NeuroRx Presents Phase 2 Efficacy & Safety Data for NRX-101, a Breakthrough Therapy Targeting Suicidal Bipolar Depression

Findings suggest potential for NRX-101 in maintaining remission from Severe Bipolar Depression with Acute Suicidal Ideation following initial stabilization with ketamine

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WILMINGTON, Del.--(BUSINESS WIRE)--NeuroRx, a clinical stage biopharma company focused on the development of Rapid Acting Antidepressants (RAADs) that target the brain's NMDA receptor, announced results from its Phase 2 STABIL-B study of NRX-101 versus lurasidone in patients with Severe Bipolar Depression and Acute Suicidal Ideation & Behavior (ASIB). Findings were presented yesterday at the American Congress of Neuropsychopharmacology (ACNP) in Hollywood, Florida. The results of the STABIL-B trial, which was intended to demonstrate feasibility, tolerability, and blood exposure levels of NRX-101, were presented by Professor Daniel Javitt, M.D., Ph.D., Chairman of NeuroRx's Scientific Advisory Board, in conjunction with researchers from Massachusetts General Hospital, University of Alabama Birmingham, and Baylor College of Medicine.

In this double-blind study, patients with Severe Bipolar Depression and ASIB received either NRX-101 or lurasidone after stabilization with a single intravenous infusion of NRX-100 (ketamine). Though not powered for efficacy, results of this 6-week Phase 2 study, unexpectedly, showed a statistically significant 11 point difference on the Montgomery Åsberg Depression Rating Scale (MADRS) between NRX-101 and lurasidone groups at day 14 (P=0.03). Patients also maintained separation between groups over the six-week duration of the trial, with a lower depression score in the NRX-101 group at a trend level of significance (P=0.059). None of the 10 NRX-101 patients met the trial's definition for relapse, while 2 of the 5 lurasidone patients relapsed. Relapse was defined as a ≥50% increase in MADRS depression scores versus baseline, suicidality levels requiring hospitalization (CSSRS ≥4)[1], the need for a new treatment plan.

Overall the drug was well tolerated, with no serious adverse events or discontinuations for side effects. Hallucinations and dissociative side effects, along with blood pressure increases were seen during ketamine infusions, as expected. However, these effects were not seen in association with oral NRX-101. The presentation also included safety data documenting no evidence of abuse liability, as measured by rodent self-administration, compared to both ketamine and S-ketamine, which demonstrated substantial abuse liability. Last month, NeuroRx presented findings documenting lack of neurotoxicity in rodents, even at maximal, systemically toxic doses of NRX-101. Ketamine, particularly with repeat administration, is well-known to be neurotoxic in some circumstances, as has been documented in FDA drug warnings.[2]

NRX-101 is a patented, oral, fixed-dose combination of D-cycloserine (DCS), an NMDA antagonist, and lurasidone, which has 5-HT2a receptor antagonis
t activity. In contrast with all currently approved antidepressant drugs, which primarily raise serotonin levels in the brain, DCS is shown to raise levels of two neurotransmitters: glutamate and

[1] Columbia Suicide Severity Rating Scale; https://cssrs.columbia.edu/wp-content/uploads/ScoringandDataAnalysisGuide-for-Clinical-Trials-1.pdf

[2] Kale, R. ; Development of Cyclurad™, a Novel Treatment for Acute Suicidal Crisis in Bipolar Depression: Preclinical Acute Neurotoxicity Study; Poster T1030-01-001 at AAPS 2018

glutamine (Glx). As such, NRX-101 may represent a new class of antidepressants with the potential to decrease suicidal thoughts, whereas serotonin-based antidepressants are associated with an increase in risk of suicide in certain vulnerable patient populations. In April 2017, the FDA granted NeuroRx a Biomarker Letter of Support to continue to study this novel mechanism of action and recently granted Breakthrough Therapy Designation to NRX-101.

"This study represents the development of NRX-101 as the potentially first oral medicine for suicidal bipolar depression," said Andrew A. Nierenberg, M.D., study principal investigator, director of the Dauten Family Center for Bipolar Treatment Innovation and the Thomas P. Hackett Endowed Chair in Psychiatry at Massachusetts General Hospital, as well as Professor of Psychiatry at Harvard University. "Substance abuse is very high in this population. Therefore, this medicine could become an important treatment choice for this population."

"Although we sized the STABIL-B trial as a feasibility study, we are excited to see additional evidence that acutely suicidal patients, who are first stabilized with intravenous ketamine, can maintain their remission from depression and suicidal ideation with an oral, non-hallucinogenic, and non-addictive home use drug. These data are consistent with prior studies of DCS in depression," said Professor Daniel Javitt, who is a co-founder of NeuroRx, and invented NRX-101. "Bipolar Depression and suicide have reached epidemic proportions in the United States. The sad truth is that if you know two people with bipolar depression, on average, one will attempt suicide. If you know five people with bipolar depression, one is likely to succeed. For too long, the only FDA-approved therapy for suicidal depression has been electroconvulsive therapy (ECT), which appears to work by raising Glx in the brain. We, at NeuroRx, aspire to develop a drug that confers the clinical benefits of ECT without the well-known, negative side effects and also without the hallucinogenic and addictive side effects of repeated administration of ketamine."

"For too long, patients with suicidal ideation have been excluded from clinical studies in bipolar depression. NeuroRx aims to bring hope to a population of patients with a lethal brain condition, who have extraordinary potential to lead productive, and successful lives," said Jonathan Javitt, co-founder, CEO, and Chairman of NeuroRx.

NeuroRx is in the process of initiating its pivotal Phase 2b/3 study of NRX-101 under Special Protocol Agreement (SPA).

About Bipolar Depression and Acute Suicidal Ideation & Behavior

Bipolar disorder, which affects 5.7 million Americans, is characterized by significant changes in mood, from mania or hypomania to depression, often quite severe. The depressive phase can trigger suicidal thoughts and behaviors. Currently the only FDA-approved treatment for suicidal bipolar depression is electroconvulsive therapy (ECT), which is shown to increase levels of Glx in the brain. Despite its effectiveness, ECT has a myriad of well-known adverse side effects, including confusion and memory loss. Unfortunately, most commonly-used antidepressants bear an FDA-mandated warning label identifying the potential to increase the risk of suicide.

Each day, approximately 100 Americans, and more than 2,100 people worldwide, end their lives by suicide, according to the American Foundation for Suicide Prevention (AFSP) and the World Health Organization (WHO). Individuals who suffer from bipolar depression are at far greater risk of suicide than those with major depressive disorder and are believed to represent between 25% and 40% of

the 45,000 who end their lives each year in the United States. 11%-20% of those diagnosed with bipolar disorder are believed to take their lives at some point. Overall, suicide has become a national epidemic and is the 10th leading cause of death in the United States.

About NRX-101

NRX-101 is a patented, oral, fixed-dose combination of two FDA approved drugs: D-cycloserine, a N-methyl-D-aspartate (NMDA) receptor modulator, and lurasidone, which has D2/5-HT2a receptor antagonist activity. D-cycloserine has shown activity against depression in four clinical studies. It has also shown an effect on suicidality in some of these studies. NRX-101 is designed to address bipolar depression with suicidal ideation, an indication for which there is no currently approved drug and for which the only FDA-approved treatment remains electroconvulsive therapy (ECT). NeuroRx was granted Fast Track designation by the U.S. FDA for this indication in August 2017. In May of 2018 NeuroRx was awarded a Special Protocol Agreement (SPA) by the FDA for the NRX-101 phase 2b/3 trial. In April 2018, NeuroRx received a biomarker letter of support from the FDA, documenting that the company had shared evidence of increased Glx levels associated with oral administration of D-cycloserine, a phenomenon not seen with serotonin-targeted (SSRI). In November of this year, the FDA awarded NeuroRx Breakthrough Therapy designation for NRX-101.

About NeuroRx, Inc.

NeuroRx draws upon 30 years of basic science and clinical expertise in the role of N-methyl-D-aspartate (NMDA), a receptor that regulates human thought processes, particularly depression and suicidality, as well as PTSD. The company is privately funded and led by former senior executives of Johnson & Johnson, BMS, Pfizer Inc., Eli Lilly, and Sunovion. NeuroRx's Board of Directors and Advisors includes Hon. Sherry Glied, former Assistant Secretary for Planning and Evaluation, Department of the U.S. Health and Human Services; Chaim Hurvitz, former President, TEVA International Group; Wayne Pines, former Associate Commissioner of the U.S. Food and Drug Administration, and Daniel Troy, former Chief Counsel, U.S. Food and Drug Administration.

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