February 13, 2023

NRx Pharmaceuticals Reports Minutes of Recent U.S. Food and Drug Administration (FDA) Meeting on the Development of NRX-101 to Treat Severe Bipolar Depression in Patients with Suicidality

- FDA discussed a broader indication of "treatment of recently acutely suicidal patients" with Bipolar Depression.
  - This broader indication does not require ketamine as the only stabilization agent.
  - The Company estimates this substantially increases the addressable acute population for its treatment.
- FDA encouraged NRX to request a Breakthrough Therapy Planning Meeting for NRX-101.
- FDA suggested the NRX-101 clinical development program be enlarged to allow for chronic treatment of patients with Bipolar Depression and intermittent suicidality.
  - This expanded development program could enable the use of NRX-101 by a broader segment of the approximately 7 million individuals in the U.S. with Bipolar Disorder on a long-term basis.
  - The Company is considering expanding its current phase 2 clinical trial to a potential registration study based on the FDA current guidance using newly released commercial-scale NRX-101 product.
- FDA deemed the Company's remaining nonclinical development plan to be reasonable and indicated that deferring Pediatric and Adolescent trials until after drug approval appears reasonable.

RADNOR, Pa., Feb. 13, 2023 /PRNewswire/ -- NRx Pharmaceuticals, Inc. (Nasdaq: NRXP) ("NRx Pharmaceuticals", the "Company"), a clinical-stage biopharmaceutical company, today reported the minutes of a Type B meeting with the U.S. Food and Drug Administration's Division of Psychiatry Products held on January 11, 2023.

NRx Pharma Announces FDA Guidance from January 11, 2023, Type B Meeting

The purpose of the meeting was to discuss requirements for submission of a New Drug Application for NRX-101. FDA noted in written correspondence that the Special Protocol Agreement (SPA), granted in April 2019 remains in effect. Additionally, the FDA suggested during the meeting that a broadening of the addressable population of the indication (under the SPA or otherwise) to patients with Severe Bipolar Depression and Recent Acute Suicidality regardless of how the initial stabilization was accomplished could represent a more straightforward development program. This broader indication would enable the Company to potentially demonstrate the use of NRX-101 to maintain stabilization from suicidality in patients stabilized either with ketamine or with other standard of care therapeutic approaches. This broader indication is not expected to delay the acute care trial expected to be completed in 2023. FDA noted that, should the results of such a study be driven primarily by subjects stabilized with ketamine, a New Drug Application for ketamine would also be required.

The FDA further guided the Company to broaden the study of NRX-101 to include chronic/intermittent treatment of patients with Bipolar Depression and suicidality. This could enable a pathway for the use of NRX-101 by a broader segment of the approximately 7 million individuals in the U.S. with Bipolar Disorder on a long-term basis. A portion of this population is already being addressed in the Company's ongoing phase 2 trial, which recently passed its first Data Safety Monitoring Board (DSMB) safety review. Based on this guidance, the Company is considering expanding its current phase 2 clinical trial to a potential registration study now that the manufacture of phase 3/commercial-stage NRX-101 has been completed. The Company previously announced completion of

a Type C meeting in which FDA agreed to the Company's Chemical Manufacturing Control and stability program for drug manufacture. As previously announced, the Company currently expects a DSMB evaluation of efficacy data from this trial by the end of Q1 2023.

The FDA further advised the Company that as a chronic, or chronic-intermittent treatment, the safety database requirement under ICH guidelines for NRX-101 should be 1,500 patients, with at least 100 treated for 1 year. The Company is evaluating the timing and cost of expanding clinical access to this larger population. In addition to its ongoing clinical trials, the Company is considering augmenting its safety database via an expanded access program, which is now enabled by the availability of commercial-stage NRX-101 and is expected under federal law governing Breakthrough Therapy Designation. The Company will seek cost reimbursement for operating this Expanded Access Program as permitted under current FDA regulations.

In related comments, the FDA accepted the Company's rationale for deferring pediatric and adolescent studies with NRX-101 until after drug approval and advised the Company to include this rationale in its regulatory filings. The FDA will consider the Company's submission of an Advice Request to evaluate waiving or deferring chronic carcinogenicity testing as a post-approval commitment. Finally, the FDA's Controlled Substances Staff advised the Company to closely monitor abuse-related adverse events and possible cases of abuse during clinical trials.

"We appreciate the FDA's support for the development of a drug that might offer the first approved medicine to patients with bipolar depression and acute and subacute levels of suicidality" said Stephen Willard, Chief Executive Officer of NRx Pharmaceuticals. "With their guidance, we aim to expand our development program to address the needs of the broader population of patients with subacute suicidal ideation, while continuing to focus on those with bipolar depression with acute suicidal ideation and behavior as per our Breakthrough Therapy Designation. We anticipate amending the indication under our SPA to align with the broader stabilized patient population, and we will discuss this issue further with the FDA at our Breakthrough Therapy Planning Meeting. FDA has guided us to a path that potentially serves a significantly greater proportion of the approximately 7 million patients in the U.S. who have bipolar disease, half of whom are reported to attempt suicide at some point in their lives. Our completion of phase 3 commercial stage drug supply enables us to embark upon that path without delay."

About NRX-101

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 bipolar depression and acute suicidal ideation & behavior (ASIB) remains electroconvulsive therapy (ECT). 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. 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 PTSD and other indications. To date, NRX-101 is the only oral NMDA investigational medicine focused on bipolar depression in patients with acute and sub-acute suicidality.

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 program NRX-101, an oral, fixed-dose combination of D-cycloserine and lurasidone, 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. NRx Pharmaceuticals has also initiated a Phase 2b clinical trial in patients with Sub-Acute Suicidality, a substantially broader indication. 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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