NRx Pharmaceuticals, Inc. (NASDAQ:NRXP) Re-Files Abbreviated New Drug Application (ANDA) for KETAFREE™, Preservative-Free IV Ketamine

September 29, 2025

- KETAFREE™ to provide innovative, preservative-free IV ketamine formulation, eliminating toxic preservatives, in keeping with current HHS priorities to eliminate toxic preservatives from foods and drugs
- Filing is based on FDA interaction and approval of Suitability Petition for NRx's proposed strength of preservative-free ketamine
- This presentation of ketamine represents a reshoring of a strategically important drug to the US, in keeping with the Presidential Executive Order signed on May 5, 2025. Ketamine faces a current US drug shortage not expected to abate in the near future[1]
- Current ketamine market estimated at $750 million and projected to reach $3.35 billion globally in 2034.[2] NRx anticipates marketing KETAFREE™ for currently approved ketamine indications
- The Company has filed a citizen's petition with the FDA to remove benzethonium chloride, a known neurotoxic and cytotoxic substance, from all presentations of ketamine intended for intravenous use
- This formulation of ketamine is distinct from the formulation used in the ongoing NDA submission for NRX-100 in suicidal ideation in depressed patients, including bipolar depression, which was recently granted Fast Track designation by the FDA

WILMINGTON, Del., Sept. 29, 2025 (GLOBE NEWSWIRE) -- NRx Pharmaceuticals, Inc. (Nasdaq: NRXP), a clinical-stage biopharmaceutical company, today announced the re-filing of its Abbreviated New Drug Application (ANDA) to the U.S. Food and Drug Administration (FDA) for KETAFREE™, its preservative-free IV ketamine formulation, for use in all existing approved indications. The filing follows FDA grant of approval of its Suitability Petition for NRx's proposed strength of preservative-free ketamine.

The current annual ketamine market is estimated at $750 million, with global demand for ketamine projected to grow to $3.35 billion by 2034. This does not include the widespread use of compounded ketamine by clinics unable to obtain manufactured drug. NRx aims to capture a significant share of the current market. According to a 2021 survey, an estimated 5.1 million Americans had received ketamine for medical uses in their lifetime[3], a number that continues to grow with increased clinical focus on this important medication. Ketamine currently faces a severe drug shortage according to the American Society of Hospital Pharmacists. Accordingly, NRx is seeking priority review from FDA.

The Company previously filed a citizen's petition with the FDA to remove benzethonium chloride (BZT), a known neurotoxic and cytotoxic substance, from presentations of ketamine intended for intravenous use. The FDA has previously disallowed the use of BZT in hand cleansers and topical antiseptics. A related preservative, benzalkonium chloride has demonstrated corneal and conjunctival toxicity in artificial tears and glaucoma medications, leading to use of preservative-free alternatives. NRx has filed expert testimony from accredited toxicologists regarding the toxicity of BZT, which is not generally recognized as safe (GRAS) by the FDA. Removal of potentially harmful preservatives from foods is a stated priority in the MAHA report and HHS leadership has additionally targeted preservatives in vaccines. BZT was originally added to ketamine when it was first formulated in the 1970s to maintain stability and sterility using the container closure systems then available. NRx has demonstrated long term stability and sterility with a patented preservative-free formulation using modern manufacturing methods.

Return of strategic drugs to US manufacture (Reshoring) is a current US priority as stated in a Presidential executive order issued on May 5, 2025. This initiative particularly applies to drugs that are critical for inpatient care, such as ketamine. The NRx product is manufactured in partnership with Nephron Pharmaceuticals of West Columbia, SC.

The formulation filed under the ANDA is distinct from that used in the New Drug Application (NDA), for which the Company has received Fast Track Designation for Treatment of Suicidal Ideation in Depression, including Bipolar Depression. The Company anticipates submitting clinical trial data from more than 1,000 patients and real-world data from more than 180,000 patients in which ketamine demonstrated superiority to placebo and active placebo, with noninferiority to electroconvulsive therapy. Should both the ANDA and the NDA be approved, the resulting commercial products would have different, non-substitutable product numbers and different commercial paths.

"We appreciate FDA's rapid response to our suitability petition and look forward to advancing our preservative-free ketamine presentation to market," said Jonathan Javitt, MD, MPH, Chairman and CEO of NRx Pharmaceuticals. "KETAFREE™ is designed

to replace older formulations that rely on potentially neurotoxic and cytotoxic preservatives for stability and sterility, and to reshore the manufacture of a strategically-important drug to the US. We have filed a US patent on our novel, preservative-free formulation, which anticipates three years of room-temperature shelf stability."

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 had a Suitability Petition granted, allowing re-filing of 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 depression.

About HOPE Therapeutics, Inc.

HOPE Therapeutics, Inc. (www.hopetherapeutics.com), a subsidiary of NRx Pharmaceuticals, is a Healthcare delivery company that is building a best-in-class network of interventional psychiatry clinics 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. 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.

For further information:

Matthew Duffy
Chief Business Officer, NRx Pharmaceuticals
mduffy@nrxpharma.com

Brian Korb
Managing Partner, astr Partners
(917) 653-5122
brian.korb@astrpartners.com

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[1] https://www.ashp.org/drug-shortages/current-shortages/drug-shortage-detail.aspx?id=391
[2] https://www.factmr.com/report/injectable-ketamine-market
[3] https://www.radars.org/system/publications/NMURx%20Ketamine%20Use%20Poster_fin2.pdf