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NRx Pharmaceuticals, Inc. (Nasdaq: NRXP) Announces FDA Qualified Infectious Disease Product (QIDP) and Fast Track Designation of NRX-101 in Complicated Urinary Tract Infection and Pyelonephritis

- *NRX-101 has demonstrated potent activity against resistant urinary pathogens upon FDA review*
- *QIDP designation grants Priority Review and an additional 5 years of additional product exclusivity*
- *3 million Americans develop complicated Urinary Tract Infection (cUTI) each year at a cost that ranges from $4497 to $17,431 with a high rate of antibiotic resistance and need for inpatient hospitalization*[1]
- *Unlike many advanced-generation antibiotics, NRX-101 is not contra-indicated in sulfa and penicillin allergic patients and is not believed to disrupt the normal intestinal microbiome, potentially leading to reduced risk of C. difficile infection*
- *Data have been accepted for posting on biorxiv and are under review at a peer-reviewed journal*[β]

RADNOR, Pa., Jan. 16, 2024 /PRNewswire/ -- NRx Pharmaceuticals, Inc. (Nasdaq: NRXP) ("NRx Pharmaceuticals", the "Company"), a clinical-stage biopharmaceutical company, today announced that it has received Qualified Infectious Disease Product (QIDP) and Fast Track designation from the US FDA for NRX-101 in the treatment of complicated urinary tract infections (cUTI) and pyelonephritis. Receipt of QIDP designation confers Priority Review, and critically, five additional years of data-exclusivity to NRX-101's already strong Intellectual Property position. The FDA also granted NRX-101 Fast Track designation for cUTI, which additionally allows for rolling submission of the Company's New Drug Application. In addition to the marketplace protections conferred by QIDP designation in the US, NRx has composition of matter patent protection on NRX-101 through at least 2033 in all major global markets. The data that formed the basis of FDA's QIDP approval have been submitted for publication. On the basis of this advance, NRx is seeking partners with active involvement in urology, infectious disease and/or women's health for commercialization of NRX-101.

The active antibiotic ingredient of NRX-101 is D-cycloserine (DCS) that was developed as an antibiotic in the 1950's and used worldwide for the treatment of tuberculosis. However, it fell out of favor with the development of trimethoprim/sulfa and various penicillins, cephalosporins, and tetracyclines, in part because of the CNS effects associated with DCS-induced blockade of the brain's NMDA receptor. In the course of its CNS research, NRx pharmaceuticals has demonstrated that small doses of lurasidone counteract those CNS effects, potentially providing a new therapeutic life to DCS as an antibiotic. Over the ensuing decades, increased antibiotic resistance has rendered standard treatments for UTI ineffective in many cases and today 3 million Americans suffer from cUTI requiring increasingly toxic antibiotics, increasingly frequent intravenous therapy, and increased need for hospital admission.[1]

Because DCS has the unique property of being highly concentrated, unmetabolized, in the urine with oral administration, the Company believes, and previous literature has suggested that DCS may effectively treat, and therefore help prevent, the need for intravenous and inpatient treatment of cUTI. Moreover, because DCS is rapidly absorbed and excreted in the urine, the Company is optimistic that NRX-101 will have a minimal tendency to disrupt the microbiome of the intestine and which can lead to secondary *Clostridium difficile* infection. *C. diff* associated colitis doubles hospital mortality and costs the American healthcare system up to $1.6 billion each year.[2] Additionally, DCS has no known association with C. diff or with pulmonary fibrosis, a rare, lethal condition

that has been associated with macrolide (tetracycline family) antibiotics.

"When we embarked on the development of NRX-101 for treating bipolar depression, we did not imagine that it would develop a new utility as a potentially lifesaving antibiotic. However, the antibiotics we have relied upon for decades are increasingly failing to control resistant pathogens and those that are able to do so are increasingly toxic. NRx thanks the US FDA for its rapid award of QIDP designation for cUTI and pyelonephritis. These conditions impact 3 million Americans annually and can carry significant co-morbidities, including sepsis and death," said Dr. Jonathan Javitt, Founder, Chairman and Chief Scientist of NRx Pharmaceuticals." Whereas the 12 million Americans who contract uncomplicated UTI each year can expect rapid relief from well-known antibiotics, those who contract cUTI frequently require intravenous therapy, and hospitalization, with frequent serious side effects"

Dr. Michael Manyak, noted Professor of Urology and former Global Thought Leader for Glaxo SmithKline's urology business added "As a Urologist, I am excited about the potential availability of NRX-101 for patients suffering from cUTI; this is a very serious condition in desperate need of new treatment options. Receipt of QIDP and Fast Track should make NRX-101 even more attractive to potential partners in this multi-billion-dollar market." Dr. Manyak serves as NRx's Medical Thought Leader for urology.

The data presented to the FDA have now been accepted for posting on the biorxiv pre-print server and are under review by a peer-reviewed journal.[3]

About NRx Pharmaceuticals
NRx Pharmaceuticals is a clinical-stage biopharmaceutical company developing therapeutics based on its NMDA platform for the treatment of central nervous system disorders, specifically suicidal bipolar depression, chronic pain and PTSD. The Company is developing NRX-101, an FDA-designated investigational Breakthrough Therapy for suicidal treatment-resistant bipolar depression and chronic pain. NRx has partnered with Alvogen Pharmaceuticals around the development and marketing of NRX-101 for the treatment of suicidal bipolar depression. NRX-101 additionally has potential to act as a non-opioid treatment for chronic pain, as well as a treatment for complicated UTI.

NRx has recently announced plans to submit a New Drug Application for ketamine in the treatment of suicidal depression, based on results of well-controlled clinical trials conducted under the auspices of the US National Institutes of Health and newly obtained data from French health authorities, licensed under a data sharing agreement. NRx was awarded Fast Track Designation for development of ketamine (NRX-100) by the US FDA as part of a protocol to treat patients with acute suicidality.

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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[1] Lodise TP, et. al. Open Forum Infectious Diseases https://doi.org/10.1093/ofid/ofac307

[2] Drozd EM, et. al. Mortality, Hospital Costs, Payments, and Readmissions Associated With Clostridium difficile

Infection DOI: 10.1097/IPC.0000000000000299
[3] https://doi.org/10.1101/2024.01.14.575572

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