Revive Therapeutics Provides Update on FDA Phase 3 Clinical Trial for Bucillamine in COVID-19 with Plans on Emergency Use Access

TORONTO, Dec. 23, 2020 -- Revive Therapeutics Ltd. ("Revive" or the "Company") (CSE: RVV, USA: RVVTF), a specialty life sciences company focused on the research and development of therapeutics for medical needs and rare disorders, is pleased to announce an update on the Company's U.S. Food & Drug Administration ("FDA") Phase 3 clinical trial (the "Study") to evaluate the safety and efficacy of Bucillamine in patients with mild to moderate COVID-19. The Company is on pace to meet its enrollment goals for the Independent Data and Safety Monitoring Board ("DSMB") to review the safety and efficacy data from the 210 patients as part of the first interim analysis of patients treated and followed up for 28 days after randomization.

The Company's clinical safety team has actively monitored the ongoing interim data of patients and found there have been no safety concerns and no severe adverse events during the interim analysis enrollment period. In the event of any serious safety concerns, the DSMB would be notified to determine any risks and provide its recommendations. To date, there have been no serious safety concerns that required the DSMB to be notified.

There are currently nine clinical sites participating in the Study with an additional six more clinical sites joining the Study in January to satisfy the overall enrollment goal of up to 1,000 patients.

Further to the DSMB review and recommendations on the interim analysis periods, the Company aims to file for an Emergency Use Authorization ("EUA") of Bucillamine for mild to moderate COVID-19 with the FDA. In November 2020, the FDA also issued an EUA to permit the emergency use of bamlanivimab (manufacturer Eli Lilly) and the combination of casirivimab and imdevimab (manufacturer Regeneron) for the treatment of mild to moderate COVID-19.

A recently published study, titled "Thiol-based drugs decrease binding of SARS-CoV-2 spike protein to its receptor and inhibit SARS-CoV-2 cell entry" from the University of California San Francisco, shows that thiol-based drugs, like Bucillamine, decrease the binding of SARS-CoV-2 spike protein to its receptor, decrease the entry efficiency of SARS-CoV-2 spike pseudotyped virus, and inhibit SARS-CoV-2 live virus infection. The findings uncovered a vulnerability of SARS-CoV-2 to thiol-based drugs and provide rationale to test thiol-based drugs as novel treatments for COVID-19. Bucillamine, a cysteine derivative with two thiol groups, has been shown to be 16 times more potent as a thiol donor in vivo than N-acetyl-cysteine. Bucillamine has a well-known safety profile with over 30 years of use as a treatment for rheumatoid arthritis in Japan and South Korea.

"We are pleased with the progress we have made to date in our Phase 3 clinical trial with the potential for Bucillamine to become the first orally administered drug to obtain emergency use access from the FDA and also potentially providing another therapeutic option for healthcare professionals to use in treating mild to moderate COVID-19," said Michael Frank, CEO of Revive.

About the Phase 3 Clinical Trial (ClinicalTrials.gov Identifier: NCT04504734)

The Phase 3 confirmatory clinical trial titled, "A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Study of Bucillamine in Patients with Mild-Moderate COVID-19", will enroll up to 1,000 patients that will be randomized 1:1:1 to receive Bucillamine 100 mg three times a day ("TID"), Bucillamine 200 mg TID or placebo TID for up to 14 days. The primary objective is to compare the frequency of hospitalization or death in patients with mild-moderate COVID-19 receiving Bucillamine therapy with those receiving placebo. The primary endpoint is the proportion of patients meeting a composite endpoint of hospitalization or death from the time of the first dose through Day 28 following randomization. Efficacy will be assessed by comparing clinical outcomes (death or hospitalization), disease severity using the 8-category NIAID COVID ordinal scale, supplemental oxygen use, and progression of COVID-19 between patients receiving standard-of-care plus Bucillamine (high dose and/or low dose) and patients receiving standard-of-care plus placebo. Safety will be assessed by reported pre-treatment adverse events and treatment-emergent adverse events (including serious adverse events and adverse events of special interest), laboratory values (hematology and serum chemistry), vital signs (heart rate, respiratory rate, and temperature), and peripheral oxygen saturation.

An interim analysis will be performed by an Independent Data and Safety Monitoring Board ("DSMB") after 210 patients have been treated and followed up for 28 days after randomization. The DSMB is independent from the Company, the investigators of the Study, or anyone involved in the clinical care of the Study subjects and oversees the safety of participating patients by reviewing the Study's accumulating safety and efficacy data for Bucillamine. The better performing Bucillamine dose at the interim analysis will be selected and patients will then be randomized 2:1 to the selected Bucillamine dose or placebo. Additional interim analyses will be performed after 400, 600, and 800 patients have reached this same post-treatment timepoint. The independent DSMB will actively monitor interim data for the ongoing safety of patients and will recommend continuation, stopping or changes to the conduct of the study based on the interim analysis reports.

Scientific Rationale of Bucillamine for COVID-19

Preclinical and clinical studies have demonstrated that reactive oxygen species contribute to the destruction and programmed cell death of pulmonary epithelial cells.[3] N-acetyl-cysteine (NAC) has been shown to significantly attenuate clinical symptoms

in respiratory viral infections in animals and humans, primarily via donation of thiols to increase antioxidant activity of cellular glutathione.[4-7] In addition, it was found that thiol-based drugs decrease binding of SARS-CoV-2 spike protein to its receptor, decrease the entry efficiency of SARS-CoV-2 spike pseudotyped virus, and inhibit SARS-CoV-2 live virus infection.[8] Bucillamine (N-(mercapto-2-methylpropionyl)-l-cysteine) has a well-known safety profile and is prescribed in the treatment of rheumatoid arthritis in Japan and South Korea for over 30 years. Bucillamine, a cysteine derivative with two thiol groups, has been shown to be 16 times more potent as a thiol donor in vivo than NAC.[2] The drug is non-toxic with high cellular permeability. The basis of the clinical study will analyze if Bucillamine has the potential, via increasing glutathione activity and other antioxidant and anti-inflammatory activity, to lessen the destructive consequences of SARS-CoV2 infection in the lungs and attenuate the clinical course of COVID-19.

The Company is not making any express or implied claims that its product has the ability to eliminate or cure COVID-19 (SARS-2 Coronavirus) at this time.

About Revive Therapeutics Ltd.

Revive is a life sciences company focused on the research and development of therapeutics for infectious diseases and rare disorders, and it is prioritizing drug development efforts to take advantage of several regulatory incentives awarded by the FDA such as Orphan Drug, Fast Track, Breakthrough Therapy and Rare Pediatric Disease designations. Currently, the Company is exploring the use of Bucillamine for the potential treatment of infectious diseases, with an initial focus on severe influenza and COVID-19. With its recent acquisition of Psilocin Pharma Corp., Revive is advancing the development of Psilocybin-based therapeutics in various diseases and disorders. Revive's cannabinoid pharmaceutical portfolio focuses on rare inflammatory diseases and the company was granted FDA orphan drug status designation for the use of Cannabidiol (CBD) to treat autoimmune hepatitis (liver disease) and to treat ischemia and reperfusion injury from organ transplantation. For more information, visit **www.ReviveThera.com**.

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