**CONFERENCE CALL SCRIPT**

**Fourth Quarter 2020 Earnings Conference Call**

**March 2, 2020**

**Carlo Tanzi, Ph.D.**

Thank you and good morning. Our press release with the company's fourth quarter 2020 financial results and a business update became available at 7:00 a.m. Eastern Time this morning, and can be found on the Investors & Media section of the company's website.

I'd like to remind you that we will be making forward-looking statements relating to the timing, enrollment, and results of our clinical studies, potential regulatory approval, and the promise and potential impact of our microbiome therapeutics. Actual results may differ materially. Additionally, these statements are subject to certain risks and uncertainties, which are discussed under the Risk Factors section of our recent SEC filings. Any forward-looking statements made on today's call represent our views as of today only. We may update these statements in the future, but we disclaim any obligation to do so.

On today's call, with prepared remarks, I'm joined by President and Chief Executive Officer, Eric Shaff; Chief Medical Officer, Dr. Lisa von Moltke; and Chief Scientific Officer, Dr. Matt Henn. Dr. Terri Young, Chief Commercial and Strategy Officer, and Dr. David Ege, Chief Technology Officer, will also be available for Q&A.

With that, I'll pass the call over to Eric.

**Eric Shaff:**

Thank you, Carlo, and good morning everyone.

2020 was a pivotal year for Seres as we moved an important step closer to realizing our goal of translating microbiome insights into an entirely new class of medicines. The year was highlighted by positive data from our Phase 3 SER-109 ECOSPOR III study in patients with recurrent *C. difficile* infection, marking our transition towards becoming a fully integrated commercial organization.

Since then, we have been taking actions necessary to file a SER-109 BLA submission and preparing for a successful commercial launch following an FDA approval. As an organization, our top priority right now is to obtain the required SER-109 safety database by completing our ongoing open-label study.

We are also continuing supportive market assessment work, including primary research with physicians and payers, and pricing and reimbursement analyses. Furthermore, we have been scaling our market education efforts, including the hiring and training of an MSL team.

We recognize that as we are working in an entirely new field of medicine, there is understandably a knowledge gap in the healthcare community regarding the broad and important role of the microbiome in human health and disease. We are looking forward to continuing to engage with patient groups, physicians, and payers to educate the market about the substantial value of our microbiome therapeutic approach.

We have also made strides to increase our drug supply capacity. Our SER-109 process is already at commercial scale, and we have activities underway to expand our production capacity with the goal of ensuring that we are able to meet future commercial demand, and assume rapid and broad uptake into the recurrent CDI population , as well as support our expanding clinical trial activity.

In addition to SER-109, we are advancing a pipeline of additional investigational microbiome therapeutics led by SER-287, our Phase 2b candidate for ulcerative colitis. SER-287 has the potential to transform the management of this disease, intended to provide an effective alternative treatment approach that is well tolerated and is not immunosuppressive. We are pleased to report today that the SER-287 Phase 2b study has achieved target enrollment of 201 patients, and we look forward to reporting topline data in mid-year.

With that, I'll now turn the call over to Lisa.

**Lisa von Moltke:**

Thanks, Eric and good morning everyone.

I'll begin with a review of our SER-109 program.

Last summer, we reported topline interim results from the ECOSPOR III Phase 3 study that demonstrated SER-109 met the study's primary efficacy endpoint in patients with recurrent C difficile infection, showing a substantial absolute reduction of recurrent infection compared to placebo at 8 weeks post-treatment.

We have subsequently obtained ECOSPOR III data through the final 24-week timepoint. These results reflect the final categorization of all subjects in the protocol-specified intent-to-treat population following study completion and full unblinding. This completed analysis reflected minimal changes from the Interim analysis, and demonstrated a remarkable sustained clinical response rate of approximately 88% at eight weeks post-treatment. The primary endpoint showed an absolute reduction of recurrence of CDI of 27% compared to placebo at 8 weeks post-treatment, which is a relative risk reduction of 69%. Study results show that SER-109 administration resulted in similar efficacy when examined by groups stratified by age, or by the prior antibiotic therapy. Additionally, the data demonstrate that SER-109 efficacy is maintained over the duration of the 24-week study.

From a tolerability perspective, we were also extremely pleased with the Phase 3 study data. We observed a highly favorable safety profile, with SER-109 adverse events being similar to placebo.

The need for an approved new therapeutic approach, with a favorable safety profile, is highlighted by the recent announcement from a major stool bank stating that it plans to halt operations.

We believe our SER-109 Phase3 data represent a substantial advancement over the standard of care, with the potential to transform how CDI is managed. Furthermore, we believe that SER-109 has the

potential to improve treatment of CDI, a disease that results in the death of over 20,000 people in the U.S. each year.

In October of last year, we presented our preliminary SER-109 Phase 3 study results at the American College of Gastroenterology Annual Scientific Meeting, and we plan to present additional data at medical meetings later this year.

In January, we participated in the Keystone Symposium presenting mechanistic support for the efficacy observed in the Phase 3 study, and Matt will discuss those data in more detail.

We look forward to submitting the remarkable SER-109 Phase 3 study results for this novel treatment modality to a leading journal for publication.

Importantly, SER-109 ECOSPOR III study results far exceeded the efficacy threshold communicated to us by the FDA, and we expect this single study to provide the efficacy basis for a SER-109 BLA filing. The FDA position is at least 300 patients will be required for a SER-109 safety database to support the BLA, and we continue to enroll our ongoing SER-109 open-label study in patients with recurrent CDI. We expect this study to fulfill the remainder of our required safety database. We continue to make progress, activating new clinical sites across the U.S. and Canada.

Next let's turn to our ongoing SER-287 Phase IIb study in patients with mild to moderate ulcerative colitis. SER-287 is an orally administered drug candidate comprised of commensal bacterial spores isolated from the healthy human gastrointestinal tract. Our objective with SER-287 is to develop a first-in-class microbiome therapeutic that modulates the microbiome and microbiome-associated metabolites to treat ulcerative colitis. We believe that SER-287 may provide a much-needed non-immunosuppressive treatment option for UC. SER-287 is intended to reduce the impact of a disrupted microbiome as both a trigger and an amplifier of inflammation. We believe that SER-287 has the potential to be used as both a monotherapy and potentially also in combination with other approved agents.

Data from the Phase 1b study demonstrated that SER-287 administration was associated with high rates of clinical remission, endoscopic improvement, modulation of the gastrointestinal microbiome, and a favorable safety profile. These results and data supporting the underlying mechanisms of action were recently highlighted as the cover article in the January 2021 print edition of the peer-reviewed journal, *Gastroenterology*.

To remind you, the SER-287 Phase 2b ECO-RESET study is a randomized, placebo-controlled, 3-arm induction trial designed to enroll 201 patients with active, mild to moderate ulcerative colitis who have failed prior therapy. In Arm A, patients receive a short course of vancomycin preconditioning followed by 10 weeks of the same daily regimen that was used in the arm of the previous 1B study that showed the highest clinical remission rate. In Arm B, patients receive vancomycin preconditioning followed by 2 weeks of the same SER-287 daily regimen used in Arm A, followed by 8 weeks of a lower dose. In Arm C, patients receive placebo.

As Eric mentioned, we have achieved target enrollment, with several patients remaining in the screening process. And in an acceleration of our previous expectations, we now expect topline study results from ECO-RESET in mid-2021.

As a well-designed and meaningfully-sized Phase 2b study, we expect to learn a great deal from the trial. Clinically, our primary objective is to demonstrate that SER-287 results in a significantly higher rate of patients achieving clinical remission than those administered placebo. We believe that the safety profile of our microbiome therapeutic approach, based on commensal healthy bacteria, is a major advantage and anticipate that the safety profile of SER-287 will be highly favorable, particularly as compared with the current standard of care which can be immunosuppressive. We expect that if we are able to achieve this clinical profile, and with an orally-administered therapy, SER-287 would represent a highly attractive new medicine with the potential for wide adoption. With this targeted product profile, SER-287 has the potential to provide mild-to-moderate UC patients, representing a majority of all UC patients, with an effective treatment option that is not immunosuppressive.

The SER-287 study will also be important to inform our broader, multi-product and longer-term efforts to develop transformative new medicines for inflammatory bowel disease and more broadly,

modulating host immunity. The development of the microbiome therapeutic field remains in its adolescence, and as a learning, data-driven, science-based organization, we expect that Seres will gain important insights both from our pending Phase 2b clinical data and from mechanistic data coming later this year, that could inform the further development of SER-287, as well as that of SER-301 and other future compositions designed to modulate host inflammation and immune pathway signaling.

With that, I'll now turn the call over to Matt.

**Matt Henn:**

Thank you, Lisa, and good morning, everyone.

Seres continues to invest significantly in our reverse translational discovery and development platforms that can delineate at high-resolution microbiome biomarkers from human clinical data and integrate these data with preclinical assessments using human cell-based assays and in vitro, ex vivo, and in vivo disease models to evaluate drug mechanism of action and to design consortia of bacteria with specific pharmacological properties. We reported earlier this year at the Keystone Microbiome Symposium on SER-109 Phase 3 predefined microbiome readouts that confirmed the drug candidates' mechanisms of actions. The Phase 3 study data demonstrate that SER-109 bacterial species rapidly engraft into the gastrointestinal tract. Engraftment was observed as early as one-week post-treatment and found to be durable through 24 weeks. The presence of SER-109 bacteria was significantly greater in subjects that received SER-109 versus Placebo and all differences were maintained in all subpopulation analyses. SER-109 administration also rapidly shifted the gastrointestinal metabolic landscape, including a significant decrease in primary bile acids and an increase in secondary bile acids, providing a mechanistic basis for both the inhibition of *C. difficile* spore germination and vegetative growth. Notably, in early timepoint samples, *C. difficile* and other bacterial pathogens known to harbor antibiotic resistant genes were significantly more prevalent in Placebo treated subjects. These data confirm observations from Seres' prior trials that SER-109 resulted in a reduction of other clinically relevant bacterial pathogens. The detailed mechanistic learnings we have obtained from SER-109, combined with our ability to link these learnings to clinical outcomes, and confirm observations in human subjects in a nonclinical setting to demonstrate causality has proven immensely beneficial, and we are already applying this knowledge to the design of future planned microbiome therapeutic compositions.

Moving now to our SER-301 program. SER-301 is a next-generation, orally dosed, rationally designed, cultivated microbiome therapeutic candidate for the treatment of ulcerative colitis. The consortia of bacteria in SER-301 is designed to modify the microbiome and microbe-associated metabolites in the gastrointestinal tract to reduce the presence of proinflammatory bacteria and modulate pathways linked to gastrointestinal inflammation and epithelial barrier integrity in patients with ulcerative colitis.

SER-301 was designed using Seres' reverse translation discovery and development platforms. The design incorporated learnings from the SER-287 Phase 1B study related to the bacterial species and the microbiome functional signatures associated with clinical efficacy. Additionally, the design incorporated insights on the engraftment dynamics of different bacteria and also the association of specific bacteria with the modulation of inflammatory and immune pathways in human subjects that have been observed across our broader clinical portfolio and confirmed using our nonclinical human-cell based assays and in vivo models. In November of 2020, we announced the dosing of the first patient in our SER-301 Phase 1B study in adults with mild to moderate ulcerative colitis and enrollment is ongoing.

The study is being conducted in Australia and New Zealand a target enrollment 65 patients in total. The objectives for the study are to evaluate drug safety and pharmacokinetics, and further to evaluate clinical remission and other measures of efficacy as secondary endpoints. The Data Safety Monitoring Board recently reviewed preliminary safety data from the first set of patients enrolled, and we are encouraged to see that drug tolerability has been favorable.

Turning to our Phase 1b study for SER-401. SER-401 is an orally administered microbiome therapeutic candidate, comprised of bacteria associated with response to checkpoint inhibitor immunotherapy.
Our objective with SER-401 is to enhance the efficacy of approved immunotherapies by modulating the patient's immune response to these medicines. As we have previously discussed, the SER-401 study has been impacted by COVID-19 and enrollment has therefore been slower than anticipated. We are currently evaluating our SER-401 development plans with our study collaborators, the Parker Institute for Cancer Immunotherapy and MD Anderson Cancer Center.

Moving now to SER-155. SER-155 is an orally dosed, rationally designed, cultivated microbiome therapeutic candidate designed to prevent mortality due to gastrointestinal bacterial infections and bacteremia and graft versus-host disease in immunocompromised patients, in patients receiving allogeneic hematopoietic stem cell transplantation. SER-155 builds on our expertise in both infectious disease and immunology and is designed to both prevent bacterial infections, particularly those that harbor antibiotic resistance genes, and the onset of GvHD autoimmune disease.

The SER-155 program is supported by a CARB-X grant that provides financial and operational support. We are making continued progress advancing SER-155 into the clinic, in collaboration with our partners at Memorial Sloan Kettering Cancer Center, and we expect to submit an IND during the first half of this year.

We continue to resource our microbiome pipeline in a number of indications beyond both SER-155 and SER-301, which over time will serve as a product engine for our growing commercial organization. Our clinical programs and our reverse translation discovery platforms continue to provide meaningful insight and knowledge into the underlying mechanisms by which microbes in the GI tract engage pathogenic bacteria and human cells and tissues to impact disease. Moreover, advances in Seres microbial cultivation and bioprocessing know-how and commercial scale GMP capabilities continue to advance and broaden access to the diversity of microbes in the human GI that can be harnessed in potential new product candidates and development programs.

With that, I'll now turn the call back to Eric.

**Eric Shaff:**

Thank you, Matt.

Our fourth quarter and full year P&L financials are included in this morning's press release, so I won't reiterate them here. Seres ended the year 2020 with approximately $303.4 million in cash, cash equivalents and short and long-term investments.

We enter 2021 in a position of strength, and poised for growth as we continue to advance our pipeline and transition to a fully integrated commercial organization. Seres is building upon our microbiome platform leadership position, and driving forward a multi-product clinical pipeline that is led by SER-109. We believe that our SER-109 ECOSPOR III results provide validation and support for the broader Seres pipeline and our capabilities in this new area of medicine. Seres has advanced, non-commoditized, unique platforms that are being deployed for the development of microbiome therapeutics. These technologies, and our proprietary scientific insights, have already generated a pipeline of promising microbiome therapeutic candidates, each targeting a serious medical condition, and each providing the potential to fundamentally transform how diseases are treated.

Our top priority is preparing for a high quality BLA submission for SER-109 as well as readying the Company for a successful commercial launch for what we expect will be the first FDA approved microbiome product. We are continuing to advance what we believe to be a highly promising pipeline, led by SER-287. In addition, we intend to continue to invest in core microbiome drug discovery and CMC capabilities to ensure that Seres is well-positioned to continue to lead the microbiome therapeutics field in these important areas.

We expect 2021 to be an eventful year for the company. We are looking forward to:

- continued enrollment in our SER-109 open label study and progress with pre-commercial activities;
- top-line results from the SER-287 Phase 2b study;
- advancement of our multiple earlier stage clinical programs; and
- further strengthening our microbiome platform capabilities, enabling us to bring the next wave of therapeutic candidates into the clinic.

Seres has a strong and experienced team in place, and are working with urgency to achieve our goals and fulfill our mission of transforming the lives of patients worldwide with revolutionary microbiome therapeutics. We look forward to keeping you informed on our progress.

With that, Operator, we'll now open up the call to questions.