Relief Therapeutics and NeuroRx Announce Enrollment of First Patients with RLF-100 in Phase 2b/3 Clinical Trial in Patients with COVID-19 Associated Acute Respiratory Distress

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•First participants treated at the University of Miami Miller School of Medicine with intravenous RLF-100
•Clinical trial to enroll 144 patients total with expansion to additional sites including the University of California, Irvine and Thomas Jefferson University Hospital, Philadelphia
•RLF-100 is a patented formulation of Aviptadil (synthetic human Vasoactive Intestinal Polypeptide VIP), which binds to alveolar type 2 cells in the lungs inhibiting pro-inflammatory cytokines. Type 2 cells are essential to oxygen exchange and are selectively targeted by the SARS-CoV-2 virus

MIAMI, June 01, 2020 (GLOBE NEWSWIRE) -- RELIEF THERAPEUTICS Holding AG (SIX:RLF) (Relief) and its U.S. partner, NeuroRx, Inc. today announced treatment of the first patients with RLF-100 at the University of Miami Miller School of Medicine, Fla. This is part of a Phase 2b/3 clinical trial to assess RLF-100 as a treatment for Acute Respiratory Distress Syndrome (ARDS) in COVID-19 patients on mechanical ventilation. RLF-100 is a patented formulation of Aviptadil, a synthetic human vasoactive intestinal polypeptide (VIP), that targets alveolar type 2 cells in the lungs that could be the major target of the SARS-CoV-2 virus. VIP is known from numerous animal models of lung injury and lung disease to inhibit inflammatory cytokines and to protect pulmonary epithelial cells that line the air sacs (alveolae) of the lungs.

“ARDS is the primary cause of COVID-19 related deaths triggered by acute inflammation in the air sacs (alveolae) of the lungs. As a result, they fill with fluid rendering them unable to deliver oxygen to the body. There is an urgent need for a treatment that can specifically protect type 2 alveolar cells and suppress excessive inflammation,” said Dushyantha T Jayaweera M.D., principal study investigator at the University of Miami. “We are pleased to be the first site to treat patients with RLF-100, it reflects our commitment to advancing clinical research on COVID-19 to provide critically ill patients the best care and improve their chances of survival.”

Jonathan Javitt, M.D., MPH, CEO of NeuroRx, added, “RLF-100 previously showed promising phase 1 results in ARDS related to sepsis and promising phase 2 results in the treatment of other inflammatory lung conditions. Aviptadil specifically binds to the cells in the lung that are essential to transmitting oxygen to the body and to making surfactant that is essential to oxygen exchange (the Alveolar Type II cells). These are the same cells that are targeted and killed by the SARS-CoV-2 virus. Fifty years of research into the biology of VIP suggests that it may protect the vulnerable cells in the lungs while inhibiting the inflammatory cytokines that contribute to disease progression, without impairing the immune response necessary to clear the infection.”

The multicenter randomized placebo-controlled trial aims to enroll 120 patients with COVID-19 who have Acute Respiratory Distress and require intensive care with mechanical ventilation. Patients will be randomized to intravenous (IV) RLF-100 plus maximal intensive care or placebo plus maximal intensive care. The primary endpoints will be mortality and index of respiratory distress. The secondary endpoint will include levels of TNFα and multi-system organ failure free days. For more details on the clinical trial, go to the government’s website: www.clinicaltrials.gov (NCT04311697).

Relief Therapeutics and NeuroRx are engaging clinical trials authorities in the European Union, the United Kingdom, Russia, and Australia in order to broaden the clinical study and increase access to RLF-100.

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. 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 Acute Respiratory Distress Syndrome (ARDS). The trigger for ARDS is widely attributed to a cytokine storm in the lungs, in which the virus causes release of inflammatory molecules called cytokines. As a result, the air sacs (alveolae) of the lungs fill with water and become impermeable to oxygen, even in the setting of mechanical ventilation. Before this acute phase, however, there is evidence of early viral infection of the alveolar type 2 cells.1 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. Although not yet shown for COVID-19, the coronavirus that causes SARS (SARS-CoV) is 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. 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 are essential for oxygen exchange. Patients with early COVID-19 lung injury commonly describe “crackling sounds” in their lungs, combined with extreme shortness of breath. No currently proposed treatments for COVID-19 specifically target these vulnerable type 2 cells.

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.

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.

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 Ageny 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.

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

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