



NeuroRx Announces that ZYESAMI™ (Aviptadil) has Successfully Demonstrated 10-Day Accelerated Recovery from Respiratory Failure in Critically Ill Patients with Covid-19 Treated with High Flow Nasal Oxygen at 28-Day Interim Endpoint
NeuroRx to File for Emergency Use Authorization in This Patient Population if Positive Results Continue to be Demonstrated at Day-60 Endpoint in Line with FDA's New Guidance

RADNOR, Pa., Feb. 23, 2021 /[PRNewswire](#)/ -- NeuroRx, Inc. announced today that the Phase 2b/3 trial* of ZYESAMI™ (aviptadil, previously RLF-100™) for the treatment of Respiratory Failure in critically ill patients with Covid-19 has demonstrated multidimensional benefit around its prespecified primary endpoint of Recovery from Respiratory Failure with discharge from hospital and ICU (without relapse) by day 28 in patients with critical Covid-19 who were treated with High Flow Nasal Oxygen. Although not envisioned at the start of the clinical trial, High Flow Nasal Oxygen has become the predominant form of treatment in Covid-19 respiratory failure, with mechanical ventilation reserved for those whose blood oxygen levels cannot be maintained on this less invasive modality. The trial was conducted at 10 U.S. hospitals under the direction of NeuroRx in collaboration with RELIEF THERAPEUTICS Holding AG (SIX: RLF; OTCQB: RLTF). NeuroRx has signed an agreement to complete a business combination with Big Rock Partners Acquisition Corporation (NASDAQ:BRPA).

The clinical trial was originally approved as a 28-day study at FDA's direction. In December, NeuroRx added a 60-day endpoint based on the recognition that the traditional 28-day endpoint adopted in the 1990s for trials in Acute Respiratory Distress Syndrome is not appropriate for critically ill patients with Covid-19, who are frequently maintained in the ICU with advanced technologies well beyond this time point. NeuroRx and other clinical trial sponsors alerted FDA to this trend and yesterday the FDA published formal guidance† changing the required time for measuring the prespecified endpoint of "alive and free of respiratory failure" in critically ill patients to 60 days. Interim data are being reported because they were unblinded as per the original protocol and the last patient in the trial reached day 60 yesterday. Therefore, study conduct cannot be adversely influenced by release of these interim findings.

At 28 days, patients treated with ZYESAMI™ demonstrate 35% higher likelihood of recovery from respiratory failure with continued survival compared to patients treated with placebo (Hazard Ratio 1.53; $P=.08$). In tertiary care hospitals, ZYESAMI-treated patients were 46% more likely to recover and return home before day 28 (Hazard Ratio controlling for age and severity 1.84; $P=.058$). Should these trends continue through day 60, they have the potential to reach statistical significance. At day 28, a highly significant 10-day difference in median time to recovery and hospital discharge has emerged in ZYESAMI-treated patients compared to those treated with placebo ($P<.006$).

Should the above trends continue through day 60, NeuroRx anticipates filing a request for Emergency Use Authorization in this population of critically ill patients (i.e. those on High Flow Nasal Oxygen) who have exhausted all currently approved treatments. FDA decisions implement a benefit/risk framework. NeuroRx previously announced the high degree of safety observed with use of ZYESAMI. This safety has continued to be documented in the more than 300 additional patients treated under the Expanded Access Protocol and in patients who have filed requests under the federal Right to Try act.

Yesterday's guidance emphasizes the importance of analyzing patient outcomes by treatment subgroup and, in this case, the study did not recruit enough patients treated with mechanical ventilation to confirm the benefit seen in open-label studies. In the seven months that have elapsed since the trial began, mechanical ventilation has gone from first-line therapy to treatment of last resort for patients with Covid-19. Recognizing this, NeuroRx signed clinical trial agreements with the I-SPY clinical trial platform and the National Institutes of Health under which ZYESAMI will continue to be evaluated in patients who require mechanical ventilation.

The study's principal investigators, Dushyantha Jayaweera, M.D., FACP (University of Miami), Professors J. Georges Youssef, M.D. (Houston Methodist Hospital), and Richard Lee, M.D. (University of California, Irvine), commented, *"We are excited to report that ZYESAMI demonstrates a highly significant reduction in time to recovery compared to patients treated with placebo in those treated with High Flow Nasal Oxygen, together with increased likelihood of recovery and excellent safety. We look forward to learning whether this benefit can also be shown for patients treated with other stages of Covid-19 with inhaled forms of ZYESAMI. We look forward to working with the sponsor to secure emergency use authorization for ZYESAMI in this population of patients."*

Jonathan C. Javitt, M.D., M.P.H., CEO of NeuroRx, added, *"We look forward to reporting the final 60-day efficacy data shortly. We are indebted to the researchers, patients, and families who have helped us demonstrate this meaningful clinical benefit for ZYESAMI. We are honored to name the drug in honor of the late Prof. Sami Said, who discovered its active ingredient, VIP. Additional efficacy data on patients who require mechanical ventilation will be obtained from ongoing research supported by BARDA and the National Institutes of Health, in addition to our newly initiated study of inhaled use ZYESAMI in hospitalized patients who have not yet developed respiratory failure."*

About VIP in COVID-19

Vasoactive Intestinal Polypeptide (VIP) was first discovered by the late Dr. Sami Said in 1970, for whom ZYESAMI™ is named. 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 500 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 in the production of lung surfactant that is essential to transmission of oxygen from the air to the blood by the pulmonary epithelial cells that line the air sacs (alveoli) of the lung. Initial radiographic changes in Covid-19 are suggestive of collapse of these alveoli.

Covid-19-related respiratory failure is caused by selective infection of the ATII cell by the SARS-CoV-2 virus. The ATII cells 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. To our knowledge, other than ZYESAMI™, no currently proposed treatments for Covid-19 specifically target these vulnerable Type II cells. Recent laboratory findings suggest that VIP directly interferes with the spike protein complex of the SARS-CoV-2 virus.

About NeuroRx, Inc.

NeuroRx draws upon more than 100 years of collective drug development experience from senior executives of AstraZeneca, Eli Lilly, Novartis, Pfizer, and 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, M.D., M.P.H., 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. NeuroRx recently announced a plan to complete a business combination with Big Rock Partners Acquisition Corp (NASDAQ:[BRPA](#)) ("BRPA") and intends to apply for listing on the NASDAQ under the proposed symbol "NRXP". For

more information, visit www.neurorxpharma.com.

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. Its lead drug candidate RLF-100™ (aviptadil) is being investigated in two placebo-controlled U.S. late-stage clinical trials in respiratory deficiency due to COVID-19. Relief holds a patent issued in the United States and various 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 OTCQB under the symbol RLTF. www.relieftherapeutics.com Follow us on LinkedIn.

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This communication expressly or implicitly contains certain forward-looking statements concerning RELIEF THERAPEUTICS Holding AG. The results reported herein may or may not be indicative of the results of future and larger clinical trials for the treatment of respiratory failure from COVID-19 or other respiratory diseases. 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 to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Such forward-looking statements do not constitute guarantees of future performance and are subject to a variety of risks and uncertainties, including whether the results described herein will be sufficient to gain any regulatory approvals for RLF-100™. RELIEF THERAPEUTICS Holding AG is providing this communication as of this date and do not undertake to update any forward-looking statements contained herein as a result of new information, future events or otherwise.

Cautionary Note Regarding Forward Looking Statements – NeuroRx:

Statements contained in this press release that are not historical facts may be forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Forward-looking statements generally relate to future events or NeuroRx's future financial or operating performance. In some cases, you can identify forward-looking statements because they contain words such as "may," "will," "should," "expects," "plans," "anticipates," "could," "intends," "target," "projects," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these words or other similar terms or expressions that concern NeuroRx's expectations, strategy, plans or intentions. Such forward-looking statements may relate to, among other things, the outcome of any discussions or applications for the future use of ZYESAMI, the approvals, timing, and ability to complete the proposed business combination with BRPA, and the combined company's ability to continue listing on Nasdaq after closing the proposed business combination. Such forward-looking statements do not constitute guarantees of future performance and are subject to a variety of risks and uncertainties. NeuroRx does not undertake any obligation to update forward-looking statements as a result of

new information, future events or developments or otherwise.

Additional Information and Where to Find It

This press release relates to a proposed business combination and related transactions (the "Transactions") between NeuroRx and BRPA. This press release does not constitute an offer to sell or exchange, or the solicitation of an offer to buy or exchange, any securities, nor shall there be any sale of securities in any jurisdiction in which such offer, sale or exchange would be unlawful prior to registration or qualification under the securities laws of any such jurisdiction. BRPA has filed a registration statement on Form S-4 ("Registration Statement"), which includes a preliminary proxy statement for the solicitation of the approval of BRPA's stockholders, a preliminary prospectus for the offer and sale of BRPA's securities in the Transactions and a preliminary consent solicitation statement of NeuroRx, and other relevant documents with the SEC. The proxy statement/prospectus/consent solicitation statement will be mailed to stockholders of NeuroRx and BRPA as of a record date to be established for voting on the proposed business combination. INVESTORS AND SECURITY HOLDERS OF NEURORX AND BRPA ARE URGED TO READ THE REGISTRATION STATEMENT, PROXY STATEMENT/PROSPECTUS/CONSENT SOLICITATION STATEMENT AND OTHER RELEVANT DOCUMENTS THAT WILL BE FILED WITH THE SEC CAREFULLY AND IN THEIR ENTIRETY WHEN THEY BECOME AVAILABLE BECAUSE THEY WILL CONTAIN IMPORTANT INFORMATION ABOUT THE PROPOSED TRANSACTIONS. Investors and security holders will be able to obtain free copies of the registration statement, proxy statement, prospectus and other documents containing important information about NeuroRx and BRPA once such documents are filed with the SEC, through the website maintained by the SEC at <http://www.sec.gov>. In addition, copies of the documents filed with the SEC by BRPA can be obtained free of charge on BRPA's website at www.bigrockpartners.com or by directing a written request to BRPA at 2645 N. Federal Highway, Suite 230 Delray Beach, FL 33483.

Participants in the Solicitation

NeuroRx, BRPA and their respective directors and executive officers, under SEC rules, may be deemed to be participants in the solicitation of proxies of BRPA's stockholders in connection with the proposed Transactions. Investors and securityholders may obtain more detailed information regarding the names and interests in the proposed Transactions of NeuroRx's and BRPA's respective directors and officers in BRPA's filings with the SEC, including the proxy statement/consent solicitation statement/prospectus statement. You may obtain a free copy of these documents as described in the preceding paragraph.

*(www.clinicaltrials.gov NCT04311697)

† COVID-19: Developing Drugs and Biological Products for Treatment or Prevention. <https://www.fda.gov/media/137926/download>

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