Revive Therapeutics Announces Submission of Investigational New Drug Application (IND) with U.S. FDA for Phase 3 Confirmatory Study for Bucillamine in COVID-19

TORONTO, June 30, 2020 -- Revive Therapeutics Ltd. ("Revive" or the "Company") (CSE: RVV), a specialty life sciences company focused on the research and development of therapeutics for medical needs and rare disorders, is pleased to announce it has submitted today its Investigational New Drug ("IND") application to the U.S. Food and Drug Administration ("U.S. FDA") for a Phase 3 confirmatory study for Bucillamine as a potential treatment in COVID-19. Once the U.S. FDA allows the IND to go into effect, Revive will initiate a randomized, double-blind, placebo-controlled study of Bucillamine in patients with mild-moderate COVID-19 in Q3-2020.

"We are very pleased in achieving this major milestone of filing our IND for a Phase 3 confirmatory study to evaluate Bucillamine in the treatment of patients with mild-moderate COVID-19, which was based on the recommendation from the U.S. FDA from our pre-IND meeting earlier this year," said Michael Frank, Revive's Chief Executive Officer. "We are preparing plans for initiating the Phase 3 study upon the IND becoming active by the U.S. FDA and we look forward to advancing Bucillamine as a potential new treatment option for patients with a confirmed diagnosis of COVID-19 globally."

Phase 3 Confirmatory Clinical Study Design

The Phase 3 confirmatory clinical study titled, "A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Study of Bucillamine in Patients with Mild-Moderate COVID-19", will enroll up to 800 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 frequency of hospitalization and mortality in patients with mild-moderate COVID-19 receiving Bucillamine therapy with those receiving placebo. The primary endpoint is the proportion of patients with the following outcomes attributed to COVID-19 from time of the first dose through Day 28 following randomization: death, alive and hospitalized, and alive and not hospitalized. Efficacy will be assessed by comparison of clinical outcome (death and hospitalization), disease severity using the eight-category National Institute of Allergy and Infectious Diseases ("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 incidence and severity of 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 a total of 28 days after randomization. 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 300, 400, 500, 600, and 700 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 pulmonary inflammation, cytokine dysregulation, and acute lung injury.[1] 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[2,3,4,5]. 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 [6]. Bucillamine 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 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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References

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