RLF-100 (aviptadil) clinical trial showed rapid recovery from respiratory failure and inhibition of coronavirus replication in human lung cells

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- Rapid recovery of patients on ventilators and ECMO (extracorporeal membrane oxygenation) was seen in patients with severe medical comorbidities after three days of treatment with RLF-100 under FDA Emergency Use IND authorization at multiple clinical sites

- Aviptadil is being developed as the first COVID therapeutic to block replication of the SARS-CoV-2 virus in human lung cells and monocytes

- 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. 2, 2020 /PRNewswire/ -- NeuroRx, Inc. and Relief Therapeutics Holdings AG (SIX:RLF, OTC:RLFTF) "Relief" today announced that RLF-100 (aviptadil) showed rapid recovery from respiratory failure in the most critically ill patients with COVID-19. At the same time, independent researchers have reported that aviptadil blocked replication of the SARS coronavirus in human lung cells and monocytes.

RLF-100 has been granted Fast Track designation by FDA and is being developed as a Material Threat Medical Countermeasure in cooperation with the National Institutes of Health and other federal agencies. Further research will be conducted.

The first report of rapid clinical recovery under emergency use IND was posted by doctors from Houston Methodist Hospital. The report describes a 54-year-old man who developed COVID-19 while being treated for rejection of a double lung transplant and who came off a ventilator within four days.1 Similar results were subsequently seen in more than 15 patients treated under emergency use IND and an FDA expanded access protocol which is open to patients too ill to be admitted to the ongoing Phase 2/3 FDA trial.

Patients with Critical COVID-19 were seen to have a rapid clearing of classic pneumonitis findings on x-ray, accompanied by an improvement in blood oxygen and a 50% or greater average decrease in laboratory markers associated with COVID-19 inflammation.2 clinicaltrials.gov NCT04311697.

The clinical findings may be based on evidence that VIP inhibits the replication of the SARS-CoV-2 virus in human lung cells and immune cells (monocytes). The work was reported by Brazilian researchers working in a level-4 biocontainment laboratory.3 The same researchers reported a case-control study in which patients who survived being on ventilators for COVID-19 had significantly higher levels of VIP in their blood than those who died of respiratory failure.

"No other antiviral agent has demonstrated rapid recovery from viral infection and demonstrated laboratory inhibition of viral replication," said Prof. Jonathan Javitt, CEO and Chairman of NeuroRx. "We are conducting placebo-controlled trials to see whether the observations made in the case-control and open-label studies will be confirmed for less ill patients with COVID-19-related respiratory failure. Our independent Data Monitoring Committee will be conducting an interim analysis of these data later this month."

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. 2 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 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. patent1 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 Youssef, J.G.; Zahiruddin, F.; Al-Saadi, M.; Yau, S.; Goodarzi, A.; Huang, H.J.; Javitt, J.C. Brief Report: Rapid Clinical Recovery from Critical COVID-19 with Respiratory Failure in a Lung Transplant Patient Treated with Intravenous Vasoactive Intestinal Peptide . *Preprints* 2020, 2020070178 (doi: 10.20944/preprints202007.0178.v1). https://www.preprints.org/manuscript/202007.0178/v1

2 http://ssrn.com/abstract=3665228.

3 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/rlf-100-aviptadil-clinical-trial--showed-rapid-recovery-from-respiratory-failure-and-inhibition-of-coronavirus-replication-in-human-lung-cells-301104384.html

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