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NRx Pharmaceuticals, Inc. (NASDAQ:NRXP) Announces New Data on NRX-101 Demonstrating No Damage to Intestinal and Vaginal Flora in Validated Rodent Models Compared to Standard Antibiotics: Potential Implications for Avoidance of C. Difficile infections

- New data demonstrates no impact of NRX-101 on gut or vaginal flora – considered primary causes of pseudomembranous colitis due to *C difficile* and vaginal yeast infections
- NRX-101 previously demonstrated potent activity against resistant urinary pathogens and has been shown to be fully excreted, unmetabolized, in the urine
- NRX-101 has received FDA Qualified Infectious Disease Product (QIDP) and Fast Track Designation in Complicated Urinary Tract Infection (cUTI) and Pyelonephritis

RADNOR, Pa., April 17, 2024 /PRNewswire/ -- NRx Pharmaceuticals, Inc. (Nasdaq:NRXP) ("NRx Pharmaceuticals", "NRx", the "Company"), a clinical-stage biopharmaceutical company, today announced new data that demonstrate that in a rodent model NRX-101 shows no measurable damage to either intestinal or vaginal flora, compared to the significant negative effect caused by drugs such as ciprofloxacin. Antibiotics commonly used to treat complicated urinary tract infections (cUTI) are associated with pseudomembranous colitis caused by *Clostridium difficile* (*C diff)* and vaginal yeast infections, primarily owing to their impact on normal flora.

C. diff causes an intractable diarrhea in approximately 500,000 Americans each year and kills 1 in 11 Americans over age 65 who contract the infection. Costs of *C. diff* are estimated at $24,000 per patient and are significantly higher when *C. diff* occurs as part of a hospital admission. Whereas most antibiotics have substantial effect in the large bowel, the key component of NRX-101 (D-cycloserine) is entirely absorbed in the small intestine and excreted unmetabolized in the urine. If the nonclinical data reported today are replicated in patients, NRX-101 could represent the first antibiotic for cUTI and pyelonephritis that has essentially no risk of causing *C. diff* infection or vaginal yeast infection. There is an extensive literature surrounding the use of D-cycloserine to treat tuberculosis and cases of *C. Diff* are unknown.

D-cycloserine's effect as an antibiotic is based on its propensity to substitute for the amino acid alanine in the formation of the bacterial cell wall.

Dr. Michael Manyak, noted Professor of Urology and former Global Medical Director for Urology at Glaxo SmithKline stated "As a Urologist, I'm acutely aware of the importance of avoiding common side effects of current antibiotics. NRX-101's lack of impact on normal flora could potentially confer a distinct advantage for the product in for the treatment of cUTI and pyelonephritis. This profile could change the lives of the half million Americans each year who contract *C. diff* and save lives among the tens of thousands who die from antibiotic-induced *C. diff* infections. These potential advantages 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.

"While we have primarily focused on NRX-101 as a drug to treat CNS disease, these new and highly provocative findings suggest that NRX-101 could find a home as a first line treatment for cUTI and pyelonephritis, which afflicts more than 3 million Americans each year. Should the rodent model findings prove applicable to the people, the use of NRX-101 to treat cUTI without increasing the risk of *C. diff* infection could have multibillion dollar

potential," said Stephen Willard, JD, Chief Executive Officer of NRx pharmaceuticals.

About D-Cycloserine in cUTI

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. (Lodise TP, et. al. Open Forum Infectious Diseases https://doi.org/10.1093/ofid/ofac307)

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, NRX-101 has now been shown to have minimal tendency to disrupt the microbiome of the intestine and vagina and which can lead to secondary *Clostridium difficile* and/or yeast infections. *C. diff* associated colitis doubles hospital mortality and costs the American healthcare system up to $1.6 billion each year. (Drozd EM, et. al. Mortality, Hospital Costs, Payments, and Readmissions Associated With Clostridium difficile Infection DOI: 10.1097/IPC.0000000000000299) Additionally, DCS has no known association pulmonary fibrosis, a rare, lethal condition that has been associated with macrolide (tetracycline family) antibiotics.

NRX-101 has received FDA Qualified Infectious Disease Product (QIDP) and Fast Track Designations in Complicated Urinary Tract Infection and Pyelonephritis.

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 and Lotus 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 HTX-100 (IV ketamine), through Hope Therapeutics, 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.

About HOPE Therapeutics, Inc.

HOPE Therapeutics, Inc. (www.hopetherapeutics.com) is a Specialty Pharmaceutical Company, wholly-owned by NRX Pharmaceuticals focused on development and marketing of an FDA-approved form of intravenous ketamine for the treatment of acute suicidality and depression together with a digital therapeutic-enabled platform designed to augment and preserve the clinical benefit of NMDA-targeted drug therapy.

Notice Regarding Forward-Looking Statements

The information contained herein includes forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended. These statements include, among others, statements regarding the proposed public offering and the timing and the use of the proceeds from the offering. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as "may," "will," "should," "would," "expect," "plan," "believe," "intend," "look forward," and other similar expressions among others. These statements relate to future events or to the Company's future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause the Company's actual results to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. You should not place undue reliance on forward-looking statements since they involve known and unknown risks, uncertainties and other factors which are, in some cases, beyond the Company's control and which could, and likely will, materially affect actual results, levels of activity, performance or achievements. Any forward-looking statement reflects the Company's current views with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to the Company's operations, results of operations, growth strategy and liquidity. More detailed information about the Company and the risk factors that may affect the realization of forward-looking statements is set forth in the Company's most recent Annual Report on Form 10-K and other filings with the Securities and Exchange Commission. Investors and security holders are urged to read these documents free of charge on the SEC's website at http://www.sec.gov. Except as may be required by applicable law, The Company assumes no obligation to publicly update or revise these forward-looking statements for any reason, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, whether as a result of new information, future events or otherwise.

SOURCE NRx Pharmaceuticals, Inc.

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