

Part 1: “Elevator” Introduction

Only 1 in 10 drug candidates that enter human clinical trials is found to be effective and safe enough to receive FDA approval, i.e., a large portion of the \$141 billion spent worldwide on pharmaceutical R&D is wasted. A major reason for this poor outcome is that animal models or cell cultures used for testing efficacy and toxicity in the drug development process do not properly replicate the complexity of the human body, and do not predict human responses well. Therefore, tissue models have been developed to re-create the complex interaction of cells in the human body. The ultimate goal of these so called Organ-on-a-Chip models is to improve the predictive value of the toxicity and efficacy of drug tests prior to human clinical trials. The goal is to determine earlier in the drug development process which drugs will likely fail in clinical trials, saving time and money. BMSEED’s **MicroElectrode Array Stretching Stimulating und Recording Equipment (MEASSuRE)** improves these Organ-on-a-Chip models by simulating the mechanical and electrical environment of cells in the body in a controlled environment. Organ tissues grown in this environment are more reflective of the mature human organ, thus increasing the predictive value of early drug testing. MEASSuRE also reproduces the biomechanics of a traumatic brain injury, concussion, and spinal cord injury, which are caused by mechanically stretching and compressing the cells in the brain and spinal cord, providing a screening platform to assess the efficacy of drugs and other treatment strategies based on the electrophysiology of the injured cells. The critical component of MEASSuRE is the stretchable microelectrode array, which incorporates our patented soft and elastically stretchable microelectrodes. Our long term goal is to apply our technology to therapeutic and diagnostic clinical applications, such as the stimulation of the spinal cord to alleviate chronic pain and the more accurate localization of seizures prior to epilepsy surgery.

Part 2: Market and Industry Analysis

Market and Growth: The global market for Organ-on-a-Chip devices is valued at \$31.5 million in 2015, with an expected Compound-Annual-Growth-Rate (CAGR) of 70% until 2020. The research market for *in vitro* extracellular electrophysiology and mechanical stretching equipment, which includes traumatic brain injury and concussion research, is valued at \$90-110 million and \$30-40M, respectively, for a total available market (TAM) of \$120-150M with a CAGR of 12%. We believe that MEASSuRE will capture a significant share of this market. The total available market for clinical neurological stimulation and recording devices is significantly larger than the *in vitro* market. The *Neurology Devices Market Report* from Transparency Market Research states that the global neurology market was valued US\$5.0 billion in 2012 and is expected to reach US\$13.6 billion in 2019, growing at a CAGR of 15.4%. BMSEED will address this market with future products. To that end, an SBIR was awarded to BMSEED in May 2016 to adapt our core technology to electrically interface directly with the brain. **Competition:** The competition for MEASSuRE, which are small to medium sized companies, falls into three categories: (1) cell stretchers are produced by Strex, Flexcell International, Nepagene, and CellScale; (2) *In vitro* extracellular electrophysiology equipment is produced by MultiChannel Systems, Tucker Davis Technologies, MED64, and others; and (3) commercial devices that combine the capability to mechanically stretch and electrically stimulate cell or tissue cultures are available from by Strex and Ionoptix. The companies and laboratories working on Organ-on-a-Chip applications could be customers or partners of BMSEED. Entry to this market is currently crowded by several companies with microfluidics based technology (e.g., Emulate, Hurel, Nortis, TISSUSE, Mimetas).

Part 3: Go-to-Market Plan

Customers: The target customers for MEASSuRE are (i) research institutions working on neurotrauma and regenerative medicine, (ii) pharmaceutical companies working on neuroprotective drugs, (iii) biomedical companies working on tissue engineering, and (iv) “organ-on-a-chip” companies working on human organ models for drug testing. We anticipate that MEASSuRE will be ready for beta testing in Q2 2017. We are engaged with three research groups to test MEASSuRE for different market segments. Dr. M. Nikkhah from Arizona State University will evaluate MEASSuRE for the Organ-on-a-Chip customer segment, growing cardiomyocytes into a mature myocardium. Dr. C. Good from the Army Research Laboratory will evaluate MEASSuRE for traumatic brain injury research using dissociated cell cultures. Dr. B. Firestein from Rutgers University will evaluate MEASSuRE for spinal cord injury research using tissue slices. Our goal is to launch MEASSuRE to the marketplace in Q3 2017, once the distribution agreement is signed. We have raised market awareness of MEASSuRE and engaged with potential customers at the recent MEA 2016 and the Society for Neuroscience conferences. **Distribution:** For the North American market, BMSEED is engaged in discussions of a sales, marketing, and distribution agreement with ALA Scientific and AutoMate Scientific. Both companies are already marketing and selling research equipment for the neuroscience research market and are therefore a good fit. For the European market, BMSEED is working with MultiChannel Systems (MCS; Germany) to adapt their amplifier to our sMEAs. We plan to negotiate a marketing and distribution agreement with MCS after successful beta testing. Commercial solutions exist for (i) mechanical stimulation (stretch), and (ii) electrical recording and stimulation of cell and tissue cultures *in vitro*, but **not** both. **Differentiation:** BMSEED will offer three distinct product configurations: (1) a “Mechanical Configuration” (includes optical imaging) that addresses the mechanical stretching market, (2) an “Electrical Configuration” that addresses the electrophysiology market, and (3) the complete MEASSuRE configuration, which is unique and combines mechanical stretching (including optical imaging) and electrophysiology applications. The value proposition for these products is superior compared to the incumbent competition because the Mechanical Configuration and the Electrical Configuration are cheaper than the competition, and both can be upgraded to the MEASSuRE configuration. The MEASSuRE configuration is more than simply a combination of two tools into one. The new capabilities that MEASSuRE provides enables entirely new approaches to biomechanical and bioelectrical applications. We therefore believe that our products will be competitive in these three markets.

Part 4: Technical Product Description and Plan

Product Description: BMSEED is developing MEASSuRE as a tool that is capable to simulate the mechanical and electrical environment of cells *in vivo* in a controlled environment *in vitro*. The critical component of MEASSuRE is the stretchable microelectrode array (sMEA), which incorporates our patented elastically stretchable gold film. The critical capability of sMEAs is that the microelectrodes remain functional when mechanically stretched. MEASSuRE is a capital equipment whereas the sMEA is a consumable that needs to be replaced after 5-10 uses. **Technology Validation:** The founder of BMSEED has developed the core technology to fabricate sMEAs at Princeton University in collaboration with Prof. B. Morrison at Columbia University. This work was funded by a grant from NIH and the New Jersey Commission on Brain Injury Research, and the results of this research were published 8 peer-reviewed scientific journals. A Phase I SBIR was awarded to BMSEED in July 2014 with the goal to produce sMEAs at cost, quantities, and quality required for commercial applications, and to validate these sMEAs for the neurotrauma application. We succeeded to achieve the goals of the project. We have also built a prototype to integrate the sMEAs with the hardware and software required for mechanical stimulation, electrophysiology, and optical imaging to offer a complete and easy to use commercial system (i.e., MEASSuRE) that provides an “all-in-one solution” for our customers. **Product Development Risks:** The remaining product development risks are twofold. First, the sMEAs have been validated for the neurotrauma application (traumatic brain injury) using hippocampal tissue slices. The validation for other applications with different cells remains, and is planned for a submitted Phase II SBIR. Second, the complete MEASSuRE prototype needs to be evaluated and validated, which is also a major part of the Phase II SBIR technology objective. **Product Advantages:** MEASSuRE provides the following capabilities: (1) Reproduce the mechanical and electrical environment of cells in the body: Existing commercial devices are either able to reproduce the mechanical or the electrical environment, but **not** both; (2) Direct assessment of the functional impact of a traumatic brain injury or spinal cord injury on the cellular processes: MEASSuRE allows the direct functional assessment of the healthy tissue and the injured (i.e., stretched) tissue because the microelectrodes stretch together with the tissue; (3) Repeated stretch: The microelectrodes stretch elastically, allowing the investigation of the cellular and molecular mechanisms of repeated concussions, which is poorly understood, in part due to the lack of reproducible injury models; (4) High reproducibility and versatility of the mechanical stretch: Any stretch pattern within the limits of the actuator can be programmed using macros; (5) Maintenance of sterility: The sMEAs can be sterilized and are biocompatible for long-term studies; and (6) Optical imaging: The high speed camera captures images of the stretched cells at up to 1700 frames per second, allowing verification that the stretch of the cells and detection of morphological changes. In future clinical applications, the major benefit of our electrodes is that they are soft, with mechanical properties akin to human tissue, i.e., our electrodes will not be recognized by the human body as a foreign object, therefore last longer. Current hard and stiff electrode are rejected by the body due to the large mismatch in mechanical properties between the electrodes and the tissue, limiting their useful life. **IP:** BMSEED has an exclusive licensing agreement with Princeton University for all applications for the patent “Stretchable and elastic interconnects” (US Patent # 7,491,892). This patent includes the use of microcracked gold thin films, which are critical to all of BMSEED’s products. Most future patents that BMSEED will file are likely to be subordinate to this patent. BMSEED does not plan to patent the trade secrets regarding the fabrication of sMEAs in order to keep from having to disclose this important information. A non-provisional patent application for the use of microcracked gold conductors in soft and compliant pressure sensors was filed in April 2014. BMSEED will pursue patents as necessary for *in vivo* applications of our products. **Non-IP Barriers to Entry:** The reliable and repeatable fabrication of sMEAs is BMSEED’s core competency. The details of the parameters of the fabrication process are critical trade secrets. The challenge for BMSEED will be to find a distribution partner that does not charge excessive distribution fees. A Break-Even Analysis shows that the break-even revenue without distribution charges is \$630,000, whereas the break-even revenue increases to \$1.3M for a distribution charge of 35%.

Part 5: Risk vs. Talent Narrative

Mitigated Risk and Risk-Reduction Milestones: The major risk reduction was the successful development of a reliable and reproducible fabrication process for stretchable microelectrodes. This is BMSEED’s core competency and critical for MEASSuRE as well as future products. The next major risk reduction milestone is the completion of the development of MEASSuRE and the successful product launch. **Key Team Members:** Oliver Graudejus, PhD, the founder of the company, is responsible for the technical direction and business development. Prior to founding BMSEED, he worked for over 6 years as a key account technologist at Novellus Systems (now LAM Research). He developed the core technology at Princeton University. Ruben Ponce Wong, PhD, the director of technology, is a mechanical and biomedical engineer from Arizona State University, and is in charge of the technical development work. **Recruiting Needs:** We plan will hire an electrical engineer in 2017, and a manufacturing engineer and a technician to support production growth in 2018. Eva Garland Consulting is in charge of accounting until BMSEED has the revenue to support a full time CFO. We also plan to hire a CEO with experience and contacts in the biosciences who can help grow the company from a pre-revenue startup to an annual revenue of \$10 Million in five years. **Key Advisors:** Tom Schumann and Patti DuBois at CEI, and Christine Bailey, Tom Fulcher and Greg Bischak at NACET provide support in our commercialization effort through consultation, mentoring in market research, customer development, financial projections, and investment preparation. We are working with Frank deBernardis (founder of medical device start-ups, former national sales manager at Medtronic, and partner at Gore Range Ventures) on sales and marketing strategy.