

Breakthrough First-in-Human Study Shows Vagus Nerve Stimulation Significantly Reduces Rheumatoid Arthritis Symptoms, Inhibits Cytokine Production

– Clinical Data Published in *Proceedings of the National Academy of Sciences (PNAS)* –

– Delivery of Electric Current to Vagus Nerve Could Provide More Treatment Options and Alternatives to Costly Immunosuppressive Drugs –

Amsterdam, Manhasset, NY and Valencia, CA – July 4, 2016 – Clinical trial data published in the *Proceedings of the National Academy of Sciences (PNAS)* demonstrates stimulating the vagus nerve with an implantable bioelectronic device significantly improved measures of disease activity in patients with rheumatoid arthritis (RA). RA is a chronic inflammatory disease that affects 1.3 million people in the United States and costs tens of billions of dollars annually to treat. The findings, announced by the Academic Medical Center/University of Amsterdam, the Feinstein Institute for Medical Research and SetPoint Medical, appear online in *PNAS Early Edition* and will appear in an upcoming print issue.

The publication, titled “Vagus nerve stimulation inhibits cytokine production and attenuates disease severity in rheumatoid arthritis,” highlights a human study designed to reduce symptoms of RA, cytokine levels and inflammation by stimulating the vagus nerve with a small implanted device.

“This is the first study to evaluate whether stimulating the inflammatory reflex directly with an implanted electronic device can treat RA in humans,” said Professor Paul-Peter Tak, MD, PhD, FMedSci, the international principal investigator and lead author of the paper at the Division of Clinical Immunology & Rheumatology of the Academic Medical Center/University of Amsterdam. “We have previously shown that targeting the inflammatory reflex may reduce inflammation in animal models and in vitro models of RA. The direct correlation between vagus nerve stimulation and the suppression of several key cytokines like TNF as well as reduced RA signs and symptoms demonstrates proof of mechanism, which might be relevant for other immune-mediated inflammatory diseases as well.”

“Our findings suggest a new approach to fighting diseases with bioelectronic medicines, which use electrical pulses to treat diseases currently treated with potent and relatively expensive drugs,” said Anthony Arnold, Chief Executive Officer of SetPoint Medical. “These results support our ongoing development of bioelectronic medicines designed to improve the lives of people suffering from chronic inflammatory diseases and give healthcare providers new and potentially safer treatment alternatives at a much lower total cost for the healthcare system.”

“This is a real breakthrough in our ability to help people suffering from inflammatory diseases,” said co-author

Kevin J. Tracey, MD, president and CEO of the Feinstein Institute for Medical Research, discoverer of the inflammatory reflex and co-founder of SetPoint Medical. “While we’ve previously studied animal models of inflammation, until now we had no proof that electrical stimulation of the vagus nerve can indeed inhibit cytokine production and reduce disease severity in humans. I believe this study will change the way we see modern medicine, helping us understand that our nerves can, with a little help, make the drugs that we need to help our body heal itself.”

While focused on rheumatoid arthritis, the trial’s results may have implications for patients suffering from other inflammatory diseases, including Crohn’s, Parkinson’s, Alzheimer’s and others.

Study Methodology and Results

In the study, a stimulation device was implanted on the vagus nerve during a surgical procedure, then activated and deactivated based on a set schedule to measure response over 84 days, with primary endpoints measured at day 42 using DAS28-CRP, a standard disease activity composite score for RA that includes counts of tender and swollen joints, patient’s and physician’s assessment of disease activity and serum C-reactive protein (CRP) levels.

Of 17 patients with active RA in the study, several patients that had failed to respond to multiple therapies, including biologicals with different mechanisms of action, demonstrated robust responses. The findings indicate that active electrical stimulation of the vagus nerve inhibits TNF production in RA patients and significantly attenuates RA disease severity.

Several patients reported significant improvements, including some who had previously failed to respond to any other form of pharmaceutical treatment. In addition, no serious adverse side effects were reported.

The emerging field of bioelectronic medicine aims to target disorders traditionally treated with drugs and instead uses advanced neuromodulation devices that may offer significant advantages. SetPoint is developing a novel proprietary bioelectronic medicine platform to treat a variety of immune-mediated inflammatory diseases, using an implanted device to stimulate the vagus nerve.

About Academic Medical Center at the University of Amsterdam

The Academic Medical Center (AMC) is one of the foremost research institutions of the Netherlands as well as one of the largest hospitals. The AMC complex houses the university hospital and the medical faculty of the University of Amsterdam, as well the Netherlands Institute Neurosciences and, the medical department of the Royal Tropical Institute. In the coming years, a national Neuroimaging Center will arise next to the AMC. Also a number of biotech companies – partly AMC spin-offs - are located on the premises. This concentration of expertise makes the AMC a breeding ground for fruitful scientific collaboration. The AMC houses all medical specializations that are recognized in the Netherlands, and all types of top clinical patient care. www.amc.nl

About The Feinstein Institute for Medical Research

The Feinstein Institute for Medical Research is the research arm of Northwell Health, the largest healthcare provider in New York. Home to 50 research laboratories and to clinical research throughout dozens of hospitals and outpatient facilities, the 2,000 researchers and staff of the Feinstein are making breakthroughs in molecular medicine, genetics, oncology, brain research, mental health, autoimmunity, and bioelectronic

medicine – a new field of science that has the potential to revolutionize medicine. For more information about how we empower imagination and pioneer discovery, visit FeinsteinInstitute.org.

About SetPoint Medical

SetPoint Medical is a privately held biomedical technology company dedicated to treating patients with debilitating inflammatory diseases using bioelectronic therapy. SetPoint’s approach is intended to offer patients and providers an [alternative](#) for the treatment of RA and other chronic inflammatory diseases with less risk and cost than drug therapy. SetPoint’s therapy is being evaluated in an open-label clinical study for Crohn’s Disease.

SetPoint is developing a novel bioelectronic medicine platform consisting of an implantable miniature neuromodulation device and iPad prescription pad application. The implantable device stimulates the vagus nerve to activate the body’s natural inflammatory reflex, which is intended to produce a potent systemic anti-inflammatory effect. The company has published positive results from a first-in-human open-label proof-of-concept trial in rheumatoid arthritis in *Proceedings of the National Academy of Sciences* (PNAS) and presented positive results at the American College of Rheumatology. Current investors in the company include Morgenthaler Ventures, Flare Capital Partners, Topspin Partners, Medtronic, GlaxoSmithKline’s Action Potential Venture Capital Limited and Boston Scientific. For more information, visit www.setpointmedical.com.

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