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**NAUREX INC. REPORTS POSITIVE TOP-LINE PHASE I RESULTS FOR ITS NOVEL MECHANISM  
NMDA RECEPTOR MODULATOR GLYX-13 IN TREATMENT-RESISTANT DEPRESSION**

**— Good Overall Safety with No Schizophrenia-Like Side Effects Seen in First-in-Human  
Clinical Trial of this Novel and Selective GFPA Mechanism Drug Candidate—**

**EVANSTON, IL, February 10, 2010** -- Naurex Inc., a clinical stage company developing innovative treatments for depression and other CNS disorders based on its novel glycine site functional partial agonist (GFPA) NMDA receptor modulators, today reported positive top-line results from its Phase I clinical trial of lead compound GLYX-13. GLYX-13 is a GFPA selective modulator of the NMDA receptor. It is initially being developed as a therapy for treatment-resistant depression in severely depressed patients. In the Phase I trial, adverse events were similar for subjects receiving GLYX-13 and placebo and were all rated as mild. There were no signs of the schizophrenia-like side effects associated with other NMDA receptor modulator drugs.

“These encouraging data in humans are consistent with the excellent safety profile demonstrated in preclinical studies of GLYX-13,” said Ronald Burch, M.D., Ph.D., chief medical officer at Naurex. “In view of the history of schizophrenia-like side effects caused by NMDA receptor modulators such as ketamine<sup>1</sup> and CP-101,606<sup>2</sup>, we are very pleased that there were no signs of these effects in this first trial of GLYX-13 in humans, even at higher doses than we expect would be required to provide antidepressant effects. The pharmacokinetics of GLYX-13 also was encouraging, with similar or greater drug exposure seen in humans than in animals at the same doses. These positive results will allow us to proceed to Phase II clinical trials in patients with severe treatment-resistant depression, a condition with an urgent need for better treatment options.”

The GLYX-13 Phase I trial was a randomized, double-blind, placebo-controlled single ascending dose level study of the safety, tolerability and pharmacokinetics of four dose levels of GLYX-13 in healthy volunteers. The primary outcome measures included observational and laboratory-confirmed safety parameters. Schizophrenia-like side effects were specifically evaluated.

The efficacy of NMDA receptor glycine site functional partial agonists has been demonstrated in animal models in a number of CNS disorders, including major depressive disorder, neuropathic pain, schizophrenia, anxiety, Alzheimer's disease and other cognition disorders. In these studies, GFPA modulators did not exhibit the schizophrenia-like side effects associated with NMDA receptor blockers that interact with other binding sites on the receptor complex.<sup>3,4</sup> In preclinical studies, GLYX-13 has demonstrated a wide therapeutic ratio ( $\geq 500:1$ ) between efficacy and side effects, which is the largest therapeutic ratio of any reported molecule that interacts at the NMDA receptor. Preclinical studies also showed that the antidepressant effects of GLYX-13 were evident within 20 minutes and demonstrated a lasting antidepressant effect of at least four days' duration after administration of a single dose. In these studies, GLYX-13 affected both positive and negative symptoms of depression-like states in animals.<sup>5</sup>

**About NMDA Receptor Modulators and Depression**

The glutamate receptor subtype known as N-methyl-D-aspartic acid (NMDA) plays a central role in modulating aspects of brain activity, such as synaptic transmission, synaptic plasticity and excitotoxicity. Major pharmaceutical firms have been developing NMDA receptor modulators for more than 20 years, and a few, including Memantine<sup>®</sup>, ketamine, D-cycloserine, and dextromethorphan are marketed for other indications, generating annual sales of more than \$1 billion. The antidepressant potential of modulating the NMDA receptor has been confirmed by data from clinical studies with known NMDA receptor

antagonists, which produced reductions in depression scores in patients with treatment-resistant depression. The efficacy in these studies was significant, with response rates of greater than 50%, fast onset of action within hours of a single dose, and a long duration of effect lasting as long as seven to 30 days after a single dose. These data have confirmed the NMDA receptor as a novel target of high interest in depression – representing a potentially entirely new way to treat patients who do not respond to current therapies. But the known NMDA receptor drugs are also associated with significant toxicities at doses that are very close to the therapeutic dose.<sup>3, 4</sup> These side effects include schizophrenia-like effects, sedation, and abuse and addiction potential, perhaps best illustrated by the fact that ketamine has achieved notoriety as a drug of abuse. Until now, the narrow margin between therapeutic effects and adverse effects has limited the therapeutic potential of these agents. In studies to date, Naurex's novel NMDA receptor glycine site functional partial agonists have shown the significant therapeutic efficacy of other NMDA receptor modulators but without their limiting side effects.

<sup>1</sup> Zarate CA Jr, Singh JB, Carlson PJ, Brutsche NE, Ameli R, Luckenbaugh DA, Charney DS, Manji HK, A randomized trial of an N-methyl-D-aspartate antagonist in treatment-resistant major depression. *Arch Gen Psychiatry* 2006; 63:856-864.

<sup>2</sup> Preskorn SH, Baker B, Kolluri S, Menniti FS, Krams M, Landen JW. (Pfizer), An innovative design to establish proof of concept of the antidepressant effects of the NR2B subunit selective N-methyl-D-aspartate antagonist, CP-101,606, in patients with treatment-refractory major depressive disorder., *J Clin Psychopharmacol.* 2008 Dec;28 (6):631-7.

<sup>3</sup> Skolnick P, Popik P, Trullas R., (2009) Glutamate-based antidepressants: 20 years on, *Trends Pharmacol Sci.* Nov; 30 (11):563-9.

<sup>4</sup> Machado-Vieira R, Salvadore G, Luckenbaugh DA, Manji HK, Zarate CA Jr., Rapid onset of antidepressant action: a new paradigm in the research and treatment of major depressive disorder., *J Clin Psychiatry.* 2008 Jun;69 (6):946-58.

<sup>5</sup> Joseph Moskal, Jeffery Burgdorf. Northwestern University, Evanston, IL, The anti-depressant and anxiolytic properties of GLYX-13: a Glycine-site Functional Partial Agonist (GFPA), a novel mechanism for modulating NMDA receptors. Presented at the 2009 Annual Meeting of the American College of Neuropsychopharmacology.

### **About Naurex**

Naurex, Inc. is a private company developing novel therapies for depression and other CNS disorders based on the work of founder Dr. Joseph R. Moskal and colleagues now at The Falk Center for Molecular Therapeutics at Northwestern University, who discovered a new mechanism of action for modulating the NMDA receptor. Naurex has used these discoveries to generate novel chemical drug classes known as glycine site functional partial agonists (GFPAs). Naurex's first GFPA NMDA modulator, GLYX-13, has shown promising signs of antidepressant activity with excellent safety in preclinical studies. These safety results have now been confirmed in a Phase I clinical trial, and preparations for a Phase II evaluation in patients with severe treatment-resistant depression are underway. A second-generation series of compounds is advancing rapidly in preclinical development. Naurex has patented these novel chemistry classes and key molecular features that represent a new platform for modulating NMDA receptors in a novel way. For more information, visit [www.naurex.com](http://www.naurex.com).