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NeuroRx and Relief announce topline efficacy data from patients treated with RLF-100™ (aviptadil) under the U.S. FDA Expanded Access Protocol authorization for respiratory failure related to critical COVID-19

- RLF-100™ therapy associated with a 9-fold increased probability of survival and recovery from respiratory failure in an open-label, prospective study

- Top-line data from randomized, placebo-controlled Phase 2b/3 trial expected this quarter

GENEVA and RADNOR, Pa., Oct. 13, 2020 /PRNewswire/ -- RELIEF THERAPEUTICS Holding AG (SIX: RLF, OTCQB: RLFTF) ("Relief" or the "Company") and NeuroRx, Inc., today announced topline results from 45 patients assessed in an open-label prospective study where 21 patients admitted to an intensive care unit (ICU) with critical COVID-19 and respiratory failure were treated with RLF-100™(aviptadil) and compared to 24 control patients treated in the same setting. All patients had severe comorbidities that rendered them ineligible for the ongoing randomized controlled phase 2b/3 trial being conducted to ascertain safety and efficacy of RLF-100™, and all patients were deteriorating despite treatment with approved therapies for COVID-19.

Overall, 81% of RLF-100™-treated patients survived beyond 60 days, compared to 17% of control patients. Patients treated with RLF-100™ demonstrated a 9-fold increased probability of survival and recovery from respiratory failure, with a high degree of statistical significance. Statistical analysis was performed by Prof. Phil Lavin, FASA, FRAPS of the Boston Biostatistical Research Foundation.

"We are encouraged by these initial results in highly comorbid patients with COVID-19 respiratory failure, and we are pleased that the majority of these patients have returned safely to their families. We look forward to the upcoming results from the randomized, double-blind, prospective trial in less severely comorbid patients for confirmation of these results," said Jihad Georges Youssef, MD, section chief of General Academic Pulmonary Medicine at the Houston Methodist Hospital, who serves as the study's principal investigator at Houston Methodist and also serves as national co-chair for the ongoing randomized controlled trial.

"The patients included in this study are representative of those who are too ill to be included in the clinical trials of any known treatment for COVID-19," said Dr. Jonathan Javitt, CEO and Chairman of NeuroRx, Inc. "We are grateful to Dr. Youssef and to the Houston Methodist Hospital for having the courage to treat and study patients at this level of risk. The results suggest that there may be substantial hope to mitigate the attack of the coronavirus on the delicate cells that line the lung with a natural peptide that has been protecting the lung's lining since humans first walked the earth. While the number of patients treated at Houston Methodist is modest, the initial results in our nationwide expanded access program suggest similarly encouraging survival with RLF-100™. We continue to closely monitor treatment with RLT-100TM in other hospitals."

Raghuram (Ram) Selvaraju, Chairman of the Board of Relief commented: "The encouraging EAP topline data give us continued motivation to remain focused on the rapid clinical development of RLF-100™. We look forward to topline results from our randomized, placebo-controlled study this quarter. We remain dedicated to our goal of providing therapeutic relief to critical COVID-19 patients as quickly as possible."

Scientific findings of the analysis have been submitted for peer review.

About VIP in Lung Injury
Vasoactive Intestinal Polypeptide (VIP) was first discovered by the late Prof. 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 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 are 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 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 can be found here: 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, 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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