Seres Therapeutics Reports First Quarter 2021 Financial Results and Provides Business Updates

May 4, 2021

– Topline clinical data from SER-287 Phase 2b study in patients with mild-to-moderate ulcerative colitis expected in mid-2021, microbiome biomarker data anticipated in H2 2021 –

– Ongoing enrollment in SER-109 open label study for recurrent C. difficile infection; On track to achieve 300 subject enrollment target in Q3 2021 –

– Virtual ulcerative colitis microbiome therapeutic investor event to be held June 21, 2021 –

– Conference call at 8:30 a.m. ET today –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 4, 2021-- Seres Therapeutics, Inc., (Nasdaq: MCRB), a leading microbiome company developing a novel class of multifunctional bacterial therapeutics designed to functionally interact with host cells and tissues to treat disease, today reported first quarter 2021 financial results and provided business updates.

"We continue to make steady progress across our broad microbiome pipeline and we look forward to an eventful remainder of the year with important clinical milestones," said Eric Shaff, President and Chief Executive Officer of Seres. "Our SER-287 ECO-RESET Phase 2b study in mild-to-moderate ulcerative colitis patients is fully enrolled and we anticipate topline clinical results in mid-year. Following successful SER-109 Phase 3 pivotal results in patients with recurrent *C. difficile* infection, we continue to enroll an open label study to expand our safety database. We are very pleased with the pace of study enrollment and we anticipate achieving target enrollment during the third quarter of 2021. Completion of the required SER-109 safety database will support a Biologics License Application (BLA) filing, and potentially pave the way for SER-109 to become the first-ever FDA-approved microbiome therapeutic."

Program and Corporate Updates

SER-109 Phase 3 ECOSPOR III study in recurrent *C. difficile* infection: SER-109, an investigational oral, live microbiome therapeutic, achieved a high rate of sustained clinical response in Seres' Phase 3 clinical trial in patients with recurrent *C. difficile* infection (CDI).

In August 2020, Seres announced positive topline interim results from the SER-109 Phase 3 study, ECOSPOR III. The Phase 3 study (ClinicalTrials.gov identifier: NCT03183128) was a multicenter, randomized, placebo-controlled study that enrolled 182 patients with multiply recurrent CDI. Patients were randomized 1:1 to receive either SER-109 or placebo after standard of care antibiotic treatment. Study results demonstrated that ECOSPOR III achieved the study's primary endpoint at eight weeks and demonstrated a sustained clinical response rate of approximately 88% at eight weeks post-treatment. SER-109 resulted in a 27% absolute reduction of recurrence of CDI compared to placebo at eight weeks post-treatment, which is a relative risk reduction of 68%. SER-109 was well tolerated, with no treatment-related serious adverse events (SAEs) observed in the active arm and an adverse event profile comparable to placebo. In addition, subsequent 24-week end-of-study data indicate that the clinical effect of SER-109 is durable.

Following the topline Phase 3 study results, the FDA reaffirmed its prior position regarding the efficacy requirements to support a SER-109 BLA submission, which were exceeded by the positive SER-109 ECOSPOR III study results, as well as its prior position that the safety database should be at least 300 subjects. Seres believes that ECOSPOR III will be a single pivotal efficacy study supporting product registration and expects to reach target enrollment for the safety database study in the third quarter of 2021.

In January 2021, Seres presented Phase 3 microbiome and metabolomic endpoint data at the Keystone Symposium, which provide mechanistic support for the SER-109 efficacy observed. The 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 was durable through eight weeks, confirming the biological activity of SER-109. SER-109 administration was also observed to 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 inhibition of *C. difficile* spore germination and vegetative growth.

Seres is conducting an ongoing SER-109 open-label study in patients with recurrent CDI (ClinicalTrials.gov identifier: NCT03183128), which also admits patients with a single recurrence of CDI, to expand the SER-109 safety database. The SER-109 open label study is being enrolled at more than 100 sites across the U.S. and Canada, representing a substantial increase over those that recruited subjects into the SER-109 Phase 3 ECOSPOR III study. Additional information is available at serescdiffstudy.com.

Seres continues to execute activities necessary to enable a SER-109 BLA submission. The Company is completing supportive market assessment work, including primary research with physicians and payers, and pricing and reimbursement analyses. Seres continues to hire, train, and deploy a medical science liaison team in order to increase market education efforts. The Company believes that a substantial commercial opportunity exists for SER-109. The recurrent CDI population includes approximately 170,000 patients in the U.S.

SER-287 Phase 2b ECO-RESET study in ulcerative colitis (UC): SER-287, an oral microbiome therapeutic candidate consisting of a bacterial consortium, is designed to restructure the gastrointestinal microbiome and reduce inflammation in individuals with UC. Seres has obtained FDA Fast Track designation for SER-287 in active mild-to-moderate ulcerative colitis. SER-287 targets restructuring the microbiome to reduce proinflammatory activity and modulate UC-relevant inflammatory pathways, potentially providing a much-needed non-immunosuppressive treatment option to patients suffering from ulcerative colitis. SER-287 has the potential to be used as both a monotherapy and in combination with other approved agents.

The SER-287 Phase 2b ECO-RESET study is a randomized, placebo-controlled, three-arm induction trial that has enrolled 203 patients with active mild-to-moderate ulcerative colitis who have had inadequate response or loss of response on prior therapy. In arm A, patients receive a short course of vancomycin preconditioning followed by ten weeks of the same daily regimen used in the arm of the Phase 1b trial that showed the highest clinical remission rate. In arm B, patients receive vancomycin preconditioning followed by two weeks of the SER-287 daily regimen as in the first arm, followed by eight weeks of a lower dose of SER-287. In arm C, patients receive placebo. The study's primary endpoint is the proportion of patients achieving clinical remission at ten weeks. The study will assess endoscopic improvement as a secondary endpoint, as well as a range of microbiome and metabolomic measures.

Seres has completed enrollment in the SER-287 Phase 2b ECO-RESET induction study in patients with active mild-to-moderate ulcerative colitis and expects to report topline clinical study results in mid-2021, with additional microbiome biomarker data becoming available in H2 2021.

Publication of SER-287 Phase 1b study results: Data from a 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 tolerability profile. The paper, titled "A Phase 1b Safety Study of SER-287, a Spore-Based Microbiome Therapeutic, For Active Mild-To-Moderate Ulcerative Colitis," was published as the highlighted cover article in the January 2021 print edition of the leading journal *Gastroenterology*.

SER-301 Phase 1b study in adults with mild-to-moderate ulcerative colitis: Seres is enrolling its Phase 1b study for SER-301, an investigational oral, rationally-designed, cultivated microbiome therapeutic, and study enrollment is ongoing. SER-301 is being evaluated in a Phase 1b study in adults with mild-to-moderate ulcerative colitis. The study is being conducted in Australia and New Zealand and is designed to enroll approximately 65 subjects. The study objectives are to evaluate drug safety and pharmacokinetics and to evaluate clinical remission and other measures of efficacy as secondary endpoints.

The consortia of bacteria in SER-301 is designed to modify the microbiome and microbe-associated metabolites in the gastrointestinal tract 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 December 2020, Seres received a $10 million milestone payment associated with the Phase 1b SER-301 clinical study initiation from Nestlé, the Company's ex-North American collaborative partner for this program.

SER-155 Phase 1b clinical study activities: SER-155 is an investigational oral, rationally-designed, cultivated microbiome therapeutic designed to reduce the incidence of gastrointestinal infections, bacteremia, and graft versus host disease (GvHD) in immunocompromised patients, including patients receiving allogeneic hematopoietic stem cell transplantation. SER-155 is a consortium of bacterial species selected using microbiome biomarker data and from human clinical data and nonclinical human cell-based assays and in vivo disease models. The composition aims to decrease infection and translocation of antibiotic-resistant bacteria in the gastrointestinal tract and modulate host immune responses to decrease GvHD.

The SER-155 program is supported by a CARB-X grant. Seres continues to advance SER-155 toward a Phase 1b clinical study initiation in collaboration with Memorial Sloan Kettering Cancer Center.

SER-401 program update: Seres, in collaboration with study partners, The Parker Institute for Cancer Immunotherapy and The University of Texas MD Anderson Cancer Center, had announced the voluntary discontinuation of further enrollment in the Melanoma Checkpoint and Gut Microbiome Alteration With Microbiome Intervention (MCGRAW) study evaluating the safety and drug activity of SER-401 or fecal microbiota transplant (FMT) in combination with nivolumab in patients with metastatic melanoma. Seres has deprioritized further development of SER-401, and will prioritize rationally-designed, cultivated leads designed using the Company's reverse translational platforms and learnings from the SER-401 trial. Future oncology programs aim to modulate host immunity/inflammation to improve response and tolerability of cancer drugs.

Upcoming investor event: Seres plans to hold a webcast and conference call on June 21, 2021 with a focus on the Company's efforts to develop microbiome therapeutics for ulcerative colitis and the substantial opportunity for safe, effective alternative therapeutics for the over 700,000 individuals (U.S. estimate) suffering from UC. The event will include discussion of the ongoing SER-287 Phase 2b study, and SER-301 Phase 1b study. The Company anticipates topline SER-287 Phase 2b study clinical results in mid-2021, and additional microbiome biomarker data in H2 2021. Further details will be provided closer to the event.

Financial Results

Seres reported a net loss of $35.5 million for the first quarter of 2021, as compared with a net loss of $19.9 million for the same period in 2020. The first quarter net loss was driven primarily by clinical and development expenses, personnel expenses and ongoing development of the Company's microbiome therapeutics platform.

Research and development expenses for the first quarter of 2021 were $29.3 million, compared with $21.7 million for the same period in 2020. The research and development expenses were primarily related to Seres' late stage SER-109 and SER-287 clinical development programs.

General and administrative expenses for the first quarter of 2021 were $11.7 million, compared with $6.1 million for the same period in 2020. General and administrative expenses were primarily due to headcount, professional fees and facility costs.

Seres ended the first quarter of 2021 with approximately $272.5 million in cash, cash equivalents and short and long-term investments.

Conference Call Information

Seres' management will host a conference call today, May 4, 2021, at 8:30 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 9967338. To join the live webcast, please visit the "Investors and News" section of the Seres website at www.serestherapeutics.com.

A webcast replay will be available on the Seres website beginning approximately two hours after the event and will be archived for at least 21 days.

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' SER-287 program has obtained Fast Track and Orphan Drug designations from the FDA and is being evaluated in a Phase 2b study in patients with active mild-to-moderate ulcerative colitis. Seres is evaluating SER-301 in a Phase 1b study in patients with ulcerative colitis, and SER-155 to prevent mortality due to 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 the potential market for SER-109, the timing of study enrollment, the impact of the microbiome and metabolomic data on our other programs, the potential approval of SER-109 and its potential status as a first-in-class therapeutic, the timing of topline results and microbiome analysis from the SER-287 study, the safety results observed to-date in our clinical studies, the promise of our microbiome therapeutics, our development plans, the potential impact of the COVID-19 pandemic, and other statements that are not historical facts.

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 and manufacture our product candidates, if approved; our ability to retain key personnel and to manage our growth; and our management and principal stockholders have the ability to control or significantly influence our business. These and other important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K filed with the Securities and Exchange Commission, or SEC, on March 2, 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.

SERES THERAPEUTICS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share data)

	March 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 66,579	$ 116,049
Short term investments	176,221	137,567
Prepaid expenses and other current assets	6,574	5,774
Accounts receivable	2,604	9,387
Total current assets	251,978	268,777
Property and equipment, net	13,580	13,897
Operating lease assets	8,386	9,041
Restricted investments	1,400	1,400
Long term investments	29,749	49,825
Other non-current assets	602	—
Total assets	$ 305,695	$ 342,940
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 4,879	$ 4,018
Accrued expenses and other current liabilities	13,153	14,226
Operating lease liabilities	5,250	5,115
Short term portion of note payable, net of discount	3,339	454
Deferred revenue - related party	21,242	22,602
Total current liabilities	47,863	46,415
Long term portion of note payable, net of discount	21,872	24,639
Operating lease liabilities, net of current portion	9,194	10,561
Deferred revenue, net of current portion - related party	82,284	85,572
Other long-term liabilities	777	1,003
Total liabilities	161,990	168,190
Commitments and contingencies		

Stockholders' deficit:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized at March 31, 2021 and December 31, 2020; no shares issued and outstanding at March 31, 2021 and December 31, 2020	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at March 31, 2021 and December 31, 2020; 91,588,264 and 91,459,239 shares issued and outstanding at March 31, 2021 and December 31, 2020, respectively	92	91
Additional paid-in capital	727,869	723,482
Accumulated other comprehensive (loss)	(15)	(47)
Accumulated deficit	(584,241)	(548,776)
Total stockholders' equity	143,705	174,750
Total liabilities and stockholders' equity	$ 305,695	$ 342,940

SERES THERAPEUTICS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share data)

	Three Months Ended March 31,	
	2021	**2020**
Revenue:		
Collaboration revenue - related party	$ 4,648	$ 5,462
Grant revenue	1,070	739
Collaboration revenue	—	1,988
Total revenue	5,718	8,189
Operating expenses:		
Research and development expenses	29,303	21,743
General and administrative expenses	11,741	6,138
Total operating expenses	41,044	27,881
Loss from operations	(35,326)	(19,692)
Other (expense) income:		
Interest income	966	159
Interest expense	(696)	(716)
Other (expense) income	(409)	368
Total other (expense) income, net	(139)	(189)
Net loss	$ (35,465)	$ (19,881)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.39)	$ (0.28)
Weighted average common shares outstanding, basic and diluted	91,527,800	70,821,514
Net loss	(35,465)	(19,881)
Other comprehensive income (loss):		
Unrealized gain (loss) on investments, net of tax of $0	32	(10)
Total other comprehensive income (loss)	32	(10)
Comprehensive loss	$ (35,433)	$ (19,891)

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