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21 February, 2007

# Company Announcement Excellent Results from Australian Ropren Trials

The Directors of Solagran Limited are pleased to provide a summary of the key findings and implications of the Ropren Neurocognitive Effects Trial conducted by the Brain Research Institute (BSI) at Swinburne University in Melbourne. This trial, which was conducted throughout 2006, produced findings consistent with previous research in Russia and provides excellent baseline data in relation to the impact of Ropren treatment on healthy elderly volunteers.

### **Context and Purpose**

The Swinburne Neurocognitive Effects Trial was initiated for two reasons:

- To understand and calibrate the impact of Ropren treatment on the cognitive functioning of healthy elderly volunteers. Trials conducted in Russia had already established that Ropren had a multi-faceted impact on clinical populations – including patients suffering from Alzheimer's Dementia;
- 2. To begin to engage with the Australian research community. Over the past few years, commentators in Australia have questioned the veracity of the results of trials undertaken with Ropren at prestigious Russian research institutions. These doubts appeared to stem from the extent of the biological activity noted in the findings from the Russian trials, as well as a general scepticism directed towards Russian scientific research.

Prior to the commencement of the Swinburne trials, a number of trials had been completed in Russia to assess the impact of treatment with Ropren on the brain. The most significant were:

- A comprehensive three stage research program undertaken at the I.M. Sechenov Institute of Evolutionary Physiology and Biochemistry in St Petersburg during the period from late 2003 to mid 2005. One of the aims of this research was to understand the effects of Ropren on three key enzymes in the liver and brain, namely Acetylchoninesterase (AChE), Butyrylcholinesterase (BuChE) and Monoamine Oxidase (MAO). All three enzymes are involved in neurotransmission. The principal findings from this research were communicated to the market on 4 October, 2005. The results of the first stage of this research have already been published in the prestigious Annals of the Russian Academy of Sciences. The results of the remaining two stages will be published in due course;
- A pilot trial conducted with Alzheimer's Dementia patients in early 2005 at the Skvortsova-Stepanova Psychiatric Hospital in St Petersburg. A summary of the results of this trial were contained in an announcement to the ASX on 20 September, 2005.

The Institute of Evolutionary Physiology's Neurotransmission Studies demonstrated that Ropren quickly restored damaged enzymatic systems in both the liver and the brain of laboratory animals, and also helped to restore damaged neurotransmission. Significantly,

Ropren was able to restore the rate of catalytic serotonin deamination reactions in the brain to normal levels, pointing to the recovery of damaged neurohumoral regulation throughout the entire body. The lead researcher, Professor Khovanskikh, suggested that this may have been due to Ropren's direct participation in the process of repairing damaged cellular membranes. He also considered that the speed with which Ropren acted was extremely significant – potentially fast enough to prevent the onset of delayed neuronal cell death in instances of brain trauma, hypoxia following a stroke or heart attack, and ischemia where a blockage or constriction of a blood vessel leads to brain damage. This research program also provided solid evidence in support of the contention of Solagran's Executive Chairman in relation to the existence of a causal link between liver function and the incidence of neurodegenerative disorders, emphasising the importance of maintaining balance in the enzymatic systems of both the liver and the brain.

The Skvortsova-Stepanova Alzheimer's Trial involved 40 patients who had been suffering from Alzheimer's Dementia for between six months and four years. 25 were given Ropren and 15 were given Gliatilin (Choline Alphoscerate). Four months treatment with Ropren led to an average 38 percent improvement in cognitive function based on the Mini Mental State Examination (MMSE), together with the elimination of most of the other symptoms associated with Alzheimer's disease, including depression. The trial also demonstrated that treatment with Ropren led to a normalisation of the activity of key enzymes in blood plasma—again pointing to a link between liver degeneration and the incidence of neurodegenerative disorders like Alzheimers's Dementia. The research team was surprised to find that eleven patients experienced an improvement of 50 percent or more in their MMSE score. Six experienced an improvement of 100 percent or more.

Understanding the impact of Ropren treatment on healthy volunteers was therefore of great interest.

## **Principal Findings of the Swinburne Trials**

100 healthy volunteers aged 60-85 were recruited for the double blind, placebo controlled Neurocognitive Effects Trials conducted by Swinburne's Brain Sciences Institute (BSI). The trial involved oral administration of Ropren delivered in *VegeCaps* manufactured by Cardinal Health in Melbourne for a period of 12 weeks. The effect of Ropren was measured using blood biochemical analysis, batteries of cognitive and other psychological tests, computerised brain analyses and EEGs. Blood tests and EEGs were taken at the beginning and at the end of the 12 week period. Cognitive and psychological testing occurred every four weeks. 80 participants completed the full trials program.

The results of the trials are entirely consistent with the findings from previous Russian research – even though the *VegeCaps* used for this trial only had the *Bioeffective R* dose concentration developed for the treatment of chronic liver disease, not the higher concentration used in the Russian Alzheimer's trials.

In his confidential report to Solagran, the BSI team leader Professor Con Stough noted that the Australian trials results provide "substantial evidence that Ropren is an interesting and exciting compound that improves a range of cognitive, brain and biochemical variables in healthy elderly adults."

The trials report also states that:

- Several cognitive variables were improved due to Ropren. These were all complex rather than simple cognitive processes. Nearly all involved some form of memory rather than just executive functioning or decision making. For example, Ropren treatment led to:
  - Consistently improved spatial working memory over the three month treatment period

- Significant improvement in the speed of retrieval of information from long term memory
- Improved verbal learning and consolidation of verbal material into long term memory
- An important finding was the speeding up of brain Event Related Potential (ERP) responses during working memory tasks. ERP is an electrical brain response to a cognitive task. The components of ERP portray how the brain processes information. For example, one component is associated with attention another with decision-making. Ropren caused a consistent improvement in both latency and amplitude measures of ERP components. Latency means the speed with which the brain processes information. Amplitude means the strength of the response, with higher amplitude suggesting more efficient and stronger processing of the signal by the brain. This finding, which is underpinned by EEG data, indicates improved neural efficiency and better cortical information processing.
- EEG measures strongly support the changes in cognitive function observed.
- Several blood biochemical markers were improved perhaps the most significant findings being an improvement in liver function and a normalisation of cholesterol levels, as evidenced by a reduction in Low Density Lipoproteins (LDL) and an improvement in the LDL/HDL ratio.
- Further analysis can be done with the existing data to try to determine whether the changes observed in blood biochemical markers correlate with the observed improvements in cognitive functioning.
- There were no differences in the reported side-effects between the placebo group and the Ropren experimental group.
- Ropren treatment was well tolerated by trial participants.

#### **Potential Implications**

There are four potential implications from this work that the Solagran Board considers important:

- 1. Research conducted in Australia has now added to the already strong body of evidence suggesting that Ropren has the potential to be used as a safe and effective means with which to both prevent and treat brain and neurodegenerative disorders, as well as chronic liver disease. A good deal more evidence will be revealed when Solagran is able to release the results of the chronic alcoholics trial completed in St Petersburg late last year. Leading Russian psychiatrists and neurologists privy to these results have already advised Solagran that they are planning to use Ropren to treat drug induced psychoses and other psychiatric and neurological conditions arising from drug and alcohol abuse, once Ropren is entered into the Russian Pharmacopoeia.
- 2. Solagran now has further evidence suggesting that cholesterol levels could be able to be normalised by balancing the enzymatic function of the liver with Ropren, rather than by blocking the liver's synthesis of an enzyme required to produce cholesterol, as is the case with existing cholesterol lowering drugs like Lipitor. Solagran's research makes this doubly important now. Not only is there the risk of liver side effects arising from long term Lipitor use. There is now the emerging possibility of a link between the incidence of these side effects and the onset of neurodegenerative disorders.

- 3. The improvement in cognitive function achieved during the trial is significant, since all trial participants were healthy volunteers having what was considered to be sound cognitive functioning at the commencement of the trial. The normalisation of cholesterol levels which occurred in parallel with an improvement in liver function is equally significant. Further testing of these effects in clinical populations (i.e. patient groups with impaired cognitive function or abnormal cholesterol levels) will provide additional important information about the activity of Ropren.
- 4. The fact that Ropren appears to enhance cognitive function in healthy volunteers, while at the same time normalising enzymatic activity known to be associated with neurotransmission, raises the possibility of it being used as a prophylactic to help prevent neurodegenerative disorders, as well as a potential treatment with which to overcome them.

## **Next Steps**

Over the next few weeks, Solagran, its patent attorneys, and its research partners in St Petersburg, will review the Swinburne trials report and underlying data – particularly the blood biochemistry and EEG results. They will then discuss the path forward with the Swinburne BSI team. This process will enable data related to Ropren's effect on healthy volunteers to be compared to that relating to Alzheimer's patients. This will lead to both a deeper understanding of the activity of Ropren and a joint publication in a peer reviewed journal.

The BSI has recommended a number of further research projects to learn more about Ropren's potential. It has also recommended that Solagran conduct a similar study with a much larger population using brain imaging technology to more clearly demonstrate the nature and the speed of Ropren's impact on the brain.

These recommendations will be considered in the context of Solagran's overall clinical trials program — and particularly in the light of the results of the yet-to-be-released chronic alcoholics trial. The results of that trial are far more significant than those being revealed today in this announcement. A summary of the key findings of the alcoholics trial will be released as soon as all relevant intellectual property protection work is complete.

Once Ropren has entered the Russian pharmacopoeia as a new pharmaceutical substance to treat chronic liver disease – as is expected to occur soon – the opportunity to complete Phase IV trials to address other indications will open up.

### **Commercial Consequences**

The Directors believe that the apparent ability of Ropren to normalise cholesterol levels and balance enzymatic activity in both the liver and the brain is significant – particularly once the link between liver function and neurodegenerative disorders has been established unequivocally. This would mean that Ropren could be used as a prophylactic against such disorders – as well to help prevent cardiovascular disease. It could also enable patients with abnormal cholesterol levels to treat their condition, without the risk of long term liver side effects potentially leading to a neurodegenerative condition later in their life. Russian trials have already demonstrated that it should be possible for those who already have liver problems arising from the side effects of cholesterol lowering drugs, to use Ropren to quickly restore a healthy liver function.

The Directors consider that there is now substantial evidence supporting Solagran's contention that Ropren can potentially be used as a safe and effective treatment for neurodegenerative disorders, as well as for chronic liver disease. This evidence is already sufficient to satisfy a number of opinion-leading Russian psychiatrists and neurologists who have been privy to the results of recent Ropren trials in Russia. These clinicians plan to use

Ropren in their clinical practice as soon as it receives regulatory approval from the Russian Ministry of Health.

In the opinion of the Directors, the commercial consequences for Solagran arising from these potential applications for Ropren are considerable.

Peter Stedwell

Company Secretary

On behalf of the Board of Directors

Solagran Limited