Seres Therapeutics Reports Fourth Quarter and Full Year 2021 Financial Results and Provides Business Updates

March 1, 2022

– SER-109 Phase 3 study results in recurrent C. difficile infection published in New England Journal of Medicine

– Biologics License Application (BLA) filing for SER-109 anticipated in mid-2022 –

– Investor webcast highlighted the broad potential of microbiome therapeutics as a novel approach for Infection Protection in medically compromised individuals –

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

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 1, 2022-- Seres Therapeutics, Inc. (Nasdaq: MCRB), a leading microbiome therapeutics company, today reported fourth quarter and full year 2021 financial results and provided business updates.

“The progress made throughout 2021 has set the stage for an exciting year ahead for Seres, highlighted by the anticipated BLA filing for SER-109 with the U.S. Food and Drug Administration (FDA) for recurrent *C. difficile* infection (rCDI) in mid-2022 which, if approved, we expect to be the first ever microbiome therapeutic” said Eric Shaff, Chief Executive Officer at Seres. “In collaboration with Nestlé Health Science, we are executing on our plans for a successful SER-109 product launch. Together, we are committed to bringing this potentially transformative therapeutic option to patients suffering with rCDI.”

“As highlighted during our recent investor event, we are also advancing our earlier stage efforts in Infection Protection, including the recently initiated SER-155 Phase 1b study to evaluate safety and efficacy in individuals undergoing allogeneic hematopoietic stem cell transplantation. We believe that our microbiome approach has the potential to result in transformative new medicines for Infection Protection, a therapeutic category in great need of innovation,” continued Mr. Shaff.

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 its primary endpoint of superiority to placebo in reducing CDI recurrence in a Phase 3 clinical trial in patients with rCDI. The Company continues to prepare for a BLA filing with the FDA.

Seres has achieved target enrollment in its open-label study of SER-109 in patients with rCDI (ClinicalTrials.gov identifier: NCT03183141), which also admits patients with a single recurrence of rCDI, to expand the SER-109 safety database. Based on FDA commentary, Seres believes the ECOSPOR III efficacy results should support a BLA filing as a single pivotal study. Seres intends to finalize a BLA submission, including data from the open-label study, in mid-2022.

While executing multiple activities necessary to support the BLA submission, Seres is also preparing for a successful product launch with Aimmune, the division within Nestlé Health Science leading commercialization efforts. The Company believes that a substantial commercial opportunity exists for SER-109. The cost of a patient with recurrence of CDI has been estimated to result in approximately $34,000 in annual direct healthcare expenses; this does not include the substantial indirect costs associated with this disease. There are approximately 170,000 cases of rCDI annually in the U.S. and CDI results in over 20,000 deaths.

In January 2022, the *New England Journal of Medicine (NEJM)* published data from the SER-109 Phase 3 ECOSPOR III study evaluating SER-109 for the treatment of rCDI. The publication highlights key results including that SER-109 was superior to placebo in reducing CDI recurrence, with 88% of SER-109 patients achieving a sustained clinical response compared to 60% on placebo. SER-109 was well tolerated, with a side effect profile comparable to placebo and no serious drug-related adverse events observed.

In November 2021, the Company initiated a SER-109 expanded access program at various sites across the U.S. The program is designed to enable eligible adults with rCDI to obtain access to SER-109 prior to a potential FDA product approval.

In October 2021, Seres announced the presentation of an exploratory analysis of its SER-109 Phase 3 ECOSPOR III study at the American College of Gastroenterology 2021 Annual Meeting. Data demonstrate that SER-109 reduced the risk of rCDI, as compared to subjects administered placebo, in individuals with risk factors for recurrence, including those taking acid-reducing medications such as proton pump inhibitors and H2 blockers.

In November 2021, Seres announced a collaboration with Bacthera, a specialized contract development and manufacturing organization to manufacture SER-109, Seres’ lead product candidate for rCDI. The collaboration is designed to expand upon existing production capacity to meet demand growth beyond the initial phase of an anticipated product launch.

SER-155 Phase 1b clinical study activities: In December 2021, Seres announced the enrollment of the first patient in the Company’s Phase 1b clinical study of SER-155 designed to evaluate safety, microbiome alterations, and the impact on infections and/or graft versus host disease (GvHD) associated with SER-155 in adult subjects who are undergoing allogeneic hematopoietic stem cell transplantation (allo-HSCT). The study is currently being conducted with Memorial Sloan Kettering Cancer Center and the University of Chicago.

SER-155 is an investigational oral, rationally designed, cultivated microbiome therapeutic designed to reduce the incidence of gastrointestinal infections, bloodstream infections, and graft versus host disease (GvHD) in patients receiving allo-HSCT. SER-155 is a consortium of bacterial species selected using Seres' reverse translation discovery and development platforms. The design incorporates microbiome biomarker data from human clinical data and nonclinical human cell-based assays and in vivo disease models. The SER-155 composition aims to decrease infection and translocation of antibiotic-resistant bacteria in the gastrointestinal tract and modulate host immune responses to decrease GvHD. In addition to SER-109, SER-155 represents Seres' second active development program in its Infection Protection franchise.

Infection Protection Investor Event: In January 2022, Seres held a webcast event that highlighted development of microbiome therapeutics as a novel approach for Infection Protection in medically compromised individuals. Building upon SER-109, and in addition to SER-155, Seres is also evaluating additional preclinical stage programs in indications such as cancer neutropenia, solid organ transplant, and antimicrobial resistant infections more broadly.

Ulcerative colitis (UC) development efforts: In July 2021, Seres announced topline results from the Phase 2b ECO-RESET study evaluating SER-287, a donor-derived investigational microbiome therapeutic candidate, in patients with mild-to-moderate UC. The study did not meet its primary endpoint of improving clinical remission rates compared to placebo. Both dosing regimens of SER-287 were generally well tolerated. In December 2021, Seres announced preliminary microbiome drug pharmacology analyses from the study. Engraftment of SER-287 bacteria was statistically significant in patients receiving SER-287 versus placebo ($p \leq 0.001$ at all timepoints), however, unlike the Phase 1b study, anticipated changes in disease-relevant metabolites post-administration with SER-287 in the Phase 2b study were not observed. As previously reported, SER-287 Phase 2b clinical and microbiome data suggest that there may be an opportunity to utilize biomarker-based patient selection in future UC development efforts.

Seres has completed preliminary data analysis data from the first cohort of the SER-301 Phase 1b study in subjects with mild-to-moderate UC, which included 15 subjects. Evaluation of the first cohort data by an independent Data Safety Monitoring Board indicated that it would be safe to proceed to the placebo-controlled second cohort. While clinical efficacy was not a defined endpoint in the first cohort, evaluation of outcome data indicated that no subjects achieved clinical remission as defined by the FDA using the Three-Component Modified Mayo Score after 10 weeks of treatment, though there were improvements in one or more individual components, (endoscopic, stool frequency and rectal bleeding sub scores) in some patients.

SER-301 led to modulation of the metabolic landscape in the gastrointestinal tract, including in short-chain and medium-chain fatty acids, tryptophan-derived metabolites, bile acids, and other microbe-associated metabolites, as well as host metabolites associated with a non-disease state. SER-301 strains were observed to engraft in subjects across the trial period. The degree of metabolic changes observed following SER-301 administration appeared to be dependent on the baseline metabolic profile of the study subjects, providing support for the potential for microbiome therapeutics to be developed in biomarker-identified UC patient subpopulations.

The SER-287 and SER-301 clinical and drug pharmacology data sets obtained to date provide a robust set of insights into the role of the microbiome in UC, and Seres continues to conduct analyses of data from our SER-287 and SER-301 programs to inform next steps for further development.

Appointment of Executive Vice President, Chief People Officer: In February 2022, Seres announced that Paula Cloghessy joined Seres, bringing more than 20 years of human resources expertise with broad business experience. She most recently served as Chief People Officer at Translate Bio, Inc., where she led the talent architecture and people strategy. She previously served as vice president of human resources at Joule Unlimited Technologies, Inc. She has also held human resources positions at Interleukin Genetics, Inc. and NUCRYST Pharmaceuticals, Inc.

Financial Results

Seres reported a net loss of $65.6 million for the full year of 2021, as compared to a net loss of $89.1 million for the prior year. Seres reported a net loss of $50.0 million for the fourth quarter of 2021, as compared to a net loss of $18.3 million for the same period in 2020.

Research and development expenses for the fourth quarter of 2021 were $36.8 million, as compared to $24.9 million for the same period in 2020. The research and development expenses were primarily related to Seres' late-stage SER-109 clinical development program and manufacturing costs, as well as personnel expenses.

General and administrative expenses for the fourth quarter were $20.5 million, as compared to $10.6 million for the same period in the prior year. General and administrative expenses were primarily related to personnel expenses, professional fees, including SER-109 commercial readiness and pre-launch expenses, and facility costs.

Seres amended its debt financing agreement with Hercules Capital in February 2022, providing the Company with an additional $50 million in capital, for up to $100 million in total. Upon closing, Hercules advanced $50 million to the Company under the facility, of which $22.1 million was previously outstanding, resulting in proceeds of $27.6 million, net of fees and expenses. The Company will make interest only payments through December 31, 2023, extendable to December 31, 2024 with SER-109 approval. There are two subsequent tranches of $25 million each, one of which becomes available to the Company upon the FDA's approval of the BLA for SER-109 by December 15, 2023 and the second of which becomes available upon the satisfaction of certain conditions, including Hercules' investment committee approval.

Seres ended the 2021 year with approximately $291.2 million in cash, cash equivalents and short and long-term investments as compared with approximately $353.2 million at the end of the third quarter 2021.

Conference Call Information

Seres' management will host a conference call today, March 1, 2022, 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 6277858. 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 to reduce the recurrence of *C. difficile* infection and has potential to become a first-in-class FDA-approved microbiome therapeutic. Seres is evaluating SER-301 in a Phase 1b study in patients with ulcerative colitis and SER-155 in a Phase 1b study in patients receiving allogeneic hematopoietic stem cell transplantation to reduce incidences of gastrointestinal infections, bloodstream infections and graft-versus-host disease as well as additional preclinical stage programs targeting Infection Protection in medically compromised patients.

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 approval of SER-109 and its status as a first-in-class therapeutic, the timing of a BLA filing, the market for SER-109, and our capacity for commercial supply of SER-109; the anticipated indication and potential impact of infection protection microbiome therapeutics; the ability to utilize biomarker-based patient selection in UC development; plans, timing and potential impact of the release of additional preclinical and clinical data; our development opportunities, including the future of development in UC; the ultimate safety and efficacy data for our products; the potential of microbiome therapeutics to treat and prevent disease; the safety, efficacy and regulatory and clinical progress of our product candidates; the potential benefits of our collaborations; and other statements which are not historical fact.

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, manufacture our product candidates and develop and commercialize our product candidates, if approved; and our ability to retain key personnel and to manage our growth. 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, 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.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share data)

	December 31,	
	2021	**2020**
Assets		
Current assets:		
Cash and cash equivalents	$ 180,002	$ 116,049
Short term investments	110,704	137,567
Prepaid expenses and other current assets	12,922	5,774
Accounts receivable	—	9,387
Total current assets	303,628	268,777
Property and equipment, net	17,938	13,897
Operating lease assets	18,208	9,041
Restricted cash	8,000	—
Restricted investments	1,401	1,400
Long term investments	495	49,825
Other non-current assets	5,189	—
Total assets	$ 354,859	$ 342,940
Liabilities and Stockholder's Equity		
Current liabilities:		
Accounts payable	$ 13,735	$ 4,018
Accrued expenses and other current liabilities (1)	45,094	14,226
Operating lease liabilities	6,610	5,115
Short term portion of note payable, net of discount	—	454
Deferred revenue - related party	16,819	22,602
Total current liabilities	82,258	46,415
Long term portion of note payable, net of discount	24,643	24,639
Operating lease liabilities, net of current portion	17,958	10,561
Deferred revenue, net of current portion - related party	86,998	85,572
Other long-term liabilities (2)	11,495	1,003
Total liabilities	223,352	168,190
Commitments and contingencies		
Stockholders' equity:		

Preferred stock, $0.001 par value; 10,000,000 shares authorized at December 31, 2021 and 2020; no shares issued and outstanding at December 31, 2021 and 2020	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at December 31, 2021 and 2020; 91,889,418 and 91,459,239 shares issued and outstanding at December 31, 2021 and 2020	92	91
Additional paid-in capital	745,829	723,482
Accumulated other comprehensive loss	(60)	(47)
Accumulated deficit	(614,354)	(548,776)
Total stockholders' equity	131,507	174,750
Total liabilities and stockholders' equity	$ 354,859	$ 342,940

[1] Includes related party amounts of $21,098 and $0 at December 31, 2021 and December 31, 2020, respectively

[2] Includes related party amounts of $10,585 and $0 at December 31, 2021 and December 31, 2020, respectively

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

	Year Ended December 31,		
	2021	**2020**	**2019**
Revenue:			
Collaboration revenue - related party	$ 143,857	$ 11,897	$ 27,188
Grant revenue	1,070	4,157	1,102
Collaboration revenue	—	17,161	6,215
Total revenue	144,927	33,215	34,505
Operating expenses:			
Research and development expenses	$ 141,891	$ 90,570	$ 80,141
General and administrative expenses	69,261	30,775	24,748
Collaboration (profit) loss sharing - related party	(1,732)	—	—
Restructuring expenses	—	—	1,492
Total operating expenses	209,420	121,345	106,381
Loss from operations	(64,493)	(88,130)	(71,876)
Other (expense) income:			
Interest income	2,870	946	1,033
Interest expense	(2,910)	(2,924)	(502)
Other (expense) income	(1,045)	981	1,066
Total other (expense) income, net	(1,085)	(997)	1,597
Net loss	$ (65,578)	$ (89,127)	$ (70,279)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.72)	$ (1.12)	$ (1.24)
Weighted average common shares outstanding, basic and diluted	91,702,866	79,789,220	56,649,220
Other comprehensive loss:			
Unrealized loss on investments, net of tax of $0	(12)	(47)	—
Currency translation adjustment	(1)	—	—
Total other comprehensive loss	(13)	(47)	—
Comprehensive loss	$ (65,591)	$ (89,174)	$ (70,279)

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