NRx Pharmaceuticals Announces Positive Recommendation to Continue Enrollment in the Ongoing Trial of NRX-101 in Patients with Suicidal Treatment-Resistant Bipolar Depression

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· The independent Data Safety Monitoring Board recommended continuation of patient enrollment as planned

· No safety or futility signals were reported in the first 50 patients

· This patient population could represent up to 1 million bipolar depression patients in the US and represents a portion of the indication expansion recommended in recent correspondence with the FDA

· Trial has been upgraded to a Phase 2b/3 study that may be used for a registrational filing

RADNOR, Pa., March 27, 2023 /PRNewswire/ -- **NRx Pharmaceuticals, Inc. (Nasdaq: NRXP)** ("NRx Pharmaceuticals", the "Company"), a clinical-stage CNS biopharmaceutical company, today reported that the independent Data Safety Monitoring Board (DSMB) reviewed the safety and efficacy findings of the first fifty enrolled participants in the Company's clinical trial of NRX-101 for the treatment of Severe Bipolar Depression and Subacute Suicidal Ideation or Behavior (**www.clinicaltrials.gov** NCT NCT03395392). NRX-101 is a proprietary fixed dose combination of D-cycloserine and lurasidone. The people enrolled in this trial had bipolar depression and suicidal thoughts. They were being treated in the outpatient setting. Going forward, NRx will use the term "Suicidal Treatment-Resistant Bipolar Depression" to describe this potential indication.

The DSMB found no futility signal at this stage of the trial. Similarly, no safety signals were identified in association with NRX-101 and the DSMB recommended that enrollment in the trial continue as planned. According to the study's statistical analysis plan, the failure to identify futility requires that a numerical advantage of the investigational drug relative to the comparator treatment must be observed by the DSMB. The DSMB will continue to monitor safety and efficacy in the trial.

Based on the DSMB findings, together with the recent completion of Phase 3/ anticipated commercial stage manufacture of NRX-101, the Company has upgraded the ongoing trial to a phase 2b/3 trial whose results may be used in a future registrational filing, should the primary endpoint be met. We expect top-line data from this trial in the fourth quarter of 2023. In the Type B meeting conducted with the FDA, the Company was guided to explore the use of NRX-101 in this broader population of patients who may benefit from NRX-101 without prior use of ketamine. The Company plans to discuss the path to approval in this population of people with Suicidal Treatment Resistant Bipolar Depression in the planned Comprehensive Breakthrough Therapy Meeting with FDA that is planned for the second quarter of 2023.

NRX-101 is the first oral NMDA-targeted medicine to be developed for patients with suicidal bipolar depression. Moreover, this trial, together with the phase 3 trial for which the Company has been granted a Special Protocol Agreement by FDA, represent the only known clinical trials in which patients with active suicidal ideation or behavior have been enrolled. All known previous studies of oral antidepressants have excluded patients with active suicidality. There is reason to believe that people with bipolar depression may derive particular benefit from NMDA-targeted drugs, based on a recent trial in France demonstrated that ketamine, a potent NMDA-targeted drug, may be seven-fold more effective in reducing suicidal ideation in people with bipolar depression compared to those with major depressive disorder. Unlike ketamine, however, NRX-101 is an oral medicine for home use that has been shown not to be neurotoxic, not to produce psychedelic effects in prior studies, and to have no potential for addiction in standard screening tests.

In the US alone, nearly 1 million people are believed to have Treatment-Resistant Bipolar Depression, a lethal condition that ultimately leads to a suicide attempt in half of those with bipolar disorder. Currently, there is no approved medicine for patients with this condition and the only FDA-approved treatment is electroshock therapy, which has numerous known side-effects. To date, no drug-related Serious Adverse events have been identified in clinical trials of NRX-101.

NRx Pharmaceuticals' CEO Stephen Willard said: "We are encouraged by the DSMB's advice to continue this trial in patients with Suicidal Treatment-Resistant Bipolar Depression, who represent an extraordinary unmet medical need. The crisis of suicide in our society demands action now, with an American attempting suicide every 27 seconds. We are committed to investigating NRX-101 as a potential solution for this crisis. While all known trials of oral antidepressants have excluded patients with suicidal ideation, we have embraced them and – so far – demonstrated that they can be safely welcomed into a clinical trial of a medicine that may provide benefit. Now that we have a manufactured inventory of Phase 3/commercial stage NRX-101, we have upgraded this trial to a Phase 2b/3 registrational study. Additionally, we are opening an Expanded Access Program as required for all Breakthrough Therapy Medicines to make this investigational medicine more broadly available and to accrue the safety database previously requested by the FDA."

About NRx Pharmaceuticals
Clinical-stage biopharmaceutical company developing therapeutics for the treatment of central nervous system disorders, specifically suicidal depression and post-traumatic stress disorder (PTSD). The company's lead medicine, NRX-101, is an oral, fixed-dose combination of D-cycloserine and lurasidone. NRX-101 targets the brain's NMDA receptor and is being investigated in a Phase 3 trial under an FDA Special Protocol Agreement and Breakthrough Therapy Designation in patients with bipolar depression and suicidal ideation, an indication for which the only approved treatment is electroshock therapy. The Breakthrough Therapy Designation and Special Protocol Agreement were awarded by the FDA based on the Company's prior STABIL-B trial that demonstrated substantial improvement over available therapy in reducing depression and suicidality compared to placebo when patients were treated with NRX-101 after a single dose of ketamine.

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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