

# **REGEN THERAPEUTICS PLC**

**ANNUAL CITY PRESENTATION**

**13<sup>th</sup> DECEMBER 2004**

[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 relate to ReGen's objectives, estimates and goals. Any statements that are not statements of historical fact should be considered forward-looking statements. The company's business is subject to numerous risks and uncertainties, including the necessity to conduct further clinical trials and related studies (such as toxicity and bio-equivalence), the ability to develop and manage 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 certain acquisitions and the ability to successfully integrate acquisition targets. These and other risks and uncertainties could cause ReGen's actual results and developments to be materially different from those expressed or implied by any of these forward-looking statements.

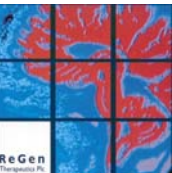
The financial projections contained in this document and the presentation to which it relates have been prepared for illustrative purposes only and are based on assumptions, some of which are described below. Although ReGen's management believes that such assumptions are reasonable, projections are necessarily speculative. Unanticipated events and circumstances may occur. Actual results may vary materially and adversely from the projections, and therefore, the projections may not give an accurate representation of the future performance of ReGen.

Key assumptions made in preparing the financial projections include:

- We assume the final development work on Colostrinin™ as a nutraceutical treatment for mild cognitive impairment is taken on by a third party by 1st half 2005.
- Most development costs beyond 1st half 2005 refer to work to be carried out in the preclinical area to explore the potential of Colostrinin™ peptides in the treatment of Alzheimer's disease and several other CNS diseases.
- We do not expect sales of Colostrinin™ as a nutraceutical before 2006, but we do expect signing on fees before then.
- We do not expect any milestone payments for Colostrinin™ constituent peptides as a treatment for Alzheimer's disease or other CNS illnesses before 2007.

## Legal Notice

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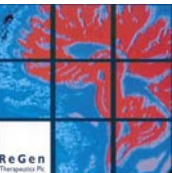


# **REGEN THERAPEUTICS PLC**

## **Introduction**

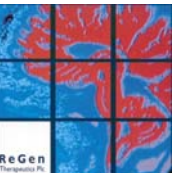
Percy Lomax

Chairman and Chief Executive



# **The Company and its Business**

- ReGen Therapeutics Plc was founded in 1998 to acquire IP related to Alzheimer's disease
- The Company now has three businesses - drug development, nutraceuticals and by acquisition conducting clinical trials
- Acquired Guildford Clinical Pharmacology Unit Limited (GCPUL) October 2004
- ADR live 10th December 2004

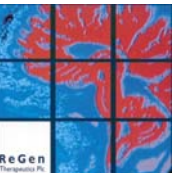


# Our Business

- Drug Development:

The focus of drug development is Colostrinin™ and its constituent peptides as a potential treatment for Alzheimer's disease.

ReGen is developing two commercial applications for Colostrinin™ and its constituent peptides: pharmaceutical and nutraceutical.

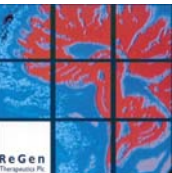


# **REGEN THERAPEUTICS PLC**

## **Partnering/development Update**

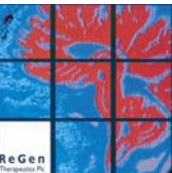
Tim Shilton

Development Director

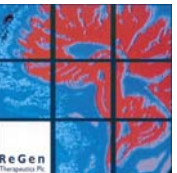
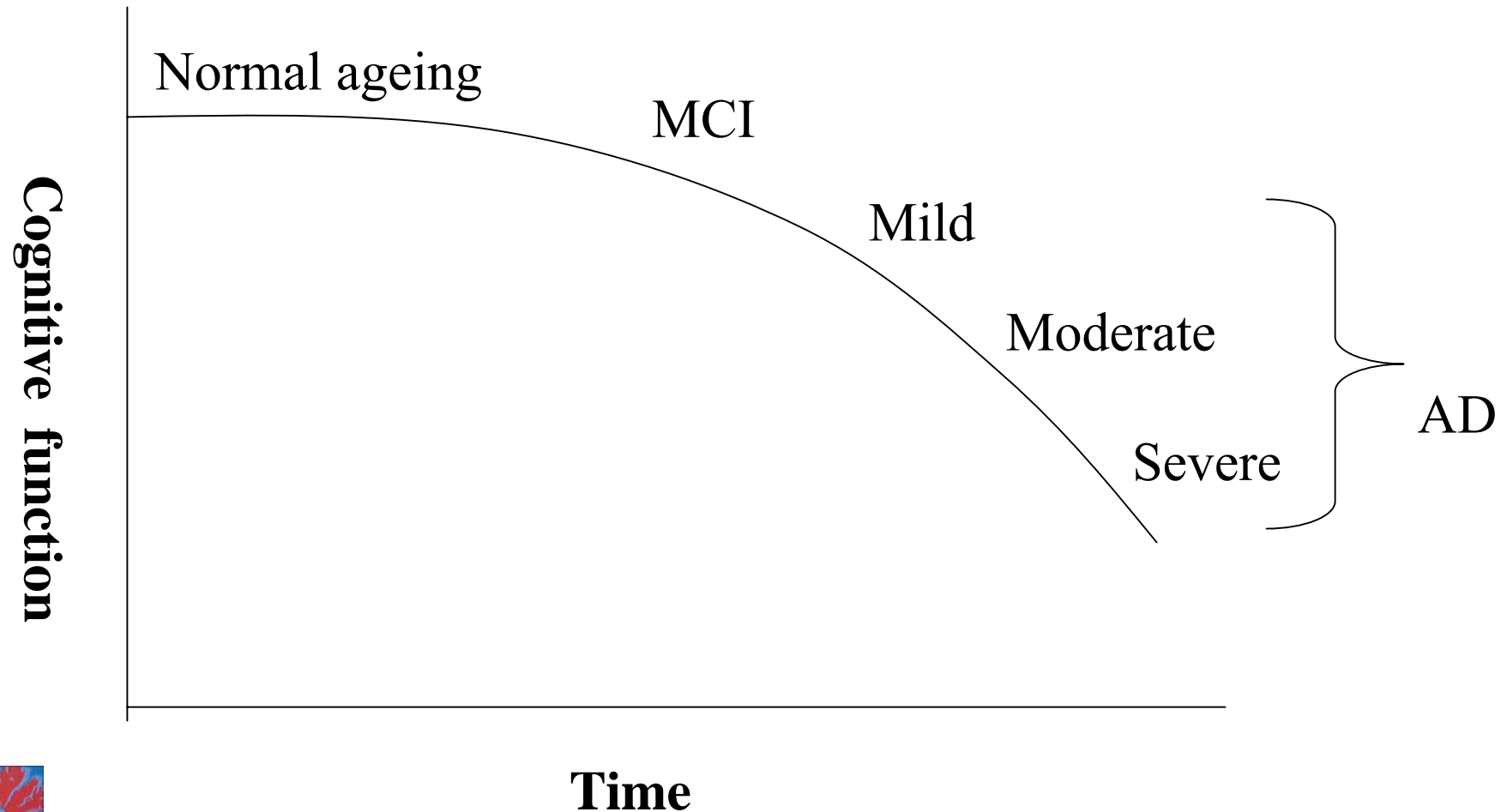


# The Colostrinin™ Opportunity

- Prophylaxis and treatment of age-related neurodegenerative disorders involving cognitive impairment
  - Age-related memory impairment
  - Mild cognitive impairment (MCI)
  - Alzheimer's disease (AD)
- Colostrinin™ and peptides available for licensing/co-development



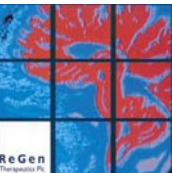
# Continuum of Cognitive Decline





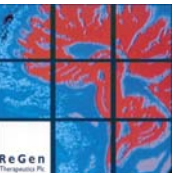
# Partnering Status?

- Discussions to date suggest:
- **Nutraceutical** opportunity real subject to:
  - GMP Manufacturing resolved
  - Toxicology/Clinical data in target population on production material
  - Same/close product not for pharmaceutical use
- **Pharma** more interested in the exact nature of the active component(s)

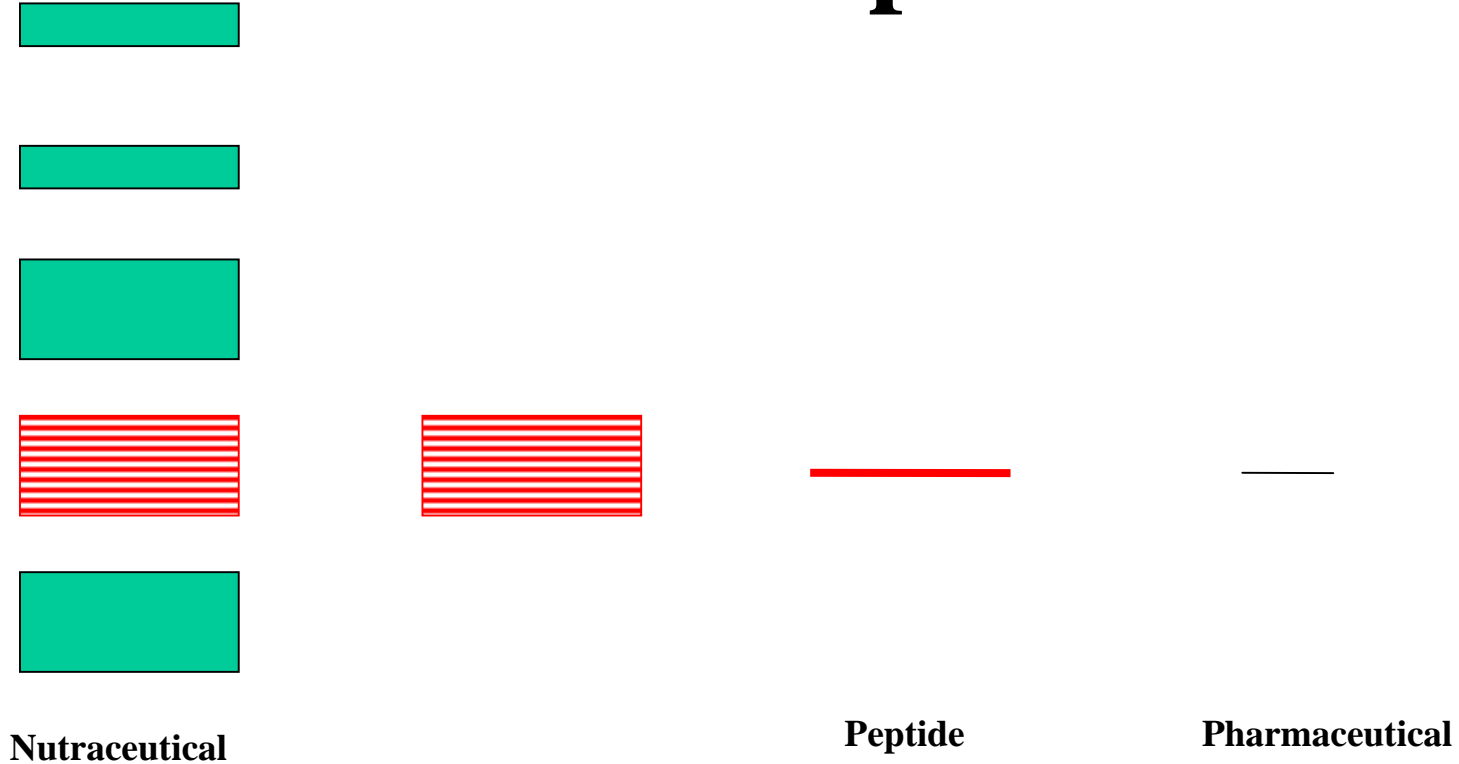


# Intended Strategy

- Complex ‘peptide extract’ for nutraceutical use
- Pursue source of ‘exquisite activity’ as potential pharmaceutical



# Product Options



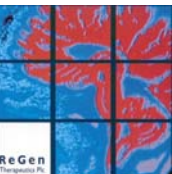
Increased margin/long-term value

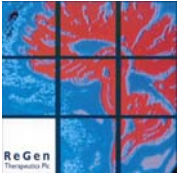
Increased timeline, technical/regulatory hurdles, costs and risk



# Nutraceutical Timeline

Material	Q1/05
Toxicology start	Q2/05
Clinical Study	Q4/05
Launch	Q3/06





# Peptide-based Pharmaceutical

- Fractionate Colostrinin
- Characterise peptides
- Make peptides
- Screen peptides
- Identify target(s)
- Develop HT screen
- Screen library
- Chemistry around hits
- Select leads/optimise
- Pre-clinical, clinical etc

6 Months

Typically  
24+ Months

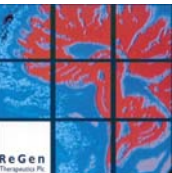
Q3/07

# **REGEN THERAPEUTICS PLC**

## **Science Highlights**

Dr. Marian Kruzel

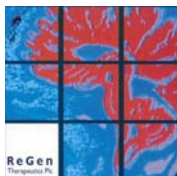
Senior Scientific Adviser



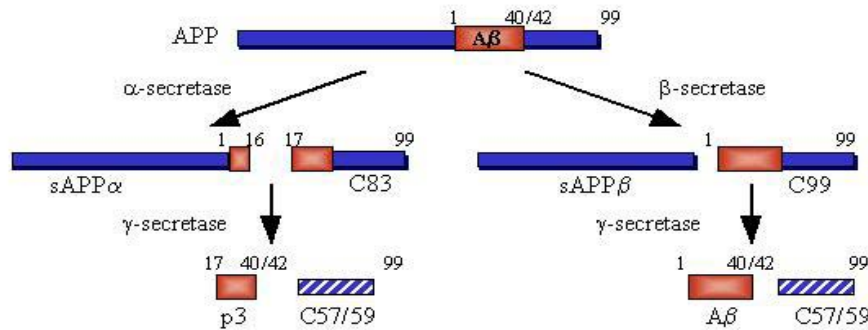
# 2004 Science Highlights

## *CLN Mode of Action*

- *In vitro* cell culture – UTMB Galveston, Texas – Regulation of intracellular level of reactive oxygen species (ROS) and subsequent regulation of p53 pathway
- *In vitro* cell culture – Roswell Park Cancer Institute, Buffalo New York - Protection against toxic effects of Amyloid- $\beta$  aggregates (plaques)

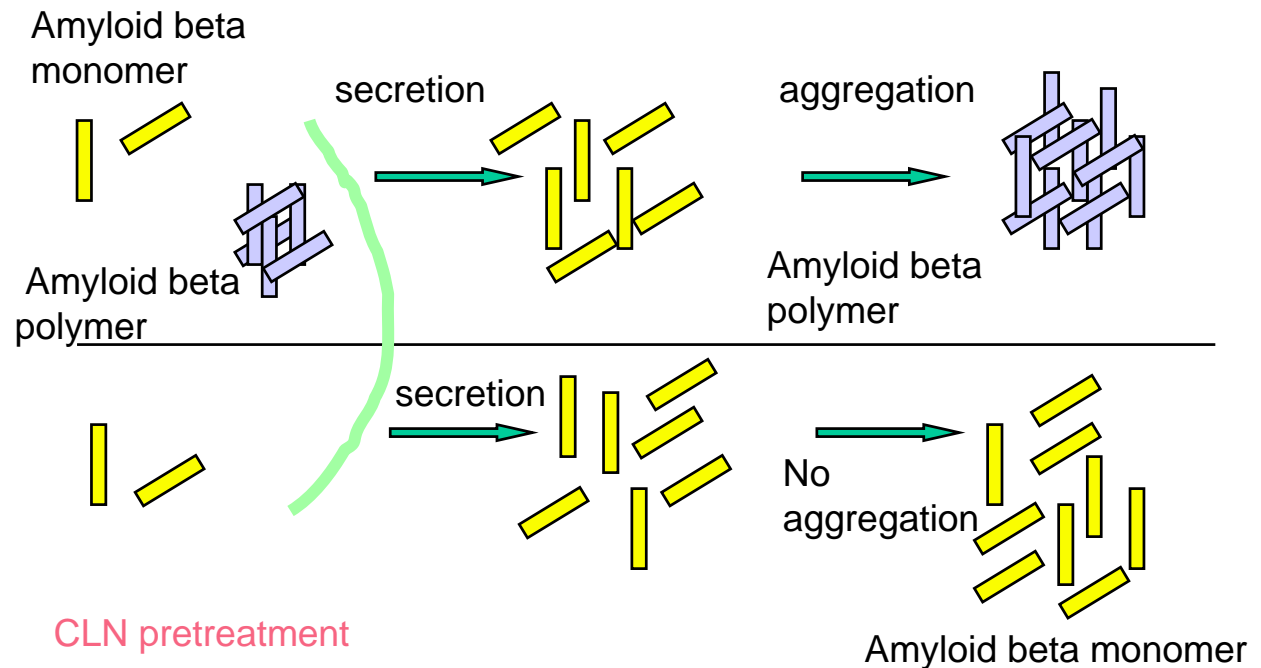


# 2004 Science Highlights



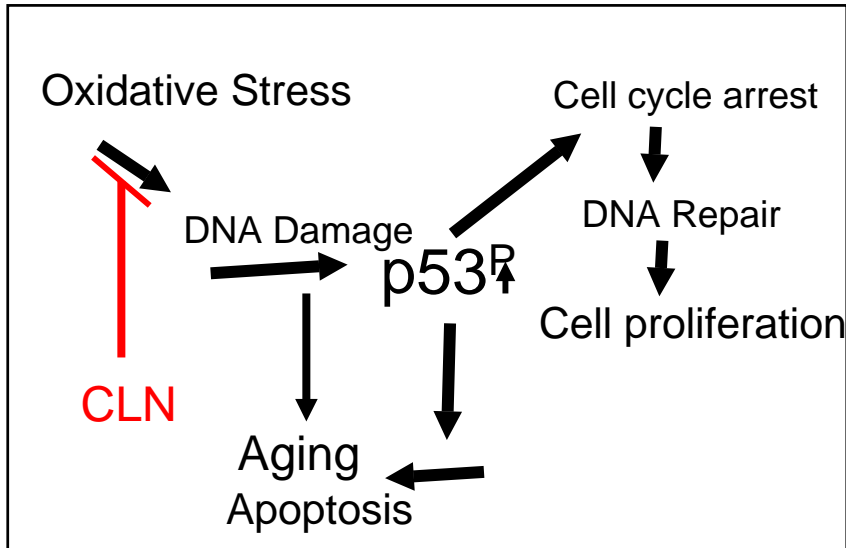
## Proteolytic Processing of Amyloid Beta Precursor

## Amyloid Beta Interactions

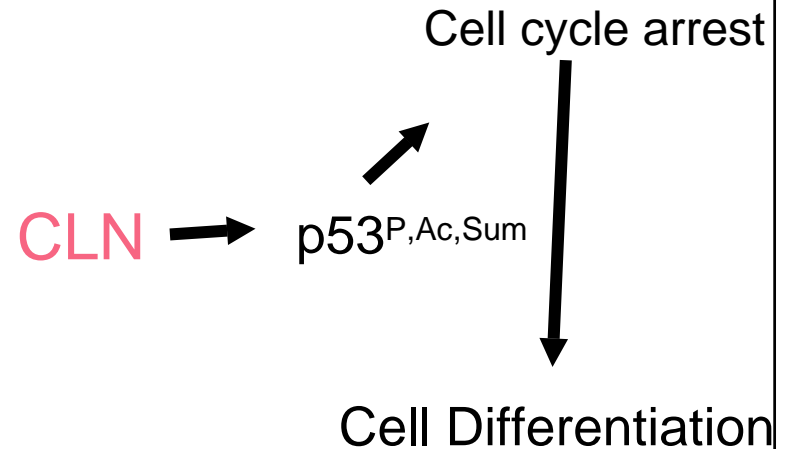
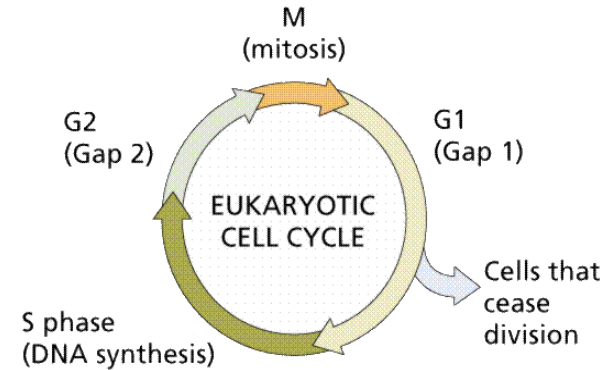




# 2004 Science Highlights



CLN regulates p53 activity



# 2004 Science Highlights

## *CLN Biological Compatibility*

- *In vitro* cell culture – UTMB Galveston, Texas – inhibition of 4HNE-induced p53 activation – ovine *versus* bovine
- *In vivo* chick model – Open University, UK - Memory enhancement in newly hatched chicks – ovine *versus* bovine



# 2004 Science Highlights

## *CLN Production Simplified*

The quality of new, two-step purification protocol confirmed in a pilot production by the US contract manufacturer



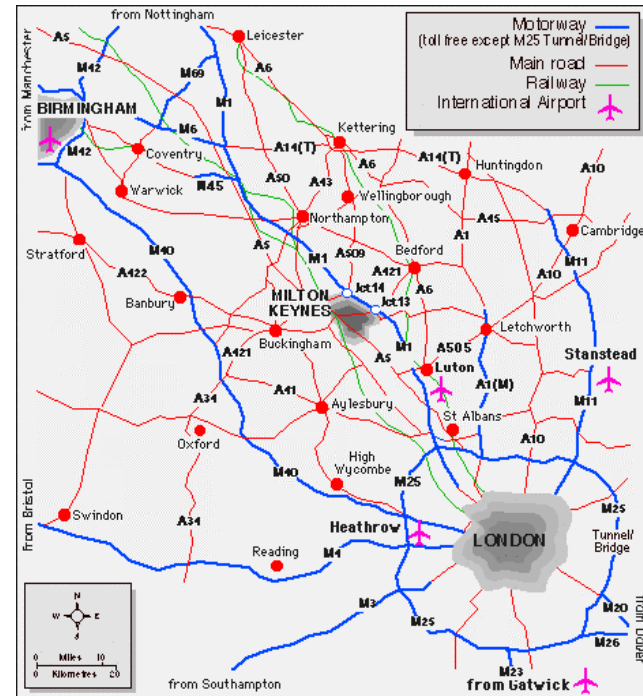
**The efficacy of Colostrinin™ (a proline-rich polypeptide complex) on memory retention in day-old chicks (*Gallus domesticus*) for a one-trial passive-avoidance paradigm**

Prof. Mike Stewart, Dr Duncan Banks,

Dept of Biological Sciences, Open University,

Walton Hall, Milton Keynes, UK

# Open University, Walton Hall, Milton Keynes

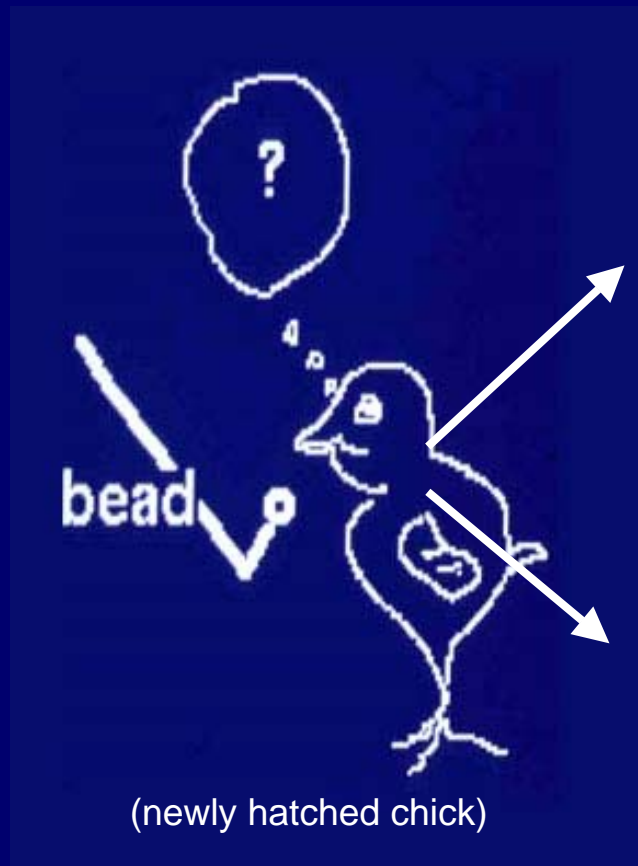


## Advantages of the chick as a behavioural model

- Chick learning models can be timed precisely - noise of other learning kept to a minimum
- Drug administration simple by virtue of thin skull and minimal blood-brain barrier
- Inexpensive subjects, easy to handle and results can be obtained relatively quickly

# Passive avoidance training

(to peck or not to peck)



DRY  
Chrome bead

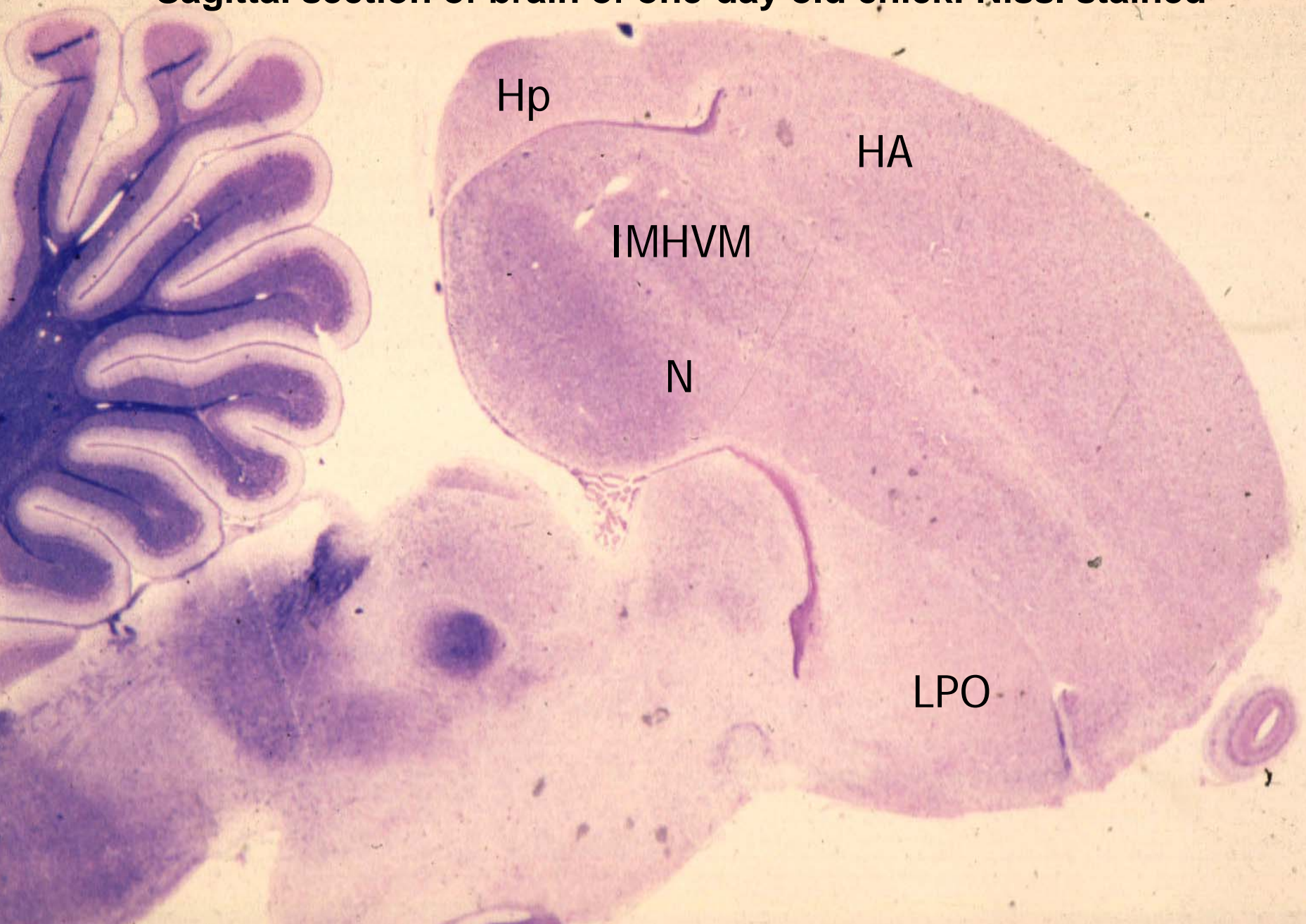
OK, peck again  
(control)

MeA-dipped  
Chrome bead

YUK! Never again  
(trained)

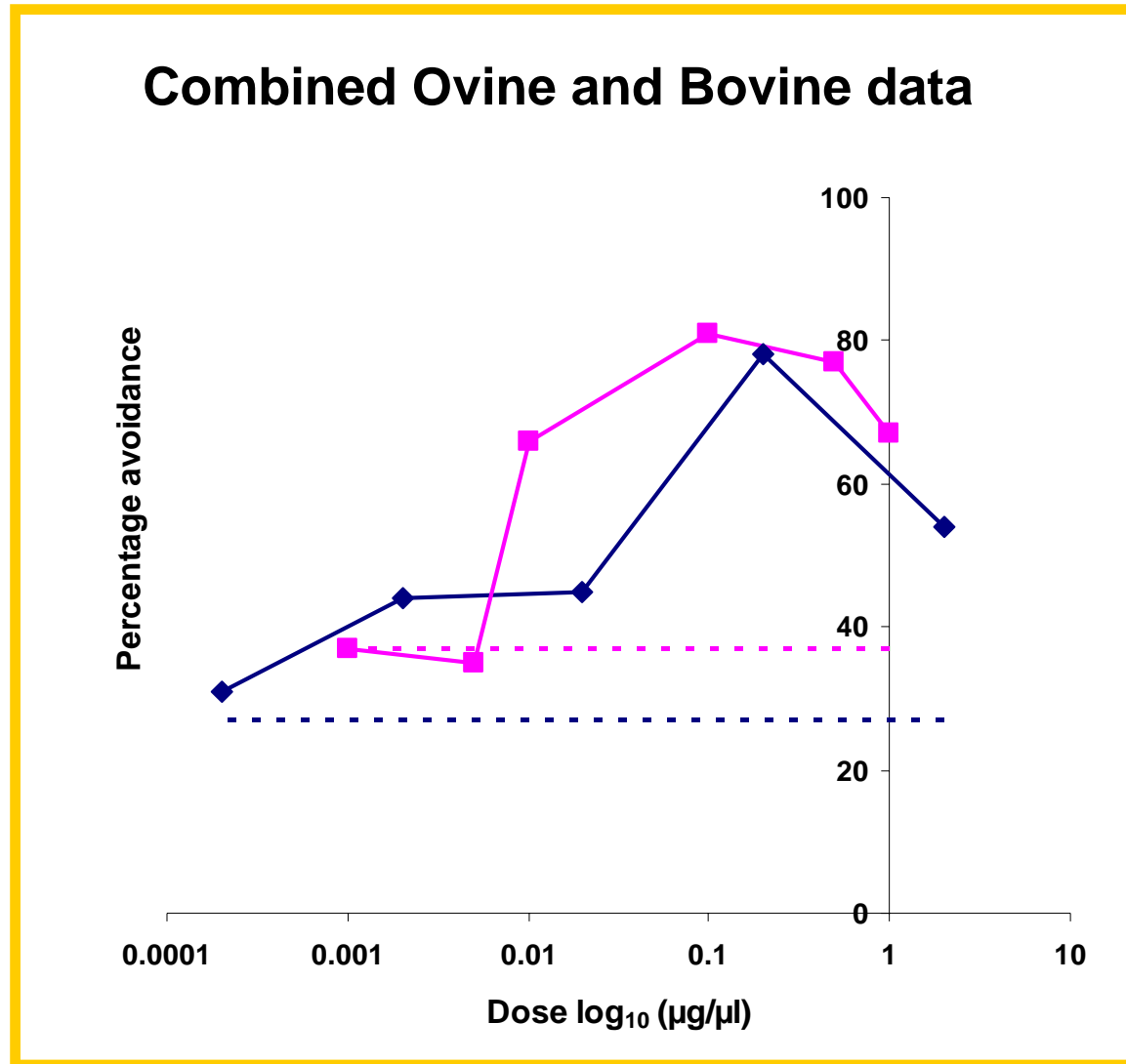


**Sagittal section of brain of one-day old chick: Nissl stained**

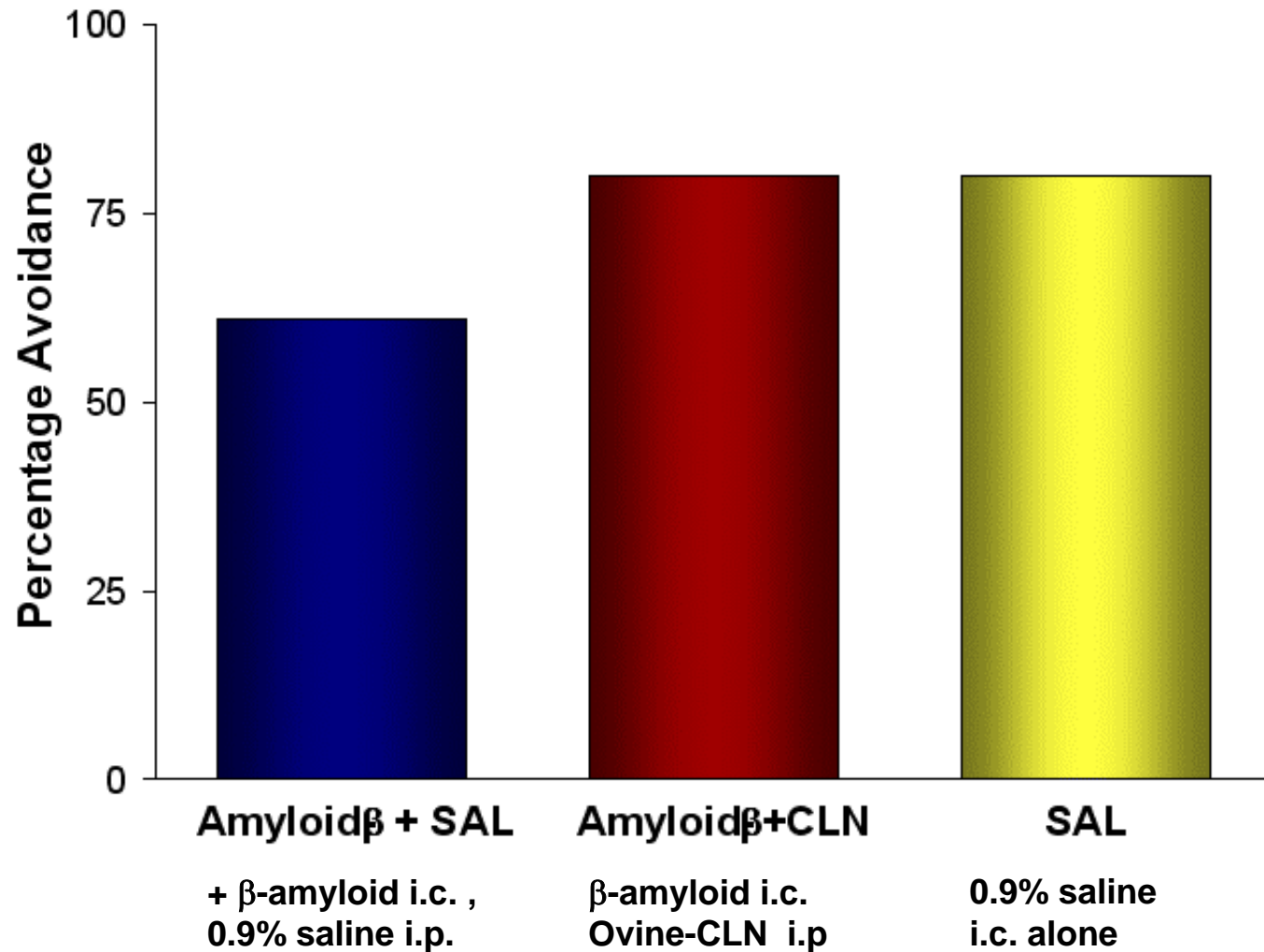




The effect of i.c. injections of 0.9% SALINE (dashed lines) or Colostrinin (Bovine, **blue**; Ovine, **mauve**) on the passive avoidance learning response to 10% MeA in 1-day old chicks.



**The neuroprotective effect of 0.1µg/g Ovine-CLN injected i.p.  
40 mins prior to training with 100% MeA.**



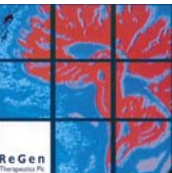
# CONCLUSIONS

- Colostrinin exhibits potency as a cognitive enhancer of avoidance training on an aversive stimulus in newly hatched chicks.
- This extends the known efficacy of Colostrinin from mammals (rats & humans) to aves.
- Colostrinin efficacy shows a dose response curve with potency over a 100 fold range and is equally effective via the intraperitoneal or intracranial route.
- Colostrinin did not remove the memory block caused by i.c. injection of  $\beta$ -amyloid. However, when given prior to  $\beta$ -amyloid administration, showed an ability to reduce the severity of the  $\beta$ -amyloid induced memory block.
- These results indicate that Colostrinin may have efficacy in the treatment of memory disorders including Alzheimer's disease.

# **REGEN THERAPEUTICS PLC**

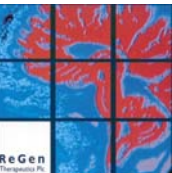
## **Guildford Clinical Pharmacology (GCPUL)**

Dr. Andrew Sutton  
Medical Director



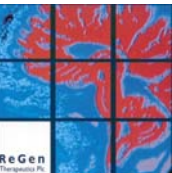
# Guildford Clinical Pharmacology Overview

- Guildford Clinical Pharmacology Unit Ltd was acquired by ReGen in October 2004 for a consideration of £250,000 satisfied by ordinary shares
- GCPUL is a contract research organisation, established over 10 years, with experience in measuring pain and motility of the gastrointestinal system
- It works closely with Royal Surrey County Hospital where many of its clinical studies are carried out and it has an international list of clients
- The acquisition of GCPUL will assist ReGen, as a drug development company, in the management of its expenditure and operations in this area



# Guildford Clinical Pharmacology Personnel

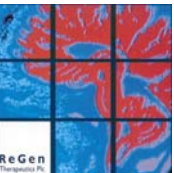
- Dr Andrew Sutton, Guildford's medical director has over 20 years experience in conducting phase 1 and 2 clinical trials and has directed units at Beecham, Roussel and Abbott
- Dr Graham Mould has a similar period of experience in pharmacokinetics and interactions between drugs. He was an adviser to NHS South West Thames Region on drug absorption and metabolism
- Guildford has a core of experienced personnel complemented by a team of nurses and technicians, experienced in good clinical practice, that work for the company on a project basis
- The expertise of Drs Sutton and Mould provides a valuable resource to the ReGen Therapeutics board to support the Colostrinin™ programme and in developing applications for its derivatives



# Guildford Clinical Pharmacology

## Skills and Experience

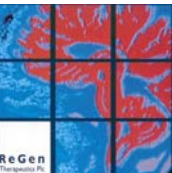
- Global level expertise in analgesic studies
- Leader in UK trials on Japanese volunteers
- Unique models for measuring effects of gastrointestinal tract
- 69 volunteer studies and 39 patient studies completed to date
  - Volunteer studies include: first single dose to man, first repeat dose to man, Bioequivalence, Immunoglobulin, Japanese volunteers, laser pain threshold
  - Patient studies include: Oncology, H Pylori, Migraine, Chronic Pain, Viagra in angina
- Clients include: Pfizer, Hoffman La Roche, GSK, Novartis



# **Guildford Clinical Pharmacology**

## **Future Plans**

- Acquire small clinical unit to permit more cost-effective and timely patient studies
- Develop and publish models
- Develop marketing databases and marketing support to increase visibility
- ReGen management support will aid future development with minimal additional expenditure





# **REGEN THERAPEUTICS PLC**

## **Colostrinin™ as a Companion Animal Product**

Martin Small

New Projects Director



# Background

- Emerging market for non-prescription health products targeted at household pets
- Canine dementia widely acknowledged
- Project proposed to ReGen by Nick Mills, respected veterinary surgeon
- Potential evaluated over last year and development planning underway



# Canine Dementia

- In dogs, dementia is known as Canine Cognitive Dysfunction Syndrome or CCDS
- 1-in-4 dogs over the age of eight suffer a degree of CCDS
- Clinical signs associated with certain age related behavioural changes include:-
  - Disorientation
  - Less human interaction
  - Disturbed sleep pattern
  - Loss of house training



# Diagnosis of CCDS

- First reports on age-associated neuropathology in dogs published in 1914
- Other types of neuropathology in aged-canine brains, including “Alzheimer-like” conditions, reported in 1950’s
- Research suggesting dogs would be useful models of human brain ageing and dementia published 1971
- Parallels between Alzheimer’s disease and cognitive decline in humans and CCDS
- Many researchers now including study of dogs in ongoing investigations of cognitive impairment
- Established methods of ascertaining decline



# Project Attributes

- Manufacturing process and product validation similar to human nutraceutical
- Increasing public awareness of CCDS resulting in a growing commercial market for effective treatments
- Currently few products on the market aimed at the condition
- Petcare products generally distributed in UK through two main networks
- Global supply networks readily accessible



# Potential Market - Dogs

- 7.4 million dogs in UK - 3.2 million over the age of eight
- 1-in-4 dogs over the age of eight suffers a degree of canine dementia
- Potential target market in UK: 800,000 dogs
- Potential world-wide market: 20 million dogs



# Potential Market - Cats

Some evidence that cats also suffer cognitive defects and dementia, but less published research in the area. More research needs to be done, but potentially:-

- 8.7 million cats in the UK
- Potential target market for feline-version of a dog product in UK: 850,000 cats
- Potential target market worldwide: 20 million cats



# Existing Commercial Market

- Pedigree® is a major global player in the sector and has its “Dentastix” range of chews etc for maintaining animal dental health.
- Several other similar “chew” products available.
- Hills Pet Nutrition Inc. markets “Canine b/d™” as part of their “Prescription Diet™” range internationally.
- Tesco recently reported in the press as having sold 2.4 million packs of “*Dentastix*” in the last year and demand growing.





# Summary of Development Intentions

- Conduct initial small-scale feasibility study to establish perceivable effect of Colostrinin™ on dogs
- Investigate contract product manufacture
- Conduct clinical study, in collaboration with veterinary surgeon
- Approach potential development partners
- Approach potential product distributors (initially for UK market)
- Investigate potential for world-wide distribution

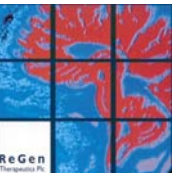


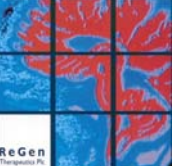
# **REGEN THERAPEUTICS PLC**

## **Financials**

Norman Lott

Finance Director





# Spend Analysis

	<b>Historically to 12/04 £m</b>	<b>Yr to 12/04 £(,000) (Estimated)</b>
<b>Development</b>	5	550
<b>Overheads</b>	6.4	1000
<b>% Development</b>	44%	35%

- Over £5m spent on development of the project to date incorporating
  - Initial acquisition of the rights to Colostrinin™ and patent protection
  - Successful completion of clinical trials
  - Continuing development of a manufacturing process
  - Extensive research and development

# Cash burn

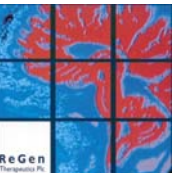
	<b>2004</b>
<b>Cash burn per month:</b>	
<b>Overheads</b>	83k
<b>Overall</b>	130k

# **REGEN THERAPEUTICS PLC**

## **Summary**

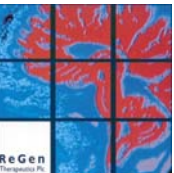
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Chairman and Chief Executive



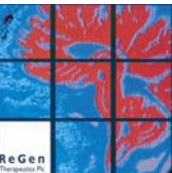
# Equity

- RGT - Alternative Investment Market (AIM)
- Stock price - 2.75p
- Market cap - £7.9m/\$14.6m
- Average trading volume - 1 million
- 52-week range - 1.5p - 7.4p
- Shares outstanding - 287,658,850



# Summary

- General manufacturing process being scaled-up
- Co-development partners currently being actively sought
- Anticipated that further human subject trials will be covered within the terms of any contract with a development partner
- One strategic acquisition made October 2004 - expansion plan currently being developed
- Further acquisition targets identified
- ADR live 10th December 2004



# The Vision

- By end of 2006 to have a self sustaining profitable Healthcare business

