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NeuroRx Initiates Phase 2/3 Study of Inhaled ZYESAMI™ for Severe COVID-19 with UCI Health

RADNOR, Pa. and IRVINE, Calif., Feb. 3, 2021 /PRNewswire/ -- NeuroRx, Inc. today announced initiation of a Phase 2/3 clinical trial investigating the role of inhaled ZYESAMI™ (aviptadil) for the treatment of patients with Severe COVID-19 in partnership with UCI Health of the University of California, Irvine. UCI Health was also a key site in the recently-completed study of ZYESAMI™1 for intravenous administration in patients with Critical COVID-19 Respiratory Failure. The objective of the current study is to determine whether aviptadil, administered at the earlier (Severe) stage of COVID-19 can reduce the likelihood of progression to Critical COVID-19 with respiratory failure: the predominant cause of death in COVID.

ZYESAMI™ is a synthetic form of human Vasoactive Intestinal Peptide (VIP). Emerging data indicate that the drug protects the alveolar type II cells upon which the lung depends for production of surfactant and which are the primary target of the SARS-CoV-2 Coronavirus. Loss of surfactant causes the alveolar collapse that is the hallmark of radiographic change in COVID-19. VIP blocks replication of the Coronavirus, increases production of pulmonary surfactant, and blocks the virus-induced production of inflammatory cytokines in laboratory experiments.

"We are excited to be the first clinical site for this crucial study, which aims to prevent patients from progressing to respiratory failure and being admitted into the ICU," said Dr. Richard Lee, Interim Chief of UCI Health's Division of Pulmonary Diseases and Critical Care Medicine and the Principal Investigator for the clinical trial. "We have seen the devastation of COVID-19 firsthand and recognize the importance of investigating all potential therapeutics, especially one like ZYESAMI™. Its mechanism holds promise as a treatment for patients in the ICU with Critical COVID-19 and possibly also in the earlier stage of the disease, to reduce disease progression and respiratory failure."

Reducing the progression of COVID-19 could have a profound impact in mitigating the ICU and hospital occupancy crisis in the US. Nearly 90 million Americans currently live in a county where ICU bed occupancy averages 90% or greater, according to data provided by the US Department of Health & Human Services (HHS). In Orange County, CA, where UCI Health is located, 90.0% of ICU beds and 80.7% of hospital beds are currently occupied, underscoring the dire need for a treatment that mitigates COVID-19 progression and, thereby, ICU admissions.

The placebo-controlled study is targeted to enroll 144 patients. Once clinical safety is established, NeuroRx will initiate a second outpatient cohort of patients with the aim to determine whether inhaled ZYESAMI™ can be used at home in patients with early stages of COVID-19 and perhaps other viral infections in order to prevent disease progression and hospitalization.

"We are welcome the partnership of UCI Health as our lead clinical site," said Dr. Jonathan Javitt, MD, MPH, CEO and Chairman of NeuroRx. "Their nationally recognized leadership in the treatment of COVID-19 is inspiring. As increasingly virulent strains of the Coronavirus emerge, threatening the efficacy of existing vaccines, we are counting on UCI to continue to help us chart a forward path. Naturally, we look forward to honoring our

collaboration agreement with our partner Relief Therapeutics on this important project."

Details of the study are posted on Clinical Trials NCT04360096.

About VIP in COVID-19

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 (ATII), that is critical to transmission of oxygen to the body.

COVID-19-related respiratory failure is caused by selective infection of the ATII cell by the SARS-CoV-2 virus. They are vulnerable because of their (ACE2) surface receptors, which serve as the route of entry for the virus. These specialized cells manufacture surfactant that coats the lung and is essential for oxygen exchange. Loss of surfactant causes collapse of the air sacs (alveolae) in the lung and results in respiratory failure.

VIP is shown to block Coronavirus replication in the ATII cell, block cytokine synthesis, block viral-induced cell death (cytopathy), and upregulate surfactant production. Other than ZYESAMI™, no currently proposed treatments for COVID-19 specifically target these vulnerable Type II cells.

About ZYESAMI™ (previously RLF-100™: aviptadil)

ZYESAMI™ (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 to NeuroRx for intravenous and inhaled delivery of aviptadil for the treatment of COVID-19 and awarded Fast Track designation. ZYESAMI™ 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 300 patients with Critical COVID-19 and Respiratory Failure have been treated with ZYESAMI™ between the two FDA-cleared protocols (randomized and expanded access). Information on the ZYESAMI™ Expanded Access Program can be found at https://www.neurorxpharma.com/our-services/rlf-100.

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 ZYESAMI™, 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.

About UCI Health

UCI Health comprises the clinical enterprise of the University of California, Irvine. Patients can access UCI Health at primary and specialty care offices across Orange County and at its main campus, UCI Medical Center in

Orange, California. The 418-bed acute care hospital provides tertiary and quaternary care, ambulatory and specialty medical clinics, and behavioral health and rehabilitation services. UCI Medical Center is also home to Orange County's only National Cancer Institute-designated comprehensive cancer center, high-risk perinatal/neonatal program and American College of Surgeons-verified Level I adult and Level II pediatric trauma center and regional burn center. It is the primary teaching hospital for the UCI School of Medicine. UCI Health serves a region of nearly 4 million people in Orange County, western Riverside County and southeast Los Angeles County.

CORPORATE CONTACT

US Inquiries
Jonathan C. Javitt, M.D., MPH
Chief Executive Officer
NeuroRx, Inc.
ceo@neurorxpharma.com

MEDIA CONTACT

NeuroRx (United States):
David Schull
Russo Partners, LLC
david.schull@russopartnersllc.com
858-717-2310

INVESTOR RELATIONS

Brian Korb
Solebury Trout
bkorb@troutgroup.com
917-653-5122

1 Zyesami is a trademark of NeuroRx, Inc.

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