NRx Pharmaceuticals (NASDAQ:NRXP) Announces Publication of Paper Entitled "Quality Assurance of Depression Ratings in Psychiatric Clinical Trials"

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- *NRx-developed training and monitoring methodology in recently completed phase 2b/3 clinical trial of NRX-101 documents higher interrater reliability (IRR) on primary endpoint (MADRS depression scale) than previously reported industry standards*
- *Positive implications for conduct of future registration trials for NRX-101 and similar medications.*
- *Published in the peer reviewed* American Journal of Clinical Psychopharmacology

WILMINGTON, Del., Nov. 25, 2024 /PRNewswire/ -- NRx Pharmaceuticals, Inc. (Nasdaq: NRXP) ("NRx Pharmaceuticals", the "Company"), a clinical-stage biopharmaceutical company, today announced the publication of a paper by Sapko, *et. al*. in the peer-reviewed *American Journal of Clinical Psychopharmacology*. The paper, entitled "Quality Assurance of Depression Ratings in Psychiatric Clinical Trials,"[1] reported on the impact of a comprehensive program developed by NRx Pharmaceuticals to enhance reliability in psychometric ratings that are key to drug approval. Registration trials of drugs for depression and related conditions frequently fail because of unexpected statistical variability across study sites. NRx developed a methodology for training and monitoring the performance of the study site raters, whose measurements are key to the success or failure of all clinical trials of antidepressant drugs. This approach resulted in an unprecedented level of agreement (3 points or better on a 60 point scale) compared to prior industry practices.

"The rater training and monitoring methodology achieved by NRx's research team enabled the team to identify statistically significant improvements in recovery from suicidality and reduction in akathisia (a potentially lethal side effect of antidepressant drugs) with a compact study design of 90 patients. This methodology enabled statistical significance to be achieved with fewer than 100 participants, where typically several hundred would have been required," said Dr. Jonathan Javitt, Chairman, CEO and Chief Scientist of NRx Pharmaceuticals and senior author of the study. "Clinical trials in antidepressant drugs rely on close coordination of human psychometric raters across study sites. Improving the reliability of this methodology increases our ability to bring new, lifesaving medicines to patients."

In the NRX-101 study, trial concordance, as defined by no more than 3 points of disagreement between site raters and central raters, was seen in 94.5% of ratings, where standard industry practice was to accept substantially higher variance (i.e. up to 6 points of disagreement) between study site raters and central raters.[2] Accepting higher variance entails recruiting many more participants to achieve statistical significance with substantially higher study costs and risks of failure. The Company will be using this improved methodology in future drug development, and clinical trials conducted within its network of HOPE clinics.

About NRx Pharmaceuticals, Inc.

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 is developing NRX-101, an FDA-designated investigational Breakthrough Therapy for suicidal treatment-resistant bipolar depression and chronic pain. NRx plans to file an NDA for Accelerated Approval for NRX-101 in patients with bipolar depression and suicidality or akathisia. NRX-101 additionally has potential to act as a non-opioid treatment for chronic pain, as well as a treatment for complicated UTI.

NRx has recently announced plans to submit a New Drug Application for NRX-100 (IV ketamine) for the treatment of suicidal depression, based on results of well-controlled clinical trials conducted under the auspices of the US National Institutes of Health and newly obtained data from French health authorities, licensed under a data sharing agreement. NRx was awarded Fast Track Designation for development of ketamine (NRX-100) by the US FDA as part of a protocol to treat patients with acute suicidality.

About HOPE Therapeutics, Inc.

HOPE Therapeutics, Inc. (www.hopetherapeutics.com) is a development stage healthcare delivery company developing a best-in-class network of precision psychiatry clinics that intends to offer ketamine transcranial magnetics stimulation (TMS) and other lifesaving therapies to patients with suicidal depression and related disorders, together with a digital therapeutic-enabled platform designed to augment and preserve the clinical benefit of NMDA-targeted drug therapy.

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. These statements include, among others, statements regarding the proposed public offering and the timing and the use of the proceeds from the offering. 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. 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, uncertainties and assumptions relating to the Company's operations, results of operations, growth strategy, liquidity, Hope Therapeutic's ability to consummate the acquisitions of providers for its national network, the Company's ability to raise adequate capital to fund the Hope Therapeutics acquisitions, and the Company's ability to spin-off Hope Therapeutics. 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] Sapko, et. al., *J Clin Psychopharmacol*, 2024

[2] *Targum SD, Catania CJ. Audio-digital recordings for surveillance in clinical trials of major depressive disorder. Contemp Clin Trials Commun. 2019;14:100317*

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