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Relief, with Partner NeuroRx, Announces Enrollment of 150 Patients in Phase 2b/3 Trial of RLF-100™ for Critical COVID-19 with Respiratory Failure

- **Observations of rapid recovery on chest x-rays noted and no drug-related Serious Adverse Events reported**
- **Relief also reports exercise of 500 million warrants by main shareholder GEM**

Geneva, Switzerland, November 13, 2020 – RELIEF THERAPEUTICS Holding AG (SIX: RLF, OTCQB: RLFTF) ("**Relief**" or the "**Company**") with its partner NeuroRx, Inc., announced that as of today, 150 patients (out of a targeted enrollment of 165) have been enrolled in the ongoing phase 2b/3 trial of RLF-100™ (aviptadil) for treating respiratory failure in patients with critical COVID-19. Respiratory failure is defined, according to FDA guidance, as the need for intensive care with mechanical ventilation, non-invasive ventilation, or high-flow nasal oxygen in order to sustain adequate levels of blood oxygen. So far, no drug-related serious adverse events have been reported.

There is currently no FDA-approved drug that has shown efficacy in patients who are already in the Intensive Care Unit (ICU) with Respiratory Failure. Although NeuroRx and Relief are optimistic that RLF-100™ will also be effective in treating early COVID-19, the companies have focused first on those patients who have no available therapy and are at the highest risk of mortality. An open-label prospective study in patients with Critical COVID-19 has already shown a nine-fold hazard ratio advantage in both survival and recovery from respiratory failure (http://dx.doi.org/10.2139/ssrn.3665228) with both statistically significant ($P < .001$). More than 110 patients with similar severity have additionally been treated nationwide under an FDA-sanctioned Expanded Access Protocol (NCT04453839).

Although the phase 2b/3 study remains blinded, illustrative blinded recoveries from signs of Critical COVID-19 on Chest x-ray within 10 days have been reported by study sites and shared with the study's Data Monitoring Committee and FDA (see figure). Until the study is unblinded, it cannot be known whether this rapid recovery was more frequent among patients treated with RLF-100™ compared to those treated with placebo. However, in the open-label prospective study, more rapid recovery was seen among 21 patients treated with RLF-100™ than those treated with standard of care with an average of nine fewer ICU days in the RLF-100™ treated patients compared to those treated with Standard of Care.

Completion of enrollment is anticipated in the coming weeks. Enrollment was uniquely challenged by the devastating effects of the pandemic. It strained the capacity of hospitals and caused the temporary incapacity of investigators and study coordinators at several study sites, who themselves contracted COVID-19 in the course of their duties.

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"Should RLF-100™ prove to be safe and effective for treating COVID-19 Respiratory Failure, the nation will owe an eternal debt of gratitude to the front-line healthcare workers, technicians, study coordinators, nurses, and doctors who worked seven days a week to help develop this treatment while risking their own health to do so. They are the true heroes," said **Prof. Jonathan Javitt, CEO and founder of NeuroRx, Inc**.

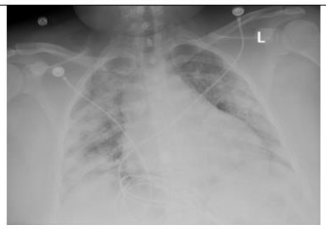
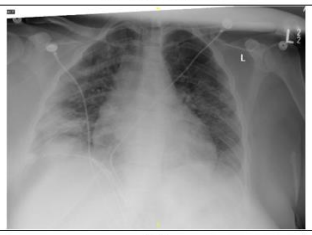
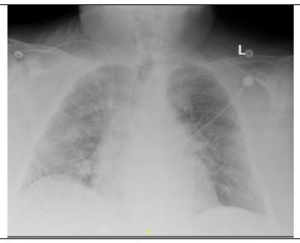
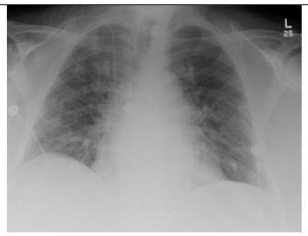
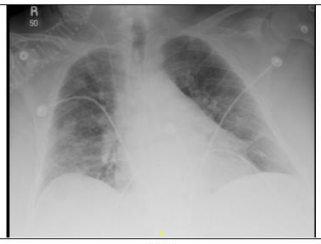
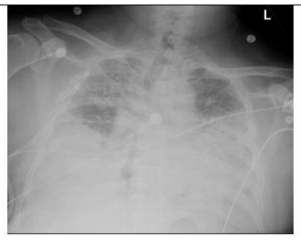
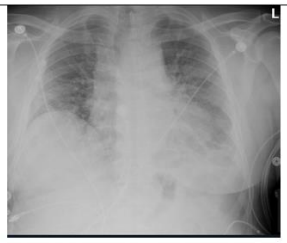
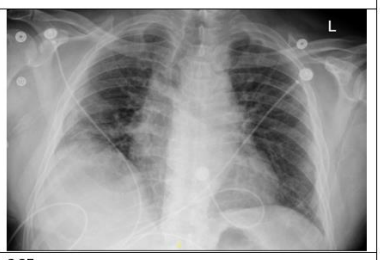
	At randomization	48-72 hours	7-10 days
Patient 1 Discharged from ICU 72 hours after infusion #3 went home on room air			Discharged home on Day 5
PaO2:FiO2	100	158	291
Patient 2 Discharged within 1 week on 2L oxygen for underlying COPD			
PaO2:FiO2	123	165	344
Patient 3 discharged on room air, 12 days after last infusion			
PaO2:FiO2	100	202	265

Figure: Unexpected rapid recovery from COVID-19 lung findings on chest x-ray seen in randomized prospective trial. Patients are randomized to RLF-100™ vs. placebo. Similar findings were seen in 19 of 21 patients treated with open label RLF-100™ (source: NeuroRx, Inc.)

GEM Exercises Warrants

Relief also reported today that the Company's main shareholder, GEM Global Yield LLC SCS ("GEM"), has exercised 500 million warrants. GEM has 86.66 million warrants remaining in Relief. Following this exercise, Relief's available cash balance totals approximately CHF 49,800,000. Upon issuance of the shares, the total amount of shares outstanding will be 3,160,068,581.

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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 2 cell, that is critical to 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 alveolar type 1 cells. These same alveolar type 2 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 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, alveolar type 2 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 alveolar type 2 cells.

ABOUT RLF-100™

RLF-100™ (Aviptadil) is a formulation of Vasoactive Intestinal Polypeptide (VIP) that was developed based on Prof. Sami Said's original work at Stony Brook University, for which Stony Brook was awarded an FDA Orphan Drug Designation in 2001. VIP is known to be highly concentrated in the lungs, where it inhibits coronavirus replication, blocks the formation of inflammatory cytokines, prevents cell death, and upregulates the production of surfactant. FDA has now granted IND authorization for intravenous and inhaled delivery of RLF-100™ for the treatment of COVID-19 and awarded Fast Track designation. RLF-100™ is being investigated in two placebo-controlled US Phase 2b/3 clinical trials in respiratory deficiency due to COVID-19. Since July 2020, more than 150 patients with Critical COVID-19 and Respiratory Failure have been treated with RLF-100™ under FDA-approved protocols. Information on the RLF-100™ Expanded Access program is at https://www.neurorxpharma.com/our-services/rlf-100.

ABOUT RELIEF THERAPEUTICS HOLDING AG

Relief focuses primarily on clinical-stage programs 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 holds orphan drug designations from the U.S. FDA and the European Union for the use of VIP to treat ARDS,

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pulmonary hypertension, and sarcoidosis. Relief also holds a patent issued in the U.S. and multiple other countries covering potential formulations of RLF-100™.

RELIEF THERAPEUTICS Holding AG is listed on the SIX Swiss Exchange under the symbol RLF and quoted in the U.S. on the OTCQB under the symbol RLFTF.

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 in suicidal bipolar depression and is currently in Phase 3 trials. Its executive team is led by Prof. Jonathan C. Javitt, MD, MPH, who has served as a health advisor to four Presidential administrations and worked on paradigm-changing drug development projects for Merck, Allergan, Pharmacia, Pfizer, Novartis, and Mannkind, together with Robert Besthof, MIM, who served as the Global Vice President (Commercial) for Pfizer's Neuroscience and Pain Division. 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.

Disclaimer: This communication expressly or implicitly contains certain forward-looking statements concerning RELIEF THERAPEUTICS Holding AG, NeuroRx, Inc. and their businesses. The results reported herein may or may not be indicative of the results of future and larger clinical trials for RLF-100™ for the treatment of COVID-19. Such statements involve certain known and unknown risks, uncertainties and other factors, which could cause the actual results, financial condition, performance or achievements of RELIEF THERAPEUTICS Holding AG and/or NeuroRx, Inc. to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. RELIEF THERAPEUTICS Holding AG is providing this communication as of this date and does not undertake to update any forward-looking statements contained herein as a result of new information, future events or otherwise.

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