

# ReGen Therapeutics Plc

R and D Update

10/12/03

[www.regentherapeutics.com](http://www.regentherapeutics.com)

# REGEN THERAPEUTICS PLC

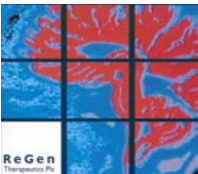
## Forward Looking Statements

This document and the presentation to which it relates includes forward-looking statements that involve risks and uncertainties. Any statements that are not statements of historical fact should be considered forward-looking statements. Important factors that could cause actual results to differ from those indicated by such forward looking statements include uncertainties relating to the necessity to conduct further clinical trials and related studies (such as toxicity and bio-equivalence), the ability to develop a scaleable manufacturing process for Colostrinin™, product testing and regulatory approval, efficacy and safety of Colostrinin™ in the treatment of any disease or condition, the completion of acquisition targets and the ability to integrate such acquisition targets.

The financial projections contained in this document and the presentation to which it relates have been prepared for illustrative purposes only and are based on reasonable assumptions, but because of the nature of the information and the factors that may affect these assumptions it may not give a true picture of the future performance of ReGen.

Key assumptions made in preparing the financial projections include:

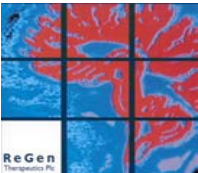
- We assume the development work on Colostrinin™ as a treatment for Alzheimer's is taken on by a third party by 4th quarter 2004.
- Development costs beyond 4th quarter 2004 refer to work to be carried out in the preclinical area to explore the potential of several additional uses of Colostrinin™.
- We do not expect any sales of Colostrinin™ as a treatment for Alzheimer's before 2006, but we do expect signing-on fees and milestone payments before then.



# **ReGen Therapeutics Plc**

## **Introduction**

- Presentation Team:
- Percy Lomax - Executive Chairman
- Tim Shilton - Development Director
- Marian Kruzel - Chief Scientific Adviser
- Martin Small - New Projects Director
- Norman Lott - Finance Director



# Overview and Strategy

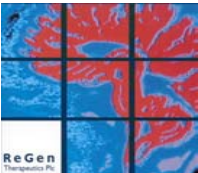
## Percy Lomax - Executive Chairman

- Continue Colostrinin™ pharmaceutical development programme.
- Explore Colostrinin™ nutraceutical development programme.
- Continue scientific programme.



# Overview - continued

- Cut costs - first half 2003 costs down 46% versus first half 2002.
- Raise cash - £1.95m raised this year so far.
- Make corporate and project acquisition.
- Working with licensing company to assist with finding codevelopment/commercialisation partner



# Colostrinin Update

Tim Shilton, Development Director



# Colostrinin Progress 2003 (A)

- Clinical trial - Published 2/04 (JAD)
- MOA defined - 1st publication (J.Mol.N)
- In-vitro assays/in-vivo models
- New process – patent filed
- Switched from ovine to bovine colostrum
- Scale-up ongoing with US colostrum processor



# Update/Process Development

## US Bovine Colostrum Co. – Benefits

- Know-how/facilities and equipment
- Collection/pooling/standardised raw material
- Cost/time-effective production of clinical grade (cGMP) material





# Colostrinin Progress 2003 (B)

- Started working with Pharm/tox CRO; programme planned and costed
- Clinical trials possible around end 2004
- Proteomics screen - offers prospect of better understanding of MOA and new potential disease targets/uses



# Colostrinin Update

Dr. Marian Kruzel





# EPIDEMIOLOGY OF ALZHEIMER'S DISEASE

*Alzheimer's Disease is a silent epidemic of dementia  
that is occurring in societies with aging populations*

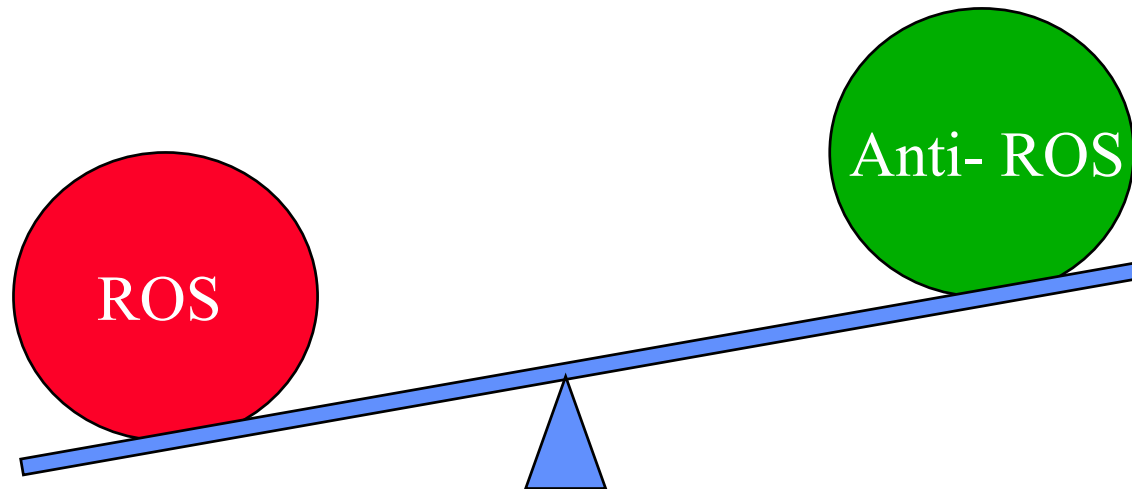


# MOLECULAR PATHOLOGY OF ALZHEIMER'S DISEASE

- Reduced level of Acetylcholine
- Accumulation of extracellular amyloid- $\beta$
- Overproduction of reactive oxygen species (ROS)



# OXIDATIVE STRESS AND AGE-RELATED DISORDERS



Oxidative Stress is defined as a disturbance in the pro-oxidant to anti-oxidant balance. It is a function of aging processes and describes a state of damage caused by reactive oxygen species.

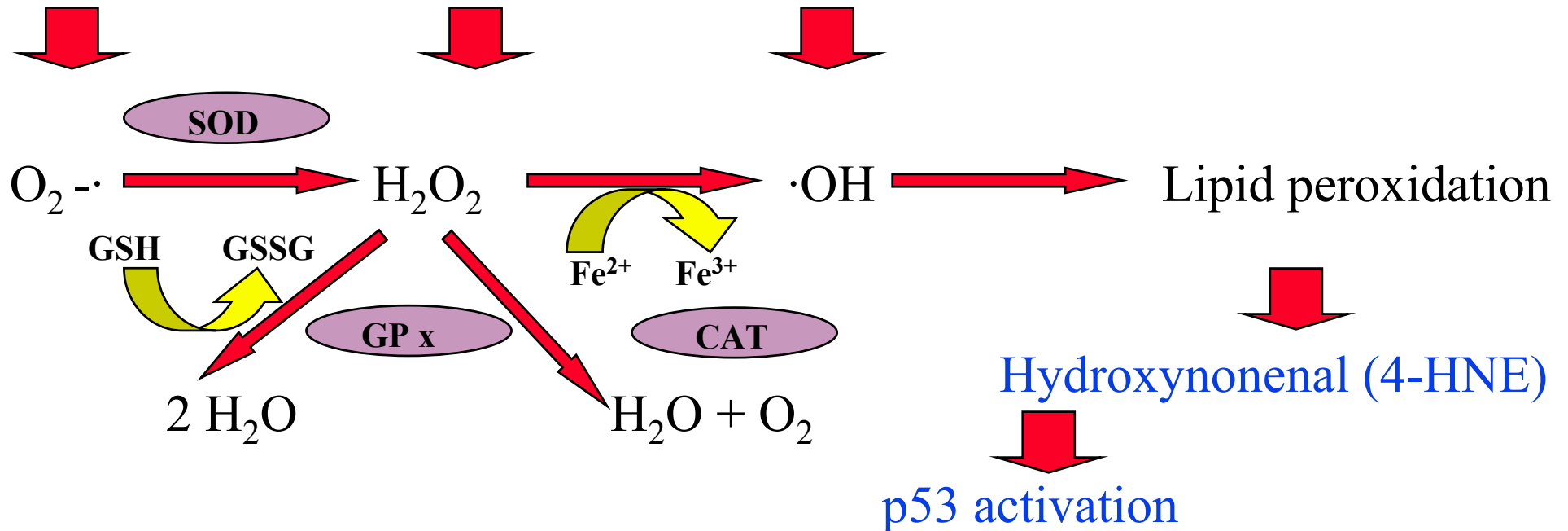


# NORMAL METABOLISM AND ROS

Health (growth & development)

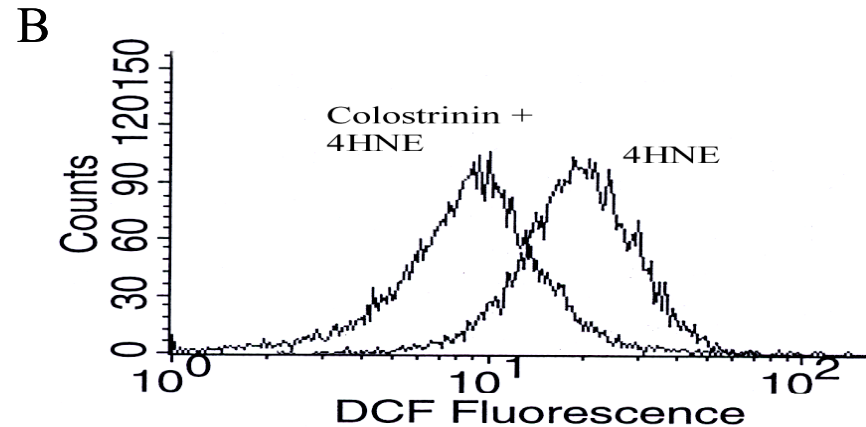
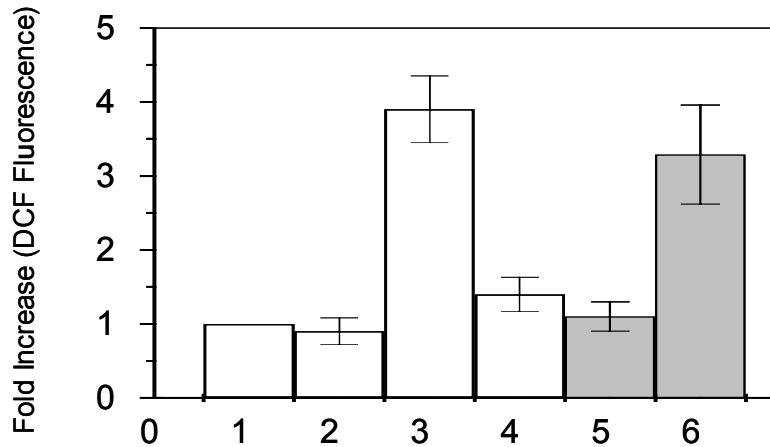
Disease (infection, inflammation  
radiation, drugs, aging)

Reactive Oxygen Species





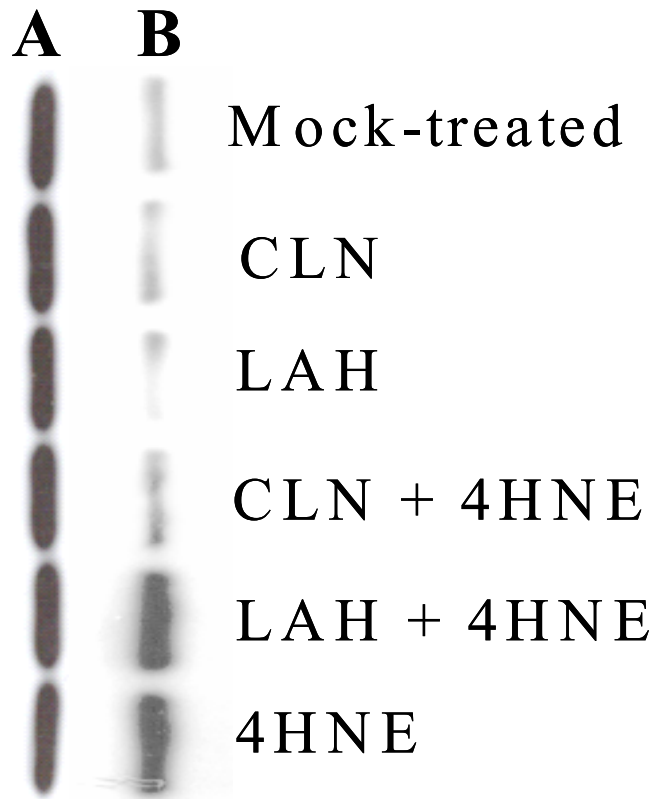
# CLN AND ROS



1, control; 2, colostrinin (10  $\mu\text{g/ml}$ ); 3, 4HNE (25 nM); 4, 4HNE (25 nM) plus colostrinin (10  $\mu\text{g/ml}$  /ml); 5, lactalbumin hydrolysate (10  $\mu\text{g/ml}$ ); 6, lactalbumin hydrolysate (10  $\mu\text{g/ml}$  /ml) plus 4HNE (25 nM). **B**: A representative FACS histogram of fluorescence of cells treated with 4HNE (25 nM) and CLN (10  $\mu\text{g/ml}$ ) plus 4HNE.



# COLOSTRININ AND p53 ACTION



PC12 cells were pre-treated with CLN or LAH and exposed to 4HNE. Three hours after treatment cell lysates were analyzed by Western blot analysis. **B**, p53; **A**, corresponding alpha tubulin. 4HNE (25 nM), CLN (10  $\mu$ g/ml), LAH 10 (mg/ml).



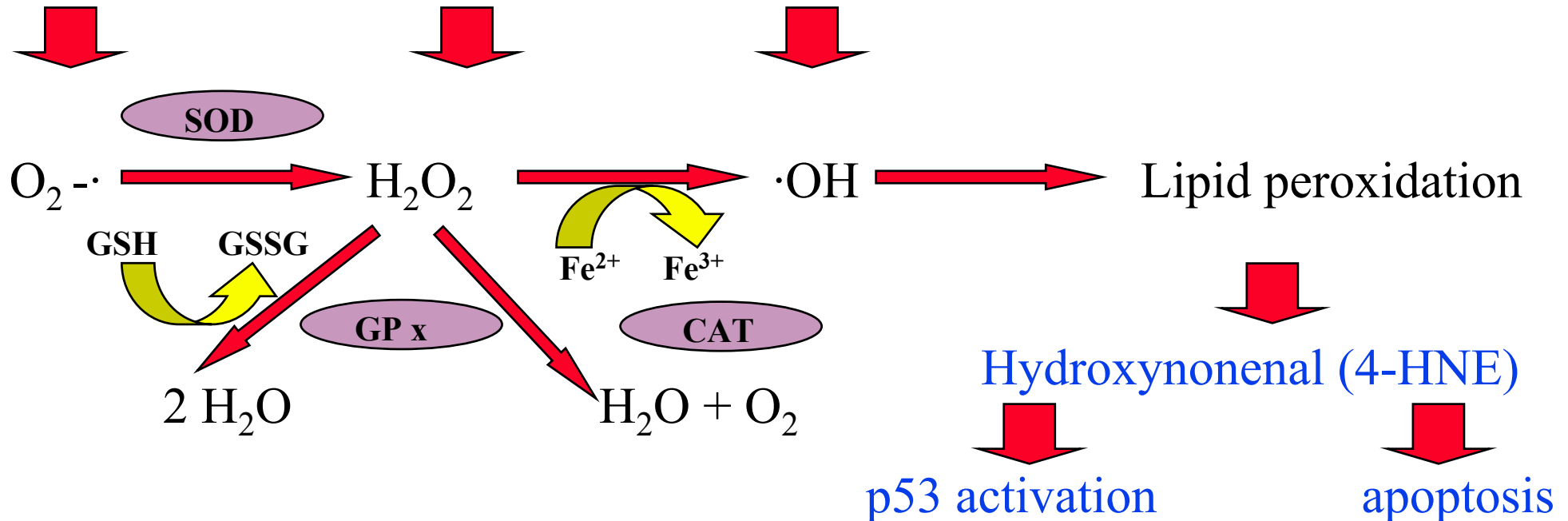


# NORMAL METABOLISM AND ROS

Health (growth & development)

Disease (infection, inflammation  
radiation, drugs, aging)

Reactive Oxygen Species





# CLN STRUCTURE FUNCTION ASSAYS

- Confirming CLN Mode of Action in a dose response inhibition of 4-HNE induced activation of p53 –quantitative bio-assay
- Confirming CLN Anti-Apoptotic Activity (4-HNE induced apoptosis; Beta amyloid induced apoptosis) – quantitative bio- and immunological assays



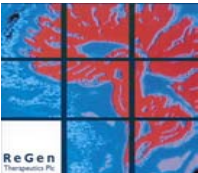
# R&D FUTURE OBJECTIVES

- CLN Anti-apoptotic and Cell Differentiating Activities: Abstract pending for presentation at the 14<sup>th</sup> European Conference on AD; Manuscript Completion
- Validation of CLN Structure-Function Assays
- CLN *in vivo* protocols to identify new clinical applications – proteomic analyses

# COLOSTRININ™ AS A NUTRACEUTICAL

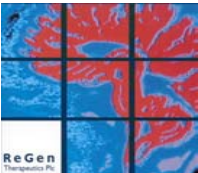
Martin Small

New Projects Director



# What is a nutraceutical?

- A term adopted by the food marketing industry to describe a product isolated or purified from foods, generally sold in medicinal forms and demonstrated to have a beneficial, functional or physiological effect or to provide protection against chronic disease
- Examples include isolated nutrients, dietary supplements, specific diets, GM foods, herbal products and bio-engineered vegetable foods



# Project Attributes

- A market exists for the treatment of early forms of cognitive impairment e.g. age-related memory impairment suggested by increasing forgetfulness.
- We believe a nutraceutical form of Colostrinin™ can be developed largely in tandem with the pharmaceutical project.
- Licensing revenues from a nutraceutical product could be generated much sooner than from a pharmaceutical version
- We are about to appoint a licensing specialist to target and initiate discussions with prospective co-development partners for the major nutraceutical markets in USA, Japan, Far East and Europe.



# Attraction of Colostrinin™ as a nutraceutical

- Derived from natural sources.
- Proven activity in clinical studies.
- Good safety profile in animal and clinical studies.



# Nutraceutical market value

US industry reference *Nutritional Business Journal* (2000) estimated that:-

- The global market to be US\$140bn, equal to about one half of the global pharmaceuticals market
- The US market accounts for 35% of the worldwide market

Overall, the European market is of a similar size to the US, but regulatory requirements remain fragmented and each country must be approached individually.

Japan and the Far East are increasingly important sectors





# **Regulatory classification of Colostrinin™ as a nutraceutical**

Independent evaluation of regulatory requirements for nutraceuticals indicates that Colostrinin™ best fits current US DSHEA regulations for a New Dietary Ingredient within the Dietary Supplement category.



# Distribution channels

*Taking the US nutraceutical market as an example:-*

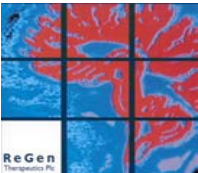
- Total market value in 2001: US\$17.7bn
- Approximate split between distribution channels in 1998; pharmacies 8%, specialist stores 49%, supermarkets/mass merchandisers 17%, and direct sales (including mail order and internet) 26%
- Internet is fastest growing sector; 22% increase in 2001

Source: *Nutrition Business Journal, Annual Industry Review 2002*



# Summary

- General manufacturing process being scaled-up.
- Manufacturing process applicable to both nutraceutical and pharmaceutical production.
- Dose Optimisation work will include defining a form, dose and method of presentation suited to a nutraceutical product.
- Anticipated that further human subject trials will be covered within the terms of any contract with a development partner.
- Co-development partners being more actively sought from January 2004



# Finance

Norman Lott, Finance Director



# Spend Analysis

	<b>Yr to 12/02</b>	<b>Yr to 12/03</b>	<b>Yr to 12/04</b>
	<b>Estimate</b>	<b>Estimate</b>	<b>Estimate</b>
	<b>£(,000)</b>	<b>£(,000)</b>	<b>£(,000)</b>
<b>Overheads</b>	1,212	900	875
<b>Development</b>	580	400	1,475
<b>% Development</b>	33%	31%	63%

- Overhead savings of over 25% in 2003
- Overheads are running at 60% of 2001 levels
- More concentration on development costs in 2004



# Cash burn/Liquid funds

	2002	2003	2004 Estimate
<b>Cash burn per month:</b>			
<b>Overheads</b>	100k	75k	70k
<b>Overall</b>	150k	110k	190k
<b>Liquid funds Dec 03</b>		800k	

- Increasing cash burn in 2004 reflecting higher development spend
- Liquid funds invested on the money market



# Summary/Q and A

Percy Lomax, Executive Chairman



# SUMMARY- Percy Lomax

- Focused action plan.
- Build on three legs.
- Raise money.





# Funding

- Liquid resources - £0.8m
- Cash raising by:
- *share issue for cash.*
- *Cash generation from acquisition.*
- *External partnering sources.*
- *Other innovative instruments*



# The Vision

- By 2006 to have a self sustaining profitable Healthcare business.

