November 13, 2018

NeuroRx Receives FDA Breakthrough Therapy Designation for NRX-101, First Oral Drug Targeting Suicidal Bipolar Depression

First oral Rapid-Acting Antidepressant to be granted Breakthrough Designation

WILMINGTON, Del. - NeuroRx, a clinical stage biopharma company focused on the development of Rapid Acting Antidepressants (RAADs) that target the brain's NMDA receptor, has been granted Breakthrough Therapy Designation by the U.S. Food and Drug Administration (FDA) for development of NRX-101. The designation is for treatment of Severe Bipolar Depression with Acute Suicidal Ideation & Behavior (ASIB) after initial stabilization with ketamine or other effective therapy. In April, the FDA also issued a Special Protocol Agreement (SPA) for the design of the upcoming pivotal Phase 2b/3 clinical trial. The company recently reported encouraging top- line data from its STABIL-B study, which demonstrated that the drug was well- tolerated with no serious adverse events or discontinuations for side effects.

NRX-101 is a patented, oral, fixed-dose combination of D-cycloserine (DCS), an NMDA antagonist, and lurasidone, which has 5-HT2a receptor antagonist 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 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.

The FDA decision to award Breakthrough Designation to NRX-101 was based in part on clinical data obtained in a multicenter STABIL-B feasibility study designed to evaluate the clinical effect of NRX-101 compared to a lurasidone control group. These data will be presented next month at the annual meeting of the American College of Neuropsychopharmacology.

"The FDA grant of Breakthrough Therapy Designation to NRX-101 recognizes the extraordinary unmet medical need that confronts patients with Severe Bipolar Depression," said Jonathan Javitt, M.D., M.P.H., CEO of NeuroRx. "These patients have previously been excluded from clinical trials of nearly all currently marketed antidepressants. We aspire to change that reality for more than 150,000 Americans each year who present for emergency care and more than 25,000 each year who lose their lives to this lethal condition."

Patients with bipolar depression are at uniquely high risk for suicide, with more than 50% attempting suicide at some point and up to 20% succumbing to suicide. 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. 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) antidepressants.

NeuroRx is initiating a pivotal Phase 2b/3 clinical trial under the SPA comparing daily oral NRX-101 to standard therapy (lurasidone) in patients with Severe Bipolar Depression and Acute Suicidal Ideation following initial stabilization with ketamine. The FDA previously granted FAST TRACK designation for this protocol in 2017.

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, which is called "bipolar depression," can trigger suicidal thoughts and behaviors. Standard of care consists of hospitalized observation and electroconvulsive therapy (ECT). 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. NeuroRx was additionally awarded a Biomarker Letter of Support by FDA. In November of this year, the FDA awarded NeuroRx Breakthrough Therapy designation for NRX-101.

About Breakthrough Therapy Designation

The U.S. Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA) created the Breakthrough Therapy designation to expedite development and review of drugs and biologics intended to treat serious or life-threatening conditions for which preliminary clinical evidence may demonstrate substantial improvement over existing therapies. From program inception through 2017, Breakthrough Designation has been awarded to only 46 approved drugs, of which fewer than 20% target Central Nervous System (CNS) disease.1 Breakthrough Designation allows FDA to provide "intensive guidance on efficient drug development" and "rolling review."2 From program inception through the end of 2017, Breakthrough designation has been awarded to 46 drugs, the majority of which (38) are for the treatment of cancer or infectious or metabolic disease. Award of Breakthrough designation connotes FDA's commitment to and intensive guidance on efficient drug development2 and is associated with substantially shorter median development times (4.8 years vs. 8 years) compared to drugs with other FDA priority programs or no priority designation.3 Of the 23 non- oncology Breakthrough products tracked through 2016, 91% were approved on their first review cycle, compared to the industry benchmark of 76% first-cycle success.4 Breakthrough designation was previously awarded to two investigational Rapid-Acting Antidepressants (RAADs), Esketamine® (J&J) and Rapastinel® (Allergan), which respectively require intranasal and intravenous administration in a clinic setting. NRX-101 is the first orally bioavailable home-use RAAD to be awarded Breakthrough Designation.

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. 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.

Learn more at NeuroRxpharma.com.

1 Puthumana J, Wallach JD, Ross JS. Clinical trial evidence supporting FDA approval of drugs granted breakthrough therapy designation. JAMA 2018;320(3):301-303.
2 US Food and Drug Administration. Guidance for industry: expedited programs for serious conditions—drugs and biologics. https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf. Accessed March 14, 2018.
3 Hwang TJ, Darrow JJ, Kesselheim AS. The FDA's expedited programs and clinical development times for novel therapeutics, 2012-2016. JAMA 2017;318(21):2137-2138
4 Poirer AF, Murphy WR. The impact of Breakthrough Therapy Designation on development strategies and timelines for non-oncology drugs and vaccines. Clin Pharmacol Ther 2016;100(6):603-605.

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Source: NeuroRx, Inc.

Released November 13, 2018

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