FOR IMMEDIATE RELEASE

Potential therapeutic for traumatic brain injury (TBI)
Testing cathepsin B as a therapeutic target for TBI

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TBI is all too common with over 10 million people worldwide suffering such an injury each year and at least 1.7 million cases annually in the United States, where it is a leading cause of death among the young and the elderly. TBI was a signature injury for US Service Members in Afghanistan and Iraq. Despite decades of research and a rising number of TBI cases annually, there is currently no drug therapy for TBI.

The complexity of adverse outcomes after TBI includes cell death, inflammation, breakdown of blood vessel walls, lack of oxygen, aneurysms, hemorrhage, and swelling. Research has not revealed how all of these events are regulated and how they may be prevented.

A recent review was published by Dr. Greg Hook, of ALSP Inc., and colleagues* which presents supporting evidence for a potentially important therapeutic to treat traumatic brain injury (TBI) - cathepsin B.

The target enzyme, cathepsin B, is a member of the cysteine protease family of enzymes, known for degrading specific proteins. Cathepsin B levels are elevated in trauma patients and animal models of TBI. It is likely cathepsin B escapes its normal, controlled environment in a cell because of trauma and enters the cell's liquid interior or exits the cell completely. Once free within the cell or outside the cell, the enzyme's protein-destroying power causes cellular destruction and inflammation in the brain. Adverse outcomes from TBI include behavioral dysfunction and pathology in pre-clinical models as a result of TBI.

Dr. Angela M. Boutté of the Brain Trauma Neuroprotection and Neurorestoration Branch at the Walter Reed Army Institute of Research, is conducting experimental trials to better understand cathepsin B and how its inhibitors may change the course of injury in pre-clinical studies of specialized, militarily relevant models of TBI. Certain cathepsin B inhibitors show encouraging results as therapeutics, as they have been used in TBI-related epilepsy and Alzheimer's disease models. A review of the literature shows that this research is quite promising in mitigating adverse outcomes caused by TBI.

The collaboration between ALSP, Inc. and the Walter Reed Army Institute of Research (WRAIR) utilizes the research advances by ALSP scientists and applies it to WRAIR's extensive capabilities for pre-clinical trials of experimental therapeutics.

About the Cathepsin B

Cathepsin B is among the most studied proteases as there are numerous reports written over the last 76 years. Its proteolytic activity was first identified in beef tissue. Originally called cathepsin II, it was

renamed cathepsin B 63 years ago and was purified 5 years after that. The first amino acid sequences were determined 32 years ago, and the first human, rat, and mouse genes were cloned 3 years later. The first X-ray crystal structure was resolved almost 25 years ago. While the first report on cathepsin B gene-deficient mice was made 17 years ago, it was not until last year that such animals were evaluated for reduced deficits after TBI.

About ALSP Inc.

ALSP Inc. is a privately held company based in San Diego, California, developing small molecule drugs for treating neurodegenerative diseases, initially focused on TBI and AD. Our approach is to identify key enzymes in the brain, called neuroproteases, which produce neuronal cell death and biologically active peptides that are thought to cause the condition. Those enzymes become targets for screening compounds that inhibit the neuroproteases and thereby reduce brain neuronal cell death and production of the harmful peptides.
For more information visit www.alspinc.com

About the Walter Reed Army Institute of Research (WRAIR)

Established in 1893, WRAIR is the oldest, largest and most programmatically diverse military research institute of the US Army Medical Research and Materiel Command and Department of Defense. WRAIR has an extensive international research network that includes sites in Africa, Thailand and elsewhere in Southeast Asia and Georgia. The Institute is comprised of the Center for Infectious Disease Research and the Center for Military Psychiatry and Neuroscience.

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For more information visit websites for WRAIR or its Clinical Trials Center.

*Front. Neurol., 02 September 2015, http://dx.doi.org/10.3389/fneur.2015.00178, Cathepsin B is a New Drug Target for Traumatic Brain Injury Therapeutics: Evidence for E64d as a Promising Lead Drug Candidate, Gregory Hook[1], J. Steven Jacobsen[2], Kenneth Grabstein[3], Mark Kindy[4,5] and Vivian Hook[6,7]

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