

Exhibit A: Project Description (Scope of Work, Special Requirements)

Project Title: Synergistic Improvement in the Diagnosis & Treatment of Mental Illness, Dementia, & Chronic Pain

Objective 1. Combine EEG and fNIRS for clinical diagnostic development for anxiety and depressive disorder. Electroencephalography (EEG) is an established, noninvasive approach for measuring neural processes associated with brain disorders. Although EEG can identify dysfunctional regional activity patterns in different disorders, its poor spatial resolution offers little information about the neural structures or networks that are involved. By contrast, functional Near Infrared Spectroscopy (fNIRS) measures blood oxygenation levels via infrared light, providing a valuable and complementary biological marker for brain dynamics. While these combined methods are routinely used in research, they are still not widely used in the clinic to develop tangible diagnoses of mental illnesses. We propose to test this combination of technologies in clinics at MSU. Dr. Rebecca Brooker (MSU) will test them on children who exhibit early symptoms of anxiety and depressive disorders (e.g., Generalized Anxiety Disorder, Major Depressive Disorder). The goal is to identify markers of neural activity that suggest a person may have a neuropsychiatric disorder that requires a specialist's attention. Drs. Aurélien Mazurie, Ph.D. and Philip Zeman Ph.D. will develop software to process EEG-fNIRS data.

Objective 2. Develop novel neurotechnologies to address cognitive function in adult patients with neurodegeneration. Non-invasive brain stimulation techniques, including dTMS, are proving to be safe and effective treatments for several psychiatric conditions, including treatment-resistant depression, post traumatic stress disorder, and obsessive-compulsive disorder. The Center for Mental Health Research and Recovery will leverage separate funds that have been allocated to purchase a dTMS system (Brainsway) to research the effectiveness of this treatment on serious mental illnesses, and established an agreement with Western Montana Mental Health Center to place the system in their Butte clinic. Recent studies in Europe and Israel have revealed the effectiveness of TMS in improving cognitive function in dementias, particularly Alzheimer's disease (AD). Given the paucity of effective treatments available for advanced AD and the dramatic rise in the prevalence of AD (one in three seniors will develop some form of dementia), it is essential that we develop the infrastructure in MT to treat our AD patients. To this end, we will assess the effectiveness of dTMS in 20 AD patients at the Western Montana Mental Health Clinic in Butte. We will also use EEG-fNIRS before and 6 weeks after dTMS to assess the mechanism of the potential efficacy of dTMS in AD, which should guide the development of improved dTMS treatments.

Objective 3: Establish efficacy and safety in a non-human primate model to facilitate clinical candidate selection of non-opioid therapeutic agents for acute and chronic pain, common correlates of anxiety, depression and neurodegeneration. The management of acute and chronic pain represents a major challenge for patients and health care providers. Existing paradigms for pain treatment rely heavily on opioid analgesics, which can often lead to addiction. This addiction potential has resulted in a growing, deadly epidemic of opioid pain medication abuse, with nearly 15,000 deaths annually in the United States. Additionally, a large

body of evidence shows there is a correlation between chronic pain, opioid addiction, depression, and suicide. Accordingly, there is an urgent need for safe and effective non-opioid pain medications. SiteOne Therapeutics, founded based on technology licensed from Stanford University and headquartered in Bozeman, Montana, is developing novel, oral, non-opioid pain therapeutics that are highly selective inhibitors of a subtype of the voltage-gated sodium channel, NaV1.7. SiteOne has created drug candidates that exhibit 20 to 1000-fold selectivity over other NaV channels and have excellent drug properties (bioavailability, metabolic stability, etc.). In order to advance SiteOne's program, a non-human primate model is needed to reliably and efficiently evaluate the efficacy, safety and other drug characteristics of the most promising drug candidates for the selection of a lead clinical candidate molecule to move forward into initial human studies. This research project involves a collaboration between SiteOne Therapeutics, Montana State University, and Dr. David Yeomans (Stanford University and MSU), to develop and implement a non-human primate model in the MSU animal facility to evaluate SiteOne's therapeutic candidates.

Objective 4: Prevent suicide and improve mental health in high school students with the Youth Aware of Mental Health intervention. Montana has a rate of youth suicide that is amongst the highest in the US and twice that of the national average. This project will develop the foundation for a major multi-site comparative effectiveness study that will extend findings of the Youth Aware of Mental Health (YAM) intervention study. This trial demonstrated a 50% reduction in suicide attempts and serious suicidal thoughts in the largest and most rigorous suicide prevention study to date involving 11,000 high school freshmen in 10 European countries [18] With the already-committed collaboration of the European investigators who developed YAM, the proposed study will evaluate the feasibility, acceptability, and impact of this promising intervention when adapted to the rural Montana setting. The study team will start by working with stakeholders, parents, and school admin/staff to establish support for delivering YAM to the entire freshman class of 8-10 high schools. Private sector mental health professionals from "outside of the school system" will deliver the 5 hourly sessions of YAM as in the original study to improve the comfort of students in discussing mental health issues, which are the focus of the intervention. In keeping with the theme of our proposal on technology development, an internet-based enhancement of YAM for computer and smart-phone utilization will be developed by private sector Montana companies. These and future efforts should improve the mental health of students, and provide sustained federally-funded research grants for the CMHRR, while establishing MSU as a national leader in preventative mental health research of youth. Extension of this initial study to a much larger study and potentially to standard use for all high schools in the state will dramatically expand the growth of private sector companies that support the technology enhancement and intervention delivery of YAM.