NRx Pharmaceuticals Announces Strategic Change in Development of NRX-100 (IV Ketamine) at Dawson James Small Cap Investor Conference

October 12, 2023

- *Previously announced data sharing agreement for intravenous ketamine*
- *Newly available data highlight the need for a labeled form of IV ketamine that can qualify for insurance reimbursement*
- *Need for intravenous ketamine is heightened by recent failure of intranasal ketamine to treat suicidality. Currently approved esketamine is not available for patients with bipolar depression*
- *The importance of appropriately labeled intravenous ketamine is highlighted by recent FDA warning letter and prior warning letters against compounding and off-label uses of ketamine for psychiatric care*

JUPITER, Fla., Oct. 12, 2023 /PRNewswire/ -- NRx Pharmaceuticals, Inc. (Nasdaq: NRXP) ("NRx Pharmaceuticals", the "Company"), a clinical-stage biopharmaceutical company today announced a strategic acceleration of its plans to develop a commercial form of NRX-100 (intravenous ketamine) to treat acute depression and suicidality, based on recent data cooperation agreements and on changes in the regulatory environment. The full presentation may be viewed on the Company's web page Link. The Company further invites interested parties to subscribe to their email alert service stay up to date on company's progress here: NRX Email Alerts.

As previously announced, the Company has signed a Data Sharing Agreement to gain access to the patient level (anonymized) data from a major Ketamine study in France (*BMJ* 2022; 376 Link). The findings of this trial demonstrate a dramatic effect of intravenous ketamine in reducing acute suicidality and depression, particularly in patients with bipolar depression. The findings of this trial confirm the results reported by Grunebaum and coworkers (Am J Psychiatry 2018;175:327 Link) and numerous smaller trials.

Two simultaneous and unexpected developments augment NRx's renewed focus on offering a commercial form of intravenous ketamine:

1. A long-awaited trial of nasal ketamine for the same indication failed to meet its primary endpoints.
2. The FDA issued a second warning letter on October 10, 2023 (Link) cautioning against the compounding of ketamine, which follows its February 16, 2022 (Link) warning letter regarding the compounding of nasal forms of ketamine. Sequential warning letters of this nature are frequently followed by enforcement actions, particularly in the case of a DEA scheduled, dangerous drug, such as ketamine.

Without an approved form of intravenous ketamine for acute suicidality, its benefits will only be available to patients able to pay cash for off-label treatment, because unapproved therapies are not suitable for insurance reimbursement. Moreover, FDA's clear position regarding the illegality of compounded forms of ketamine is likely to further limit access to what appears to be a lifesaving drug.

Although NRx has long held the belief that ketamine is not suitable as a long-term treatment for depression and suicidality because of its potential for neurotoxicity, addiction, and hallucination, we have long-recognized ketamine's unique ability to provide rapid remission from acute suicidality, provided a safe, oral drug can be implemented to maintain the life-saving effect. With the availability of what are now two clinical trials that demonstrate clinically-meaningful and statistically significant benefit of ketamine vs. both placebo and midazolam (active comparator), we hope that a path to accelerated approval of NRX-100 (IV ketamine) as an agent for rapid reversal of suicidality as a prelude to long-term oral therapy can be identified. Preliminary estimates of this regulatory focused work show that this effort is within the company's current budget.

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 Suicidal Treatment Resistant Bipolar Depression (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 Acute Suicidal Ideation and Behavior (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, as well as potential use in Urinary Tract Infections (UTI).

About NRx Pharmaceutical
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 press release 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. Actual results could differ materially from those contemplated by the forward-looking statements. A discussion of these and other factors, including risks and uncertainties with respect to the Company, is set forth in the Company's filings with the Securities and Exchange Commission, including its Annual Report on Form 10-K, as may be supplemented, or amended by the Company's Quarterly Reports on Form 10-Q. Given these risks, uncertainties, and factors, you are cautioned not to place undue reliance on such forward-looking statements, which are qualified in their entirety by these cautionary statements.

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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