

NEW DATA ANALYSIS IDENTIFIES DEPRESSED PATIENTS WHO ARE MOST LIKELY TO BENEFIT FROM TREATMENT WITH NEUROSTAR TMS THERAPY®

Data further suggest that NeuroStar TMS Therapy compares favorably to antidepressant medications

Washington, DC, May 5, 2008 – New research on patients with depression who had not received adequate benefit from prior antidepressant treatment demonstrated that NeuroStar TMS (Transcranial Magnetic Stimulation) Therapy improved depression symptoms to a clinically significant degree. The best response to NeuroStar TMS Therapy was among the patients who failed to achieve satisfactory improvement from one prior antidepressant treatment at or above the minimal effective dose and duration in the current episode. These patients received a median of 4 treatment attempts, only one of which was at an adequate dose and duration. The study also found that NeuroStar® produced absolute treatment effects that were similar to or larger than the majority of approved pharmaceutical antidepressant treatments for either treatment responsive or resistant populations. The new data were presented over the weekend at a major psychiatric conference.

“A significant proportion of patients with depression do not adequately benefit from initial treatment attempts. This new analysis suggests that TMS Therapy® produced statistically and clinically significant efficacy results in patients who did not achieve

satisfactory improvement from prior antidepressant treatment, particularly in patients with a lower number of prior failures,” said Michael Thase, MD, Professor of Psychiatry at the University of Pennsylvania and the lead author of the analysis. “These efficacy results compared favorably with those observed with antidepressant medications based on a variety of accepted benchmarks.”

About NeuroStar TMS Therapy

NeuroStar TMS Therapy is administered as an outpatient procedure, does not require anesthesia or sedation, and can be performed in a psychiatrist’s office. It is administered as a 40-minute procedure, 5 times per week for 4-6 weeks. It works by delivering highly-focused, MRI-strength magnetic field pulses that stimulate nerve cells in an area of the brain that is linked to depression. The repetitive stimulation of these nerve cells helps normalize neurotransmitter function.

Neuronetics, Inc. is seeking marketing clearance from the FDA for NeuroStar TMS Therapy in the treatment of Major Depressive Disorder in patients who have failed to achieve satisfactory improvement from prior antidepressant treatment. If cleared by the FDA, NeuroStar will be the first and only non-invasive, non-systemic treatment for major depression. A final decision is expected from the FDA in the next few months.

About the New Data Analysis for NeuroStar TMS Therapy¹

The data were derived from two clinical trials that evaluated the acute efficacy of the NeuroStar TMS Therapy system in the treatment of patients with major depression who did not receive adequate benefit from one to four previous treatments at or above the minimal effective dose and duration in the current episode. The first was a 4-6 week, randomized, placebo-controlled, double-blind, monotherapy study, which was recently

published in *Biological Psychiatry*². Patients who did not respond in the randomized, controlled study entered into a 6-week, open-label monotherapy study, which was recently published in *The Journal of Clinical Psychiatry*³. An analysis for predictors of response demonstrated that the patients with the best response to NeuroStar TMS Therapy were those who had not benefited from one prior antidepressant medication at or above the minimal effective dose and duration in the current episode, which constituted 54.5% of the overall sample⁴.

This clinical study population was comprised of 164 patients with unipolar, non-psychotic major depressive disorder. Almost all of them (97%) had suffered previous depression episodes. These patients also had an extensive treatment history without a satisfactory improvement. They had received a median of 4 total prior antidepressant treatment attempts in the current episode, one of which achieved treatment adequacy at or above the minimal effective dose and duration. Forty-eight percent were unemployed due to their depression, 35% had a co-morbid anxiety disorder, and all had moderate to severe depressive symptoms.

In these patients, the following efficacy results were observed in the randomized, controlled study:

- The primary efficacy measure, the Montgomery-Asberg Depression Rating Scale (MADRS) symptom score change at 4 weeks, was statistically significantly superior to placebo ($p=.0006$), among NeuroStar-treated patients. Similar results were observed with the Hamilton Depression Rating Scale (HAMD).
- Response rates, as measured by the MADRS, for NeuroStar TMS Therapy-treated patients were statistically significantly superior to placebo ($p=0.0083$),

and were approximately twice the rate of placebo-treated patients. The response rate is the percentage of patients who had a $\geq 50\%$ improvement in symptoms.

Patients who did not respond in the randomized, controlled study entered into a 6-week, open-label treatment study. In the open-label study, which is most like real-world clinical practice, the following was observed:

- Patients treated with NeuroStar TMS Therapy achieved a 54% response rate on the HAM-D 24-item scale, at the end of 6 weeks

The outcomes observed for NeuroStar TMS Therapy compared favorably with outcomes observed for antidepressant medications, based on several reference datasets. One of the most widely-accepted methods for comparing treatments across studies is effect size. In an analysis of effect sizes from controlled trials, NeuroStar TMS Therapy was compared to a meta-analysis of antidepressant medication clinical trials. NeuroStar TMS Therapy produced an effect size (Hedges' g) of .52, which indicates a moderate effect, compared to .31 for antidepressant medications, which indicates a weaker effect.

About Depression

Depression affects at least 14 million American adults each year. Researchers estimate that by the year 2020, depression will be the second leading cause of disability worldwide. Each year, over 30,000 people in the US commit suicide, 60% of which suffer from depression. The economic burden of depression in 2000 was estimated at \$83.1 billion in the US. Women are almost twice as likely as men to suffer from depression. However, some experts feel that depression in men is under-reported. Depression has no racial, ethnic, or socioeconomic boundaries. About two-thirds of those who experience an episode of depression will have at least one other episode in

their lives. Despite major advances in treating this debilitating illness, nearly 30% of patients with depression do not benefit from or are intolerant of antidepressant therapy.

About Neuronetics

Neuronetics, Inc. is a privately held medical device company focused on developing non-invasive therapies for psychiatric and neurological disorders using MRI-strength magnetic field pulses. Based in Malvern, PA., Neuronetics is the leader in the development of TMS Therapy[®], a non-invasive form of neuromodulation. For more information, visit www.neuronetics.com.

For More Information, Please Contact:

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Caution: Investigational device. Limited by federal law to investigational use.

¹Thase M, Demitrack M. Evaluating Clinical Significance of Treatment Outcomes in Studies of Resistant Major Depression, *Biological Psychiatry*, April, 2008; Vol. 63:7s, pg. 138s.

²O'Reardon, J, et al. Efficacy and Safety of Transcranial Magnetic Stimulation Therapy in the Acute Treatment of Major Depression: A Multi-site Randomized Controlled Trial. *Biological Psychiatry*, December 2007.

³Janicak, P, et al. Transcranial Magnetic Stimulation (TMS) in the Treatment of Major Depression: A Comprehensive Summary of Safety Experience from Acute Exposure, Extended Exposure and During Reintroduction Treatment. *Journal of Clinical Psychiatry*, February 2008.

⁴Lisanby, S, et al. Daily Left Prefrontal Repetitive Transcranial Magnetic Stimulation (rTMS) in the Acute Treatment of Major Depression: Clinical Predictors of Outcome in a Multisite, Randomized Controlled Clinical Trial. Submitted.

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