Real-time Seizure Detection and Control System
using Ceramic-base Multisite Electrode

Executive Summary
1. Background

Real-time Seizure Detection and Control System using Ceramic-base Multisite Electrode project focuses on implantable Closed-Loop Neuromodulation medical devices for patients suffering from neurological disorders. Our initial product, Epilepsy Control System, focuses on the treatment of epilepsy, a neurological disorder which affects more than 50 million people in the world today. In addition to epilepsy, our closed-loop neuromodulation system has the potential to be adapted for the treatment of intractable depression and other neurological diseases which together affect hundreds of millions worldwide.

2. Product

What unmet medical need does the product address?

Epilepsy is a neurological disorder which affects more than 50 million people in the world. There are more than 2.6 million epilepsy patients in the US alone, with 100,000 new cases reported every year. Annual direct medical cost translates to approximately $12.5 billion, while indirect costs are many times that due to loss of lifetime earnings estimated at 35% for men and 25% for women. Social alienation often causes epilepsy patients to develop other neurological disorders like clinical depression and psychosis.

Current first line treatment for most types of epilepsy involves the prescription of anti-epileptic drugs (AEDs) that helps control seizures in 70% of the epilepsy patients. However, AEDs remain complicated by both short and long term side effects. Of the alternatives, epilepsy surgery offers a 50–65% probability of freedom from disabling seizures, but is possible in only 8% of chronic epilepsy patients; while vagus nerve stimulation (VNS) offers only palliative treatment.

Most importantly, about a third of all epilepsy patients do not respond to any available treatments and continue to have intractable seizures everyday.

What Technology is the Product based on?

Scientists have recently discovered that by delivering electrical stimulation to specific regions of the brain (epileptic focus), they are able to prevent the occurrence of seizures. This technique, also known as neuromodulation, is currently used in open-loop systems where uncontrolled electrical currents are delivered to the nervous system constantly. Due to fear of adverse effects, scientists have begun to focus their efforts on developing a more sophisticated closed-loop system that predicts the occurrence of seizures and delivers the stimulation only when necessary.

Current methods of closed-loop neuromodulation are developed based on prediction using EEG recordings, which is difficult and have so far only proven to be 50% effective in predicting seizures. In comparison, we aim to develop an implantable closed-loop neuromodulation device that uses single-neuron recordings to predict seizures. Single-neuron recording is a cutting edge technology in neurological signal recordings. Our Ceramic Based Multi-Site Electrode, developed by Dr. Karen Anne Moxon, Professor of Biomedical Engineering, Neurobiology and Anatomy at Drexel University, allows us to record accurately and chronically from multiple single-neurons in the brain, a feat which has so far been unattainable. This breakthrough in material science and neurological recording allows us to develop an Epilepsy Control System, an implantable device the size of a quarter that can be chronically implanted into an epilepsy patient’s neural tissues using current available surgical methods.

What clinical evidence exists that this technology works?

The data, in a rat model of epilepsy, demonstrated that the system was 100% effective (true positives) in detecting seizures when applied to continuous streams of data (Moxon et al., 2001, IEEE-EMBS Conference Proceedings and 6 recent animals; 149 seizures). The system was able to predict a seizure within four minutes.
before onset with a low false positive rate (less than 30%). An unoptimized closed-loop system was tested and successfully prevented 65% of seizures in 3 animals. Several parameters can be adjusted to further improve our success rate (manuscript in prep).

**Who Owns the Intellectual Property Rights on the Technology?**

Our device consists of three parts: 1) a patented Ceramic-based Multisite Electrode (CBMSE) (U.S. patent No. 6,838,200) that is chronically implanted into the affected neural tissue, 2) a wireless controlled neuromodulation system (U.S. patent application 11/753,256), and 3) an optoelectronic device to remotely power the system (U.S. provisional patent application 61/082,429). All patents and patent applications belong to Drexel University.

### 3. Market Size and Potential

**Who are the Customers and what is the Potential for this device?**

The potential customers of our technology include epilepsy patients, medical practitioners (neurologists and neurosurgeons), healthcare providers (hospitals) and healthcare payers (insurance agencies). To ensure buy-in from these stakeholders, we have identified their decision making criteria and seek to address them through our development process. Their concerns include safety, efficacy, ease of implementation, and the cost-benefits profile of the device.

We roughly estimate the target market is around $12 billion. We base this on the fact that there are approximately 2.5 million epilepsy patients in the U.S. Of these, roughly one third (around 800,000) do not respond adequately to medication, and are thus good candidates for device-based treatments. Vagus nerve stimulation costs around $15,000, so we have chosen this as the typical cost of a surgically implanted device for epilepsy treatment (this does not include the cost of the actual surgery, just the device). Multiplying the number of candidate patients by the cost, we calculate a potential maximum market size for the epilepsy treatment application as 800,000 times $15,000, or $12 billion.

### 4. Competitive Landscape and Advantage

Current first line treatment for epilepsy involves the prescription of anti-epileptic drugs (AEDs) that help control seizures in about 70% of epilepsy patients. However, AEDs remain complicated by both short and long term side effects that can be debilitating. Moreover, these drugs are not recommended for women of child bearing age as they are a known cause of birth defects. Of the alternatives, epilepsy surgery offers a 50–65% probability of freedom from disabling seizures, but is possible in only 8% of patients who have chronic epilepsy; while continuous vagus nerve stimulation (VNS) offers only palliative treatment. An alternative approach is to identify activity in the neuronal signal before the onset of the motor seizure that will predict the seizures onset using EEG (Neuropace). Our approach uses single neuron activity and may offer more precision and specificity than competing technologies, and may more accurately predict when the next seizure will occur.

### 5. Reimbursement

Healthcare reimbursement in the US adopts a multi-payer system. A search with the major reimbursement agencies revealed that similar devices for the treatment of Parkinson’s disease have already been approved for reimbursement under HCPCS code C1767 and C1820. The surgical procedures to implant these devices are also covered under APC 222. Other related costs associated with the hospital and physician charges are reimbursable as part of the Craniotomy Diagnosis Related Group (DRG) under code C61885. As such, we expect our technology and its related treatment costs to be fully reimbursable by Medicare, Medicaid, and subsequently majority of the private healthcare insurance agencies.
6. Regulatory

Marketing of any medical devices in the US is regulated by the US FDA, CDRH division. Primary discussions with an FDA consultant suggest that we will require a Pre-Market Approval (PMA) for the technology, which is a Class III medical device. This classification requires our product to fulfill the most stringent clinical tests in order to ascertain the safety and efficacy of our device. Four critical milestones were identified using pre-validated models that will allow the technology to obtain FDA approval.

7. Execution Plan

**Human clinical study 1**  
Q2’09 – Q4’09
- Demonstrate that the sensors, inserted using a standard surgical technique, record neural signals in humans
- Demonstrate that Moxon sensors are safe
  - Pathological verification of excised tissue
  - Surgical monitoring during insertion
- IRB at Thomas Jefferson University, Philadelphia, PA has been approved
- May require IDE – Pre-IDE meeting with FDA is planned

**Human clinical study 2**  
Q4’09 – 2010
- Demonstrate that our sensors can predict seizure onset
- May require IDE – Pre-IDE meeting with FDA is planned

**Development & Testing of Seizure Disruption Technology/Device**  
2011-2012
- Utilize the electrodes to deliver local stimulation – prove out this component for a closed loop system
  - Ideally run in parallel with seizure warning device - show that stimulator can halt seizure

**Development & Testing of Closed Loop Device**  
2013-2014
- Develop a complete, closed loop device
- Pivotal study – 2013, FDA approval Q1-Q2’14

8. Amount and uses of funding required

The cost to complete preliminary human studies 1 and 2 is estimated at two million dollars. We expect to raise one-third of this from foundations, including epilepsy foundations and the remaining funds by partnering with a medium sized medical device company that manufactures other devices for epilepsy treatment. The task of developing and clinically testing the closed loop device is a cash intensive task, suited better for a large corporation.

9. The Inventor

Karen Anne Moxon, Ph.D. Dr. Moxon is Associate Professor of Biomedical Engineering, Neurobiology and Anatomy at Drexel University. She is the inventor of the core technology described here, the Ceramic Based Multi-Site Electrodes. Dr. Moxon is a leader in the field of single-neuron recording technologies. Her research interests include computational modeling, neural modeling, neurorobotics, neuromimetics, neurocontrol, and multi-unit neural recording. She is the author of numerous published research papers and was most recently awarded the Excellence in Neural Engineering Young Investigator Fellowship. (1st International IEEE-EMBS Conference on Neural Engineering, Capri, Italy).
10. Risk Analysis & Mitigation

Neuromodulation therapy is widely used for pain management and Parkinson’s disease. To mitigate the risks inherent in our industry, we will be partnering with experienced industry professionals and preeminent scientists. In addition, we will be using pre-validated clinical models to lower the development risks. The technology has also gone through preliminary proof of concept.

11. Further information and licensing inquiries

For licensing information please contact:

Alexey Melishchuk, PhD, Associate Director, Licensing
Office for Technology Commercialization
Drexel University
3225 Arch Street, Ground Floor
Philadelphia, PA 19104

Tel: 215-895-0304
Fax: 215-895-0310
Email: amelishchuk@drexel.edu