

Positive Results Reported for Phase II Randomized Double-Blind Clinical Trial for the Treatment of Drug-Resistant Epilepsy Using External Trigeminal Nerve Stimulation (eTNS™) - The USB Port to the Brain™

LOS ANGELES, April 28, 2011 /PRNewswire/ -- This afternoon, at the Antiepileptic Drug Trials XI Conference in Miami, Florida, (<http://www.epilepsy.com/etp/aedtrialxi>) Dr. Christopher DeGiorgio, principal investigator and neurologist at UCLA, presented the results of a Phase II randomized double-blind clinical trial for the treatment of refractory epilepsy. The 50-subject study was conducted at UCLA and the University of Southern California. "I'm excited to see that our non-invasive and very safe approach to neuromodulation demonstrates efficacy under double-blind controlled conditions and compares favorably with pharmaceutical and surgically-invasive approaches. We look forward to proceeding to the next phase of the regulatory approval process and clinical development for our epilepsy therapies," DeGiorgio said.

This study was a randomized double-blind, active-controlled clinical trial of external TNS (eTNS™) therapy in 50 people with drug resistant epilepsy. All subjects in the study were aged between 12 – 70 with a history of intractable seizures and exposure to at least two antiepileptic drugs at adequate doses.

The study was funded by investigator-initiated grants from the Epilepsy Therapy Project, the Epilepsy Foundation, Boston Scientific and the Milken Family Foundation. The TNS technology, including eTNS™ for the treatment of epilepsy, was originally invented and developed at UCLA.

NeuroSigma, Inc., a Los Angeles-based medical technology company established to in-license and develop early stage technologies with the potential to transform medical practice, is the exclusive worldwide licensee of UCLA's TNS intellectual property. "We are extremely pleased to be working closely with Dr. DeGiorgio and his talented and dedicated team at UCLA, to help make his vision of a safe, non-invasive therapy for epilepsy a reality," said Dr. Leon Ekchian, President and CEO of NeuroSigma.

Background - TNS

NeuroSigma is developing two embodiments of TNS: eTNS™ (TNS with external electrodes and an external pulse generator) and sTNS™ (subcutaneous electrodes and implantable pulse generator).

The eTNS™ system utilizes a self-adhesive conductive pad applied to the forehead to stimulate branches of the trigeminal nerve, which are located very close to the surface of the skin above the forehead. The trigeminal nerve is one of the largest in the body, offering a high-bandwidth pathway for signals to enter the brain. In clinical studies, eTNS™ is well tolerated and the low-energy stimulus is confined to the soft tissues of the face without penetration into the brain – hence the term "USB Port to the Brain™."

The trigeminal nerve projects to specific areas of the brain, such as the locus coeruleus, nucleus tractus solitarius, thalamus and the cerebral cortex, which are involved in epilepsy, depression, PTSD and other disorders. PET

imaging studies in humans confirms that eTNS™ activates or inhibits key regions implicated in these disorders and the changes were observed within minutes of therapy.

Once approved by regulatory agencies, patients who respond well to eTNS™ can opt to switch to the implantable sTNS™ system. NeuroSigma is developing its own proprietary eTNS™ system but contemplates partnering for sTNS™ with other medical device companies, which already have commercially available implantable neurostimulation systems.

Results

The investigators reported that patients receiving active eTNS™ treatment experienced a significant improvement in seizure reduction, while those randomized to receive the control condition ("sham" or "placebo") did not. "We showed that eTNS™ works well, under stringent clinical-trial conditions, with nearly 40% showing a clinically-meaningful response after 18 weeks of daily stimulation – there were 9 responders in the active group in contrast to 3 in the control group, where a responder experiences a greater than 50% reduction in seizures," noted Dr. DeGiorgio. In addition to reducing seizures, eTNS™ also improved mood. These results confirm and extend the findings of DeGiorgio's positive feasibility trial in epilepsy, reported in 2009 in the prestigious journal *Neurology*.

CAUTION: Both eTNS™ and sTNS™ systems are investigational devices and at this time are limited by United States law for investigational use only.