



Revive Therapeutics Explores the Use of Bucillamine as a Novel Treatment for Infectious Diseases including COVID-19

TORONTO, March 20, 2020 -- Revive Therapeutics Ltd. ("Revive" or the "Company") (CSE: RVV), a life sciences company, is pleased to announce that it is exploring the use of the drug Bucillamine as a potential novel treatment for infectious diseases including influenza and the coronavirus disease (COVID-19). The Company has applied for a provisional patent with the U.S. Patent and Trademark Office entitled "Use of Bucillamine in the Treatment of Infectious Diseases" (Serial No. 62/991,996).

"Revive was founded on the premise of finding new uses for known drugs, and we are expanding on our rich product portfolio to target infectious diseases such as the coronavirus disease or COVID-19," said Michael Frank, Revive's Chief Executive Officer. "Revive has a history in the clinical development with Bucillamine in the treatment of acute gout flares and cystinuria, and we will advance our efforts in reviving and exploring new uses of Bucillamine for unmet medical needs."

Revive has explored the use of Bucillamine in the treatment of acute gout flares and has completed a Phase 2 study in the U.S. under its Investigational New Drug ("IND") application that was accepted by the U.S. Food and Drug Administration ("FDA"). Also, the Company explored the use of Bucillamine in the treatment of cystinuria where it has received FDA orphan drug status and its IND was accepted by the FDA to conduct a Phase 2 study in the U.S.

Scientific Rationale for the Investigation of Bucillamine to Treat Infectious Diseases including Influenza or COVID-19

Current antiviral interventions for influenza have exhibited modest efficacy, especially in improving mortality in at-risk populations, such as the elderly.^{1,2} Novel antivirals have been plagued by poor oral bioavailability and lack of efficacy when not delivered early.¹ This is because these drugs mostly act to prevent the early processes of virus binding to cells or viral replication.² Thiols, particularly N-acetylcysteine (NAC), with antioxidant and reducing activity have been investigated as effective therapies that abrogate the potential for influenza to cause severe disease.^{3,4,5} Restoration of glutathione, the major intracellular thiol antioxidant, is a critical functional activity of NAC.⁶ Reactive oxygen species (ROS) generation during influenza virus infection aggravate destructive inflammation and programmed death of epithelial cells.⁷ Studies in human cells and animal models have shown that NAC works to prevent acute lung injury caused by influenza virus infection through inhibition of these ROS-mediated mechanisms.^{4,7} NAC has been investigated clinically and found to significantly attenuate clinical symptoms associated with influenza infection, especially in elderly at-risk patients.⁵ While NAC is easily taken up by cells and has low toxicity, clinical efficacy has required long-term and high-dose administration because of modest relative potency, limiting its clinical applicability.

Bucillamine (N-(mercapto-2-methylpropionyl)-l-cysteine), which has a well-known safety profile and is prescribed in the treatment of rheumatoid arthritis in Japan and South Korea for over 30 years, is a cysteine derivative with 2 thiol groups that is 16-fold more potent than NAC as a thiol donor in vivo, giving it vastly superior function in restoring glutathione and therefore greater potential to prevent acute lung injury during influenza infection.⁸ Bucillamine has also been shown to prevent oxidative and reperfusion injury in heart and liver tissues⁸ and is highly cell permeable for efficient delivery into cells.^{8,9} Bucillamine has unrealized potential for the treatment of influenza with both proven safety and proven mechanism of action similar to that of NAC, but with much higher potency, mitigating the previous obstacles to using thiols therapeutically. It is also reasonable to hypothesize that similar processes related to ROS are involved in acute lung injury during nCov-19 infection, possibly justifying the investigation of bucillamine as an intervention for COVID-19.

Revive is developing a product and clinical development plan intending to unlock the full potential of Bucillamine. The Company will announce its initiatives as they unfold.

About Revive Therapeutics Ltd.

Revive is a company focused on the research, development and commercialization of novel psychedelic and cannabinoid-based life sciences products and drug repurposing for infectious diseases. Revive's technology is being advanced to fill the medical needs for diseases and disorders such as pain, inflammation, and wound care. Revive's cannabinoid pharmaceutical portfolio focuses on rare inflammatory areas such as liver disease. The Company was granted FDA orphan drug status designation for the use of CBD to treat auto-immune hepatitis (liver disease) and FDA orphan drug status designation for the use of CBD to treat ischemia and reperfusion injury from organ transplantation. With its recent acquisition of Psilocin Pharma Corp., Revive will advance Psilocybin-based therapeutics in various diseases and disorders and will prioritize 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. The Company is also exploring the use of Bucillamine for the potential treatment of infectious diseases.

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