



Positive Stroke Rehabilitation Clinical Trial Results for the Vivistim® Paired VNS™ System Published in *The Lancet*

DALLAS, Texas – (Date TBD), 2021 – MicroTransponder Inc., (www.microtransponder.com) developer of the first Vagus Nerve Stimulation (VNS) device for post-stroke rehabilitation, announced today that the pivotal, double-blind, randomized controlled stroke rehabilitation clinical trial results for the Company's investigational Vivistim® Paired VNS™ System have been published in *The Lancet*. The purpose of the study was to evaluate the safety and efficacy of the Vivistim® Paired VNS™ System combined with intense physical therapy compared to intense physical therapy (Controls) in subjects with arm and hand impairment after chronic stroke. The study met its primary and all secondary endpoints. Subjects that received paired VNS showed statistically significant and clinically meaningful improvements in motor impairment and function that were 2-3 times greater compared to Controls that received intense physical therapy. Safety and adverse events were similar to other VNS therapies.

The study enrolled 108 participants at 19 sites in the United States and United Kingdom. Study participants were up to 10 years post-stroke with moderate to severe upper extremity impairment. They were randomized to either the VNS group (intense physical therapy paired with active VNS) or the Control group (intense physical therapy paired with sham VNS). Therefore, both groups received the same intense physical therapy, which is the best option currently available for individuals with upper limb motor deficits after stroke. The study was double-blinded, meaning that neither the subjects nor the clinical personnel involved in the delivery and outcome measurement of the therapy knew which group they were in. Subjects performed 6 weeks of the therapy at a study facility, followed by 3 months of home therapy. Subjects in the Control group then crossed over to receive active VNS (with intense physical therapy) and both groups continued to do home-based VNS treatment over the long term.

The primary endpoint was the change in the Upper Extremity Fugl-Meyer Assessment (FMA-UE) score, which is a commonly used measure to assess upper extremity impairment after stroke. FMA-UE increased by 5.0 ± 4.4 points with VNS compared to 2.4 ± 3.8 points in Controls ($p=0.001$) after 6 weeks of in-clinic therapy. After ninety days of home-therapy, 47% of the subjects in the VNS group showed a clinically meaningful response (≥ 6 -point change) on the FMA-UE score versus 24% in Controls ($p=0.01$). Improvements were also observed for the VNS group on the Wolf Motor Function Test (WMFT) compared to Controls (0.46 ± 0.40 vs. 0.16 ± 0.30 , $p<0.0001$). After VNS, subjects also showed a 2-3 times improvement over Controls in quality of life domains including Activities of Daily Living and Self-Care, reflecting improved perception of their overall well-being. After Controls crossed over to receive VNS, motor gains were similar to the gains observed in the VNS group. Preliminary results show that FMA-UE

and WMFT scores were maintained at 6 months and one-year post-therapy (data collection and assessments are currently ongoing and the final dataset analysis will be available at a later date).

“This is the first study to find clinically- and statistically-significant effects of a neuromodulation therapy for people with arm and hand weakness after chronic stroke,” said Dr. Jesse Dawson, Professor of Stroke Medicine, at the University of Glasgow and principal investigator of the trial. “We saw improvement for the VNS group in both impairment and functional measures compared to Controls. In particular, the clinically meaningful response rate doubled with paired VNS for both impairment and functional outcomes.”

Dr. Steve Cramer, Professor of Neurology at UCLA and Medical Director of Research at California Rehabilitation Institute in Los Angeles, observed, “Patients with chronic stroke have limited options for therapy, so it is encouraging to see these positive results in stroke patients up to 10 years post-stroke”.

“The long-term multiplicative benefits of VNS over control therapy across different outcome measures observed in this study suggest that this may be an important adjunct for chronic stroke patients who typically receive little or no active rehabilitation at home” noted Steven L. Wolf, PT, PhD, Professor and Director of Research in the Department of Rehabilitation Medicine, Division of Physical Therapy, Emory University School of Medicine.

Dr. Charles Liu, PhD, MD, Chair of Neurosurgery, Chief of Innovation & Research at Rancho Los Amigos and Director of the USC Neurorestoration Center commented, "I've performed hundreds of VNS surgeries including eight for this clinical study. The VNS implant procedure has been performed for over 20 years and is simple and straight forward. I look forward to the Vivistim® System hopefully becoming available to help stroke patients improve their arm and hand movements."

“The results of this clinical study suggest that the addition of VNS enhances the effect of best practice stroke rehabilitation. It is also important to note that our physical and occupational therapists were able to easily incorporate the Vivistim® System with intense rehabilitation therapy.” stated Dr. Teresa Kimberley, PhD, PT, Professor and Director of the Brain Recovery Lab at MGH Institute of Health Professions, a senior investigator on the project through both the pilot and pivotal studies. “We are looking forward to potentially establishing the therapy as part of a new standard of care for stroke rehabilitation. “

The Vivistim® Paired VNS™ System stimulates the vagus nerve while the patient does task-specific rehabilitation. The vagus nerve projects to areas of the brain that release neuromodulators such as acetylcholine and norepinephrine. These neuromodulators act within a window of opportunity to enhance the behavioral relevance of the motor task that is combined with VNS, in this case, intense physical therapy. This simultaneous and repeated pairing of task-specific movements with VNS strengthens motor circuits associated with the movement task, enabling the brain to effectively relearn the task. The Vivistim® Paired VNS™ System is intended to help patients potentially regain upper limb function over time, improving their ability to perform day-to-day activities.

Efforts to obtain marketing authorizations from regulatory authorities in both the U.S. and the EU are currently underway. MicroTransponder is rapidly expanding its team and seeks talented individuals with

a passion for stroke rehabilitation and neuromodulation. Please apply via our website at <https://microtransponder.com/en-gb/stroke/about/careers>.

Dawson J *et al*, Vagus Nerve Stimulation Paired with Rehabilitation for Upper Limb Motor Function After Ischaemic Stroke (VNS-REHAB): A Randomised, Blinded, Pivotal, Device Trial *The Lancet*, Vol 397, 2021

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About MicroTransponder, Inc.

MicroTransponder, Inc. (www.microtransponder.com) is a privately held medical device development company with a strong neuroscience research focus. An experienced team of scientists and engineers has developed a neurostimulation technology platform to treat neurological conditions, including post-stroke motor rehabilitation and tinnitus.

Interviews are available upon request.