Relief Therapeutics and NeuroRx Expand Clinical Trial of RLF-100 to All Patients with Critical COVID-19 and Respiratory Failure

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•Clinical trial expanded to patients treated with both noninvasive and mechanical ventilation in critical COVID-19
•Clinical trial to enroll 144 patients total with expansion to additional sites
•RLF-100 is a patented formulation of Aviptadil (synthetic human Vasoactive Intestinal Polypeptide VIP), which inhibits pro-inflammatory cytokines and protects alveolar type II cells in the lungs inhibiting pro-inflammatory cytokines. Type II cells are essential to oxygen exchange and are preferentially targeted by the SARS-CoV-2 virus

GENEVA and RADNOR, Pa., June 08, 2020 (GLOBE NEWSWIRE) -- RELIEF THERAPEUTICS Holding AG (SIX:RLF) "Relief" and its U.S. partner, NeuroRx, Inc. today announced that the Phase 2/3 clinical trial evaluating RLF-100 as a treatment for critical COVID-19 with respiratory failure has been expanded to include patients receiving high flow oxygen and noninvasive ventilation (CPAP), in addition to those on ventilators. RLF-100 (Aviptadil) is a patented formulation of synthetic human Vasoactive Intestinal Peptide (VIP), which has been granted Orphan Drug Designation by the U.S. Food and Drug Administration (FDA) in Acute Respiratory Distress Syndrome and chronic lung diseases.

"With the FDA's expanded definition of critical COVID-19 to include patients on all forms of ventilation and the recent trend at leading hospitals that avoids mechanical ventilators whenever possible for patients with COVID-19, we recognized the potential benefit of extending this clinical trial to patients on newer forms of treatment for respiratory failure," said Dr. Jonathan C. Javitt, M.D., MPH, CEO of NeuroRx and the national study chair. "The SARS-CoV-2 likely attacks the body by entering the small population of alveolar type II cells in the lung, almost like targeting the needle in the haystack.1 Without type II cells, the lung cannot transmit oxygen, which is exactly what happens in COVID-19. We know, from 50 years of scientific research, that VIP binds specifically to the type II cell and protects that cell against cytokines (inflammatory molecules) and a wide array of toxic and infectious injuries.2"

The multicenter clinical trial will enroll patients with critical COVID-19 and respiratory failure in the hopes that RLF-100 can decrease mortality and improve blood oxygenation in this condition by rescuing alveolar type II cells from the SARS-CoV-2 virus.

Dr. Javitt added, "In recent months, there has been significant focus on "cytokine storm" as a possible cause of death in COVID-19 and on the use of various anti-inflammatory drugs to block cytokines. While we believe cytokine storm is likely a consequence of the coronavirus infecting the type II alveolar cells, we are hopeful that a more targeted approach to blocking the effects of the coronavirus may stop the cytokine storm at an earlier stage."

The trial is being led by NeuroRx, Inc., the U.S. development partner of Relief Therapeutics, whose clinical operations are based in Radnor, PA. Patients are being treated under FDA Investigational New Drug clearance, as part of the FDA's Corona Treatment Acceleration Program (CTAP). Details of the study are posted on clinicaltrials.gov NCT04311697.

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, that is critical to 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 II 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 II cells, but not in the more numerous type I cells. 2 These same type II 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 II alveolar cells is an increasingly plausible mechanism of COVID-19 disease progression.1These specialized cells replenish the more common type I cells that line the lungs. More importantly, type II cells manufacture surfactant that coats the lung and are essential for oxygen exchange. Other than RLF-100, no currently proposed treatments for COVID-19 specifically target these vulnerable type II 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 rational. 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. patent3 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 Mason R. Pathogenesis of COVID-19 from a Cell Biologic Perspective. Eur Respir J. April 9 Epub ahead of print. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7144260/

2 Javitt JC. The Potential Role of Vasoactive Intestinal Peptide in treating COVID-19, Authorea, DOI: 10.22541/au.158940764.42332418

3 US 8,178,489 Formulation for Aviptadil

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