June 15, 2021

NRx Pharmaceuticals Announces Positive Data Results from ZYESAMI™ (Aviptadil) Expanded Access Protocol

- Expanded Access Protocol (EAP) Included 240 ICU Patients Suffering Critical COVID-19 with Respiratory Failure who had Exhausted All Approved Therapies
- Sixty-Five Percent of Patients Receiving ZYESAMI™ (Aviptadil) and Maximal Intensive Care were Alive at 28 Days
- Survival was Higher in those Treated with High Flow Nasal Cannula than those Treated with Mechanical Ventilation (76% vs. 54%)
- Results from EAP are Congruent with the Randomized Control Phase 2b/3 ZYESAMI™ (Aviptadil) Trial Data Submitted to US Food and Drug Administration (FDA) in Support of Emergency Use Authorization (EUA)
- EAP Data to be Submitted to US FDA in Support of EUA Filing

RADNOR, Pa., June 15, 2021 /PRNewswire/ -- NRx Pharmaceuticals (Nasdaq: NRXP), a clinical stage pharmaceutical company, today announced positive data from its ZYESAMI™ (Aviptadil) Expanded Access Protocol (EAP). Overall, patients receiving at least one dose of ZYESAMI™ in addition to intensive care were alive at 28 days. This EAP (https://clinicaltrials.gov/ct2/show/NCT04453839) provided an opportunity for many regional hospitals to offer ZYESAMI™ to its sickest patients, for whom no other options were available, and who could not enroll in a study due to additional risk factors. Fifty-six percent of patients enrolled were already receiving mechanical ventilation, and 44% were receiving non-invasive forms of ventilation, mostly high nasal flow cannula. (HFNC).

NRx Pharmaceuticals Announces Positive Data Results from ZYESAMI™ (Aviptadil) Expanded Access Program

"We initiated the ZYESAMI™ EAP at FDA's request, to gain real-world evidence from patient outcomes outside of the clinical trial environment. Working with 42 U.S. medical centers and hospitals, we were able to see the outcomes ZYESAMI™ provided to some of sickest of COVID-19 patients," said Jonathan Javitt, MD, MPH, CEO and Chairman of the Board, of NRx. "While vaccinations have markedly reduced the incidence of COVID-19 in some countries, effective medicines remain critical for the tens of thousands who continue contracting COVID-19 and the expanding numbers of variants associated with this virus."

Enrollment in the EAP was offered to patients who were ineligible for the ZYESAMI™ phase 2b/3 clinical trial, and who had exhausted all approved therapies for COVID-19. The enrollment included 240 patients dosed by March 19, 2021, of whom 196 received maximal intensive care. Fifty-six patients received palliative care (withdrawal of life support) as determined by their families and treating physicians. Among patients receiving maximal intensive (i.e. non-palliative) care, 76% of those treated with HFNC were discharged from the hospital or were alive and in the hospital at day 28, compared to 54% of those treated with mechanical ventilation. These numbers are congruent with the previously reported, topline, randomized, clinical data of ZYESAMI™ in Critical COVID-19 patients with respiratory failure. Many of the patients involved in this EAP had prolonged illness or had exclusion factors limiting their access to the randomized clinical trial, and were enrolled as a last resort in this EAP.

Treatment related adverse events from this EAP are congruent with those seen in the randomized controlled phase 2b/3 clinical trial of ZYESMI™. Treatment related adverse events included diarrhea (5%) and hypotension (5%). Other adverse events included tachycardia and flushing.

"So many of us have lived the past 16 months in the ICU of our hospitals taking care of desperately-ill patients suffering from the most severe symptoms of COVID-19," said Dr. Eduardo Freitas, Head of Infectious Diseases at Great Plains Health Hospital in North Platte, Nebraska, one of the participating investigators in the EAP. "A regional hospital like ours is not typically involved in clinical studies, and we greatly appreciate the opportunity to participate in the Aviptadil EAP. Every doctor caring for COVID-19 patients needs new medicines to help those critically ill with this virus recover and get back to their homes and families."

The EAP data are being provided to FDA as "real world data", in support of the findings from the ZYESAMI™ randomized controlled phase 2b/3 clinical trial.

	Expanded Access Protocol Aviptadil Treated		Phase 2b/3 Trial Aviptadil Treated
N=240	Discharged or Alive at day 28 (including palliative care) (N=240)	Discharged or Alive at day 28 (no palliative care) (N=196)	Alive at day 28 (N=131)
All Patients Evaluated	53% (127/240)	65% (127/196)	69% (90/131)
Non-Invasive Ventilation	69% (73/106)	76% (73/96)	79% (60/76)
Mechanical Ventilation	40% (54/134)	54% (54/100)	55% (30/55)

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. ZYESAMI™ is not approved by any regulatory authority, including the FDA and European Medicines Agency. Data provided within this press release are not treatment recommendations.

About NRx Pharmaceuticals
NRx (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.

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