NRx Pharmaceuticals Announces Submission of an Investigational New Drug (IND) Application for NRX-101 in the Treatment of Chronic Pain

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- *IND builds on previously-published, preliminary evidence of efficacy*
- *Filing is supported by robust manufacturing, pre-clinical and clinical data already reviewed by FDA for NRX-101 associated with treatment of bipolar depression*

RADNOR, Pa., Aug. 30, 2023 /PRNewswire/ - NRx Pharmaceuticals, Inc. (Nasdaq: NRXP) ("NRx Pharmaceuticals", the "Company"), a clinical-stage biopharmaceutical company, today announced submission an Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA) for the use of NRX-101 to treat Chronic Pain. The IND application leverages pioneering research on the use of D-cycloserine (a key ingredient of NRX-101) in the treatment of chronic pain and the recent licensure by NRx of a US Patent for the use of D-cycloserine in the treatment of pain. Nonclinical and substantial clinical data are already on file with FDA for NRX-101, which has already been granted Breakthrough Therapy Designation for the treatment of suicidal Bipolar Depression.

"One in five American adults suffers from chronic pain, a condition for which there are few good solutions, once NSAIDs and Tylenol-like drugs have been exhausted. There is a critical need for non-addictive, non-neurotoxic, oral medicines, particularly with the widespread recognition that opioids are not a viable option for treatment," said Dr. Jonathan Javitt, Founder, Chairman and Chief Scientist of NRx Pharmaceuticals, Inc. "NRX-101 targets the NMDA receptor in the brain, which has been demonstrated in extensive nonclinical and early clinical studies to mediate the pain pathway."

Dr. Javitt continued "based on the preliminary evidence of efficacy already demonstrated for the use of D-cycloserine in Chronic Pain, we plan to seek Fast Track Designation, Priority Review, and Breakthrough Therapy Designation for the use of NRX-101 to treat Chronic Pain. We have already completed the critical manufacturing components required by FDA in connection with our bipolar depression program and have sufficient quantities of our investigational drug on hand to launch registrational studies in 2024, pending the results of the recently completed clinical trial funded by the US Department of Defense."

NRX-101 in Chronic Pain

- Chronic pain is estimated to be a $72 billion industry today with the potential to grow to a $120 billion industry by 2033.
- In June 2023, concurrent with announcement of the Alvogen partnership, the Company announced an expansion of its NRX-101 program to encompass treatment of chronic pain as the next focus on NRX-101's development.
- The company recently announced the licensure of US Patent 8,653,120 related to the treatment of chronic pain with DCS and the addition of Dr. Apkar Vania Apkarian, Professor of Physiology, Anesthesia, Surgery, and Neuroscience Institute, Northwestern University Feinberg School of Medicine, to the NRx Scientific Advisory Board. Dr. Apkarian is the inventor of the patent and a global expert in pain research and has important experience studying DCS in chronic pain.
- D-cycloserine (DCS) has been shown to modulate the Pain Pathway at each point in the neural chain of 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 models and clinical studies, NMDA antagonists have demonstrated attenuation of pain and shown potential to reduce opioid craving.
- DCS has demonstrated no potential for addiction, unlike ketamine and other NMDA antagonists that bind to the "mu" opioid receptor.
- DCS was evaluated in a pilot study at Northwestern University and showed efficacy at the higher dose levels in the study (Schnitzer, 2016). DCS is currently being examined in a confirmatory trial funded by the US Department of Defense under the Congressionally Directed Medical Research Program. The trial seeks to recruit approximately 200 participants with chronic low back pain at Northwestern University (clinicaltrials.gov NCT03535688).[1] Data collection is complete and statistical results are expected in the coming months.
- 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 in NRX-101.

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] https://classic.clinicaltrials.gov/ct2/show/NCT03535688

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