

PRESS RELEASE

NeuroRx and Relief announce initial successful results from expanded access use of RLF-100™ (aviptadil) in patients with Critical COVID-19 and Severe Comorbidity: 72% survival seen in ICU patients

Geneva, Switzerland and Radnor, PA, November 24, 2020 – RELIEF THERAPEUTICS Holding AG (SIX: RLF, OTCQB: RLFTF) ("Relief" or the "Company") and NeuroRx, Inc., announced that more than 175 patients with Critical COVID-19 and Respiratory Failure who also have a severe comorbidity have now been entered into an Expanded Access Protocol (EAP) with RLF-100™ in the United States.

All patients had severe comorbidities (such as organ transplant, recent heart attack, and cancer) 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 (see [www.clinicaltrials.gov NCT 04311697](http://www.clinicaltrials.gov/NCT04311697)). Of the 90 patients who have so far reached 28 days of follow-up, 72% survived to day 28.

As previously reported by Youssef and coworkers (<http://dx.doi.org/10.2139/ssrn.3665228>), at Houston Methodist Hospital, 21 patients treated with RLF-100™ under the EAP were compared to 24 control patients treated in the same setting. Only 17% of the control patients, all treated with best available intensive care unit (ICU) Standard of Care, survived to day 28. The survival rate with RLF-100™ reported today is comparable to that seen among the open-label patients treated with RLF-100™ by Youssef et al. Despite advancements in treating COVID-19, survival for the patients at highest risk due to severe comorbidities has remained dismal in the absence of an effective therapy.

Notably, in the EAP, no drug-related Serious Adverse Events have been reported to date among these patients nor the 160 patients randomized to RLF-100™ vs. placebo in the U.S. phase 2b/3 clinical trial currently underway. Thus, from a risk/benefit perspective, while the benefit of RLF-100™ has not yet been proven in a randomized prospective trial, no serious risk has been identified so far.

Currently, 25 U.S. hospitals have enrolled patients in the EAP, nearly all of which are community hospitals, suggesting that RLF-100™ can demonstrate effectiveness in the hands of front-line physicians who deliver the majority of care to patients with Critical COVID-19. Physicians enrolling patients in the EAP have routinely reported that initial patients at their sites have frequently been in the ICU for several weeks without recovery prior to treatment with RLF-100™. As patients are treated earlier in the course of their ICU stay, there is an emerging clinical impression that RLF-100™ has an even greater impact on recovery.

PRESS RELEASE

“We are reassured that emerging real-world data on the use of RLF-100™ in improving survival in patients with Critical COVID-19 are comparable to results seen in the hands of major academic teaching centers. We hope that these findings are viewed as encouraging at a time when many Americans, including the doctors, nurses, and other front-line caregivers who are the heart of our initiative, are celebrating the Thanksgiving holiday at a distance from their loved ones. We look forward to completing enrollment and reporting the results of our pivotal U.S. clinical trial,” said **Prof. Jonathan C. Javitt, MD, MPH, CEO and founder of NeuroRx, Inc.**

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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 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 Dr. 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

PRESS RELEASE

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, 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 RLTF.

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.

PRESS RELEASE

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