February 15, 2022

NRx Pharmaceuticals Announces US National Institutes of Health Study of ZYESAMI® (aviptadil) in Critical COVID-19 is Cleared to Complete Full Enrollment

- After review of more than 448 enrolled patients in ACTIV-3b Critical Care Study, no new safety concerns identified by Independent Data Safety Monitoring Board; study cleared to continue enrollment to 640 Patients

- ZYESAMI® (aviptadil) is the sole remaining investigational medicine in ACTIV-3b with recent closures of other arms

- ACTIV-3b Critical Care Study is evaluating ZYESAMI and Veklury® (remdesivir), in Critical COVID-19 Patients, as monotherapy and in combination against placebo

- ACTIV-3b Trial to commence enrollment in Brazil, EU, UK, and Scandinavia in the coming months

RADNOR, Pa., Feb. 15, 2022 /PRNewswire/ -- NRx Pharmaceuticals (Nasdaq: NRXP), a clinical-stage, biopharmaceutical company, today announced results of a review conducted by the Therapeutics and Prevention Data Safety and Monitoring Board (DSMB) of the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH) on February 14, 2022. The DSMB reviewed data on 448 ICU patients with Critical COVID-19 Respiratory Failure who were enrolled in the ACTIV-3b (TESICO) trial[1]. The TESICO protocol was submitted by NIH and cleared by the US Food and Drug Administration (FDA) as a Phase 3 trial that, if positive, may be used in the submission of a New Drug Application for ZYESAMI®.

ACTIV-3b is a randomized, placebo-controlled clinical trial testing ZYESAMI and Veklury® (remdesivir; Gilead Sciences: Nasdaq:GILD) — alone and in combination — in hospitalized patients with acute respiratory failure due to COVID-19. The patients enrolled in TESICO are critically-ill patients in the ICU who have exhausted other approved therapies and require high-flow nasal oxygen, mechanical ventilation, or extracorporeal membrane oxygenation to maintain blood oxygen.

At a September 2021 Reagan Udall Foundation conference chaired by Dr. Francis Collins, former Director of the NIH and Dr. Janet Woodcock, Acting Commissioner of the FDA, Dr. Collins identified ZYESAMI® as one of a handful of investigational compounds selected by the NIH for Phase 3 study from among 600 candidate compounds initially considered.[2] Last week, the NIH announced the discontinuation of the PF-07304814 arm of the ACTIV-3 trial on account of futility[3] According to an NIH spokesperson, aviptadil is the sole remaining investigational medicine being offered within the ACTIV-3 trial, which targets the most critically-ill patients with COVID-19.[4]

While the continuation of this trial certainly does not guarantee success in proving the primary endpoint, NRx is encouraged to reach this level of enrollment without identifying either a safety or futility stopping point. Some of the underlying experimental hypotheses in the trial and the statistical power available at the projected study enrollment to prove those hypotheses will be presented in future corporate updates. Next week, NRx investigators will present the first peer-reviewed findings from the Company's Phase 2b/3 clinical trial, completed in March 2021.[5] These data were reviewed by the NIH as part of its decision to select ZYESAMI for inclusion in ACTIV-3b.

NRx further confirms that it has received no reports of drug-related Serious Adverse Events from the NIH and is forwarding this safety information to the FDA for inclusion in its ongoing

review. These findings increase the safety database of patients treated with ZYESAMI to more than 800 patients.

At the DSMB meeting, it was noted that recruitment into the aviptadil arms of the study is ahead of recruitment into the other arms and may potentially be completed in a matter of months patients to the. The Company views this recruitment by physicians at the TESICO study sites as an encouraging sign.The ACTIV-3b trial has now enrolled 448 Critical COVID-19 patients, representing more than 80% of the targeted recruitment. NIH is now moving forward to bring the ACTIV-3b protocol to Brazil, the European Union, the United Kingdom, and Scandinavia. NRx has manufactured investigational medicine to the standards required in those jurisdictions and reported in September 2021 that it passed a European Qualified Person (QP) audit related to that drug supply. NRx expects to complete regulatory requirements to export ZYESAMI to those regions for investigational use in the coming weeks.

"With more than 80% of the trial enrolled, we are highly encouraged that the Data Safety and Monitoring Board has continued enrollment and that trial investigators have continued to express enthusiasm for enrolling patients into the ZYESAMI arm of the trial at some of the nation's most advanced hospitals," said Prof. Jonathan Javitt, MD, MPH, Chairman and CEO of NRx. "So far, we have received no reports of drug-related Serious Adverse Events in ZYESAMI-treated patients and are sharing those data with the FDA. We are indebted to the NIH leadership for its decision to include our investigational medicine in the ACTIV program alongside investigational medicines from major pharmaceutical companies and hope that ZYESAMI will soon become an important therapeutic option that enables physicians to offer a renewed chance at life to patients who have exhausted all approved therapies."

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. In July 2021, the Government of Israel awarded NRx the exclusive worldwide right to develop and market the BriLife™ COVID vaccine developed by the Israel Institute for Biological Research. NRx continues to develop ZYESAMI® (aviptadil) for patients with COVID-19, which 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 medical technology 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.

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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[1] https://clinicaltrials.gov/ct2/show/NCT04843761
[2] https://reaganudall.org/sites/default/files/2021-10/Slide%20deck%20092821.pdf (slide 27)
[3] https://www.nih.gov/research-training/medical-research-initiatives/activ/covid-19-therapeutics-prioritized-testing-clinical-trials
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