December 28, 2021

NRx Pharmaceuticals Files Breakthrough Therapy Designation Request for ZYESAMI® (aviptadil) in Patients at Immediate Risk of Death from COVID-19 Despite Treatment with Remdesivir and Other Approved Therapies

- Breakthrough Therapy Designation request focused on patients whose respiratory failure has progressed despite treatment with Remdesivir
- Filing is based on FDA request for clinical data on the effectiveness of ZYESAMI compared to Remdesivir and other approved therapies
- Patients treated with ZYESAMI vs. placebo demonstrated a statistically significant (P=.03) 2.8-fold increased odds of being alive and free of respiratory failure at day 28 and day 60
- A highly significant (P=.006) four-fold increased odds of survival is seen in these patients
- Patients at the highest risk - those on ventilators at time of randomization - demonstrated a 10-fold increased odds of survival (P=.03)
- US National Institutes of Health-sponsored trial comparing ZYESAMI and Remdesivir individually and in combination continues to demonstrate safety and has enrolled more than 350 patients

RADNOR, Pa., Dec. 29, 2021 /PRNewswire/ -- NRx Pharmaceuticals (Nasdaq: NRXP) announced today that it has filed a new Breakthrough Therapy Designation (BTD) request with the US Food and Drug Administration (FDA) focused on patients with Critical COVID-19 and respiratory failure who are at immediate risk of death despite treatment with remdesivir and other approved therapies.

> With the FDA's support, we believe we have the chance to help more than 100,000 Americans return to their loved ones who otherwise might not live to see next year's holidays.

NRx filed the request after the FDA's request for clinical data on ZYESAMI® vs. Remdesivir in these high risk patients. Prof. David Schoenfeld, one of the world's most widely published statisticians with unique expertise in life-threatening diseases of the lung conducted the new analysis.

ZYESAMI® (aviptadil) has demonstrated a statistically significant two-fold increased odds of survival compared to placebo across all patients and hospitals studied in a randomized trial of 196 patients. However, in 70% of patients who were already treated with Remdesivir and continued to progress despite all approved therapies, ZYESAMI has demonstrated a highly significant four-fold increased odds of survival compared to placebo at 60 days (P=.006). Moreover, those treated with ZYESAMI after Remdesivir has failed demonstrate a 3-fold increased odds of being both alive and free of respiratory failure at both 28 and 60 days, compared to placebo (P=.03).

The FDA recently declined Emergency Use Authorization (EUA) and Breakthrough Therapy Designation (BTD) for ZYESAMI and invited a new request based on new clinical evidence that aviptadil may demonstrate a significant improvement in treatment over existing therapies. Based on the FDA's input, NRx has narrowed its BTD request to treatment of COVID-19 respiratory failure in patients who progress despite treatment with remdesivir and other approved therapies.

"At a time when America is entering a new COVID-related crisis, we thank the FDA for encouraging us to address the subset of patients who have no other approved treatment", said Prof Jonathan Javitt, MD, MPH, Chairman

and CEO of NRx Pharmaceuticals. "More than 2,000 Americans died from COVID-19 on Christmas eve. With the FDA's support, we believe we have the chance to help more than 100,000 Americans return to their loved ones who otherwise might not live to see next year's holidays."

About NRx Pharmaceuticals

NRx Pharmaceuticals (NRx) draws upon more than 300 years of collective, scientific, and drug-development experience to bring improved health to patients. The Company is developing the BriLife™ Covid vaccine, developed by the Israel Institute for Biological Research, under an exclusive license from the Israel Ministry of Defense. NRx is additionally developing ZYESAMI® (aviptadil) for patients with COVID-19, and has been granted Fast Track designation by the US Food and Drug Administration (FDA), and is currently undergoing phase 3 trials funded by the US National Institutes of Health, the Biomedical Advanced Research and Development Authority (BARDA) of the US Department of Health and Human Services, and the Medical Countermeasures program, part of the US Department of Defense. The FDA has additionally granted Breakthrough Therapy Designation, a Special Protocol Agreement, and a Biomarker Letter of Support to NRx for NRX-101, an investigational medicine to treat suicidal bipolar depression. NRX-101 is currently in Phase 3 trials, with readouts expected in 2022.

NRx is led by executives who have held senior roles at Allergan, J&J, Lilly, Novartis, Pfizer, and the US FDA. NRx is chaired by Prof Jonathan Javitt, MD, MPH, who has held leadership roles in six biotechnology startup companies with public exits and been appointed to advisory roles in four US Presidential Administrations. The NRx board includes Dr. Sherry Glied, former US Assistant Secretary for Health (ASPE), Daniel E. Troy, JD, former Chief Counsel of the US FDA, Chaim Hurvitz, former director of Teva and President of the Teva International Group, and General H.R. McMaster, Ph.D. (US Army, Ret.) the 26th United States National Security Advisor.

About ZYESAMI™/VIP in COVID-19

Aviptadil is a synthetic form of Vasoactive Intestinal Polypeptide (VIP) first discovered by the late Prof. Sami Said in 1970, and ZYESAMI® is named in his honor. Although primarily concentrated in the lung, it was first purified from the intestinal tract. VIP binds specifically to the alveolar type II cell (ATII) in the air sac (alveolus) of the lung, where it has been shown have potent anti-inflammatory/anti-cytokine activity in animal models of respiratory distress, acute lung injury, and inflammation. Most importantly, VIP stimulates ATII cells to make the surfactant that must coat the lining of the lungs in order for them to exchange oxygen with the blood. Loss of surfactant causes respiratory failure and alveolar collapse, which are hallmarks of COVID-19.

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. Coronavirus infection of the ATII cell shuts down surfactant production, triggers the formation of inflammatory cytokines, and causes cell death (cytopathy). VIP is shown to upregulate surfactant production, block Coronavirus replication in the ATII cell, block cytokine synthesis, and prevent viral-induced cell death (cytopathy). Other than ZYESAMI®, no currently proposed treatments for COVID-19 specifically target this mechanism of action.

About Prof. David Schoenfeld.

David Alan Schoenfeld, PhD, is a Professor (emeritus) of Medicine at Harvard Medical School and was Professor of Public Health at the Harvard TH Chan School of Public Health. He founded the statistics unit at the Harvard Mass General Hospital and 1996 and served for 15 years as the Principal Investigator for the Clinical Coordinating Center of the Acute Respiratory Distress (ARDS) Network. He has served as a member of an FDA advisory committee and two major International Data Safety and Monitoring Committees. Dr. Schoenfeld has authored more than 390 peer-reviewed publications and is ranked as one of the world's most widely cited statisticians and scientists.

Cautionary Note Regarding Forward-Looking Statements

This announcement of NRx Pharmaceuticals, Inc. includes "forward-looking statements" within the meaning of the "safe harbor" provisions of the US Private Securities Litigation Reform Act of 1995, which may include, but are not limited to, statements regarding our financial outlook, product development, business prospects, and market and industry trends and conditions, as well as the company's strategies, plans, objectives, and goals. These forward-looking statements are based on current beliefs, expectations, estimates, forecasts, and projections of, as well as assumptions made by, and information currently available to, the company's management.

The company assumes no obligation to revise any forward-looking statement, whether as a result of new information, future events, or otherwise. Accordingly, you should not place reliance on any forward-looking statement, and all forward-looking statements are herein qualified by reference to the cautionary statements set forth above.

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