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FDA grants inhaled use IND for RLF-100 (aviptadil) to treat patients with moderate and severe COVID-19 aiming to prevent progression to respiratory failure

- Aviptadil is now shown as the first COVID therapeutic to block replication of the SARS-CoV-2 virus in human lung cells and monocytes, while also preventing synthesis of cytokines in the lung

- RLF-100 is a patented formulation of aviptadil (synthetic human Vasoactive Intestinal Polypeptide, VIP), which has been granted FDA Fast Track Designation, FDA emergency use IND authorization, and an expanded access protocol.

RADNOR, Pa. and GENEVA, Aug. 6, 2020 /PRNewswire/ -- NeuroRx, Inc. and Relief Therapeutics Holdings AG (SIX:RLF, OTC:RLFTF) "Relief" today announced that NeuroRx has been granted Investigational New Drug (IND) permission to test RLF-100 (aviptadil) for inhaled use in patients with moderate and severe COVID-19 in order to prevent progression to respiratory failure.

The study is posted at https://clinicaltrials.gov/ct2/show/NCT04360096. The first phase will commence with patients hospitalized for severe COVID-19 who do not yet have respiratory failure. If promising results are seen in the inpatient setting, the trial will expand to patients at home with mild and moderate COVID-19 in order to prevent the need for hospital admission.

Professor Jonathan Javitt, MD, MPH, CEO of NeuroRx said, "Now that we know VIP suppresses replication of the SARS-CoV-2 virus in human lung cells, based on the outstanding work of the Oswaldo Cruz Institute (Rio de Janeiro).[1] We are optimistic that treatment with VIP will not only help patients on ventilators, but will help to stop the advancement of the virus in patients with earlier stages of COVID-19. By blocking cytokine synthesis in the lung cells and increasing the production of surfactant, which is key to the

lung's ability to transmit oxygen, we are hopeful that inhaled VIP will prove to be of clinical benefit across a wider array of patients suffering respiratory complications from COVID-19 infection."

The clinical trial of the inhaled formulation of RLF-100 is expected to begin on or before September 1, 2020.

About VIP in Lung Injury

Vasoactive Intestinal Polypeptide (VIP) was first discovered by the late Dr. Sami Said in 1970. Although first identified in the intestinal tract, VIP is now known to be produced throughout the body and to be primarily concentrated in the lungs. VIP has been shown in more than 100 peer-reviewed studies to have potent anti-inflammatory/anti-cytokine activity in animal models of respiratory distress, acute lung injury, and inflammation. Most importantly, 70% of the VIP in the body is bound to a rare cell in the lung, the Alveolar Type II cell, which is critical for the transmission of oxygen to the body. VIP has a 20-year history of safe use in humans in multiple human trials for sarcoidosis, pulmonary fibrosis, asthma/allergy, and pulmonary hypertension.

COVID-19-related death is primarily caused by respiratory failure. Before this acute phase, however, there is evidence of early viral infection of the alveolar type 2 cells. These cells are known to have angiotensin converting enzyme 2 (ACE2) receptors at high levels, which serve as the route of entry for the SARS-CoV-2 into the cells. Coronaviruses are shown to replicate in alveolar type 2 cells, but not in the more numerous type 1 cells. These same type 2 alveolar cells have high concentrations of VIP receptors on their cell surfaces giving rise to the hypothesis that VIP could specifically protect these cells from injury.

Injury to the type 2 alveolar cells is an increasingly plausible mechanism of COVID-19 disease progression (Mason 2020). These specialized cells replenish the more common type 1 cells that line the lungs. More importantly, type 2 cells manufacture surfactant that coats the lung and is essential for oxygen exchange. Other than RLF-100, no currently proposed treatments for COVID-19 specifically target these vulnerable type 2 cells.

About RLF-100

RLF-100 (aviptadil) is a patented formulation of Vasoactive Intestinal Polypeptide (VIP) that was developed based on Dr. Said's original work and was originally approved for human trials by the FDA in 2001 and the European Medicines Agency in 2005. VIP is known to be highly concentrated in the lungs and to inhibit a variety of inflammatory cytokines. Relief's predecessor company, Mondo Biotech, was awarded Orphan Drug Designation in 2001 by the U.S. FDA for aviptadil in the treatment of Acute Respiratory Distress Syndrome and in 2005 for treatment of Pulmonary Arterial Hypertension. Mondo was awarded Orphan Drug Designation by the European Medicines Agency in 2006 for the treatment of acute lung injury and in 2007 for the treatment of sarcoidosis. Both Mondo and Relief have worked on development of an inhaled formulation of aviptadil for several years. Both the U.S. FDA and the EMEA have granted Investigational New Drug licenses for human trials of aviptadil.

About RELIEF THERAPEUTICS Holding AG

The Relief group of companies focus primarily on clinical-stage projects based on molecules

of natural origin (peptides and proteins) with a history of clinical testing and use in human patients or a strong scientific rationale. Currently, Relief is concentrating its efforts on developing new treatments for respiratory disease indications.

Relief Therapeutics holds orphan drug designations from the U.S. Food and Drug Administration and the European Union for the use of VIP to treat ARDS, pulmonary hypertension, and sarcoidosis. Relief Therapeutics also holds a U.S. patent (US8178489 formulation for aviptadil) for RLF-100 and proprietary manufacturing processes for its synthesis.

RELIEF THERAPEUTICS Holding AG is listed on the SIX Swiss Exchange under the symbol RLF.

About NeuroRx, Inc.

NeuroRx draws upon more than 100 years of collective drug development experience and is led by former senior executives of Johnson & Johnson, Eli Lilly, Pfizer, and AstraZeneca, PPD. In addition to its work on RLF-100, NeuroRx has been awarded Breakthrough Therapy Designation and a Special Protocol Agreement to develop NRX-101 for the treatment of suicidal bipolar depression and is currently in Phase 3 trials. Its Board of Directors and Advisors includes Hon. Sherry Glied, former Assistant Secretary, U.S. Dept. of Health and Human Services; Mr. Chaim Hurvitz, former President of the Teva International Group, Lt. Gen. HR McMaster, the 23rd National Security Advisor, Wayne Pines, former Associate Commissioner of the U.S. Food and Drug Administration, Judge Abraham Sofaer, and Daniel Troy, former Chief Counsel, U.S. Food and Drug Administration.

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1 Temerozo JR, Sacramenta Q, Fintelman-Rodriques N, et. al. The neuropeptides VIP and PACAP inhibit SARS-CoV-2 replication in monocytes and lung epithelial cells, decrease the production of proinflammatory cytokines, and VIP levels are associated with survival in severe Covid-19 patients doi: https://doi.org/10.1101/2020.07.25.220806. https://www.biorxiv.org/content/10.1101/2020.07.25.220806v2.full

View original content:http://www.prnewswire.com/news-releases/fda-grants-inhaled-use-ind-for-rlf-100-aviptadil-to-treat-patients-with-moderate-and-severe-covid-19-aiming-to-prevent-progression-to-respiratory-failure-301107288.html

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