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**NEW STUDY DEMONSTRATES COST EFFECTIVENESS OF
NEUROSTAR[®] TMS THERAPY IN THE TREATMENT OF
DEPRESSION**

Cost Savings For The Health Care System May Be Expected With NeuroStar Relative to Standard Care In Patients With Inadequate Benefit to Prior Antidepressant Treatment

Malvern, PA [November 6, 2008] – Neuronetics, Inc. announced today that a new health economic study evaluating the cost effectiveness of its NeuroStar TMS Therapy[®] system in the treatment of depression was presented at the US Psychiatric and Mental Health Congress in San Diego last week. This study is the largest and most comprehensive cost effectiveness study to date of TMS Therapy[®] in patients with major depression who have failed to achieve benefit from prior antidepressant treatment, also called treatment-resistant depression (TRD).

Compared to antidepressant medication treatment as usual, NeuroStar TMS Therapy was demonstrated to be cost effective if reimbursed by third-party payers at rates up to \$400 per treatment session, when only health gains were evaluated. When productivity gains due to clinical improvement and reduced caregiver costs were also included, the cost effectiveness was substantially greater. These results were found when comparing open-label NeuroStar TMS Therapy health outcomes in the FDA-indicated patient population to the health outcomes from the antidepressant medications used in the open-label, NIMH-sponsored STAR*D (Sequenced Treatment Alternatives to Relieve Depression) study. In these open-label conditions, which are most like real-world clinical practice, NeuroStar TMS Therapy provided a net cost savings during a year of follow up when compared to antidepressant medication treatment as usual.

“Even under the most conservative modeling assumptions that we tested, TMS Therapy demonstrated an incremental cost effectiveness ratio that did not exceed the most

stringent willingness to pay benchmark in the US for a new treatment,” said Kit N. Simpson, Dr.PH, health economist at the Medical University of South Carolina and an author of the study. “NeuroStar TMS Therapy appears to be a cost effective treatment option for depressed patients who failed to benefit from prior antidepressant medications, at expected reimbursement rates,” Simpson said.

The Economic Burden of Depression

In 2000, the economic burden of depression was estimated to be \$83.1 billion in the US.¹ Patients with treatment-resistant depression (TRD) had significantly more inpatient hospitalizations, had more outpatient office visits, and used substantially more psychotropic medications.^{2,3,4} Average annual costs for TRD patients as compared to non-TRD patients ranged from between two times greater² and six times greater.⁴ TRD patients had significantly greater work loss costs (disability and absenteeism) than either non-TRD patients or average non-depressed beneficiaries.² Increased costs for depressed patient care are not limited to the cost of treating their depression, but also include increased health care utilization for non-psychiatric conditions.^{2,3}

About NeuroStar TMS Therapy

The NeuroStar TMS Therapy system is the first and only TMS Therapy[®] device cleared by the FDA for the treatment of depressed patients who failed to benefit from prior antidepressant treatment. NeuroStar TMS Therapy is a non-systemic (does not circulate in the bloodstream throughout the body) and non-invasive (does not involve surgery) form of neuromodulation. It stimulates nerve cells in an area of the brain that is linked to depression, by delivering highly focused MRI-strength magnetic pulses. Patients being treated by NeuroStar TMS Therapy do not require anesthesia or sedation and remain awake and alert. It is a 40-minute outpatient procedure that is prescribed by a psychiatrist and performed in a psychiatrist’s office. The treatment is typically administered daily for 4-6 weeks.

NeuroStar TMS Therapy is indicated for the treatment of Major Depressive Disorder in adult patients who have failed to achieve satisfactory improvement from one prior antidepressant medication at or above the minimal effective dose and duration in the current episode. In clinical trials, the patient population⁵ upon which the FDA indication is based 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.

NeuroStar TMS Therapy has not been studied in patients who have not received prior antidepressant treatment. Efficacy has not been established in patients who have failed to receive benefit from two or more prior antidepressant treatments at minimal effective dose and duration in the current episode.

In the indicated patient population, 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 ($p=0.0006$), among NeuroStar-treated patients⁵. Similar results were observed with the Hamilton Depression Rating Scale (HAMD)⁶.
- NeuroStar TMS Therapy-treated patients had statistically significant response⁶ and remission⁷ rates, which 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, and the remission rate is the percentage of patients who achieved virtually complete symptom resolution.

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 for the first time with NeuroStar TMS Therapy achieved a 54% response rate⁶ and a 33% remission rate⁷ on the HAMD 24-item scale, at the end of 6 weeks

Patients who benefited from NeuroStar TMS Therapy in either the randomized, controlled study or the open-label study were placed on antidepressant medication monotherapy and

entered into a six-month maintenance of effect study. In this study, the following results were observed⁹:

- Patients previously treated with NeuroStar TMS Therapy had less than 10% relapse rate at the end of six months
- Approximately half of patients experienced symptom breakthrough and required TMS Therapy re-treatment

Throughout the NeuroStar TMS Therapy studies, more than 10,000 active TMS treatments were safely performed. The following were the safety results observed⁸:

- No systemic side effects, such as weight gain, sexual dysfunction, sedation, nausea, or dry mouth
- No adverse effects on concentration or memory
- No seizures
- No device-drug interactions
- The most common adverse event related to treatment was scalp pain or discomfort at the treatment area during active treatments, which was transient and mild to moderate in severity. The incidence of this side effect declined markedly after the first week of treatment.
- There was a less than 5% discontinuation rate due to adverse events.
- During a 6-month follow-up period, there were no new safety observations compared to those seen during acute treatment.

NeuroStar TMS Therapy is contraindicated in patients with implanted metallic devices or non-removable metallic objects in or around the head. As with any antidepressant treatment, patients should be monitored for symptoms of worsening depression. .

About the Health Economic Analysis of NeuroStar TMS Therapy

Health care resource utilization data related to depression care only were collected during a multi-center study of NeuroStar TMS Therapy (N=301). These data were collected at the beginning of the study for each patient for the three months prior to start of treatment in order to establish a baseline. Health care resource utilization data were then collected again six months after the completion of acute treatment with NeuroStar TMS Therapy. An analysis was performed using the actual data collected to stratify the

acute treatment outcomes. A commonly-used health economic model was then used to estimate the illness course over a full year of treatment follow up.

The cost effectiveness of NeuroStar TMS Therapy is described by an incremental cost-effectiveness ratio (ICER) per quality adjusted life year (QALY) gained, a widely-accepted health economic measure. The incremental cost effectiveness ratio (ICER) is defined as the ratio of the change in costs of a therapeutic intervention compared to an alternative treatment option or to a treatment control condition. A quality adjusted life year (QALY) is a way of measuring disease burden, including both the quality and the quantity of life lived, as a means of quantifying the benefit of a medical intervention. Cost effectiveness was also assessed on a direct cost per patient basis across a range of per treatment reimbursement rates from \$250 to \$500 per treatment session. The impact of costs due to losses in work productivity and to caregiver time was also examined.

When NeuroStar TMS Therapy was compared to sham treatment, the third-party payer reimbursement rate would need to exceed \$400 per treatment session before the ICER exceeded the most stringent willingness to pay threshold for a new treatment. When productivity gains due to clinical recovery and reduced caregiver costs were included, the ICER was substantially improved. In open-label conditions comparing NeuroStar TMS Therapy (at a mid level reimbursement rate of \$350 per treatment session) to antidepressant medications used in the NIMH-sponsored STAR*D study, NeuroStar provided a net cost savings of \$1,141 per patient per year. At this reimbursement rate, treating only 10,000 patients annually would save the health care system over \$11M compared to current pharmaceutical standard of care. The cost savings increased to \$9,251 per patient per year when the costs for productivity gains were included. The analysis included 2 hours of lost productivity per treatment session for the patient to leave work to receive the 40 minute treatment.

Availability of NeuroStar TMS Therapy

Initially, NeuroStar TMS Therapy will only be available in a limited number of treatment centers around the country. For specific information on treatment locations offering NeuroStar TMS Therapy, please visit www.NeuroStarTMS.com or call the Neuronetics Customer Service Center at (877) 600-7555.

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, please visit www.neuronetics.com.

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¹Greenberg, PE, Kessler, RC, Birnbaum, HG, Leong, SA, Lowe, SW, Berglund, PA, & Corey-Lisle, PK. (2003) The Economic Burden of Depressive Disorders in the United States: How Did It Change Between 1990 and 2000? *Journal of Clinical Psychiatry*, 64 (12), 1465-1475.

²Corey-Lisle PK, Birnbaum H, Greenberg P, Claxton AJ. (2002) Identification of Claims Data "Signature" and Economic Consequences for Treatment-Resistant Depression. *Journal of Clinical Psychiatry*, 63 (8), 717-726 .

³Corey-Lisle PK, Farinpour R, Starr SR. Validation of a treatment algorithm for treatment-resistant depression. American Psychiatric Association, Philadelphia, PA. April 2002.

⁴Crown, WH, Finkelstein, S, Berndt, ER, Ling D, Poret, AW, Rush AJ, Russell, JM (2002). The impact of treatment-resistant depression on healthcare utilization and costs. *Journal of Clinical Psychiatry*, 63 (11), 963-971.

⁵Lisanby, 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. *Neuropsychopharmacology*, advance online publication, 13 August 2008; doi:10.1038/npp.2008.118.

⁶Thase M, Demitrack M. Evaluating Clinical Significance of Treatment Outcomes in Studies of Resistant Major Depression, *Biological Psychiatry*, April, 2008; Vol. 63:7s, pg. 138s.

⁷ Data on file.

⁸Janicak, 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; 69:2:222-232.

⁹ Janicak, P, et al. Durability of Acute Response to TMS in the Treatment of Major Depression: Relapse During a Continuation Pharmacotherapy Extension Study. *Biological Psychiatry*, 2007; 61:176s

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