

## Combination therapy for oxidative-stress induced nuclear damage and cell disorders

### Business Opportunity

It is well recognised that **oxidative stress** plays a pivotal role in the dysfunction and death of cells in a variety of disorders from the neurodegeneration of **Alzheimer's disease** to **premature aging of the skin**. A key component of cell death following oxidative stress is damage to the DNA. Too much DNA damage leads to over-activation of cellular repair pathways that require NAD as a substrate, leading to critical loss of NAD. As NAD is also an essential cofactor in ATP synthesis, ATP levels decline resulting in cell death. Researchers from the University of New South Wales (UNSW) have found that by simultaneously targeting these pathways there is a significant effect on DNA repair.

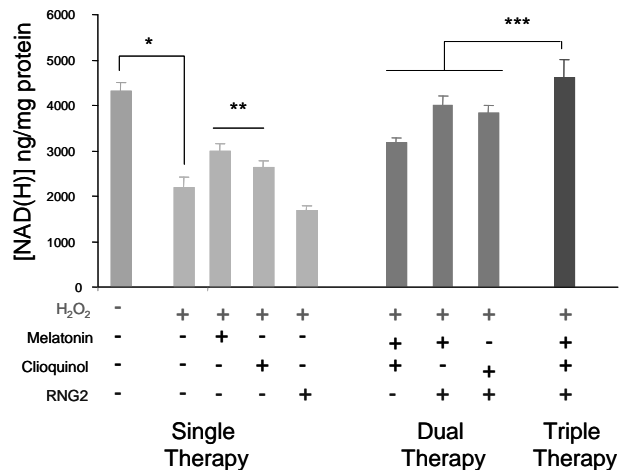
### The Market

Alzheimer's disease (AD) is considered an emerging, if not already existing, epidemic, for which presently there is no cure. In the United States alone, an estimated 4.7 million people suffered from this disease in 2007. Treatment of Alzheimer's disease is the third most expensive illness in the US, after heart disease and cancer.

The market for the other potential use of this technology; skin repair from UV damage, is in the billions of dollars.

### The Technology

This technology is based on the novel finding that a well known antioxidant-"RNG2" (used in combination with another anti-oxidant like melatonin, and a metal chelator such as Clioquinol), has an unexpected highly significant effect on a major nuclear enzyme necessary for DNA production, where it dose-dependently increases  $V_{max}$  by >500% and decreased the  $K_m$  by approximately 3 times, which suggest that "RNG2" is acting directly on the NAD salvage pathway "nuclear enzyme X" most likely through an as yet unidentified allosteric up-regulation of enzyme activity.



The figure above shows the effect of 24hour pre-treatment in **brain astrocytes** with Melatonin 5µM (antioxidant) and/or Clioquinol 10µM (Fe<sup>2+</sup>/Cu<sup>+</sup> Chelator) and/or "RNG2"100µM ("nuclear enzyme X" activator) on intracellular NAD<sup>+</sup> levels following 15 min of H<sub>2</sub>O<sub>2</sub> (100 µM) induced oxidative stress.

NAD<sup>+</sup> levels were significantly higher in cells treated with triple therapy compared to treatment with any single agent or combination of any two agents. These results have also been demonstrated in human skin (fibroblast) cells and human primary neurons.

### The Scientific Team

This technology was developed by UNSW researchers Ross Grant, Gilles Guillemin, George Smythe and Nady Braidy.

### Investment Opportunity

NSI is looking for an industry partner to further support the research and advance the proof of concept in exchange for a license option for the technology.

A provisional patent was filed in April 2008.

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