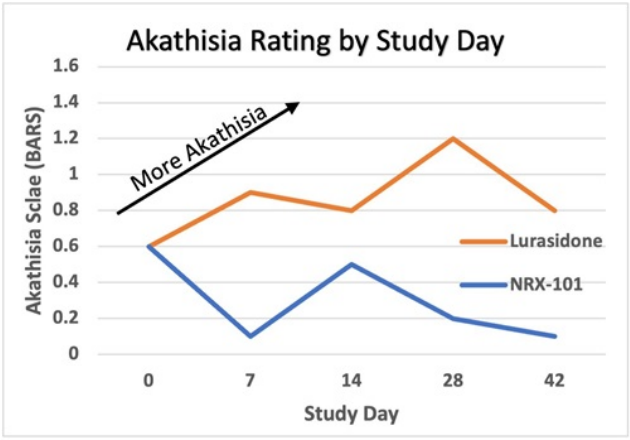
NRx Pharmaceuticals (Nasdaq:NRXP) Reports First Quarter 2024 Financial Results and Provides Business Update

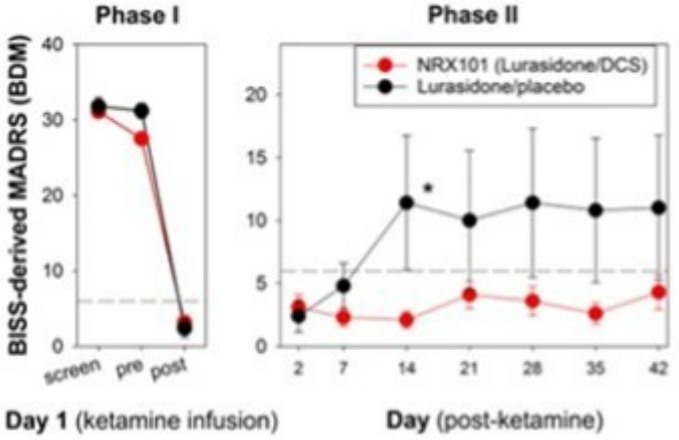
May 14, 2024

2024 Catalysts: Positive Clinical Data, Two Planned NDAs, Company Launch of Hope Therapeutics; FDA QIDP award in cUTI and New Schizophrenia Opportunity

- Executed Term Sheet from an institutional investor for an initial $7.5 million note, subject to common closing requirements, primarily to replace current debt, clearing the path to a Hope Therapeutics share distribution, with provision for funding up to $30 million to fund pipeline opportunities
- Positive data from a Phase 2b/3 trial of NRX-101 in Treatment Resistant Bipolar Depression (TRBD); trial demonstrated depression efficacy comparable to standard of care and significant reduction of akathisia (P=0.025). Akathisia is a potentially lethal side effect of all serotonin-targeted antidepressants and is associated with suicide. The study additionally demonstrated a 30% advantage in sustained remission from suicidality that was not statistically-significant at this sample size
- Above findings of reduced suicidality mirror the results of the Company's prior STABIL-B trial in acutely suicidal patients and also mirror the results of an independent published trial
- Company plans to file a New Drug Application (NDA) for Accelerated Approval under Breakthrough Therapy and Priority Review of NRX-101 in treatment of bipolar depression in people at risk of akathisia, based on the Phase 2b/3 and STABIL-B data
- Company has developed patentable pH neutral formulation for ketamine that will be suitable for both intravenous and subcutaneous administration. Ketamine efficacy data are in hand from 4 clinical trials. Three manufacturing lots are now initiated (required for NDA) and Company plans to initiate the NDA by July
- HOPE Therapeutics (which focuses on care delivery, not drug development) has partnered with representatives of ketamine clinic providers nationwide to construct a care platform that will include ketamine, operational support, and digital therapeutic extensions. In advance of FDA approval, HOPE is actively in the sales process to supply ketamine under 503b pharmacy licensure to meet the national ketamine shortage declared by FDA. HOPE is planned to be spun out as a separate company to be owned by NRx, current NRx shareholders, and new investors; Term Sheets received from prospective anchor investors for $60 million of new investment, once publicly listed
- Data expected shortly in 200-person DOD-funded trial of D-cycloserine (DCS), the key component of NRX-101, to treat chronic pain, conducted by Northwestern University. Statistical analysis plan and data unlock have been approved by Northwestern IRB
- NRX-101 in the treatment of Complicated Urinary Tract Infection (cUTI) granted Qualified Infectious Disease Product (QIDP), Fast Track, and Priority Review designations. Company has now demonstrated that NRX-101 does not damage the microbiome of the gut, in contrast to all other advanced antibiotics and is less likely to cause *C. Difficile* infection (a potentially lethal side effect of antibiotic treatment). NRx is reviewing partnership options
- Executed Memorandum of Understanding with Fondation FundaMental for rights to develop potential disease modifying drug for Schizophrenia. If successful, this would represent the first drug to reverse the underlying disease mechanism of schizophrenia, rather than simply treating symptoms.
- Management to host a conference call, May 14, 2024, at 4:30 PM ET

RADNOR, Pa., May 14, 2024 /PRNewswire/ -- NRx Pharmaceuticals, Inc. (Nasdaq: NRXP) ("NRx Pharmaceuticals", the "Company"), a clinical-stage biopharmaceutical company, today announced its financial results for the quarter ended March 31, 2024, and provided a business update.





"NRx has had an incredibly productive start to 2024, delivering positive data from our phase 2b/3 trial of NRX-101 in suicidal bipolar depression, where we demonstrated what could potentially be a best-in-class medication for people with bipolar disorder. To our knowledge, this is the first successful clinical trial ever conducted with an oral antidepressant in patients with suicidal depression who have been excluded from all antidepressant trials in the past. We plan to file a New Drug Application based on these and previous findings. In addition, we have advanced Hope Therapeutics and IV Ketamine, HTX-100, towards the filing of an NDA this summer, and continue to prepare to capitalize on the opportunity for NRX-101 in chronic pain and complicated UTI," said Stephen Willard, J.D., Chief Executive Officer and Director of NRx Pharmaceuticals. "Together these opportunities constitute treatments that can meet considerable unmet medical need in up to 75,000,000 patients across the country. Obviously, this would build incredible value for our shareholders. We are dedicated to bringing hope to life and I thank our team and shareholders for their ongoing hard work and support. Lastly, we are pleased to have signed a term-sheet to replace the toxic debt on our balance sheet with a new commitment from a solid, institutional investor."

First Quarter Clinical, Regulatory and Corporate Highlights

Development of NRX-101 for Suicidal Treatment-Resistant Suicidal Bipolar Depression

The Company announced final data from the recently completed phase 2b/3 trial of NRX-101 in suicidal bipolar depression, with a significantly improved safety profile as demonstrated by a statistically significant reduction in akathisia, an adverse event considered by many experts to be a precursor to suicide. Given the vital need for safer medications in this at-risk population, we plan to submit an NDA to the US FDA for treatment of bipolar depression patients at risk of akathisia, based on these data as well as additional data from our STABIL-B[1] trial.

	Efficacy Measures: Repeated Measures Mixed Model LS Mean Differences							
	Through Day 28				Through Day 42			
	LOCF No		LOCF yes		LOCF No		LOCF Yes	
	LS Mean Δ	p-value	LS Mean Δ	p-value	LS Mean Δ	p-value	LS Mean Δ	p-value
MADRS Depression Score	-4.0	0.09	-7.7	0.03	-3.7	0.04	-7.7	0.04
	LS Mean Δ	p-value	LS Mean Δ	p-value	LS Mean Δ	p-value	LS Mean Δ	p-value
Suicidality Rating Scale C-SSRS	-0.5	NS	-1.3	0.04	-0.6	NS	-1.5	0.02
	LS Mean Δ	p-value	LS Mean Δ	p-value	LS Mean Δ	p-value	LS Mean Δ	p-value
Clinical Global Impression CGI-SS	-0.4	NS	-2.9	0.05	-0.6	NS	-2.9	0.02

During 2024, the Company began working in unison with Alvogen and Lotus Pharmaceuticals to plan the final development and commercialization of NRX-101. These partners recently advanced $5 million of the first milestone to the Company. Final licensing

of the product, expected in Q2 2024, will yield a total of $9 million in milestone payments together with assumption of future development costs by our partners. The partnership provides for potential milestones of $329 million and a royalty reaching 15% on Net Sales.

NRX-101 for Treatment of Chronic Pain:

In 2023, the Company licensed US Patent 8,653,120 for the use of DCS in chronic pain and filed a now-accepted Investigational New Drug (IND) application with the FDA to initiate commercial drug development of NRX-101 in chronic pain. Data lock has now been achieved in a 200-person randomized prospective trial funded by the US DOD (NCT 03535688) in which patients with chronic pain were randomly assigned to DCS 400mg/day vs. placebo. Should these results support efficacy of DCS in the treatment of chronic low back pain, they are expected to provide a Breakthrough Therapy path towards treatment of chronic pain with DCS and DCS-containing medicines.

Incorporation of HOPE Therapeutics and progress towards an NDA for HTX-100 (IV ketamine) in the treatment of suicidal depression

Intravenous ketamine has now become a standard of care for acute treatment of suicidal depression, in the absence of an FDA-labeled product. Intranasal Esketamine is approved by the FDA (SPRAVATO®), but has not demonstrated a benefit on suicidality and is not approved for use in patients with bipolar depression. Attempts to use intranasal racemic ketamine for suicidal depression have failed.

The Company has formed data-sharing partnerships to license clinical trial data from a French Government-funded trial and two NIH-funded trials all of which demonstrate efficacy of racemic Intravenous ketamine against depression and two of which demonstrate statistically significant benefit vs suicidality. The Company's role is to reformat these data into the required presentation required for review by the FDA.

In contrast to nasal ketamine, Intravenous racemic ketamine demonstrates dramatic and immediate reduction of suicidality in patients with both Major Depressive Disorder and Bipolar Depression. Grunebaum and colleagues demonstrated a rapid and statistically significant reduction in Suicidal Ideation (SSI) at day 1 (p=0.0003) and in depression (P=0.0234), as measured by the Profile of Mood States (POMS) among patients randomized to IV Ketamine compared to those randomized to midazolam. This trial was published in the American Journal of Psychiatry Grunebaum, et.al.[2]. Abbar and colleagues similarly published 84% remission from suicidality on the Columbia Suicide Severity Rating Scale (C-SSRS) in patients treated with ketamine, vs. 28% in those treated with placebo (P<.0001). This trial was published in the British Medical Journal[3]. Data are expected to be transmitted to FDA by July 2024.

In November 2023, the Company initiated manufacture of ketamine together with Nephron Pharmaceuticals, Inc. (West Columbia, SC) to develop a single patient presentation of ketamine. Nine months of real-time stability is ongoing, the minimum stability time required for a New Drug Application.

A long-term challenge with ketamine is that the current formulation (KETALAR®) is highly acidic. While it is suitable for intravenous use, it cannot be administered subcutaneously. In March 2024 the Company demonstrated the formulation of a pH neutral patentable form of IV ketamine that it anticipates will have widespread applicability both in treatment of depression and chronic pain.

Treatment of Urinary Tract Infection (UTI) and Urosepsis:

Although treatment of UTI is quite different from use of NRX-101 to treat Central Nervous System disorders, D-cycloserine was originally developed as an antibiotic because of its role in disrupting the cell wall of certain pathogens. During Q3 2023, NRx tested NRX-101 and its components against resistant pathogens that appear on the Congressionally mandated Qualified Infectious Disease Product (QIDP) list and proved in vitro effectiveness against antibiotic-resistant *E. coli, Pseudomonas, and Acinetobacter.* Accordingly, NRx was granted QIDP designation, Fast Track Designation, and Priority Review by the US FDA in January 2024.

In recent years, increased antibiotic resistance to common pathogens that cause urinary tract infections and urosepsis (i.e., sepsis originating in the urinary tract) has resulted in a marked increase in cUTI, hospitalization, and death from urosepsis. The US Center for Disease Control and Prevention reports that more than 1.7 million Americans contract sepsis each year, of whom at least 350,000 die during their hospitalization or are discharged to hospice (CDC Sepsis Ref.)[4]. There are approximately 3 million patients per year who contract cUTI in the US annually (Lodise, et. al.)[5]. Additionally, should NRX-101 succeed in clinical trials, the Company will consider developing a follow-on product that is anticipated to achieve another 20 years of patent exclusivity.

A key challenge in the treatment of cUTI is the tendency of advanced antibiotics to cause C. Difficile infection, which is fatal in 10% of those who contract it over the age of 65 and results in prolonged hospitalization in many more. The Company recently announced data demonstrating that NRX-101 does not compromise the intestinal microbiome, unlike common antibiotics including Clindamycin and Ciprofloxacin. Should these findings be documented in human patients, NRX-101 would represent the only treatment for cUTI that does not cause C. Difficile infection.

In The Company does not anticipate funding this initiative with core NRx assets and is exploring structures for partnership opportunities. Should the Company or its partners succeed in serving 10% of the cUTI market, the Company believes that the revenue from NRX-101 has the potential to hundreds of million annually, based on 3 million cases per year in the US and potential

pricing of over $3,500/course of therapy.

Financial Results for the Quarter and Year Ended December 31, 2023

For the three months ended March 31, 2024, NRx Pharmaceuticals reduced net loss from $11.0 million in the first quarter of 2023 to $6.5 million in 2024, representing a 41% improvement year over year. For that same period, Research and Development expenses decreased from $3.7 million in 2023 to $1.7 million in 2024, as clinical trial enrollment concluded. The $2.0 million decrease is related primarily to a decrease of $1.6 million in clinical trial expenses, $0.2 million in regulatory and process development costs, and $0.1 million in stock-based compensation. The Company also recorded a 26% reduction in general and administrative expenses during the quarter, from $5.8 million in 2023 to $4.3 million in 2024. The decrease of $1.5 million is related primarily to a decrease of $1.2 million in insurance expenses, $0.4 million employee expense, and slightly offset by other general and administrative expenses.

As of March 31, 2024, the Company had $1.3 million in cash and cash equivalents, not including the $5.1 million of working capital committed by Alvogen. This included a reduction of corporate indebtedness to Streeterville LLC of $2.2 million. Subsequent to March 31, 2024, we increased working capital by $3.3 million from equity sales. Over the first three months of 2024 the Company improved access to working capital by $8 million in total, representing $2.9 million from equity sales and $5.1 million from the Alvogen milestone advance, while reducing corporate indebtedness by 50%.

NRx continues to implement operational efficiencies to extend cash runway and maintain focus on our path to generating revenue and value for our shareholders.

Please see detailed financials on our Form 10-Q, filed with the SEC and available on our website.

Conference Call and Webcast Details

A live webcast of the conference call will be available on the Company's website at 4:30 p.m. ET today, at https://ir.nrxpharma.com/events. An archive of the webcast will be available on the Company's website for 30 days. Participants that are unable to join the webcast can access the conference call via telephone by dialing domestically 1-800-717-1738 or internationally 1-646-307-1865.

About NRx Pharmaceuticals

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 has partnered with Alvogen and Lotus around the development and marketing of NRX-101 for the treatment of suicidal bipolar depression. 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 HTX-100 (IV ketamine), through Hope Therapeutics, in 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 Specialty Pharmaceutical Company, wholly-owned by NRX Pharmaceuticals focused on development and marketing of an FDA-approved form of intravenous ketamine for the treatment of acute suicidality and depression 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 and 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.

[1] Nierenberg et al. International Journal of Bipolar Disorders (2023) 11:28 https://doi.org/10.1186/s40345-023-00

[2] Grunebaum, et. al., Ketamine for Rapid Reduction of Suicidal Thoughts. Am J Psychiatry. 2018 Apr 1: 175(4): 327-335

[3] Abbar, et. al. Ketamine for Acute Treatment of Severe Suicidal Ideation, BMJ 2022; 376

[4] https://www.cdc.gov/sepsis/what-is-sepsis.html

[5] Open Forum Infectious Diseases, Volume 9, Issue 7, July 2022, ofac315, https://doi.org/10.1093/ofid/ofac315

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