NRx Pharmaceuticals Submits Emergency Use Authorization Application to US Food and Drug Administration for ZYESAMI® (aviptadil) to Treat Patients at Immediate Risk of Death from COVID-19 Despite Treatment with Remdesivir and Other Approved Therapies

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- Requested indication focuses on patients whose respiratory failure has progressed despite treatment with Remdesivir or other approved therapies
- Patients treated with ZYESAMI vs. placebo demonstrated statistically significant (P=.03), 2.8-fold increased odds of being alive and free of respiratory failure at day 28 and day 60 and a 4-fold increased odds of surviving to 60 days (P=.006)
- Patients at 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., Jan. 5, 2022 /PRNewswire/ -- NRx Pharmaceuticals (Nasdaq: NRXP) announced today that it has submitted an application for Emergency Use Authorization (EUA) to the US Food and Drug Administration (FDA) for the use of ZYESAMI® (aviptadil) in patients with Critical COVID-19 who are at immediate risk of death from Respiratory Failure despite treatment with approved therapy including remdesivir and who are ineligible for enrollment into the ongoing ACTIV-3b NIH-sponsored trial..

"We appreciate the detailed feedback and learnings from our previous EUA submission, and applied them to this narrower request to the FDA," said Prof Jonathan Javitt, MD, MPH, Chairman and CEO NRx Pharmaceuticals. "As the Omicron surge continues to push our hospitals far past capacity, and with more than 1200 Americans dying every day, we continue to believe ZYESAMI can provide an option to the sickest of COVID patients who have no other options and significantly increase their chances at recovering."

The filing comes with a new analysis of the Phase 2b/3 data of ZYESAMI in patients treated with Remdesivir or other approved or authorized medicines for critical COVID-19. The new analysis was conducted by Prof. David Schoenfeld, PhD, an expert statistician with unique expertise in life-threatening diseases of the lung. The analysis, requested by the FDA, demonstrated that the odds of meeting the original primary endpoint of the trial, being "alive and free of respiratory failure at 28 days" were 2.8-fold higher on ZYESAMI than on placebo (P=.03). There was a 4 fold increased odds of surviving to 60 days (P=.006). Patients at highest risk – those on ventilators at time of randomization – demonstrated a 10-fold increased odds of survival (P=.03) after doctors administered ZYESAMI. The most common side effects of ZYESAMI noted were mild to moderate diarrhea and systemic hypotension (low blood pressure).

ZYESAMI (aviptadil) is a synthetic form of Vasoactive Intestinal Polypeptide (VIP) and binds specifically to the alveolar type II cell (ATII) in the air sac (alveolus) of the lung, where it has been shown to have potent anti-inflammatory and anti-cytokine activity in animal models of respiratory distress, acute lung injury, and inflammation. VIP stimulates ATII cells to make the surfactant that must coat the lining of the lungs for them to exchange oxygen with the blood. Loss of surfactant causes respiratory failure and alveolar collapse, hallmarks of COVID-19.

NRx looks forward to working with the FDA and providing further information regarding the EUA submission upon FDA request.

In 2021, the FDA declined to issue EUA for ZYESAMI to treat patients suffering Critical COVID-19 with respiratory failure. This new EUA submission is a narrower, proposed indication for patients with no other available therapy and is supported by data requested by the FDA. ZYESAMI was selected by NIH from among 600 candidate drugs for study in the ongoing Phase 3 ACTIV-3b trial. The revised indication is designed to ensure that enrollment in this trial is not compromised.

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 to 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.

MEDIA CONTACT:
Jack Hirschfield
Head of Corporate Communications, NRx
jhirschfield@nrxpharma.com

INVESTOR RELATIONS
Eric Goldstein
LifeSci Advisors
egoldstein@lifesciadvisors.com
646-791-9729

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