Revive Therapeutics Announces Strategic Focus on Bucillamine for Infectious Diseases and Medical Countermeasures

TORONTO, Sept. 18, 2024 -- Revive Therapeutics Ltd. (“Revive” or the “Company”) (OTCQB: RVVTF) (CSE: RVV) (FRANKFURT:31R), a specialty life sciences company focused on the research and development of therapeutics for infectious diseases and medical countermeasures, announced today its strategic focus on dedicating its resources to advancing the clinical development of Bucillamine, an oral thiol-based drug with anti-inflammatory and antiviral properties. The Company has decided not to pursue the development of the Long COVID diagnostic product.

The Company will be focusing on the following programs with Bucillamine for infectious diseases and medical countermeasures:

Nerve Agent Exposure

Nerve agents are chemicals that affect the nervous system. Nerve agents are highly toxic regardless of the route of exposure. The main chemical nerve agents that are man-made and manufactured for use in chemical warfare are sarin, soman, tabun and VX. These nerve agents are known to be present in military stockpiles. Exposure to nerve agents can occur due to chemical warfare or accidental release from a military storage facility. Exposure to nerve agents can cause tightness of the chest, excessive salivation, abdominal cramps, diarrhea, blurred vision, tremors, and death.

Currently, in partnership with Defence R&D Canada – Suffield Research Centre (“DRDC”), an agency of the Canadian Department of National Defence, the Company is evaluating Bucillamine as a potential treatment for nerve agent exposure. DRDC is investigating pharmacological compounds that can mitigate nerve agent induced brain injury. Recent studies have shown that antioxidant compounds such as n-acetylcysteine (“NAC”) could be beneficial in limiting seizure activity and improving the anticonvulsant efficacy of GABA-mediating drugs such as diazepam.

Bucillamine is a significantly more effective antioxidant than NAC and has the potential to provide increased efficacy against seizure activity while limiting the anticoagulant and bleeding event liability observed with NAC. The overall objective of the research project is to investigate pharmacological means for neuroprotection of GABA(A) receptors, which are required for the effectiveness of currently fielded anticonvulsant therapies. Bucillamine and NAC will be evaluated to determine the effect on GABA(A) receptor endocytosis and the effect on diazepam effectiveness in terminating seizures. Any additional antioxidant effects on seizure activity and survival will also be assessed.

The results from this research partnership, if promising, will determine further studies to facilitate FDA and Health Canada approvals for the use of Bucillamine in nerve agents or organophosphate pesticide poisoning. Also, the Company may explore the potential of Bucillamine for traumatic brain injury caused by concussive or explosive forces.

The research study is progressing and is expected to be now completed in October 2024.

Emerging Infections

The results from the DRDC research study, if promising, may determine further studies for the potential use of Bucillamine in various viral infections, including monkeypox (“Mpox”).

In 2023, the World Health Organization released a Mpox fact sheet suggesting that severe cases of Mpox result in a number of conditions, including inflammation of the brain, heart, rectum, genital organs and urinary passages.[1]

A study in 2022 made the link between the administration of antioxidants and the improvement of virus-induced effects or to reduce viral replication yield. The suggestion that strong antioxidants such as N-acetyl-L-cysteine (“NAC”), butylated hydroxyanisole or Terameprocol could have an effect on Mpox viral infection in humans to ease severe symptoms.[2] 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.[3-6]

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.[7]

Long COVID

The CDC estimates that 7.5 percent of U.S. adults have long COVID symptoms.[8] David Cutler, PhD, a professor of economics at Harvard University, estimates in a recent research disclosure that the total economic cost of long COVID could be as much as $3.7 trillion.[9]

Currently, the Company is exploring the use of Bucillamine as a potential treatment for long COVID by leveraging the published research and data from its previous Phase 3 clinical trial. Per the results of the Type C meeting written responses

received by the Company from the U.S. Food & Drug Administration ("FDA") for the evaluation of a proposed clinical study of Bucillamine as a potential treatment for Long COVID, the FDA has recommended that the evaluation of Bucillamine for Long COVID be submitted as a new Investigational New Drug ("IND") application and may cross-reference applicable sections from the Company's current IND, that evaluated the safety and efficacy of Bucillamine in patients with mild to moderate COVID-19 in the Phase 3 clinical trial. In addition, the FDA provided valuable feedback on the appropriate design, study population, and safety and efficacy measures for assessing a therapeutic benefit in patients with Long COVID.

The Company is finalizing the proposed Phase 2 study protocol for submission to the FDA. It expects to submit it by the end of 2024. The proposed Phase 2 clinical study is expected to be approved by the FDA in Q1-2025.

As a background, on July 6, 2023, the Company announced the results of its Study evaluating the safety and efficacy of oral Bucillamine in patients with mild to moderate COVID-19. Under the Study's primary endpoint, the proportion of patients meeting a composite endpoint of hospitalization or death from time of first dose through Day 28 following randomization, there were no deaths and four hospitalizations, of which three were from the placebo arm and one from the Bucillamine low dose group (300mg/day). No hospitalizations occurred in the Bucillamine large dose group (600mg/day). The Company evaluated certain Study endpoints, including the COVID-19 clinical symptoms data (i.e. cough, fever, heart rate, and oxygen saturation). Based on preliminary analyses, the data demonstrated that for patients with oxygen saturation <96% at baseline, Bucillamine had a 29.1% improvement over placebo in time to normal oxygen saturation (SpO2). Additional analyses of the Study data may suggest Bucillamine's potential for long COVID.

A study titled, "Thiol-based drugs decrease binding of SARS-CoV-2 spike protein to its receptor and inhibit SARS-CoV-2 cell entry", showed 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. These findings uncovered a vulnerability of SARS-CoV-2 to thiol-based drugs and provided a rationale to test thiol-based drugs such as Bucillamine as novel treatments for COVID-19.

The Company would like to make it clear that it is not making any express or implied claims that its product (Bucillamine) has the ability to treat, eliminate or cure long COVID, Monkeypox (Mpox) and/or other infectious diseases and medical countermeasures indications at this time.

About Revive Therapeutics Ltd.

Revive Therapeutics is a life sciences company focused on the research and development of therapeutics for infectious diseases and medical countermeasures. Revive prioritizes its drug development efforts to take advantage of several regulatory incentives awarded by the FDA, such as Emergency Use Authorization, Orphan Drug, Fast Track, and Breakthrough Therapy designations. Currently, the Company is exploring the use of Bucillamine for the potential treatment of nerve agent exposure and long COVID. Revive is also advancing the development of Psilocybin-based therapeutics through various programs. For more information, visit www.ReviveThera.com.

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