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20 September, 2005

Company Announcement Final Results of *Bioeffective R* Alzheimer's Disease Trial

The Directors of Solagran Limited are pleased to announce that the Company has received the final results of a clinical efficacy trial of *Bioeffective R* (Ropren) in the treatment of Alzheimer's disease. Preliminary results from this trial were released in April 2005.

Clinical trials on patients with chronic liver conditions, and pre-clinical studies undertaken with animals in relation to brain activity, provided Solagran with sufficient evidence to justify undertaking a small scale clinical trial at a specialised hospital to assess the efficacy of Ropren as a treatment for elderly patients with neurodegenerative disorders.

The trial involved 25 patients (15 men and 10 women) aged 60 to 78. All were suffering from Alzheimer's type dementia, but with different pathologies and different times since diagnosis. It involved treatment with Ropren for a period of 3 months for 17 patients, and 4 months for 8 patients with a more severe form of the disease.

The trial was conducted at the Skvortsov-Stepanov Psychiatric Hospital in St Petersburg under the supervision of Dr Vladimir Agishev, the Director of the hospital and a doctor honoured by the Russian Federation for his contribution to medical science. The trials team comprised a leading consultant neurologist Dr Andrei Kulikov, and 2 of the hospital's senior consulting psychiatrists, Dr Ninel Kulikova and Dr Irina Malachova.

It was agreed at the outset to undertake this quite complex trial because Solagran's research team was confident that what had already been learned about the properties of Ropren meant that it may prove to be an effective treatment for Alzheimer's disease that did not result in side effects.

The trial demonstrated that administration of Ropren for a 3 month period was effective in the treatment of Alzheimer's type dementia for patients exhibiting the disease in its early stages. For older patients diagnosed with the disorder for more than 18 months, improvement in condition was also observed after Ropren had been administered for a period of 4 months.

The trial also demonstrated that Ropren led to normalisation of activity of key enzymes in blood plasma – pointing to a link between liver degeneration and the incidence of neurodegenerative disorders like Alzheimer's disease.

Evaluation Criteria

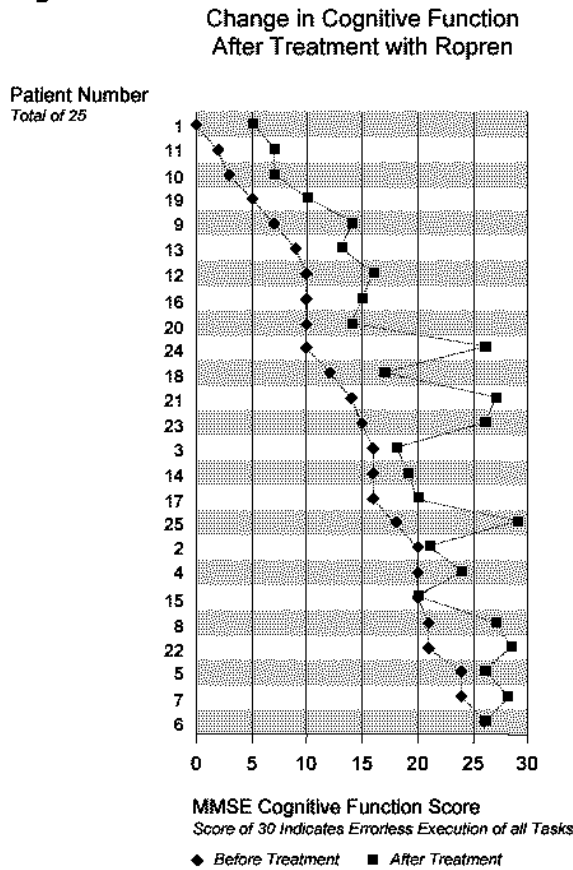
The criteria employed before and after the trial to evaluate the effect of Ropren on each patient included:

1. Clinical psychiatric examination using a semi-structured interview method
2. Evaluation of somatic-autonomic condition using a "list of symptoms" questionnaire
3. Analysis of biochemical blood parameters
4. Mini Mental State Examination (MMSE) evaluation of cognitive functions
5. Analysis of changes in Monoamine Oxidase (MAO) and Butyryl Cholinesterase (BuChE) activity

Effect of Ropren Treatment on Cognitive Function

Figure 1 shows the scores for each patient in MMSE evaluations undertaken both before and after treatment with Ropren. On a 30 point scale, the average patient MMSE score increased by 5.4 from 13.9 to 19.3, demonstrating that treatment with Ropren had a positive effect on cognitive function. The data in Figure 1 has been sorted according to patient MMSE score before beginning of treatment (the red line), with the patient exhibiting the lowest score (Patient 1) at the top of the chart. Some of these patients showed quite significant improvement, including Patients 24, 21 and 23. The most positive change to cognitive function was registered in those patients who had developed the disease in the previous 3-6 months.

Figure 1



Effect of Ropren Treatment on Symptom Severity

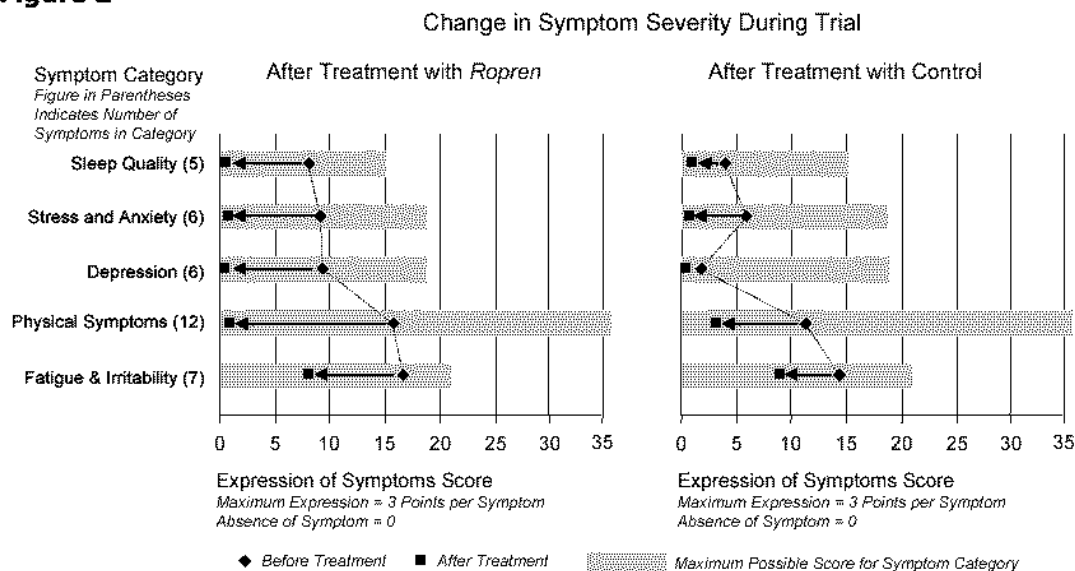
Figure 2 shows the extent of symptom severity reduction in patients treated with Ropren or the control drug (choline alfoscerate or Gliatilin – a compound used widely in the treatment of acute cerebrovascular trauma and age-related brain deficiencies). Five symptom categories were employed and 36 individual symptoms were assessed both before and after treatment. Each symptom was allocated 3 points. A score of 3 indicated maximum expression of the symptom. A score of zero indicated absence of the symptom.

Positive changes in both severity and frequency of the symptoms analysed were evident after 2 months treatment with Ropren. There was an improvement in general condition (both subjective and objective), disappearance of anxiety, and a reduction in depression and hypochondriac complaints together with more orderly behaviour. Statements like: *“it feels much better”*, *“my head is clearer”*, and *“I feel like I can do things”* were noted. Many patients noted that disturbing feelings of internal pressure, anxiety and unpleasant bodily feelings disappeared. Half the patients noted the disappearance of headaches, dizziness and loss of co-ordination while walking. There was also a reduction in emotional fragility, irritability and

tendency to affective outbursts. Sleep improved for all patients, and in 4 patients with anxiety-depressive conditions, psychotic symptoms were eliminated with a background of administration of a minimal dose of antidepressants.

The control substance also had a positive effect, but Ropren had a greater positive effect on anxious-depressive and hypochondriac symptoms.

Figure 2



After treatment with Ropren, in 40% of patients there was almost complete elimination of symptoms. These patients all exhibited better orientation. In 48% of patients, there were less pronounced but still positive changes in psychosomatic status, expressed through better adaption and self-serving skills, as well as improved orientation.

In the remaining 12% of patients, who were all older and had been diagnosed with Alzheimer's disease for more than 18 months, there were no improvements in cognitive function and the patients remained disoriented. However, they were less confused, more placid and more manageable in terms of their behaviour at the end the trial. They also became more adapted and their capacity to take care of themselves improved.

Psychological examinations revealed that patients treated with Ropren achieved improvements in memory, concentration, work capacity and vitality.

The most pronounced therapeutic effect of treatment with Ropren was registered in patients with the combined pathology of cranio-cerebral trauma and vascular dementia, as well as alcoholism. These patients exhibited an improvement of between 9 and 15 points in cognitive function (out of a possible total of 30 points on the MMSE scale), improvements in biochemical parameters of the blood and positive changes in EEG. The most positive changes in EEG data occurred in patients in the early stages of the disease.

In a majority of patients, biochemical analysis of blood showed some positive changes, including reduction in cholesterol level and blood sugar, and normalisation of liver function (despite a history of therapy using psychotropic drugs which the researchers noted can accumulate in the body during lengthy treatment programs).

All patients exhibited improvement in their general condition due largely to a reduction in depression, anxiety and hypochondriac syndromes. Out of 25 patients in the trial, 23 experienced some reduction in the symptoms of Parkinson's disease, as assessed using the

Unified Rating Scale. However, the reduction in symptoms after treatment with Ropren was greater than was observed after treatment with the comparator.

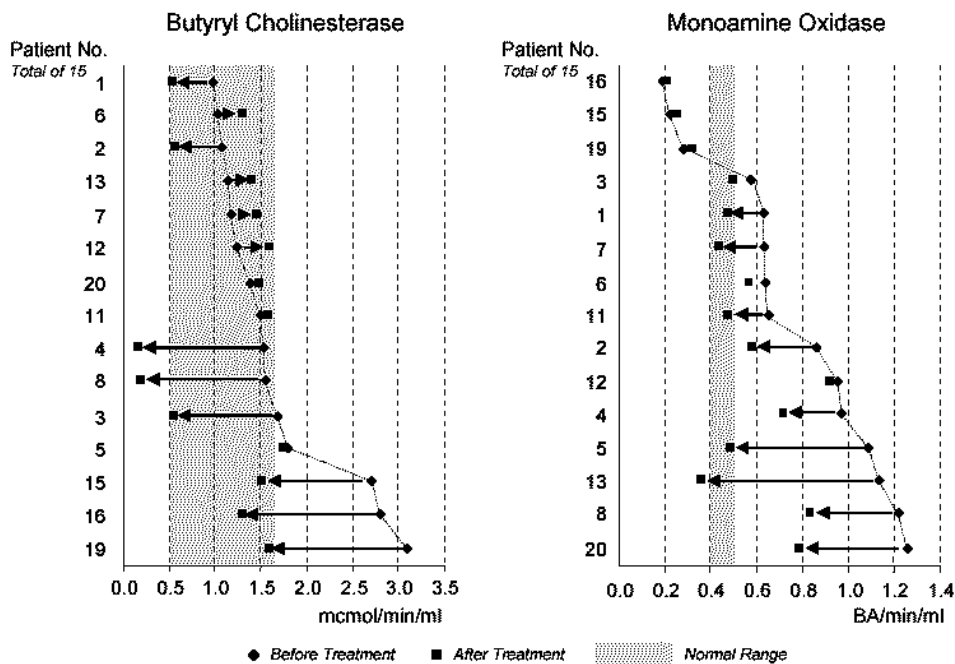
Effect of Ropren on Enzymatic Activity

Perhaps the most significant finding from this study was the demonstrated ability of Ropren to normalise enzymatic activity. The research team established that treatment with Ropren led to improvement and normalisation of brain and liver functions, as well as stabilisation of 2 key enzymes, Butyryl Cholinesterase (BuChE) and Monoamine Oxidase (MAO) – although in some cases the process of normalisation was slow. This finding supports the contention of Solagran’s Chairman, Dr Vagif Soultanov, that there is an important link between liver degeneration and the incidence of degenerative diseases in the brain like Alzheimer’s and Parkinson’s diseases. Figures 3 and 4 illustrate the extent to which treatment with Ropren enables normalisation of enzymatic activity.

Fifteen patients had BuChE activity above normal or normal, and/or MAO activity above normal. Data related to these patients is shown in Figure 3. Within this group, comprised mainly of patients with a longer history of Alzheimer’s dementia, there was a trend towards restoration of normal levels of enzymatic activity. BuChE activity was reduced sharply at first, before settling back to normal levels. MAO activity was brought back to the norm, or close to the norm.

Figure 3

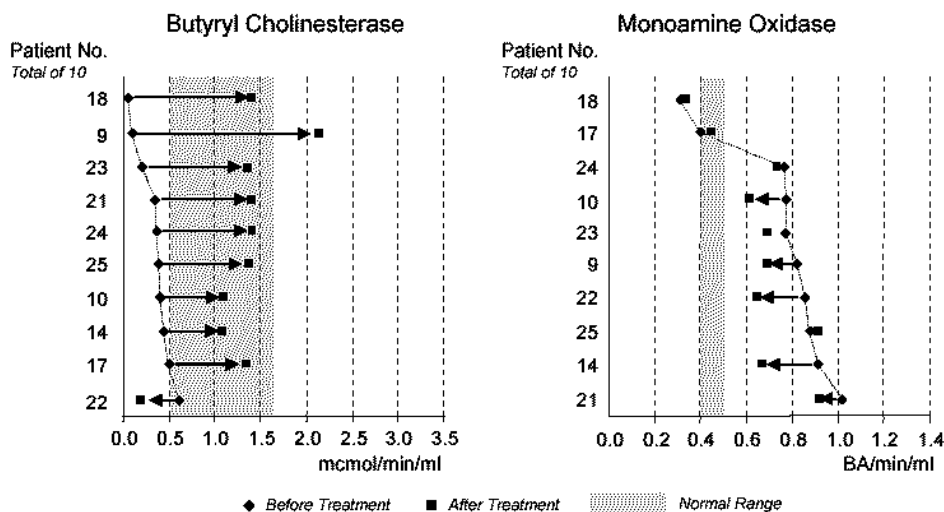
Change in Enzymatic Activity after Treatment with Ropren
(15 patients exhibiting above normal levels of enzymatic activity)



Ten patients had BuChE below the norm or at the lower limit of the normal range. Data related to these patients is shown in Figure 4. Most of these patients showed restoration of normal BuChE activity, and a reduction in MAO activity. One patient (Patient No 9) had to have surgery under general anaesthetic for an unrelated condition during the trial.

Figure 4

Change in Enzymatic Activity after Treatment with Ropren
(10 patients exhibiting lower than normal levels of BuChE activity)



Conclusion and Next Steps

With 4.5 million Americans suffering from Alzheimer's disease (at a cost to that economy estimated by the National Gerontology Institute at \$100 billion annually) and many more in other developed countries, there is significant research interest in the development of drugs to counter the disease by normalising enzymatic activity in the brain. However, as the research team from St Petersburg pointed out, newly synthesised substances developed for this purpose show toxicity and thus cannot be used over an extended period of time. The search for new therapeutics that can normalise enzymatic function with minimal side effects is ongoing.

The results of this trial, and particularly the fact that Ropren appears to normalise enzymatic function while being essentially a non-toxic substance, were important factors in opening discussions with the Centre for Neuropsychology at Swinburne University of Technology in relation to conducting clinical trials in Australia. A more detailed explanation of the role played by Ropren in a number of vital functions was provided in the recent letter to shareholders from Solagran's Chairman. Swinburne and Solagran Limited have now agreed to collaborate on a series of Australian clinical trials, which among other things will provide a better understanding of the effect of Ropren on human cognitive function.

Based on the data obtained from this trial, the research team concluded that Ropren is effective in the treatment of Alzheimer's type neurodegenerative disorders. Solagran is now planning to conduct a full series of clinical trials in St Petersburg to confirm Ropren's efficacy and determine its mechanism of action.

Peter Stedwell
Director
On behalf of the Board of Directors

Solagran Limited

Solagran Limited is an Australian company founded in 1995 with the objective of commercialising the results of a research and development program that commenced in Russia in the 1930s, and which has continued, uninterrupted, until the present day. The focus of the research program has been the extraction and utilisation of the "live elements" of tree foliage. Solagran has collectively trademarked these substances using the term Bioeffectives®.

Solagran's technology permits it to obtain many different Bioeffectives from tree and plant sources. One of the highest value Bioeffectives is a class of organic substances known as polyprenols. Polyprenols are naturally occurring precursors of dolichol, which is found in all of the vital organs of the human body, and which plays an essential role in cell metabolism and in supporting the immune system.

Solagran has committed significant resources to the development and testing of Bioeffective R – a Bioeffective comprising polyprenols. Experimental and trials results show that Bioeffective R has a very positive effect on damaged liver cells.