NRx Pharmaceuticals to discuss new NRX-101 pipeline indication for augmentation of Transcranial Magnetic Stimulation

December 3, 2025

- As previously announced, low dose D-cycloserine has been associated with augmentation of the antidepressant and antisuicidal response achieved by Transcranial Magnetic Stimulation (TMS).
- NRx has amended its Investigational New Drug filing for NRX-101 (D-cycloserine/lurasidone) to include its use in association with TMS for the treatment of depression, including suicidal depression. This protocol will be available to patients both through a clinical trial and under NRx's Expanded Access protocols.
- NRx currently has more than 25,000 manufactured investigational doses available

WILMINGTON, Del., Dec. 03, 2025 (GLOBE NEWSWIRE) -- NRx Pharmaceuticals, Inc. (Nasdaq: NRXP), a clinical-stage biopharmaceutical company, today announced that it has amended its Investigational New Drug filing for NRX-101 (D-cycloserine/lurasidone) to include the use of NRX-101 in association with Transcranial Magnetic Stimulation (TMS) for the treatment of depression, including suicidal depression.

In the third quarter, the Company identified a promising new indication for NRX-101 that potentially offers rapid path to commercialization for this Breakthrough Therapy-designated drug. Recent evidence suggests that NRX-101 may confer a significant added advantage to the clinical results of Transcranial Magnetic Stimulation. Cole and colleagues reported that patients randomized to D-cycloserine (DCS) vs. Placebo concurrent with TMS using a standard protocol experienced a greater than two-fold benefit in terms of reduction in symptoms of depression. Clinical response of 75% and remission of 40% was seen in the DCS-treated group.[1] A substantial body of nonclinical literature has been published in subsequent years demonstrating that DCS at low doses exerts a neuroplasticity effect and causes dendritic sprouting in areas of the brain associated with depression.

On November 4, 2025, Real World Data were presented in conjunction with use of a modern Theta Burst FDA-cleared TMS device and a one day TMS protocol, combined with a single administration of oral DCS. The authors reported 87% clinical response and 72% remission manifesting at 6 weeks after a single day of treatment on the Hamilton Depression Rating Scale with similar findings on other standard test measures.[2]

Nonclinical evidence suggests that D-cycloserine acts to augment neuroplasticity in association with TMS. Should the findings of these two clinical studies be replicated in registration trials conducted to current regulatory standards, the Company anticipates D-cycloserine or similar medicines will become standard of care therapy in association with TMS. The response rate from TMS with cycloserine (>80%) in these two studies compares favorably to the 30% success rate now reported in association with SSRI antidepressants, without the well known side effects of SSRI medications.

In addition to containing D-cycloserine, NRX-101 contains a low dose of lurasidone, a medicine already approved for treatment of depression and known to have anti-hallucinatory properties. D-cycloserine by itself is well known to have a low, but measurable potential for inducing low-grade hallucinations, resulting in a labeled contraindication against the use of Seromycin® (D-cycloserine) in patients with depression. This contraindication originally led the founders of NRx to develop and patent the NRX-101 drug combination, which has now obtained composition of matter patent protection in all major jurisdictions.

NRx believes that the clinical benefit demonstrated in these two published trials can be demonstrated in a well-controlled trials of approximately 120 participants. The Company is in partnership discussion with manufacturers of currently-marketed TMS devices to configure a joint clinical trial that will lead to drug registration and augmentation of FDA labeling of currently-approved TMS devices. Because TMS is already an approved and reimbursed therapy for patients with depression, the Company anticipates that such trials can be accomplished at modest expense.

Given current trends, the Company expects that more than 1 million Americans per year may be treated with TMS by the year 2030, creating a substantial new potential market for NRX-101 not previously anticipated. As required by law for Breakthrough Therapy drugs such as NRX-101, the Company has published an Expanded Access policy for this medication. Treating physicians who believe that their patients might benefit from NRX-101 in association with TMS may contact the Company for further information.

About NRx Pharmaceuticals, Inc.
NRx Pharmaceuticals, Inc. (www.nrxpharma.com), is a clinical-stage biopharmaceutical company developing therapeutics based on its NMDA platform for the treatment of central nervous system disorders, specifically suicidal depression, chronic pain, and PTSD. The Company is developing NRX-100 (preservative-free intravenous ketamine) and NRX-101, (oral D-cycloserine/lurasidone). NRX-100 has been awarded Fast Track Designation for the treatment of Suicidal ideation in Depression, including Bipolar Depression. NRX-101 has been awarded Breakthrough Therapy Designation for the treatment of

suicidal bipolar depression. NRx has recently re-filed an Abbreviated New Drug Application (ANDA), and initiated a New Drug Application filing for NRX-100 with an application for the Commissioner's National Priority Voucher Program for the treatment of suicidal ideation in patients with depression, including bipolar depression.

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. 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. The Company has reported regulatory milestones as they have been achieved but has not predicted the outcome of any future regulatory determination. 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, including uncertainties and assumptions relating to the Company's operations, results of operations, growth strategy, and, among other things, 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.

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[1] Cole J, et.al. Efficacy of Adjunctive D-Cycloserine to Intermittent Theta-Burst Stimulation for Major Depressive Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2022;79(12):1153–1161. doi:10.1001/jamapsychiatry.2022.3255

[2] Vaughn, Donald & Marino, Brooke & Engelbertson, Alex & Dojnov, Aleksandra & Weiss, Nick & Vila-Rodriguez, Fidel & Nanos, Georgine & Downar, Jonathan. (2024). Real-world effectiveness of a single-day regimen for transcranial magnetic stimulation using Optimized, Neuroplastogen-Enhanced techniques in Depression (ONE-D). 10.21203/rs.3.rs-5679327/v1.