-287 Weekly (N = 14) (%)** | **Vancomycin / SER-287 Weekly (N = 14) (%)** |
| **Clinical Remission[1]** | 1/10 (10.0)[4] | **6/15 (40.0)** | 2/14 (14.3) | 3/14 (21.4) |
| Difference from placebo (SER-287 minus placebo) | | **30.0%** | 4.3% | 11.4% |
| **Endoscopic Improvement[2]** | 1/10 (10.0) | **6/15 (40.0)** | 5/14 (35.7) | 4/14 (28.6) |
| Difference from placebo (SER-287 minus placebo) | | **30.0%** | 25.7% | 18.6% |
| **Clinical Response[3]** | 6/10 (60.0) | 9/15 (60.0) | 6/14 (42.9) | 4/14 (28.6) |
| Difference from placebo (SER-287 minus placebo) | | 0.0% | -17.1% | -31.4% |

1. Clinical remission was defined as a total modified Mayo score of less than or equal to 2, and an endoscopic sub-score of 0 or 1.
2. Endoscopic improvement was defined as a decrease in endoscopic sub score of greater than or equal to 1. Endoscopy measures were analyzed by a Central Reader
3. Clinical response was defined as a decrease of 3 or more points in total modified Mayo score from baseline along with either a decrease of greater than or equal to 1 point in the rectal bleeding sub score, or an absolute rectal bleeding sub score of 0 or 1. Clinical response did not require a change in endoscopic score.
4. A patient in the placebo study arm experienced a disease flare and was treated with corticosteroids prior to the end of treatment endoscopy. Endoscopy showed improvement and the patient was assessed as having achieved clinical remission.

Diverse analyses of microbiome data of patients in this trial, a co-primary endpoint, are expected to be completed in the coming months. Three SER-287 drug product lots, based on human donor material obtained from three separate individuals, were used in the Phase 1b study. Microbiome analyses will also be conducted to determine whether there are any recognizable differences in the drivers of response across the drug product lots.

An evaluation of SER-287 safety and tolerability was a co-primary study endpoint. The company believes the SER-287 safety and tolerability profile was very favorable, and study results demonstrated no imbalance in adverse events in SER-287 treated patients, as compared to patients treated with placebo. There were no drug related serious adverse events associated with SER-287.

The Company intends to present detailed study results at a future medical/scientific meeting.

In addition to SER-287, Seres' inflammatory bowel disease microbiome pipeline includes SER-301, a therapeutic candidate comprised of a consortium of rationally selected, fermented bacterial species. The pending SER-287 microbiome data will be used to inform the final composition of SER-301, as the Company plans a SER-301 Investigational New Drug (IND) application.

**Conference Call Information**

Seres management will host a conference call today, October 2, 2017, at 8:00 a.m. ET. A webcast of the conference call, as well as accompanying slides, may be accessed in the Investors & Media section of Seres' website at www.seresherapeutics.com. To participate in the conference call, please dial (844) 277-9450 (domestic) or (336) 525-7139 (international) and provide conference ID number 94507828.

**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. 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.[1]

**About Ulcerative Colitis**

Ulcerative Colitis 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 Ulcerative Colitis 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. 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.

**References**


1. 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.


**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 our plans to rapidly advance the development of SER-287, the conduct and expected timing of microbiome study results related to the SER-287 Phase 1b study, microbiome therapeutics' ability to provide an effective and safer alternative treatment for Ulcerative Colitis, the evaluation and assessment of SER-287 in inflammatory bowel disease, our discussions with the FDA related to SER-287, SER-287 as an important new treatment option for patients, the favorability of the safety and tolerability profile of SER-287, the presentation of detailed study results for SER-287 at a medical/scientific meeting, and plans for an IND application for SER-301.

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, which may not be available; our limited operating history; the unpredictable nature of our early stage development efforts for marketable drugs; the unproven approach to therapeutic intervention of our microbiome therapeutics; the lengthy and expensive process of clinical drug development, which has an uncertain outcome; potential delays in enrollment of patients which could affect the receipt of necessary regulatory approvals; potential delays in regulatory approval, which would impact the ability to commercialize our product candidates and affect our ability to generate revenue; any fast track or Breakthrough Therapy designation may not lead to faster development, regulatory approval or marketing approval; our possible inability to receive orphan drug designation should we choose to seek it; our reliance on third parties to conduct our clinical trials and the potential for those third parties to not perform satisfactorily; our reliance on third parties to manufacture our product candidates, which may delay, prevent or impair our development and commercialization efforts; our lack of experience in manufacturing our product candidates; the potential failure of our product candidates to be accepted on the market by the medical community; our lack of experience selling, marketing and distributing products and our lack of internal capability to do so; failure to compete successfully against other drug companies; potential competition from biosimilars; failure to obtain marketing approval internationally; post-marketing restrictions or withdrawal from the market; antikickback, fraud, abuse, and other healthcare laws and regulations exposing us to potential criminal sanctions; recently enacted or future legislation; compliance with environmental, health, and safety laws and regulations; protection of our proprietary technology; protection of the confidentiality of our trade secrets; changes in United States patent law; potential lawsuits for infringement of third-party intellectual property; our patents being found invalid or unenforceable; compliance with patent regulations; claims challenging the inventorship or ownership of our patents and other intellectual property; claims asserting that we or our employees misappropriated a third-party's intellectual property or otherwise claiming ownership of what we regard as our intellectual property; adequate protection of our trademarks; ability to attract and retain key executives; managing our growth could result in difficulties; risks associated with international operations; potential system failures; the price of our common stock may fluctuate substantially; our executive officers, directors, and principal stockholders have the ability to control all matters submitted to the stockholders; a significant portion of our total outstanding shares are eligible to be sold into the market; unfavorable or lacking analyst research or reports; 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 August 3, 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.

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