Revive Therapeutics Provides Corporate Update

TORONTO, March 12, 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 medical needs and rare disorders, announced today a corporate update on the research, clinical and regulatory initiatives with Bucillamine and its long COVID diagnostic product.

Bucillamine

The Company is advancing the research and development of Bucillamine, an oral thiol-based drug with anti-inflammatory and antiviral properties, as a potential treatment for long COVID and medical countermeasures, such as nerve agent exposure.

Chemical Warfare - 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 project is expected to be completed by June 2024.

Long COVID

The CDC estimates that 7.5 percent of U.S. adults have long COVID symptoms[1]. 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[2].

Currently, the Company is exploring the use of Bucillamine as a potential treatment for long COVID. The Company is advancing the clinical development of Bucillamine by leveraging the published research and data from its previous Phase 3 clinical trial (the “Study”) in preparing a regulatory and clinical package that includes a proposed Phase 2 clinical study for long COVID to present to the FDA and international health regulatory authorities.

The Phase 2 study protocol has been completed, and the Company is preparing its submission to the FDA. It expects to submit it by the end of March 2024. The proposed Phase 2 clinical study is expected to be approved by the FDA in Q2-2024.

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.

In addition, Revive may evaluate the potential of its proposed long COVID diagnostic product as a companion to Bucillamine.

Long COVID Diagnostic Product

The Company, under its wholly-owned subsidiary Revive Diagnostics Inc., is advancing the product development of a potential blood biomarker diagnostic that characterizes long COVID. The discovery of the biomarkers identified by a research team at Lawson, led by Dr. Douglas Fraser, was recently published in the journal, Molecular Medicine[3].

The Company entered into a license agreement with Lawson Health Research Institute for the worldwide exclusive rights to the intellectual property of novel blood biomarkers that characterize long COVID. The intellectual property includes PCT/CA2023/050145 entitled “Blood Biomarkers in Long-COVID19”; PCT/CA2023/051292 entitled “Biomarkers in Long-COVID19”; and US Provisional Patent Application No. 63/433,425 entitled “Diagnosis and Treatment of Long-COVID”.

Revive and Lawson continues to work together in completing the product development and investigational plans of a qELISA laboratory test kit and a point-of-care device for rapid testing of long COVID for FDA review, feedback and acceptability. The Company expects to submit a pre-investigational device exemption meeting package with the FDA in April 2024 and have its meeting with the FDA in early Q3-2024.

Currently, there is no FDA-approved clinical diagnosis of long COVID and it is estimated to occur in at least 10% of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections. More than 200 symptoms have been identified with impacts on multiple organ systems[4] — including fatigue, brain fog, difficulty breathing, and cardiovascular symptoms ranging from chest pain and arrhythmias to sudden cardiac death—but it remains a diagnosis of exclusion with an unknown biological basis[5].

About Revive Therapeutics Ltd.

Revive Therapeutics is a life sciences company focused on the research and development of therapeutics and diagnostics for infectious diseases, medical countermeasures, and rare disorders. 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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Sources:

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2. *"The Economic Cost of Long COVID: An Update," David M. Cutler, Harvard University, July 22, 2022, https://scholar.harvard.edu/files/cutler/files/long_covid_update_7-22.pdf*

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4. *Davis, H.E., McCorkell, L., Vogel, J.M. et al. Long COVID: major findings, mechanisms and recommendations. Nat Rev Microbiol 21, 133–146 (2023). https://doi.org/10.1038/s41579-022-00846-2; access https://www.nature.com/articles/s41579-022-00846-2*

5. *"Proteins In The Blood Hint At Biological Basis Of Long COVID", Clinical Research News, August 11, 2023, https://www.clinicalresearchnewsonline.com/news/2023/08/11/proteins-in-the-blood-hint-at-biological-basis-of-long-covid*