August 7, 2023

# NRx Pharmaceuticals Announces the Licensure of a US Patent to Support Use of NRX-101™ for Chronic Pain

- *NRx has Licensed US Patent* 8,653,120 *for use of D-Cycloserine to treat Chronic Pain*
- *Dr. Vania Apkarian, a world leader in pain and D-Cycloserine (DCS) research, has joined the NRx Scientific Advisory Board*

RADNOR, Pa., Aug. 7, 2023 /PRNewswire/ -- NRx Pharmaceuticals, Inc. (Nasdaq: NRXP) ("NRx Pharmaceuticals", the "Company"), a clinical-stage biopharmaceutical company, today announced it has made key advances in developing NRX-101 to treat Chronic Pain.

The Company has signed a License Agreement for US Patent 8,653,120 that claims the use of D-cycloserine for the treatment of chronic pain in exchange for a commitment to pay milestones and royalties as development milestones are reached in the field of chronic pain. The patent is supported by extensive nonclinical data and early clinical data that suggest the potential for NMDA antagonist drugs, such as NRX-101 to decrease both chronic pain and neuropathic pain while potentially decreasing craving for opioids. Additional published non-clinical data previously reported demonstrate that NRX-101 is not neurotoxic[1] and not addictive.[2]

NRx has signed an agreement with Dr. Vania Apkarian, Professor of Physiology, Anesthesia, Surgery, and Neuroscience Institute, Northwestern University Feinberg School of Medicine to join the NRx Pharmaceuticals Scientific Advisory Board (SAB). Over his career, Dr. Apkarian has been devoted to unravelling brain mechanisms that underlie acute and chronic pain, and more generally how the brain dynamically processes information that gives rise to perception. This has included important research into the use of D-cycloserine in Chronic Pain.

"We delighted welcome Dr. Apkarian to the NRx SAB," said Jonathan Javitt, Chief Scientist and Founder of NRx Pharmaceuticals. "Adding a scientist of Vania's caliber will be invaluable to advancing our clinical program in Chronic Pain."

NRX-101 Indication – Chronic Pain

- In June 2023, the Company announced a focus on chronic pain as the next focus on NRX-101's development.
- DCS has been shown to modulate the Pain Pathway at each point in the chain: pain transmission at dorsal horn of the spinal cord, pain perception in the thalamus ("paleo brain"), and pain memory and processing between the paleo brain and the cortex.
- In experimental mouse models and clinical studies, NMDA antagonists have demonstrated attenuation of pain and shown potential in reducing opioid craving. Additionally, DCS has demonstrated no potential for addiction, unlike ketamine, NMDA antagonists and opioids.
- Chronic pain is estimated to be a $60 billion industry today with the potential to grow to a $120 billion industry by 2033.
- D-cycloserine was evaluated in a pilot study at Northwestern University, which showed efficacy at the higher dose levels in the study.[3] DCS is currently being examined in a confirmatory trial (n>200) in lower back pain at Northwestern University.[4] Data are expected shortly.

- Research conducted by NRx Pharmaceuticals demonstrated a 25 μg/ml dose at which d-cycloserine becomes an NMDA antagonist. The 400mg dose presented in the confirmatory trial at Northwestern University is at the lower end of the threshold and suggests that the ability to increase the d-cycloserine dose beyond 400mg, where lurasidone is used to prevent CNS side effects.

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.

1. Jordan W, Sapko MT, Siegel R, Javitt J. NRX-101, a Rapid-Acting Anti-Depressant, Does Not Cause Neurotoxicity Following Ketamine Administration in Preclinical Models. *Int J Toxicol.* 2023:10915818231176971. 10.1177/10915818231176971
2. Sapko MT, Hanania T, Chang Q, Javitt JC. D-cycloserine is not susceptible to self-administration using an intravenous self-administration model in male ketamine-habituated Sprague-Dawley rats. *Pharmacol Biochem Behav.* 2023;227-228:173586. 10.1016/j.pbb.2023.173586
3. Schnitzer TJ, Torbey S, Herrmann K, Kaushal G, Yeasted R, Vania Apkarian A. A randomized placebo-controlled pilot study of the efficacy and safety of D-cycloserine in people with chronic back pain. *Mol Pain.* 2016;12. 10.1177/1744806916678627
4. D-cycloserine for the Treatment of Chronic, Refractory Low Back Pain. https://classic.clinicaltrials.gov/ct2/show/NCT03535688.

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