



**NEUROSTAR® TMS THERAPY PRODUCED SIGNIFICANT IMPROVEMENTS IN  
DEPRESSION SYMPTOMS IN RECENTLY-PUBLISHED  
RANDOMIZED, CONTROLLED TRIAL**

*Peer-reviewed Publication Suggests NeuroStar TMS Therapy May Offer a Novel  
Treatment Option for Patients with Major Depression*

Malvern, PA – June 15, 2007 – Neuronetics, Inc. announced that a study evaluating the efficacy, safety, and tolerability of its NeuroStar TMS (transcranial magnetic stimulation) Therapy system was published online today in *Biological Psychiatry*, the official peer-reviewed journal of the Society of Biological Psychiatry. The non-invasive medical device was studied in patients who had not received adequate benefit from previous antidepressant treatment. This study is the largest conducted with TMS Therapy and the first-ever international, multicenter, randomized, placebo-controlled, triple-blinded clinical trial with TMS Therapy.

"This study demonstrated that treatment with TMS produced clinically meaningful improvements in the symptoms of depression and, in addition, was very safe and well-tolerated," said psychiatrist John O'Reardon, M.D., Director of the University of Pennsylvania's Treatment Resistant Depression Clinic, a principal investigator of the trial, and the lead author of the study. "These data indicate that TMS therapy provides new hope for some of the 4 million US adults with major depression, who have not benefited from or were unable to tolerate previous treatments due to side effects. In the sense that patients studied here had not benefited from existing treatments options, TMS offers something new in treatment," O'Reardon added.

"In this study, TMS Therapy not only improved core depressive symptoms, it also had a significant effect on anxiety, somatic, and psychomotor symptoms of depression," O'Reardon added. "This is important because depression is a complex disease, where patients suffer from a broad range of symptoms."

"This study demonstrated that treatment with NeuroStar TMS Therapy produced response and remission rates that were approximately twice the rate of placebo-treated patients," said Mark A. Demitrack, MD, Neuronetics' Chief Medical Officer, a psychiatrist, and an author of the study. The response rate is the percentage of patients who had a  $\geq 50\%$  improvement in symptoms, and the remission rate is the percentage of patients who achieved virtually complete symptom resolution. "If cleared by the FDA, NeuroStar TMS Therapy could provide a truly new alternative for a great many patients suffering with depression," Demitrack added.

The NeuroStar TMS Therapy system is a non-invasive medical device studied clinically for the treatment of depression. 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 works by delivering highly focused MRI-strength magnetic field pulses that stimulate nerve cells in the brain that are thought to be linked to depression.

Neuronetics, Inc. is seeking marketing clearance for NeuroStar TMS Therapy in patients with major depression who have failed to receive adequate benefit from previous treatment. If cleared by the FDA, it will be the first and only treatment of its kind in the U.S. for the treatment of major depression.

### **About the Study**

This triple-blinded, placebo-controlled, multicenter study was conducted at 23 leading clinical research institutions throughout the U.S., Canada, and Australia to test the acute efficacy and safety of NeuroStar TMS Therapy. In the study, 301 medication-free patients with major depression, who had not benefited from at least one but no more than four fully adequate prior treatments in their current episode, were randomized to active TMS (n=155) or placebo (n=146) conditions. The study had three phases:

- Lead-in Phase: One week during which patients were on no treatment
- Acute Treatment Phase: Six-week period during which patients received daily treatment, five times per week, with active TMS or placebo
- Taper Phase: Three-week period with gradually reduced number of TMS/placebo treatment sessions. During the taper phase all patients were started on a single oral antidepressant medication.

After completion of the acute phase, if patients met pre-defined criteria for improvement, they were enrolled in a six-month maintenance of effect study. If patients failed to show meaningful clinical benefit in the acute phase, they were eligible to crossover to an open-label acute treatment study. The results of the 6-month maintenance study and the open-label study were preliminarily reported at this year's annual meeting of the American Psychiatric Association (APA), and will be fully reported in separate future publications.

The primary outcome of the study was the symptom score change as assessed at week four with the Montgomery-Asberg Depression Rating Scale (MADRS). Key secondary outcomes included changes on the 17 and 24-item Hamilton Depression Rating Scale (HAMD), response and remission rates measured by both the MADRS and HAMD, and HAMD factor scores.

### **Study Results**

Active TMS was superior to placebo on continuous outcomes at 4 and 6 week time points (MADRS:  $P = 0.057, 0.058$ , HAMD24:  $P=0.012, 0.015$ , HAMD17:  $P=0.006, P=0.005$ ). Response rates were significantly higher with active TMS on all three scales at weeks 4 and 6 ( $P < 0.05$ ). Remission rates were approximately two-fold higher with active TMS at week 6 and significant on the MADRS and HAMD24 ( $P < 0.05$ ). Active TMS was also statistically significantly superior to placebo at the 4 and 6 week time points on the HAMD core depression ( $P=0.012, P=0.008$ ), anxiety/somatization ( $P=0.025, P=0.023$ ), and psychomotor retardation factors ( $P=0.007, P=0.003$ ).

In this study, NeuroStar TMS Therapy was well tolerated with a low dropout rate for adverse events (4.5%). There were no systemic side effects such as weight gain, sexual dysfunction, nausea, dry mouth, sedation, or agitation. There was no adverse effect on cognition or auditory threshold. The most common adverse events were headache and scalp discomfort, which were transient and mild to moderate in severity. The incidence of these side effects declined markedly after the first week of treatment.

## **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. 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 percent 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](http://www.neuronetics.com).

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