



## **NRx Pharmaceuticals Announces Positive Results for ZYESAMI™ (Aviptadil-acetate) and Submits Emergency Use Authorization Application to US Food and Drug Administration to Treat Critical COVID-19 in Patients Suffering from Respiratory Failure**

June 1, 2021

- **ZYESAMI™ is the First Investigational Medicine to Show Efficacy in a Randomized, Double-Blind, Multicenter Trial, Achieving More Instances of Recovery in Critically Ill COVID-19 Patients with Respiratory Failure, Compared to Placebo**
- **ZYESAMI™ Demonstrated a Significant Treatment Advantage and Shortened Hospitalization in Patients Already Treated with All Approved Therapies for Critical COVID-19**
- **Filing Based on Data Requested from the United States Food and Drug Administration (FDA) and Marks First Emergency Use Authorization Application Based on Randomized Prospective Data for Critical COVID-19**
- **Full Data Results to be Published in a Peer-Reviewed Journal**

RADNOR, Pa., June 1, 2021 [/PRNewswire/](#) -- NRx Pharmaceuticals (Nasdaq: NRXP) (NRx), a clinical stage pharmaceutical company, today announced it has filed an application with U.S. Food and Drug Administration (FDA) requesting Emergency Use Authorization (EUA) for ZYESAMI™ (Aviptadil-acetate), to treat Critically Ill COVID-19 patients suffering with respiratory failure. Consistent with previously announced top-line data, the study identified a statistically significant increase in the likelihood that patients treated with ZYESAMI™ would be alive and free of respiratory failure at 60 days, compared to those treated with placebo, and identified a significantly shorter median hospital stay.<sup>1</sup> The clinical study report filed with FDA further documents statistically significant advantages for ZYESAMI™ on all major secondary endpoints.

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NRx Announces Positive Results for ZYESAMI™, Submits EUA to treat Critical COVID-19 with Respiratory Failure

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"The patients enrolled in our study were in the ICU, having exhausted all approved treatments for COVID-19," said Jonathan Javitt, M.D, MPH, Chief Executive Officer and Chairman of the Board, of NRx. "We look forward to working as quickly as possible with the FDA in hopes of providing critically ill patients with a new medicine that will increase their chances of recovery and survival, enabling them to leave the hospital and return to

their families significantly sooner."

Patients enrolled in the study had respiratory failure despite prior treatment with all approved medicines for COVID-19 including remdesivir. Other therapies administered included steroids, anticoagulants, and various monoclonal antibodies. Although antiviral treatment has shown advantages in treating patients with earlier stages of COVID-19. ZYESAMI™ is the first reported medicine to demonstrate increased recovery and survival in patients who have already progressed to respiratory failure. The randomized controlled trial outcomes remain similarly consistent with the open-label, administratively controlled trial reported in October 2020.<sup>2</sup>

"Since this pandemic started, there have been very few medications to effectively treat COVID-19," said Dushyantha Jayaweera, MD, Professor of Clinical Medicine and former Associate Dean, University of Miami, who served as Principal Investigator for the COVID-AIV trial. "The positive results from this trial turned into positive implications for some of our sickest COVID-19 patients and support the clinical benefit of ZYESAMI™ in critically-ill COVID-19 patients with respiratory failure. Even today, despite the availability of vaccines, we continue to see severely ill patients suffering with COVID-19, who desperately need new medicines to help them recover."

The study enrolled one hundred ninety-six participants who were randomized and treated with either ZYESAMI™ or placebo, in addition to maximal standard of care at 10 US hospitals ([www.clinicaltrials.gov](http://www.clinicaltrials.gov) NCT04311697). Patients in earlier stages of respiratory failure (those treated with high flow oxygen) were more likely to survive and recover than those who had already progressed to ventilation. However, statistically-significant benefits in the prespecified endpoint were demonstrated in both groups.

NRx previously requested limited EUA for highly co-morbid COVID-19 patients. FDA further requested randomized, prospective data regarding ZYESAMI™, which are represented in this filing.

Separately, the National Institutes of Health is conducting a confirmatory trial that randomizes patients with COVID-19 respiratory failure to ZYESAMI™ vs. Veklury® (remdesivir) and placebo in a factorial design trial ([clinicaltrials.gov](http://clinicaltrials.gov) NCT04843761). A second nationwide trial to determine if similar benefits may be achieved in critically ill patients with inhaled ZYESAMI™ is being conducted on the I-SPY platform, maintained by the Quantum Leap Healthcare Collaborative.

The COVID-AIV clinical trial was co-funded by NRx and Relief Therapeutics Holding, AG (SIX: RLF,OTCQB: [RLFTF](#)). The clinical study report has been shared with Relief Therapeutics for transmission to European health regulatory authorities.

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 NRx Pharmaceuticals

NRx ([www.nrxpharma.com](http://www.nrxpharma.com)) draws upon more than 300 years of collective, scientific and drug-development experience to bring improved health to patients. In addition to its work on Aviptadil, the United States Food and Drug Administration has granted Breakthrough Therapy Designation and a Special Protocol Agreement to NRx to develop 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 publicly traded on the Nasdaq Global Select Exchange under the stock ticker NRXP.

#### 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 U.S. 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.

1 <http://dx.doi.org/10.2139/ssrn.3830051>

2 <http://dx.doi.org/10.2139/ssrn.3665228>

#### CORPORATE CONTACT

Jack Hirschfield

Sr. Director, Head of Corporate Communications, NRx

[jhirschfield@pharma.com](mailto:jhirschfield@pharma.com)

512-674-5163

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