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17 May, 2007

**Company Announcement  
Presentation to Gastro 2007 Conference**

The Directors of Solagran Limited are pleased to provide a summary of the key elements of the presentation by Dr Vagif Soultanov to the Gastro 2007 Conference in St Petersburg on 17 May, 2007.

The presentation summarises results of Ropren Clinical Trials.

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Peter Stedwell  
**Company Secretary**  
On behalf of the Board of Directors  
Solagran Limited



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## **Report on Ropren Clinical Trial**

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*Double-blind Study of Efficacy and Safety of **Ropren** in the Treatment of Diseases of the Hepatobiliary System*

**Dr Vagif Soultanov** DSc (Hon), PhD – Solagran Limited (Melbourne)

**Prof. Victor Roschin** DSc – S.M. Kirov Forest Technical Academy (St Petersburg)

**Prof. Elena Laptiva** DMed – Medical Academy of Postgraduate Studies (St Petersburg)

May 2007

# Summary

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## **A multi-centre randomised, double-blind comparator controlled clinical trial was undertaken in 2004 to determine the efficacy and safety of *Ropren* in the treatment of chronic liver disease**

- *Ropren* is a natural substance containing *Bioeffective*<sup>®</sup> *R*. *Bioeffective*<sup>®</sup> *R* is extracted from pine foliage and comprises long chain isoprenoid alcohols (poylprenols)
- The trial was co-ordinated by the Medical Academy of Postgraduate Studies (MAPS), and was conducted in four centres:
  - S.P. Botkin Infectious Diseases Hospital (MAPS) – *Prof. Y.V. Lobzin D.Med.*
  - E.E. Eikhvald Dept. of Therapy (MAPS) – *Prof. V.I. Mazurov D.Med.*
  - Centre for Prevention and Treatment of AIDS & Infectious Diseases – *Prof. E.N. Vinogradova D.Med.*
  - St George the Sufferer Hospital – *Dr V.B. Popova PhD.*
- The trial demonstrated that treatment with *Ropren* led to a wide spectrum of positive effects in patients suffering from chronic liver disease, including:
  - Rapid normalisation of subjective and objective clinical symptoms of liver damage
  - Positive changes in cytolytic enzymatic activity together with normalisation of lipid metabolism
  - Normalisation of hepatic parenchyma
  - Activation of immunomodulating and adaptogenic mechanisms
- No side effects were registered



## ➤ Introduction

- ❑ Trial Results
- ❑ The Path Forward

# The Need for a Safe and Effective Treatment

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**There is a very real need both in Russia and throughout the world for a safe and effective treatment for chronic liver disease**

- WHO data indicates increasing global incidence of chronic liver disease. In Russia and the CIS countries, there are up to 1 million new cases each year. There are 2 billion people with liver disease worldwide and more than 300,000 cirrhosis deaths each year
- Many etiological factors contribute to development of liver disease, including viral pathogens, toxins from pollution, hormonal and metabolic disorders, poor diet, and alcohol and drug abuse
- Alcohol and pharmaceutical consumption are major problems – as is the incidence of Hepatitis C which accelerates development of cirrhosis
- The possibility of a safe new way to treat chronic liver disease of all etiologies emerged from extensive trials with laboratory animals that demonstrated the ability of *Ropren* to rapidly regenerate damaged hepatocytes and restore normal liver function

# What is Ropren?

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***Ropren* is obtained from *Bioeffective® R* which comprises polyprenols extracted from green pine and spruce needles**

- *Bioeffective® R* is a 95-98 percent concentrate of polyprenols. The complex constitutes a series of homologues each containing 12-19 isoprene units (60-95 carbon atoms) in the molecular chain
- Polyprenols are plant analogues of dolichols, which are necessary for glycosylation reactions in the dolichol-phosphate cycle during glycoprotein synthesis
- The pharmacological activity of prenols is based on their substitutive effect in the case of dolichol deficits, or deficiencies in the dolichol-phosphate cycle, which are observed with chronic inflammatory, degenerative and oncological diseases
- Pre-clinical and pilot clinical trials had established that *Ropren* had no side effects, but was able to normalise the condition of the hepatic parenchyma in experimental hepatitis models
- There was also positive experimental and clinical data on the use of *Ropren* in the treatment of chronic active Hepatitis C and HIV/AIDS patients
- Preliminary data from a 2 week trial with 18 overweight pregnant women had indicated, inter alia, that *Ropren* normalised lipid metabolism and had expressed immunomodulating properties – affecting cellular immunity in particular as evidenced by an increase in the number of T-active lymphocytes and in the T-helper/T-suppressor index
- Trials with laboratory animals had demonstrated that *Ropren* was faster acting and had a greater degree of hepatoprotective activity than the popular and effective *Essential Phospholipids Complex*



☐ Introduction

☛ **Trial Results**

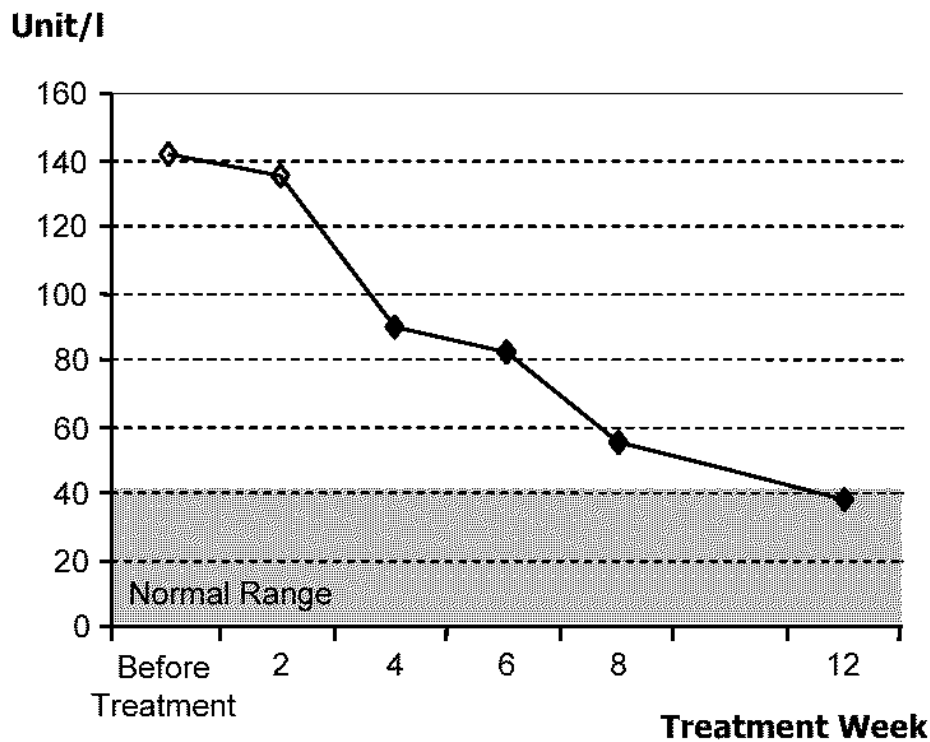
☐ The Path Forward

# Trial Results: Changes in Enzymatic Activity

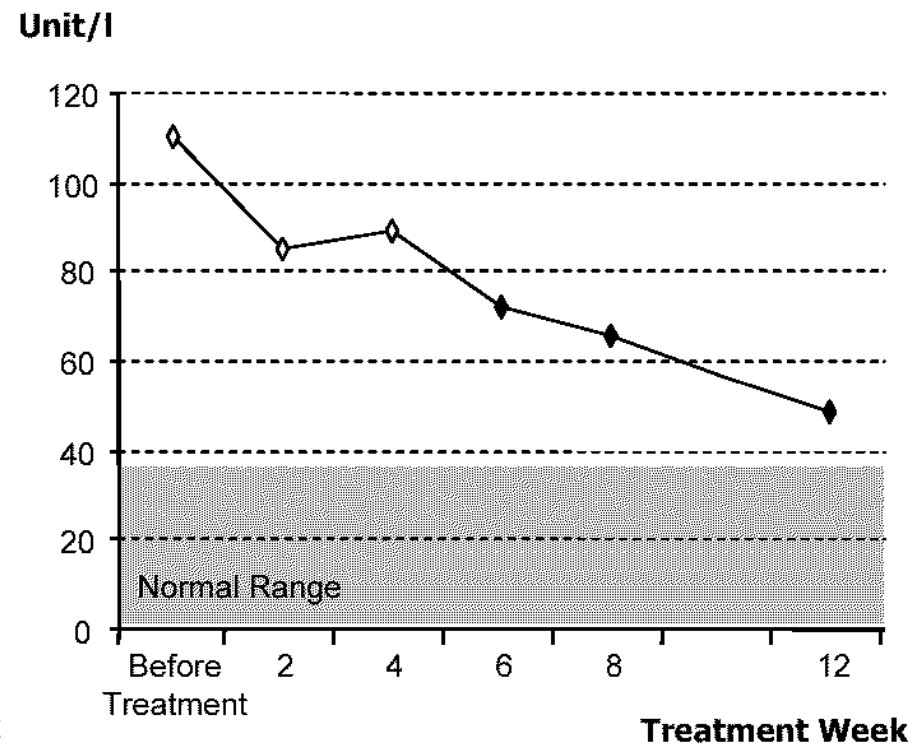


Changes in *Alanine transaminase (ALT)* and *Aspartate transaminase (AST)* content in blood plasma showed a trend towards normalisation of cytolytic enzymatic activity

### ALT Content



### AST Content



Note: Filled points indicate statistically significant,  $P \leq 0.05$

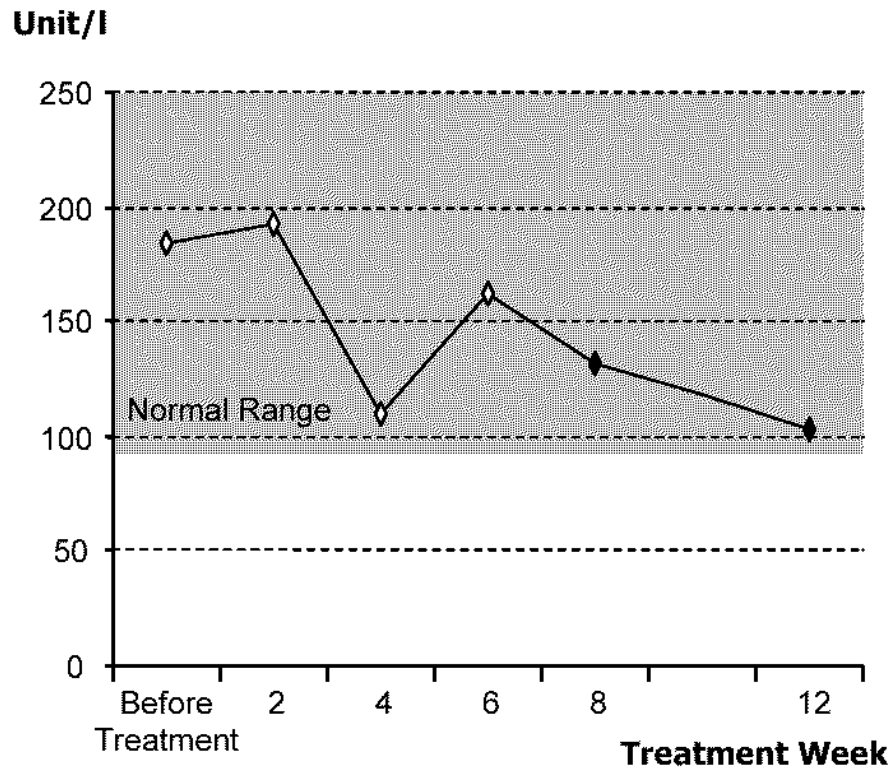


# Trial Results: Changes in Enzymatic Activity

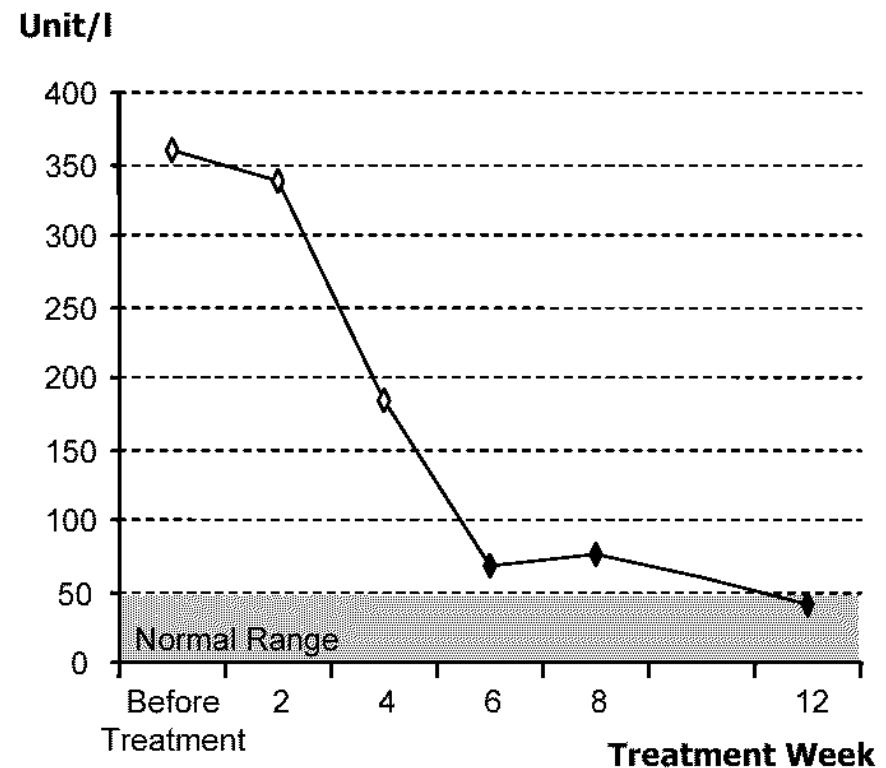


**Alkaline phosphatase (ALP) levels remained within the normal range throughout the trial.**  
**Gamma glutamyl transferase (GGT) levels returned to normal levels by Week 12**

**ALP Content**



**GGT Content**

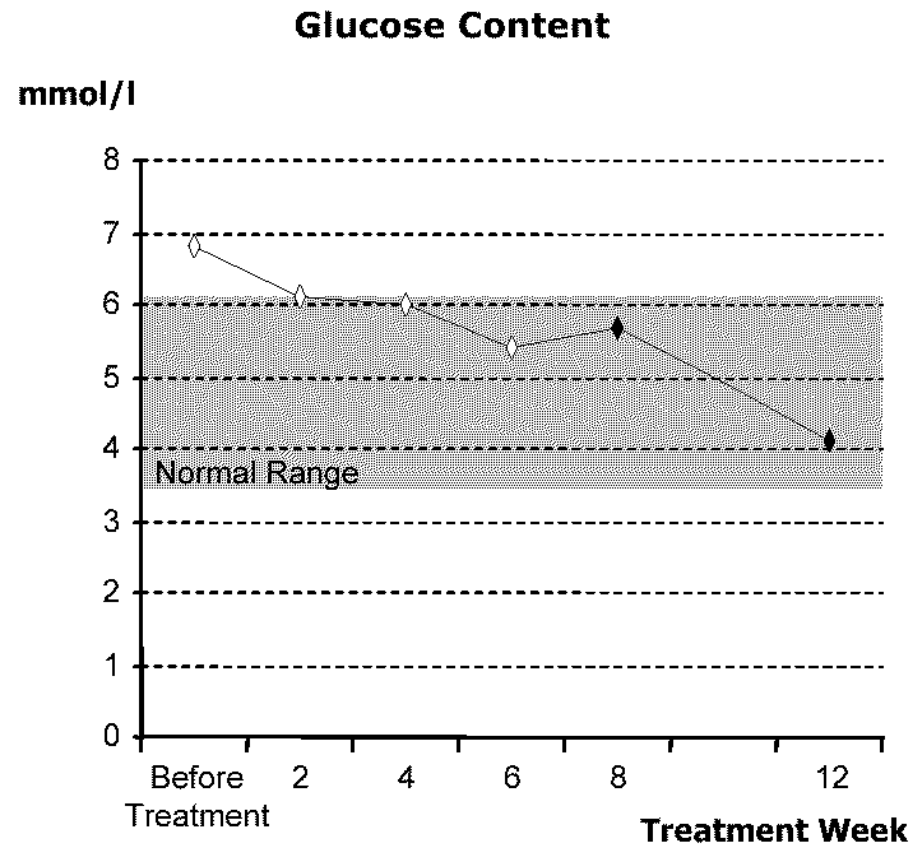


Note: Filled points indicate statistically significant,  $P \leq 0.05$

# Trial Results: Changes in Carbohydrate Metabolism



Before treatment, fasting blood serum glucose levels slightly exceeded the upper normal limit. *Ropren* treatment led to an improvement this indicator of carbohydrate metabolism



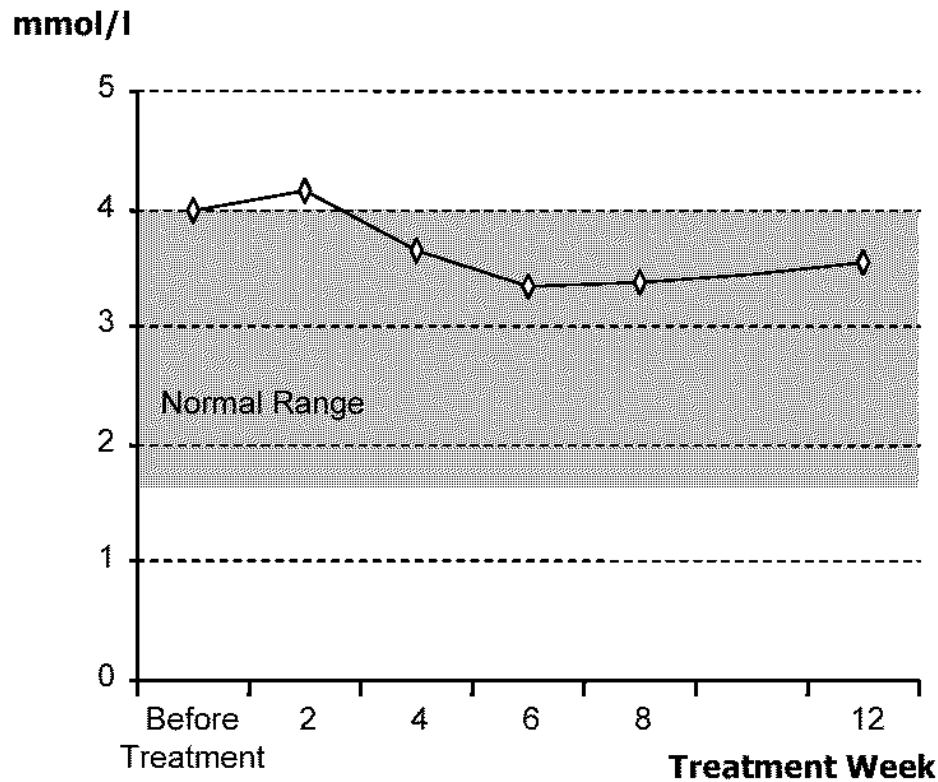
Note: Filled points indicate statistically significant,  $P \leq 0.05$

# Trial Results: Changes in Lipid Metabolism

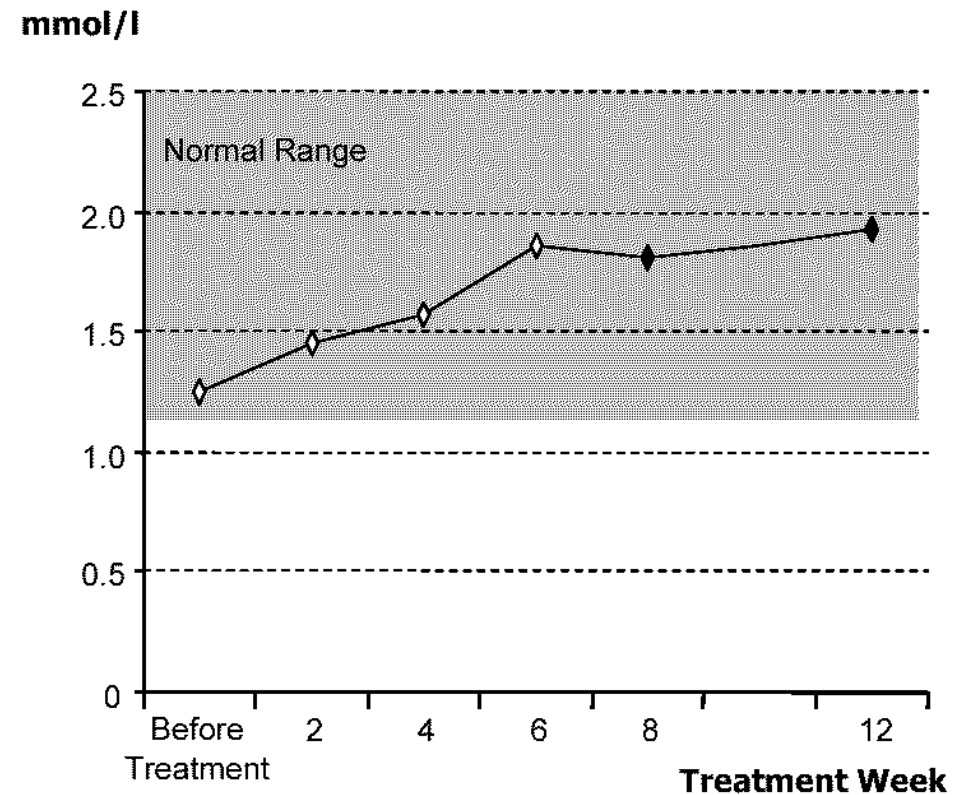


Both Low Density Lipoprotein (LDL) and Extremely Low Density Lipoprotein levels remained within the normal range throughout the trial. An increase in High Density Lipoprotein (HDL) levels was apparent by Week 6

### LDL Level



### HDL Level



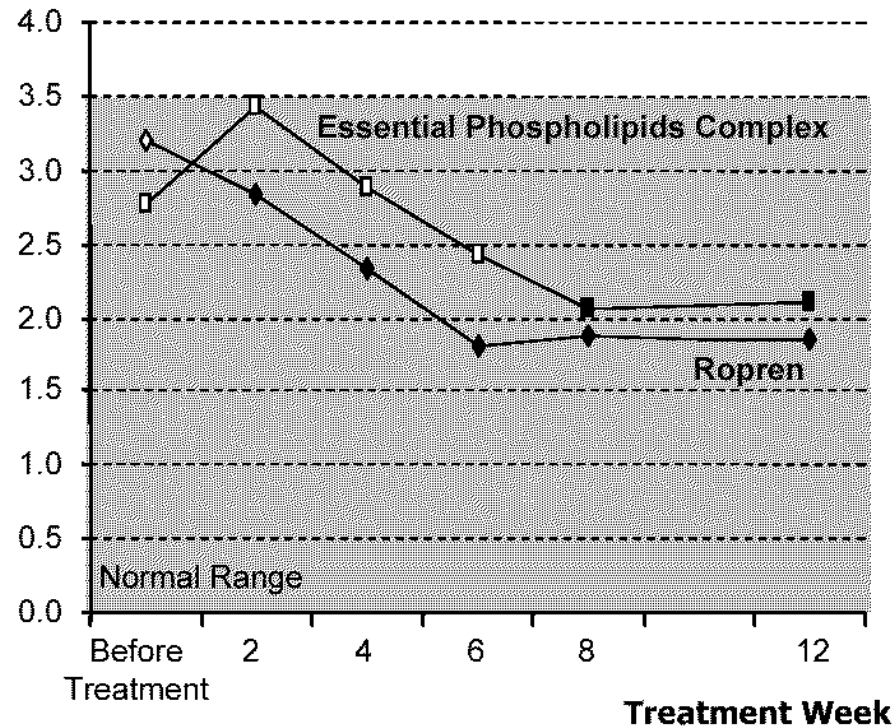
Note: Filled points indicate statistically significant,  $P \leq 0.05$

# Trial Results: Changes in LDL / HDL Ratio



The LDL/HDL Ratio improved for both the *Ropren* and the comparator groups. However *Ropren* treatment was faster and its effect greater

LDL / HDL Ratio

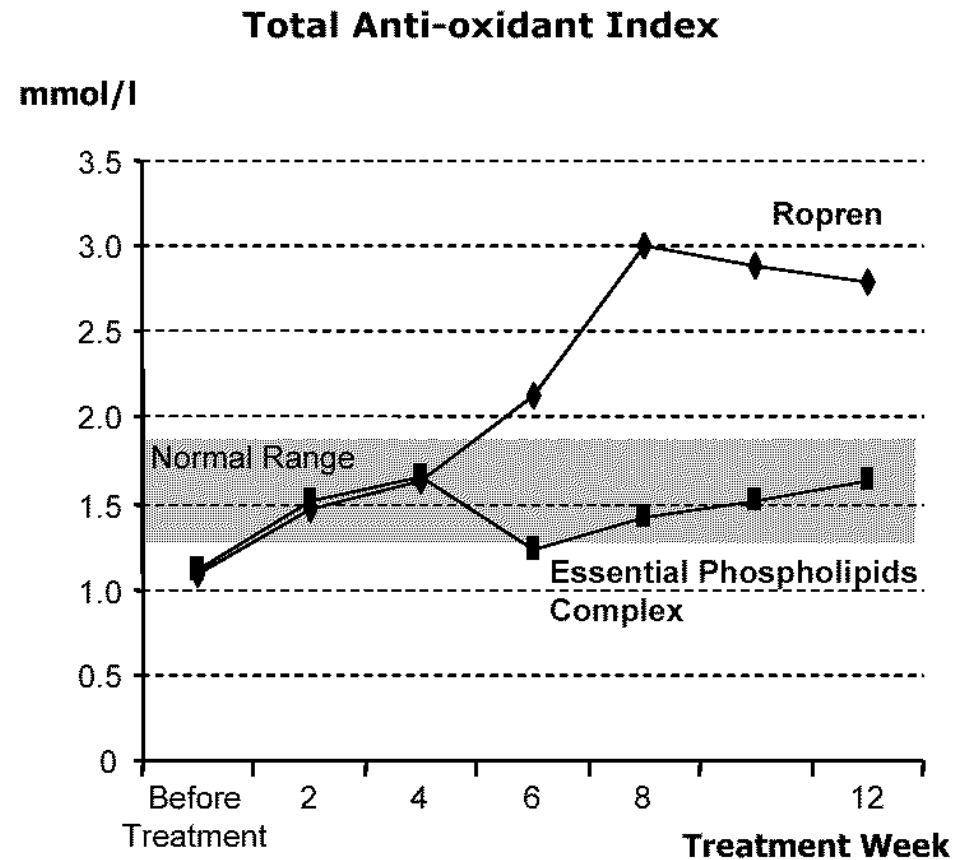


Note: Filled points indicate statistically significant,  $P \leq 0.05$

# Trial Results: Activation of Adaptogenic Mechanisms



**Ropren treatment led to a sharp increase in the total anti-oxidant index**



Note: Filled points indicate statistically significant,  $P \leq 0.05$

# Trial Results: Other Parameters

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## There were a number of other parameters measured in the trial

- The main clinical blood indices were tested at the commencement of the trial and also at two-week intervals. All parameters were within the established physiological norms for both patient groups
- Clinical analysis of protein fractions in blood was conducted at the commencement of the trial and at two-week intervals. There was no evidence of pathological changes before treatment. Throughout the trial, all parameters corresponded to the established physiological norms for both patient groups
- Triglyceride content in blood serum of both patient groups did not show any pathological deviations from normal levels either before or after treatment
- Urine analysis remained normal and did not reveal any changes indicating disorders in the excretory function of the kidneys or any signs of inflammation



Introduction

Trial Results

**The Path Forward**

# The Path Forward: Chronic Liver Disease

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***Ropren* is expected to be on the Russian market very soon**

- In February 2006, the Pharmacological Committee of the Ministry of Health gave its approval to *Ropren*. Final approval for pharmacopoeia entry is expected this month
- *Ropren* should be available on the Russian market this year



# The Path Forward: Other Indications

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**Other trials have demonstrated that *Ropren* has the potential to be effective in treating a number of other conditions**

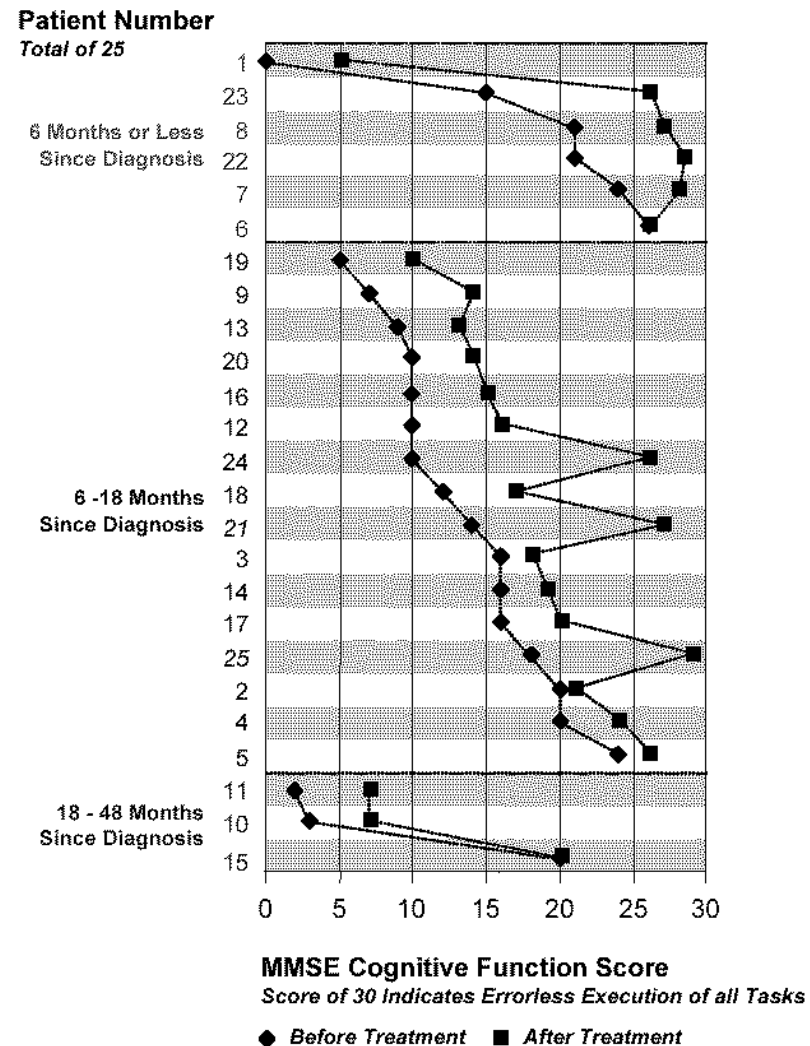
- Trials in both Russia and Australia have demonstrated that *Ropren* could be effective in both preventing and treating neurodegenerative disorders – including Alzheimer’s dementia
- We believe we are very close to proving a crucial causal link between liver degeneration and the incidence of neurodegenerative disorders including Alzheimer’s dementia
- Trials in Russia have shown that *Ropren* is an effective immunomodulating substance. It induces production of natural interferon as well as T-lymphocytes
- *Ropren’s* ability to normalise lipid metabolism is potentially one of its most important properties

# The Path Forward: Neurodegenerative Disorders



**Trials conducted with Alzheimer's patients at the Skvortsova-Stepanova psychiatric hospital demonstrated the potential of *Ropren* to re-establish lost cognitive function**

- A 25 patient trial conducted in 2005 demonstrated that *Ropren* had the potential to restore lost cognitive function in Alzheimer's patients - as measured by the Mini Mental State Examination (MMSE)
- These results were further reinforced in a 2006 trial with 100 healthy elderly volunteers conducted by the Brain Sciences Institute at Swinburne University in Melbourne
- After 3 months of treatment and with a lower dose of *Ropren* than used in the Russian Alzheimer's trials, the Australian trial revealed consistent improvement in spatial working memory, significant improvement in the speed of retrieval from long term memory, and improved consolidation of verbal material into long term memory

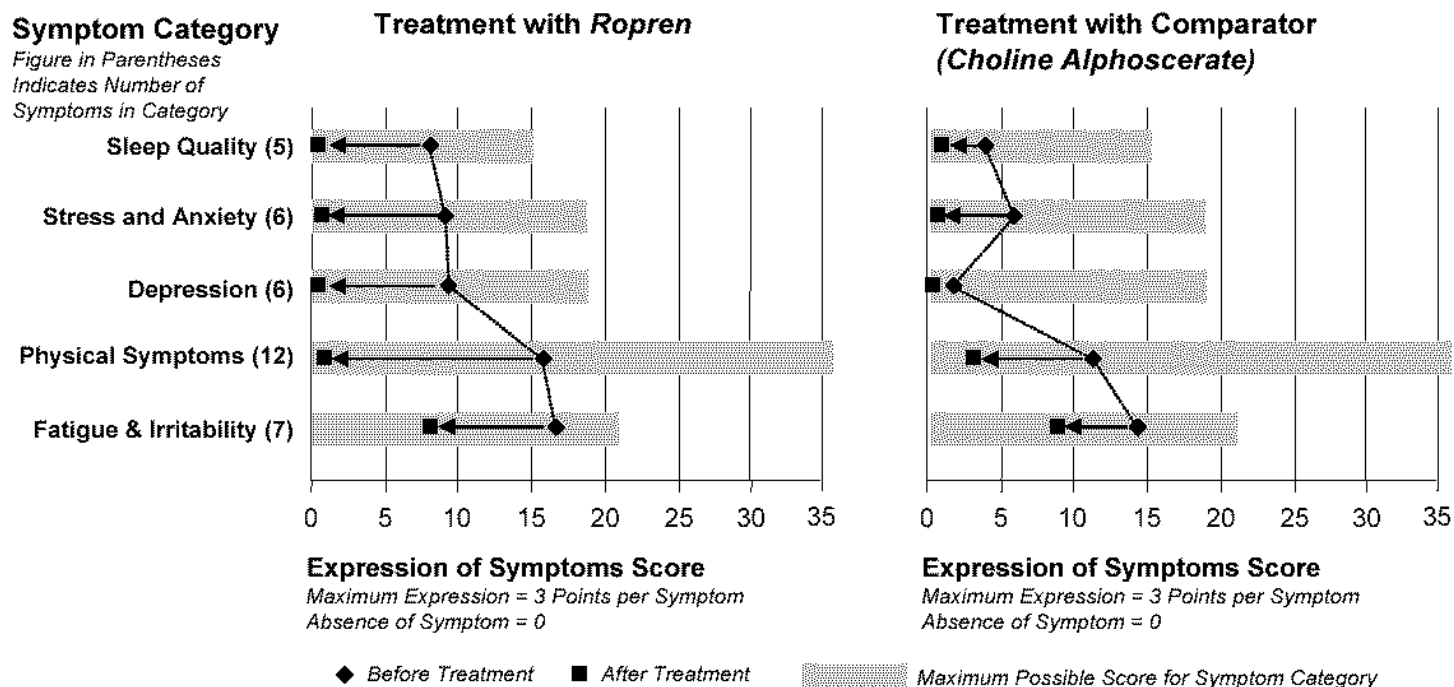


# The Path Forward: Neurodegenerative Disorders



Positive changes in both severity and frequency of the symptoms analysed were evident after four months of treatment with *Ropren*. Particularly significant was the improvement in the symptoms of depression

## Change in Symptom Severity During Trial

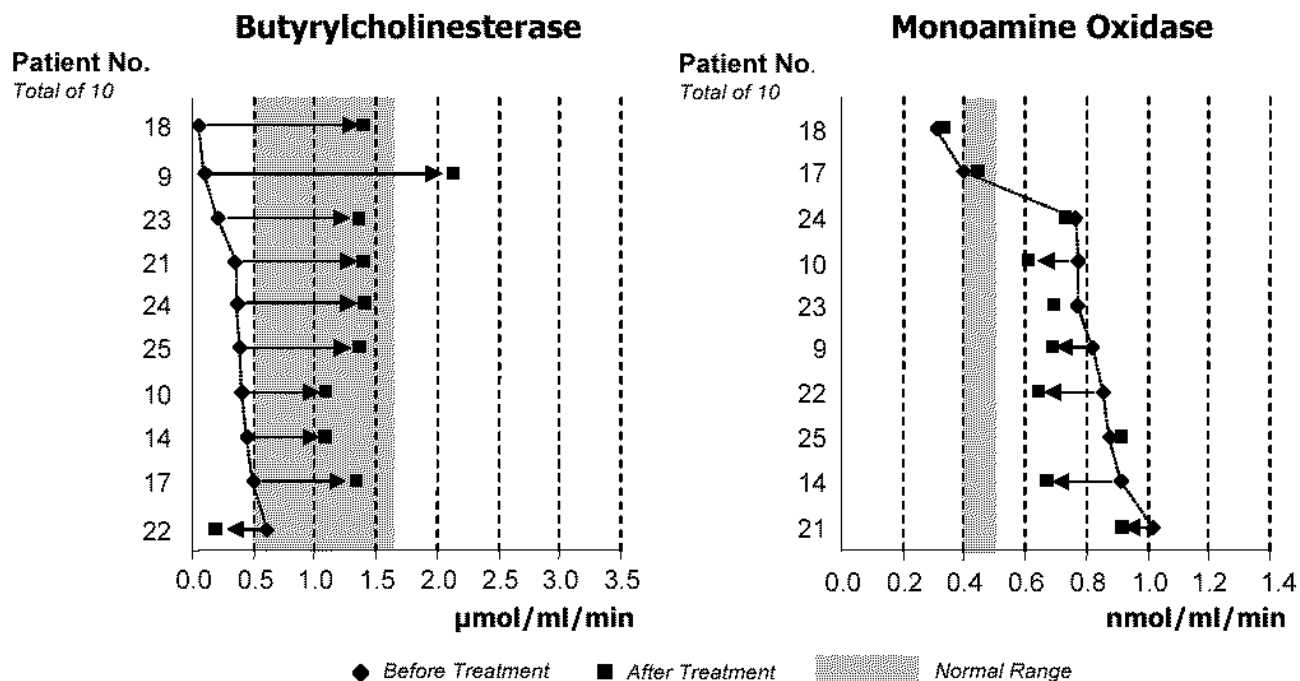


# The Path Forward: Neurodegenerative Disorders



Alzheimer's patients that had BuChE below the norm, or at the lower limit of the normal range, experienced restoration of normal BuChE activity, and a reduction in MAO activity

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



Note: One patient (Patient No 9) had to have surgery under general anaesthetic for an unrelated condition during the trial

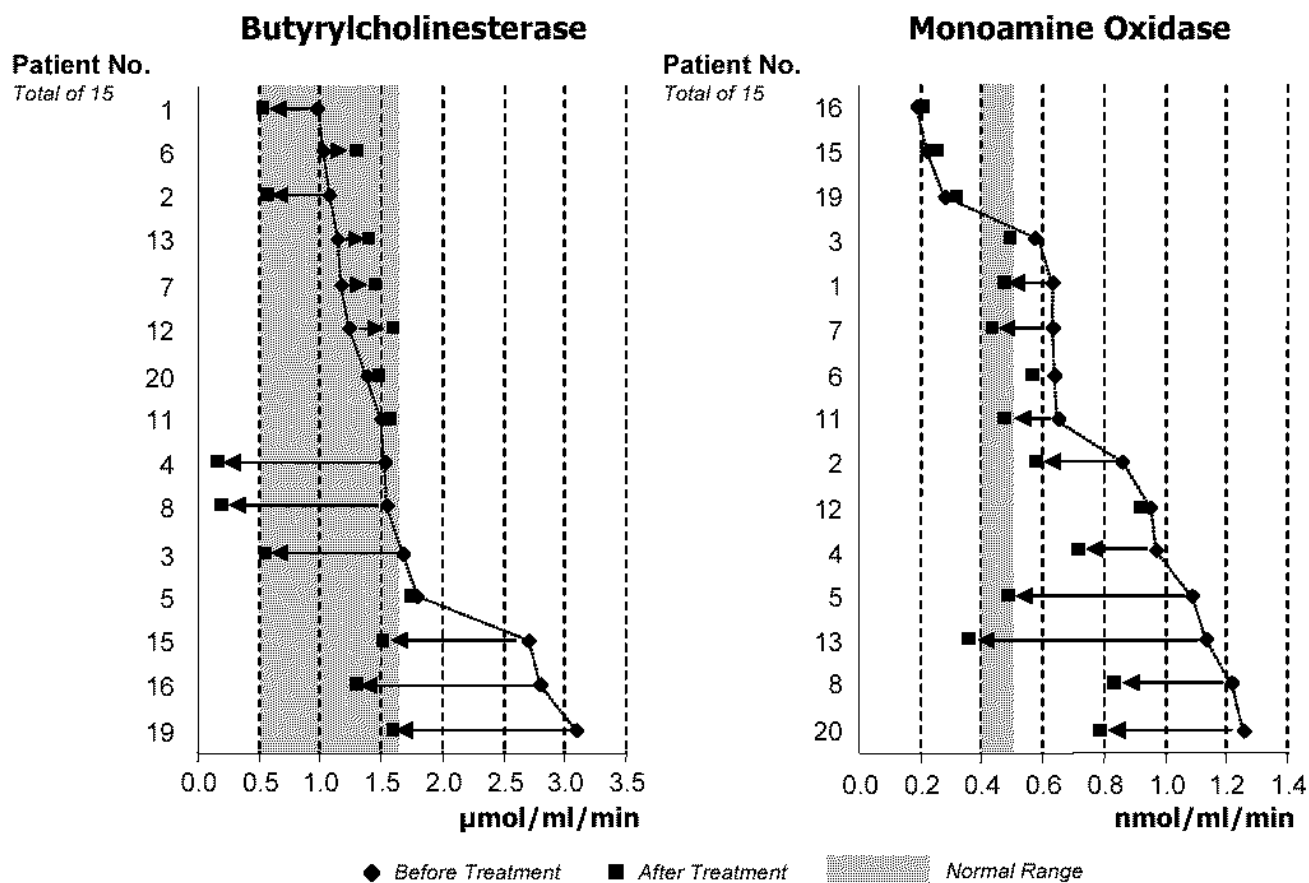
# The Path Forward: Neurodegenerative Disorders



Patients with a longer history of Alzheimer's dementia tended to have normal or above normal BuChE and MAO activity. *Ropren* treatment resulted in restoration of normal levels of activity

## Change in Enzymatic Activity after Treatment with Ropren

(15 patients exhibiting above normal levels of enzymatic activity)



# The Path Forward: Other Indications

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**Solagran is working with a number of other institutions in Russia and Australia to better understand the multi-faceted nature of *Ropren***

- A trial was completed recently at the Skvortsova-Stepanova psychiatric hospital involving critically ill opiate addicted chronic alcoholics
  - The results were outstanding and will be released as soon as patents are in place
  - Clinicians involved in the trial have already indicated that they will use *Ropren* to treat a range of conditions associated with drug and alcohol abuse, including drug and alcohol induced psychosis
  
- A number of studies have been undertaken to understand the immunomodulating properties of *Ropren*. These have included trials with:
  - Common strains of the influenza virus
  - Adenovirus
  - Erlich's carcinoma

# Concluding Comments

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***Ropren* is an innovative natural pharmaceutical with a wide range of beneficial effects**

- *Ropren* performed extremely well as a hepatoprotector in clinical trials
  
- In addition to the rapid regeneration of diseased hepatocytes and restoration of normal liver function regardless of etiology, its use appears to have a number of other beneficial effects:
  - Normalisation of lipid metabolism
  - Improvement in carbohydrate metabolism
  - Enhanced anti-oxidant activity
  - Enhanced immune response
  - Normalisation of activity of enzymes involved in neurotransmission
  - Improved cognitive function among dementia patients
  - Potential means of preventing neurodegenerative disorders including Alzheimer's dementia
  
- *Ropren* has no known side effects
  
- It should be available in Russia this year