January 3, 2022

NRx Pharmaceuticals Files Provisional Patent for Stable Compositions of Aviptadil Suitable for Human Use

- Invention by NRx scientists provides a path to long-term patent protection for ZYESAMI® (aviptadil)
- Compositions focus on buffer-free formulations with long-term shelf stability
- NRx is changing prior guidance to investors regarding the possibility of "Orange Book" protection upon FDA New Drug Approval

RADNOR, Pa., Jan. 3, 2022 /PRNewswire/ -- NRx Pharmaceuticals (Nasdaq: NRXP) announced today that it has filed a provisional composition of matter patent application with the US Patent and Trademark Office entitled "Stable, Buffer-free Compositions of Vasoactive Intestinal Peptide (VIP)." The provisional application describes compositions of vasoactive intestinal peptide, the synthetic form of which is aviptadil, that are both shelf stable and biologically active when used to treat COVID-19 and other diseases.

There have been previous attempts to create stable forms of aviptadil for pharmaceutical use that include the use of various additives, such as buffers, mannitol, and sucrose. Those additives routinely compensate for lack of strict chemical controls in drug formulations. However, NRx was advised in late 2020 that such formulations lead to inactivation of the peptide and cannot be used in human treatment.

The current invention relies on specific approaches to controlling the chemical environment of VIP, an extremely delicate peptide, in order to maintain its stability without the use of such additives. The project was led by an industry-veteran development team that collectively has more than two centuries of drug formulation and development experience.

Prior to this invention, VIP could only be manufactured for human use in small batches with a shelf-life that expired after several weeks. The invention is significant to NRx's drug development efforts because it provides a path to long-term shelf stability and a drug that can be included in national stockpiles. The patent filing also provides a path to inclusion in the FDA "orange book" of innovative drugs. Medicines that lack an orange book listing may be offered for sale by generic drug manufacturers after a statutory period that ranges from three to seven years. Orange book listed medicines, on the other hand, may not be offered for sale by generic manufacturers for the life of the patent.

The inventions identified in the recently-filed patent have already been incorporated into the manufacture of ZYESAMI® (aviptadil) and were reviewed by the FDA as part of its review of ZYESAMI's manufacturing process in September 2021. NRx anticipates that upon regulatory approval should safety and efficacy be demonstrated, ZYESAMI now has a path to drug release and innovative drug protection in the marketplace.

"In our previous guidance to investors, we advised that there were no filed patents protecting the manufacture of ZYESAMI. With the filing of this patent and the inventions described within, we at NRx believe we have a path to a long term commercial life for a stable and pharmaceutically active form of VIP as an innovative drug," said Prof Jonathan Javitt, MD, MPH, Chairman and CEO of NRx Pharmaceuticals. "Although, for obvious reasons, our initial focus has been the use of VIP in lung disease caused by COVID-19, we are now considering potential use of ZYESAMI in non COVID-related lung disease, liver disease, eye disease, and organ transplantation. We are deeply

grateful to our partners at Nephron Pharmaceuticals for working with us and embracing the painstaking work required to bring a seventy-year-old dormant drug to life."

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® (aviptadil)

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.

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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