Seres Therapeutics Announces Key Findings from SER-109 Phase 2 Study Analyses

January 31, 2017

- Findings suggest that both misdiagnosis of C. difficile recurrent infection in some patients, and dosing that may have been suboptimal in certain patients, contributed to the previously reported SER-109 Phase 2 study outcome -

- FDA discussions are ongoing regarding a new, redesigned clinical study for SER-109 -

- Conference call at 8 a.m. ET today -

CAMBRIDGE, Mass., January 31, 2017 —Seres Therapeutics Inc., (NASDAQ:MCRB), a leading microbiome therapeutics platform company, today reported that it has completed in-depth analyses of the previously reported SER-109 Phase 2, eight-week clinical study data in patients with multiply recurrent *Clostridium difficile* infection. The company also reported the full, 24-week SER-109 Phase 2 study results and open label extension study data.

"Since obtaining the unexpected SER-109 clinical study results last summer, we have undertaken a comprehensive assessment of the program to understand the reasons for the results," said Roger J. Pomerantz, M.D., President, CEO and Chairman of Seres. "We have now identified specific factors that we believe contributed to the Phase 2 results, including issues related to both the accurate diagnosis of *C. difficile* recurrent infection, and potential suboptimal dosing of certain subjects in the trial. The SER-109 analyses were recently shared with the FDA, and we are actively discussing the design of a new clinical trial for SER-109. There remains a compelling need for an effective, safe, and convenient FDA approved therapy for patients with recurrent *C. difficile* infection, and this investigation provides insights to guide further clinical development of SER-109."

Investigation Summary: *C. difficile* Diagnosis

Analysis was conducted to evaluate both the role of *C. difficile* diagnostic testing in defining the correct SER-109 Phase 2 study entry population, and in the proper diagnosis of *C. difficile* recurrences during the study. In the Phase 2 study, 81% of study subjects (72 of 89 subjects) were enrolled based on polymerase chain reaction (PCR) based testing for *C. difficile*, as well as clinical evaluation. An important and increasingly well-appreciated limitation of PCR testing is that while a positive result indicates that *C. difficile* cytotoxin genes are present, a positive PCR test does not necessarily indicate thatthe organism is viable and producing disease causing cytotoxins, nor that *C. difficile* is the source of clinical symptoms.[1]

Two separate observations were made pertaining to the effects of discordant results from PCR and cytotoxin assay on the SER-109 trial. The qualifying stool samples evaluated for Phase 2 study entry were not available for retesting for cytotoxin, however, the company was able to retest the samples associated with patients entering the open label extension trial for the presence of the *C. difficile* cytotoxin and determined that only 44% of samples (15 of 31 subjects) that tested positive by PCR testing also tested positive based on *C. difficile* cytotoxin assay. These results suggest that a substantial proportion of patients who entered the SER-109 Phase 2 study may have been *C. difficile* carriers and, therefore, *C. difficile* infection may not have been the source of the clinical symptoms. In addition, data from this analysis suggest that the use of PCR to measure *C. difficile* may have overestimated study recurrences in both treatment arms of the Phase 2 trial, further complicating interpretation of study results. This was shown by reanalysis of samples with cytotoxin assay, from patients diagnosed as recurrent in the Phase 2 study. In this retesting, between one quarter andone half of presumed study recurrences may not have been true *C. difficile* infections leading to pathology.

From the analyses described above, the company believes that misdiagnoses may have occurred both in some patients entering the SER-109 trial, as well as for recurrences diagnosed during the trial.

SER-109 Pharmacokinetics, Pharmacodynamics, & Dosing

The company performed an in-depth analysis to examine SER-109 biological activity in the Phase 2 trial, as measured by microbiome changes in patients and downstream biological effects in the gastrointestinal tract. Results demonstrated a statistically significant increase in the richness of commensal spore-forming bacterial species in patients treated with SER-109, as compared to those receiving placebo. These data demonstrate that SER-109 successfully engrafted and was biologically active in the Phase 2 study. In addition, among those patients with an increased prevalence of specific SER-109 associated bacterial species, a decreasedrate of high confidence recurrences (i.e., recurrences confirmed by *C. difficile* cytotoxin assay) was demonstrated.

The company also assessed whether the SER-109 dose impacted the degree ofmicrobiome changes observed. All Phase 2 patients received 1×10^8 bacterial spores, whereas patients in the prior SER-109 Phase 1b open label study received doses ranging approximately 700-fold, from 3×10^7 to 2×10^9 spores. The company also performed high-resolution whole metagenomics sequencing of stool samples collected from patients in both the SER-109 Phase 1b, as well as the Phase 2 trial as part of this analysis. The analysis indicated that subjects in the open-label Phase 1b study who received a higher dose achieved a significantly greater increase in diversity of commensal spore-former bacteria by 1 week post-treatment, as compared to both Phase 1b and Phase 2 subjects treated with lower doses. These results suggest that the dose used in the SER-109 Phase 2 study may have been suboptimal in certain patients, and may have resulted in a less robust drug effect, contributing to decreased efficacy in Phase 2, as compared to the Phase 1b study.

Much of the SER-109 Phase 2 microbiome-related learnings are based on advancements in the computational analytics and higher resolution whole metagenomics sequencing techniques that Seres is pioneering, and several of these methods were developed after the SER-109 Phase 2 study was

designed. Insights obtained from this work may also benefit Seres' broad preclinical and clinical microbiome development pipeline.

Analysis of SER-109 Phase 2 Study Clinical Drug Product

The company also conducted a thorough and detailed investigation of the potential impacts of manufacturing and formulation changes implemented in the Phase 2 study. No issues regarding product quality or formulation were identified which would have impacted the Phase 2 study results.

Summary of SER-109 24-Week and Open Label Extension Study Results

The full, 24-week Phase 2 study results continue to demonstrate that SER-109 was generally well tolerated. The most common adverse events associated with SER-109 included diarrhea, abdominal pain and flatulence. The Phase 2 study population represented older individuals, many in poor health, and a high rate of serious adverse events (SAEs) was reported in both study arms. A numerically higher rate of SAEs was observed in the SER-109 arm (15.0% versus 10.3% for placebo), however there was no detectable pattern in the SAEs observed, and none of these were considered to be SER-109 drug-related by the study investigators.

As expected with recurrent *C. difficile* infection, relatively few additional recurrences occurred beyond 8 weeks, and the 24-week data provides relatively little new information regarding efficacy. Based on 24-week data, five further patients recurred in the SER-109 arm, but three of the five recurrences (60%) were in patients who terminated the trial early, resulting in an imputed recurrence. In the placebo arm, one patient also terminated the trial early, resulting in an imputed recurrence. Early terminations, and loss of patients to follow-up, are common in the long safety follow-up portions of clinical trials.

Phase 2 study subjects who experienced a *C. difficile* recurrence had the option to enroll in an open label extension study, where they were treated with SER-109 and were followed for an additional 24 weeks. In total, 34 patients entered the open label extension study and 11 patients recurred during the initial 8-week study period, a 32% recurrence rate.

Conference Call Information

Seres' management will host a conference call today, January 31, 2017, at 8:00 a.m. ET. To access the conference call, please dial 844-277-9450 (domestic) or 336-525-7139 (international) and reference the conference ID number 62194071. To join the live webcast and access slides to accompany the conference call, please visit the "Investors and Media" section of the Seres website at www.serestherapeutics.com . A webcast replay and the accompanying slides will be available on the Seres website beginning approximately two hours after the event and will be archived for 30 days.

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. The Phase 2 study of Seres' program SER-109 has been completed in multiply recurrent *C. difficile* infection. Seres' second clinical candidate, SER-287, is being evaluated in a Phase 1b study in patients with mild-to-moderate ulcerative colitis (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. For more information, please visit www.serestherapeutics.com. Follow us on Twitter @SeresTx.

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 SER-109 development plans, the timing, design, and potential results of a new clinical study for SER-109, the potential for a redesigned trial to provide different results, and the impact any analysis may have on clinical outcomes.

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; anti-kickback, 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 November 10, 2016 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.

Reference:

1. Polage, C. R., et al. (2015). Overdiagnosis of *Clostridium difficile* Infection in the Molecular Test Era. JAMA Internal Medicine, 175(11), 1792–1801.

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