September 6, 2023

NRx Pharmaceuticals Announces Potent Antibacterial Activity of NRX-101 Against Common, Antibiotic Resistant Urinary Pathogens

- *NRX-101 demonstrated potent antibacterial effect against antibiotic-resistant pathogens in culture medium and in an artificial urine model*
- *D-cycloserine (DCS), a key component of NRX-101, was originally developed as an anti-infective in the 1950's but was replaced by antibiotics that have since lost effectiveness against complicated Urinary Tract Infections (cUTI)*
- *In an era when 90% of cUTI pathogens demonstrate resistance to standard antibiotics, NRX-101 may prove effective in treating cUTI and preventing urosepsis*

RADNOR, Pa., Sept. 6, 2023 /PRNewswire/ -- NRx Pharmaceuticals, Inc. (Nasdaq: NRXP) ("NRx Pharmaceuticals", the "Company"), a clinical-stage biopharmaceutical company, today announced new data that demonstrate potent *in vitro* activity of NRX-101 (D-cycloserine + lurasidone) against reference strains of Urinary Tract pathogens known to cause complicated urinary tract infections (cUTIs). D-cycloserine (DCS) was originally developed as an anti-infective in the 1950's but was never labeled for treatment of UTI, because of the prevalent and then-effective use of common antibiotics. In recent years, however, cUTI is increasingly caused by pathogens that are resistant to common antibiotics and are increasingly likely to cause sepsis, a lethal condition. Approximately 17,000 deaths per year in the United States are attributed to genitourinary sepsis.[1] The study, commissioned by NRx at Charles River Laboratories, is consistent with previously reported academic studies that demonstrate potency of DCS in antibiotic-resistant strains of urinary pathogens.

"These newly-obtained data from an internationally-recognized research organization demonstrate that NRX-101 has a potent level of in-vitro activity against dangerous pathogens, such as Pseudomonas and Acinetobacter. DCS was eclipsed by common antibiotics in the 1950s, partly because of the rarity of such pathogens at the time and the effectiveness of first and second generation antibiotics against the common urinary tract pathogens of the day. DCS additionally had an early history of causing mild hallucinations in some patients, although it remains widely used by the World Health Organization. In the studies conducted by NRx and others with DCS in combination with lurasidone and similar drugs, these CNS side effects have not been observed. At the same time, the fourth generation antibiotics that are now used to treat cUTI are increasingly associated with systemic side effects." said Dr. Jonathan Javitt, Founder and Chief Scientist of NRx Pharmaceuticals, Inc. "DCS has the advantage of being highly concentrated in the urine, suggesting that NRX-101 has potential to be developed as a safe and effective treatment of cUTI."

If successfully developed, NRX-101 could offer cUTI patients an effective therapy with a favorable safety profile. Because NRx has already completed the phase 3 manufacture of NRX-101, the Company is in a position to immediately seek investigational human use for this indication, while continuing to develop NRX-101 for suicidal depression and chronic pain.

Complicated UTI is increasingly common in the US, with an estimated 3 million new diagnoses annually.[2] Antibiotic resistance is common as well.[3] While the CNS effect of DCS is based on its inhibition of the brain's NMDA receptor, Cycloserine also inhibits cell-wall synthesis in various bacteria.

About NRX-101

NRX-101, a fixed dose combination of D-cycloserine and lurasidone, has been granted Fast Track Designation, Breakthrough Therapy Designation, a Special Protocol Agreement, and a Biomarker Letter of Support from the FDA for S-TRBD. Additionally, the product is being developed in chronic pain and PTSD.

Up to 50% of individuals with bipolar disorder attempt suicide over their lifetime, and estimates indicate that up to 20% may succumb to suicide. The only FDA-approved treatment for patients with treatment-resistant suicidal bipolar depression remains electroconvulsive therapy.

Conventional antidepressants can increase the risk of suicide in certain patients; hence their labels contain a warning to that effect. NRX-101 is a patented, oral, fixed dose combination of D-cycloserine and lurasidone, neither of which has shown addiction potential in preclinical models. Based on the results of a Phase 2 proof-of-concept study, NRX-101 received Breakthrough Therapy Designation from the FDA for the treatment of severe bipolar depression in patients with ASIB after initial stabilization with ketamine or other effective therapy.

NRX-101 is one of the first oral antidepressants currently in late-stage clinical studies targeting the NMDA-receptor in the brain, which represents potentially a key new mechanism to treat depression with and without suicidality, as well as chronic pain, PTSD and other indications.

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's lead program NRX-101, an oral, fixed-dose combination of D-cycloserine and lurasidone, targets the brain's N-methyl-D-aspartate (NMDA) receptor and is being investigated in a Phase 2b/3 clinical trial for suicidal treatment-resistant bipolar depression (S-TRBD), which includes patients with both acute and sub-acute suicidality, an indication for which the only approved treatment is electroshock therapy. The Company has partnered with Alvogen Pharmaceuticals, who owns the worldwide rights to NRX-101 for treatment of S-TRBD, to help bring NRX-101 to a global population of patients with unmet medical need. NRx Pharmaceuticals is currently exploring NRX-101's potential to act as a non-opioid chronic pain treatment option and is continuing to plan to enroll patients in an Israeli-based trial of patients suffering from post-traumatic stress disorder with depression and 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 Prest J, Nguyen T, Rajah T, Prest AB, Sathananthan M, Jeganathan N. Sepsis-Related Mortality Rates and Trends Based on Site of Infection. Crit Care Explor. 2022 Oct 10;4(10):e0775. doi: 10.1097/CCE.0000000000000775. PMID: 36248320; PMCID: PMC9556121.

2 Carreno JJ, Tam IM, Meyers JL, Esterberg E, Candrilli SD, Lodise TP, Jr. Longitudinal, nationwide, cohort study to assess incidence, outcomes, and costs associated with complicated urinary tract infection. Open Forum Infect Dis 2020; 7:ofz536

3 *Open Forum Infectious Diseases*, Volume 9, Issue 7, July 2022, ofac315

SOURCE NRx Pharmaceuticals, Inc.

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