

Neuros Medical Seeks to Commercialize Nerve Block as Treatment for Pain

by David Pope, editorial director

Neuros Medical Inc., headquartered in Willoughby, OH (about 20 miles east of downtown Cleveland) was launched in 2008 to bring to market Nerve Block, a selective and reversible neurostimulation technique for completely blocking transmission of impulses in targeted nerves. The company's initial goal is to develop an implanted device for blocking chronic pain that arises in the peripheral nervous system, such as amputation residual-limb pain, post-surgical pain, traumatic neuromas, and migraine. The neurostimulation technique also can be used to block spasticity, or muscle spasms, that occur as a result of spinal-cord injury, stroke, cerebral palsy, Tourette's syndrome, and multiple sclerosis.

Jon Snyder, founder, CEO, and president of Neuros, has more than 20 years of experience with biomedical and health-care companies including Cyberonics, Imalux, Steris, and Cardinal Health. He returned to Cleveland in early 2008 to become CEO-in-residence at BioEnterprise, a nonprofit initiative set up to help Ohio companies launch bioscience technologies. The CEO-in-residence program is funded by Ohio's Third Frontier Project. Snyder also joined Arboretum Ventures, based in Ann Arbor, MI, as a venture partner and manager of its Cleveland office. Part of his role at BioEnterprise was to search for biomedical inventions to commercialize. It did not take long to find one across the street at Case Western Reserve University. With help from BioEnterprise's staff, Snyder put together a business plan for developing and marketing the promising Nerve Block technology invented at CWRU, and incorporated Neuros Medical in October 2008.

Case Technology Ventures, an early-stage investment fund set up by the university, and JumpStart Inc., a Cleveland-based venture development organization, provided early funding of \$375,000. Joseph Jankowski, CWRU's associate vice president for technology management, joined the Neuros board of directors. In November 2009 Neuros announced a \$1.8 million series A round led by North Coast Angel Fund, which was joined by

Glengary LLC, Ohio Tech Angel Fund, Queen City Angels First Fund III, and individual investors. Claiborne Rankin of the North Coast Angel Fund and Mark Teague of Glengary LLC became directors of Neuros.

The Nerve Block technique acquired by Neuros uses two phases of electrical stimulation to temporarily depolarize the nerve membrane in the targeted nerve region. Repeated biphasic pulses make the nerve membrane incapable of conducting action potentials in that region. Animal studies indicate that the block is immediately and completely reversible. In a mixed nerve with both motor and sensory nerve fibers, it is possible to block the larger motor nerve fibers while allowing the sensory nerve fibers to continue functioning. This is done by using low-amplitude pulses. To block pain signals, the stimulus amplitude is progressively increased until both the motor and sensory nerve fibers are prevented from transmitting action potentials.

Kevin Kilgore and Niloy Bhadra of CWRU's department of biomedical engineering are credited with the development of the nerve block technique. Kilgore is an adjunct assistant professor and Bhadra is a research assistant professor. In addition, Kilgore holds positions at MetroHealth Medical Center, the Louis Stokes VA Medical Center, and is associate director at the Cleveland Functional Electrical Stimulation (FES) Center. Bhadra, who was an orthopedic surgeon before changing to biomedical engineering research, earned a Ph.D. from CWRU in 2005 for his research on biphasic, high-frequency nerve block. He also is a principal investigator at the Cleveland FES Center. Kilgore and Bhadra serve as technical advisors to Neuros.

The nerve block technology stems in part from research at CWRU in the 1990s by Warren Grill before he moved to Duke University [Grill is NBR's senior technical editor]. Kilgore, Grill, and two other researchers are listed on a fundamental patent for reversibly blocking nerve activity that was filed in 2002 and issued to CWRU in 2008. Kilgore and

Bhadra have submitted additional applications for patents.

Shortly after the series A fund raising, Neuros appointed Zi-Ping Fang chief technology officer. Fang, who has a Ph.D. in biomedical engineering from CWRU and post-doctoral training in neuroscience, is responsible for the company's technology and clinical development efforts. Fang has more than 25 years of experience in clinical research and neurostimulation technology and served previously with Nevro Corp. A clinical advisory board has been formed with Amol Soin of the Ohio Pain Clinic and Michael Stanton-Hicks of the Cleveland Clinic as members.

Battelle's medical devices and diagnostics group has been selected to develop the prototype under the guidance of Neuros' CTO Fang. "A prototype will be produced in 2010, developed with and manufactured by Battelle," according to Snyder, Neuros' president and CEO. The prototype is designed for use in patients in clinical studies.

Headquartered in Columbus, OH, Battelle is the world's largest independent research and development organization, conducting more than \$5 billion in contract research annually. The Battelle medical devices group has experience in the design, development, and manufacture of devices, as well as in the design and management of clinical studies. Its services are compliant with FDA's quality and regulatory requirements and with ISO 9001 and 13485 standards. Following the completion of a medical study managed by Battelle, the FDA requested a special presentation as an example of the design and execution of a high-quality

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Founded: 2008
Market: Chronic pain and spasticity
Privately held
President and CEO: Jon J. Snyder

Neurologists Focus on Multiple Sclerosis at 2010 AAN Annual Meeting

Staff report

Neurologists and related professionals from around the world attended the 2010 Annual Meeting of the American Academy of Neurology in Toronto, Canada earlier this month.

At the meeting, AAN named Enawgaw Mehari, of Morehead, KY, as the recipient of the Kenneth M. Viste, Jr., Patient Advocate of the Year Award. Mehari received the award for his work to improve the access to and quality of neurologic care provided to HIV/AIDS patients in his native Ethiopia.

Mehari founded People to People, a non-profit organization that allowed him to develop a neurology training program for Ethiopia's physicians, at a time when Ethiopia had only eight neurologists and two neurosurgeons serving a population of 80 million.

Numerous presentations at this year's conference were devoted to multiple sclerosis, some in conjunction with the Consortium of Multiple Sclerosis Centers, a multidisciplinary organization providing a team approach to MS care and a network for health care professionals. The consortium provides leadership in clinical research and education; develops vehicles to share information and knowledge among members; disseminates information to the health care community and to persons affected by MS; and develops and implements mechanisms to influence health care delivery.

The AAN Foundation/Consortium of Multiple Sclerosis Centers John F. Kurtzke, Clinician-Scientist Development Three-Year Award was presented to Gabriele De Luca, a neurologist at the Mayo Clinic College of Medicine in Rochester, MN,

for his research titled "Genetic-Pathologic Correlations in Multiple Sclerosis." The three-year award consists of an annual salary of \$75,000 plus \$5,000 in educational expenses per year to support a clinician scientist's research related to MS.

Actress Teri Garr hosted the AAN Foundation's newest patient education video and guidebook, *Living Well: A Guide to Managing Multiple Sclerosis for Patients and Families*, which were given to attendees to take back to their practices and share with patients. The video and guidebook are aimed at answering important questions for newly diagnosed MS patients and their caregivers.

Garr was featured in the inaugural issue of *Neurology Now* magazine, where she detailed her diagnosis and how she lives with MS. Garr is also a staunch MS patient advocate in her roles as a National Ambassador for the National Multiple Sclerosis Society and chair for the Society's Women On the Move program.

One of the scientific sessions at the conference was devoted to pseudobulbar affect, a neurologic condition of involuntary, sudden, and frequent episodes of laughing or crying quite common in patients with underlying neurologic diseases or injuries, especially those with MS and ALS. A new investigational treatment may help stop these involuntary outbursts. "These outbursts of crying and laughter at inappropriate times can have a severe impact on patient and caregiver well-being, social functioning and quality of life," said study author Erik Pioro, director of the section for ALS and related disorders at the Cleveland Clinic.

The study in patients diagnosed with PBA tested the effectiveness of a combination of two medications, dextromethorphan and low dose quinidine. The combination of the drugs is known as DMQ. After completing the blinded, placebo controlled phase of the study, participants could take part in a subsequent open label study where all of the participants would receive the DMQ drug combination for an additional 12 weeks. Of the 283 people completing the first phase, 253, or 89 percent, chose to take part in this subsequent open label study.

Participants were given daily doses of DMQ and were regularly given a test that measures the frequency and severity of their PBA. The study found that the average test score was significantly improved by 2.7 points from the start to the end of the open label study. Patients who were taking a placebo in the previous clinical trial and switched to DMQ demonstrated the most improvement.

"Our findings represent the first long-term results showing DMQ is effective in helping to control this debilitating condition afflicting patients with neurologic diseases or injuries," said Pioro. "Currently, there are no FDA approved treatments for PBA, which is problematic because currently used off-label treatments are often ineffective or may have unacceptable side-effects."

Pioro says these findings, along with additional clinical data, will serve as the basis for an application for FDA approval of DMQ as the first treatment for pseudobulbar affect. The study was supported by Avanir Pharmaceuticals, Inc.

ity medical device clinical study. The Battelle medical device group also developed the algorithms for processing brain signals from the BrainGate interface developed by Cyberkinetics Neurotechnology Systems, Inc. Battelle also developed patient-training techniques to enable paralyzed patients to learn to communicate through the BrainGate interface.

Neuros plans to have its safety and efficacy clinical trial completed in the first

quarter of 2011. The initial target market is the patient with chronic residual-limb pain following limb amputation. About 70 percent of the 1.7 million patients in the U.S. who have undergone amputation experience residual-limb pain. In addition, the high incidence of amputation in military casualties in Iraq and Afghanistan has created an urgency for developing better treatments, and the Nerve Block device may find a role in providing

pain relief to wounded veterans.

The next target for Neuros' Nerve Block platform is likely to be patients with chronic pain due to damage to nerves caused by surgery or injury. Migraine pain relief is another promising area. If patient clinical studies show that Nerve Block can prevent uncontrolled muscle spasms without affecting sensory nerve activity, a wide range of clinical applications will be possible.