R&D Briefing

December 14, 2006

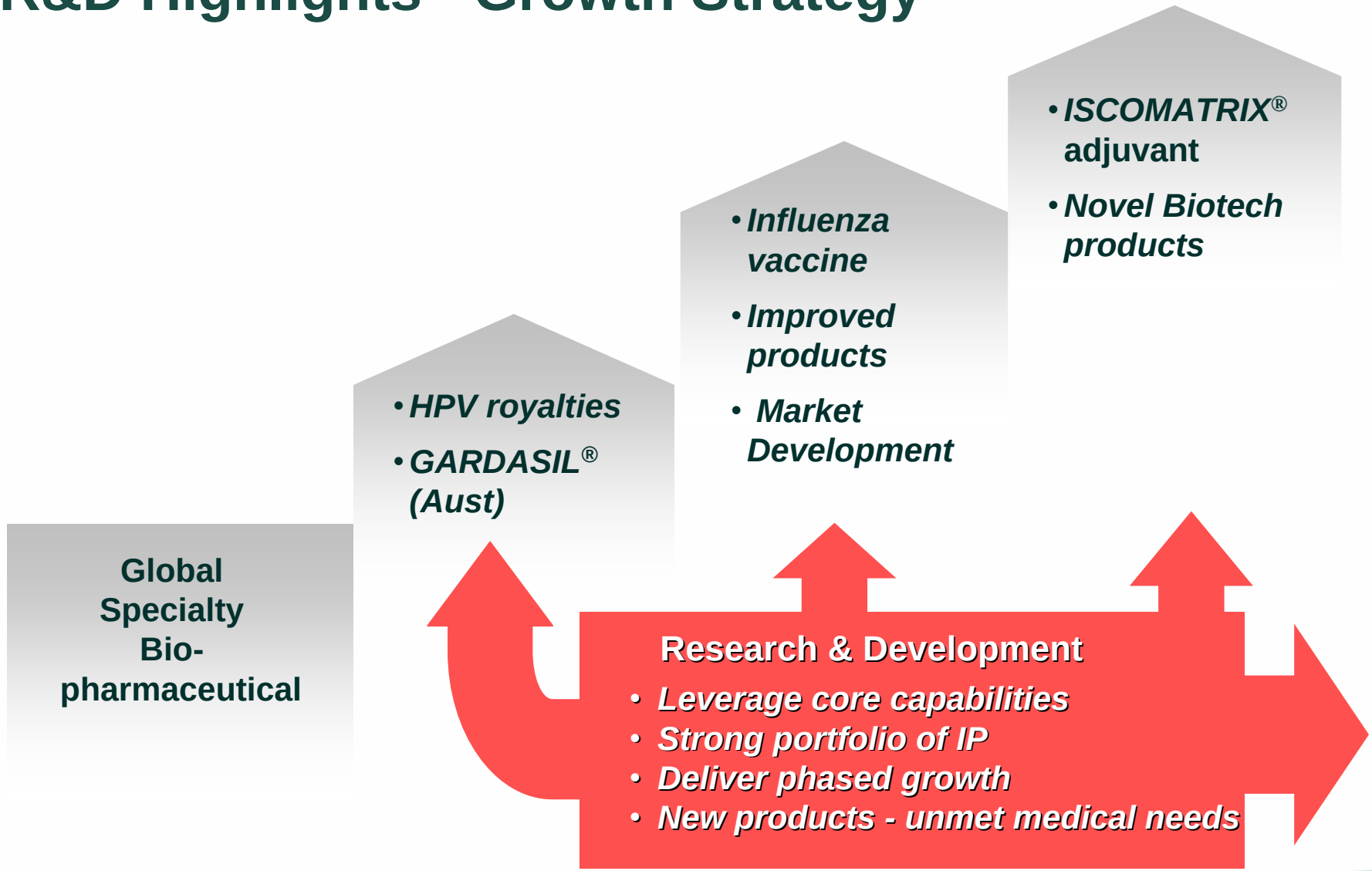
Agenda
December 2006 R&D Briefing

• Welcome	Mark Dehring
• Introduction and highlights	Andrew Cuthbertson
– Strategy, portfolio overview and budget mix	
• ISCOMATRIX® Adjuvant	Andrew Cuthbertson
• Influenza vaccine portfolio	Andrea Douglas
• Q&A	
• Tea break	
• Plasma Products	Simon Green
• Recombinant Monoclonal Antibodies	
– Introduction	Andrew Cuthbertson
– Therapeutic Leukaemia Antibody	
– Zenyth portfolio	Andrew Nash
• Summary highlights, Q&A and wrap up	

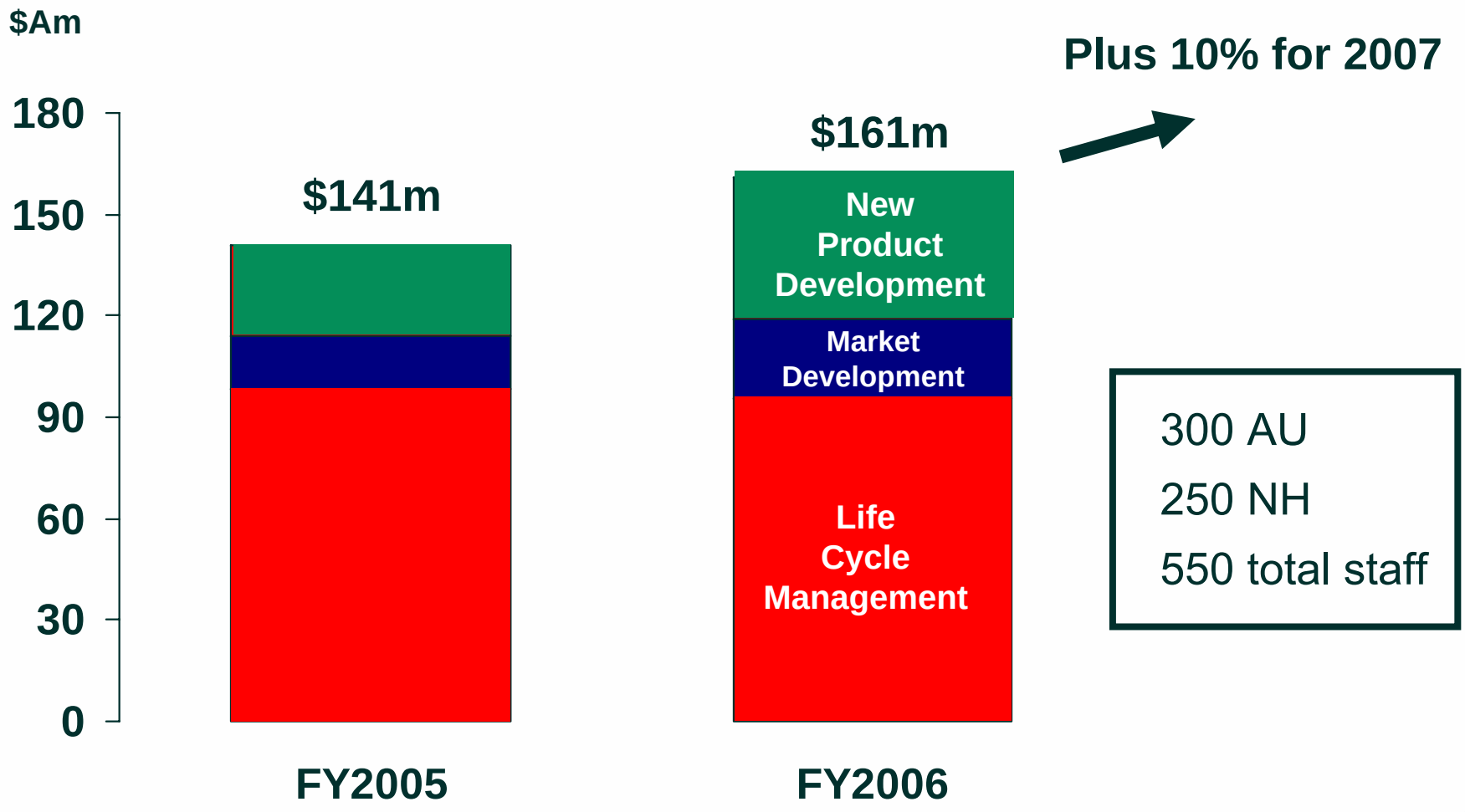
INTRODUCTION

ANDREW CUTHBERTSON

R&D Highlights - Growth Strategy



R&D Highlights – Investment

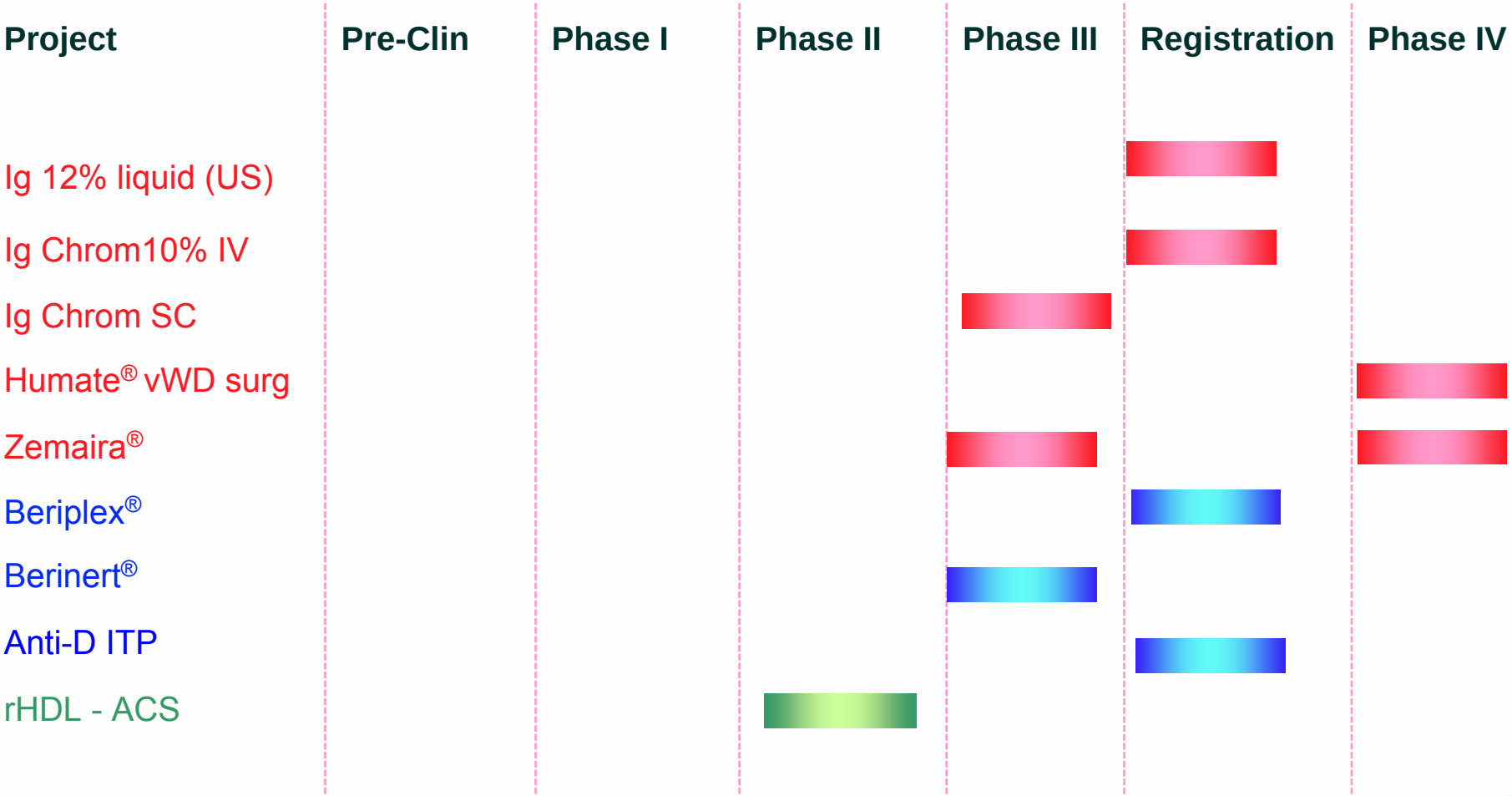


300 AU

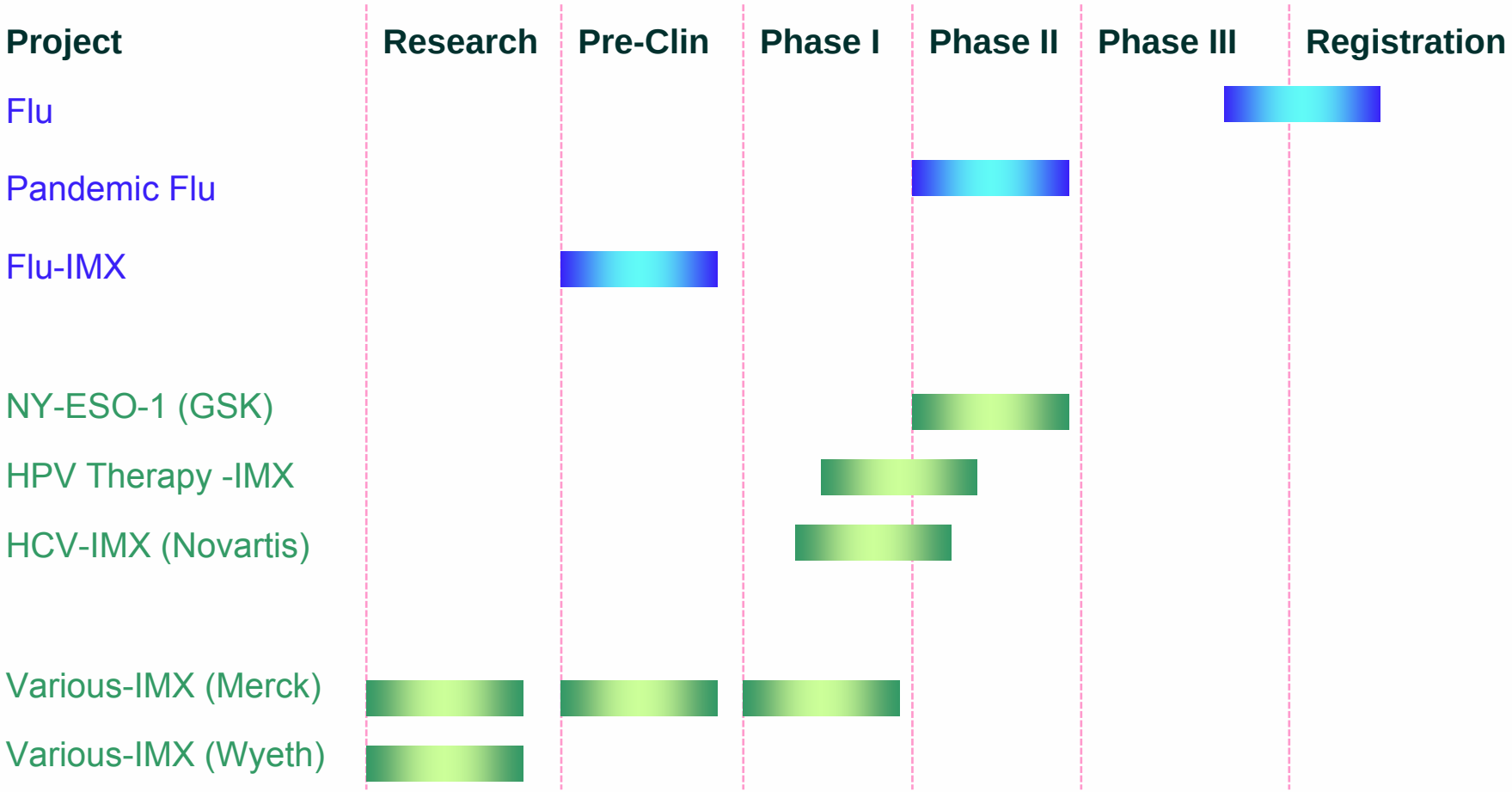
250 NH

550 total staff

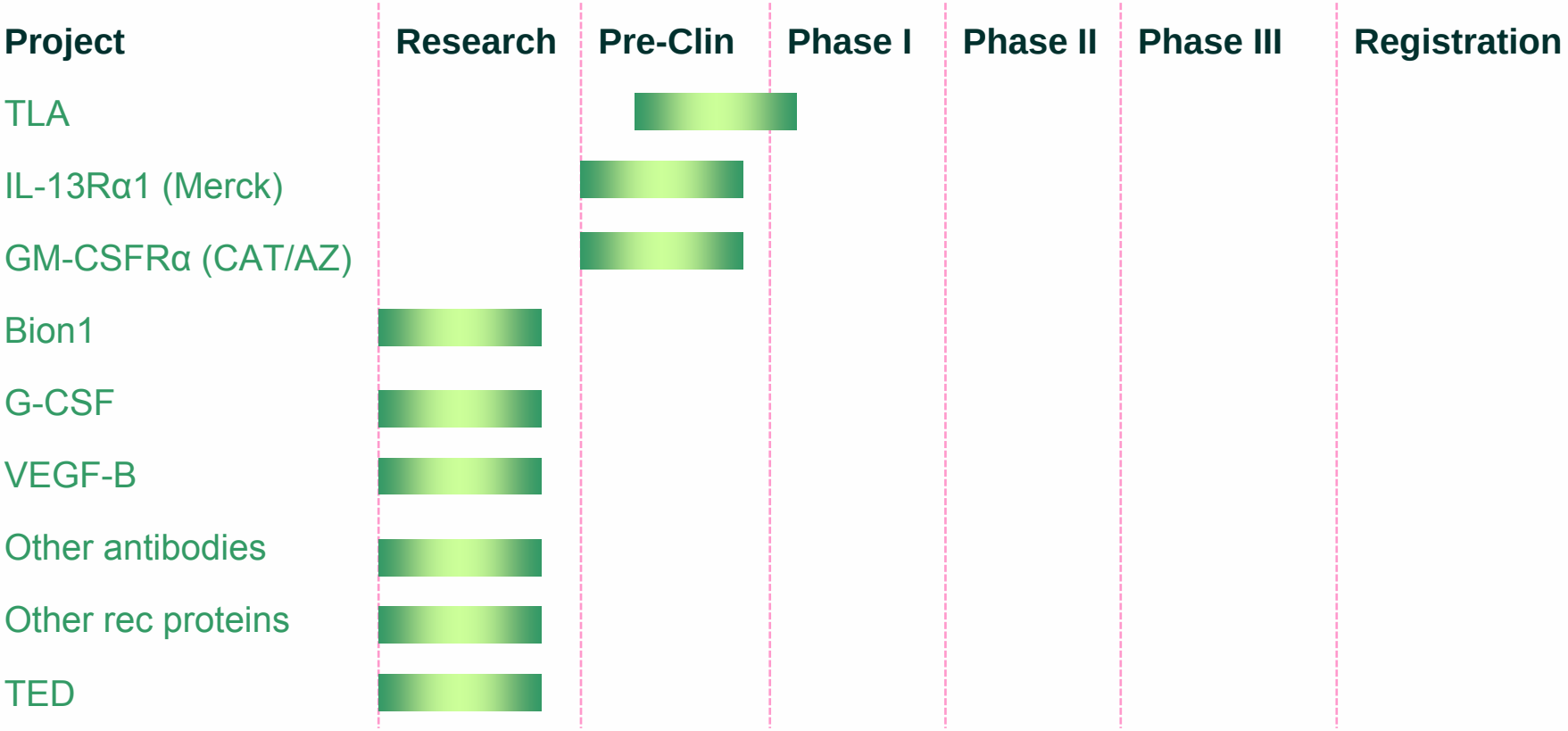
R&D Portfolio – 1



R&D Portfolio – 2



R&D Portfolio – 3



HIGHLIGHTS

- Merck Gardasil® registrations and rollout
  - Australian Government funding
- ISCOMATRIX® adjuvant commercialization
- Influenza vaccine projects
- Igs and specialty plasma products
- 3 rMAbs going into the clinic
- Zenyth integration

Merck's HPV GARDASIL®

GARDASIL®
[Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine]

- http://www.merck.com/newsroom/webcast/

- Accelerated approval in US, EU and 18 other markets for 9-26
- Broad indication for cervical cancer, genital warts and related HPV diseases
- Unanimous ACIP recommendation in the US
- Broad vaccination endorsement by professional societies
- US State efforts to achieve high immunization rates
- Reimbursed by plans covering 94% managed care lives
- States/cities covering 80% of public sector under Vaccines for Children program
- Widespread scientific presentations/publications of clinical evidence

CSL™

Merck's HPV GARDASIL®

GARDASIL®
[Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine]

- Expectation of Gardasil launches in more than 65 markets by end 07
- Product and disease awareness continues to increase. In US 50% of targeted customers now identify HPV as cause of cervical cancer vs 5% previously
- Plan to capitalize on lead to market for other populations in addition to launch market (females 9-26)
  - Estimates of market sizes:
    - Launch market – females (9-26) 118M;
    - Females (9-45) 264M;
    - Females (9-45) plus Males (9-24) cumulative cohort with sequenced roll out 374M.

CSL™

GARDASIL®: Selected ongoing clinical programs

GARDASIL®
[Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine]

- Efficacy study in mid-adult women
  - Anticipated FDA submission 4Q07
- Efficacy program in males
  - Anticipated FDA submission 2008
- Cross-protection studies
- Concomitant use studies with other adolescent vaccines

CSL™

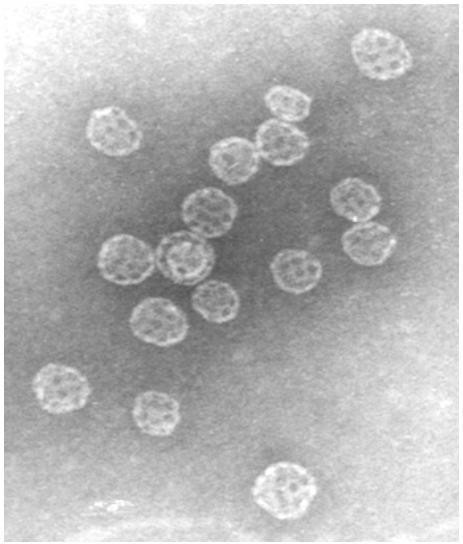
GARDASIL®: Competitive Differentiation

- First and only HPV vaccine on the market
- Proven cervical cancer protection
- Broadest cancer protection – cervical cancer, precancerous or dysplastic lesions, and genital warts caused by HPV types 6, 11, 16 and 18
- Proven 4 years+ duration of protection and immune memory

ISCOMATRIX® ADJUVANT

ISCOMATRIX® adjuvant meets all criteria for inclusion in new human vaccines

- Immunomodulator and antigen delivery
- Safe and immunogenic in humans
- Long lasting antibody and T cell responses
- Dose sparing capability
- “Industrialised”



Multiple value drivers for ISCOMATRIX® adjuvant

- Licenses
  - Upfronts
  - Milestones
  - Royalties
    - Patents
    - Know-how
- Worldwide supplier
- Internal vaccine development programs

Wyeth to use ISCOMATRIX® adjuvant

- License and option agreement
- Number of fields
- Upfronts and milestones >US$90m
- Product royalties
- Exclusive supply

ISCOMATRIX® adjuvant underpins Merck's vaccine development programs

- Aug05 Licence and Option Agreement
- Dec06 additional options added
- Upfront payment and milestones
- Royalties on products
- Distribution rights
- Exclusive supply
- Two clinical programs have been initiated

ISCOMATRIX® adjuvant being manufactured at commercial scale at Kankakee

- Facilities and expertise
- ISCOPREP® saponin
  - pilot scale
  - commercial scale
- ISCOMATRIX® adjuvant
  - commercial scale
    - process being tech transferred

Influenza Vaccine Program

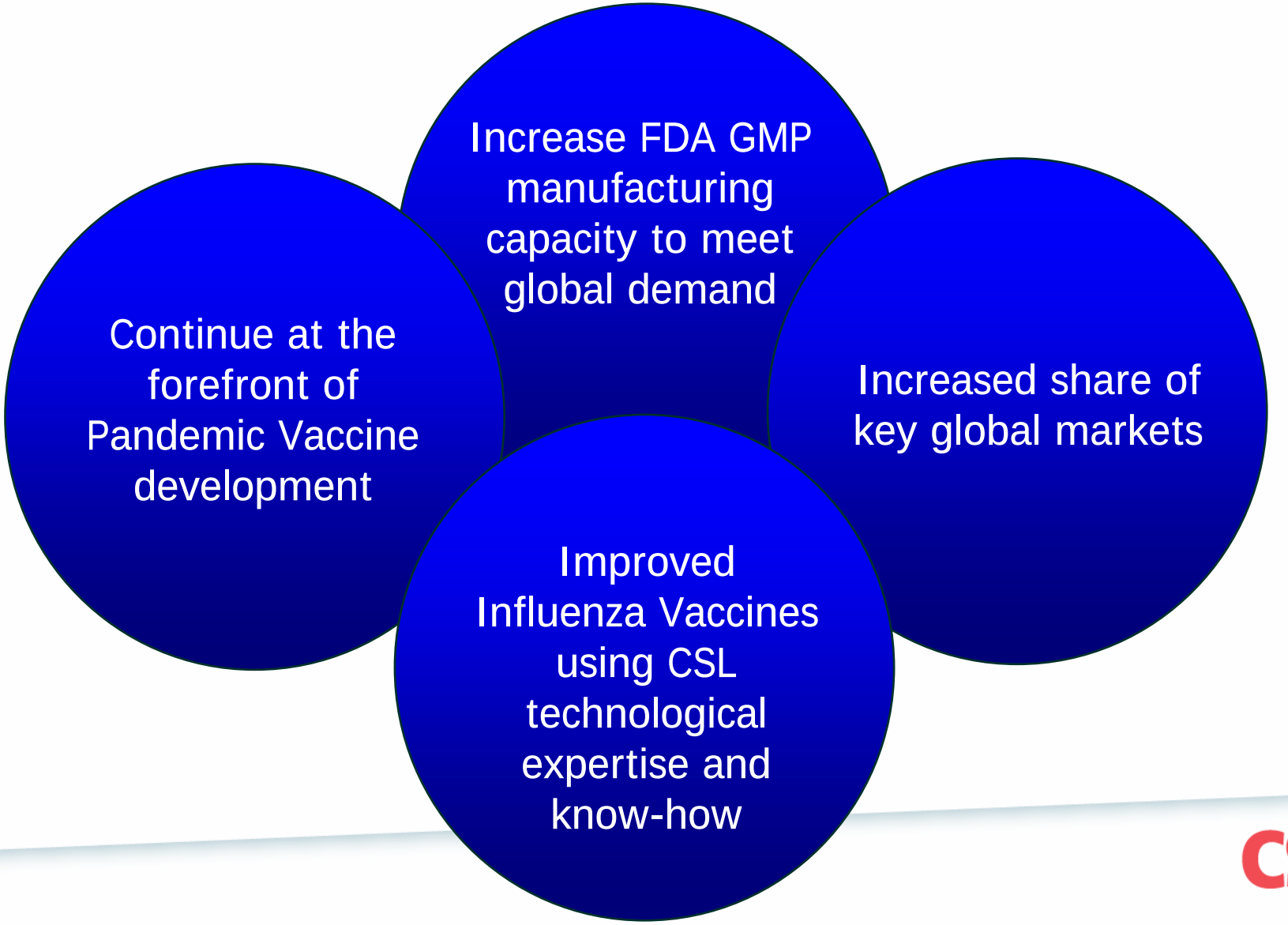
14 December 2006

Global Influenza Vaccine Business

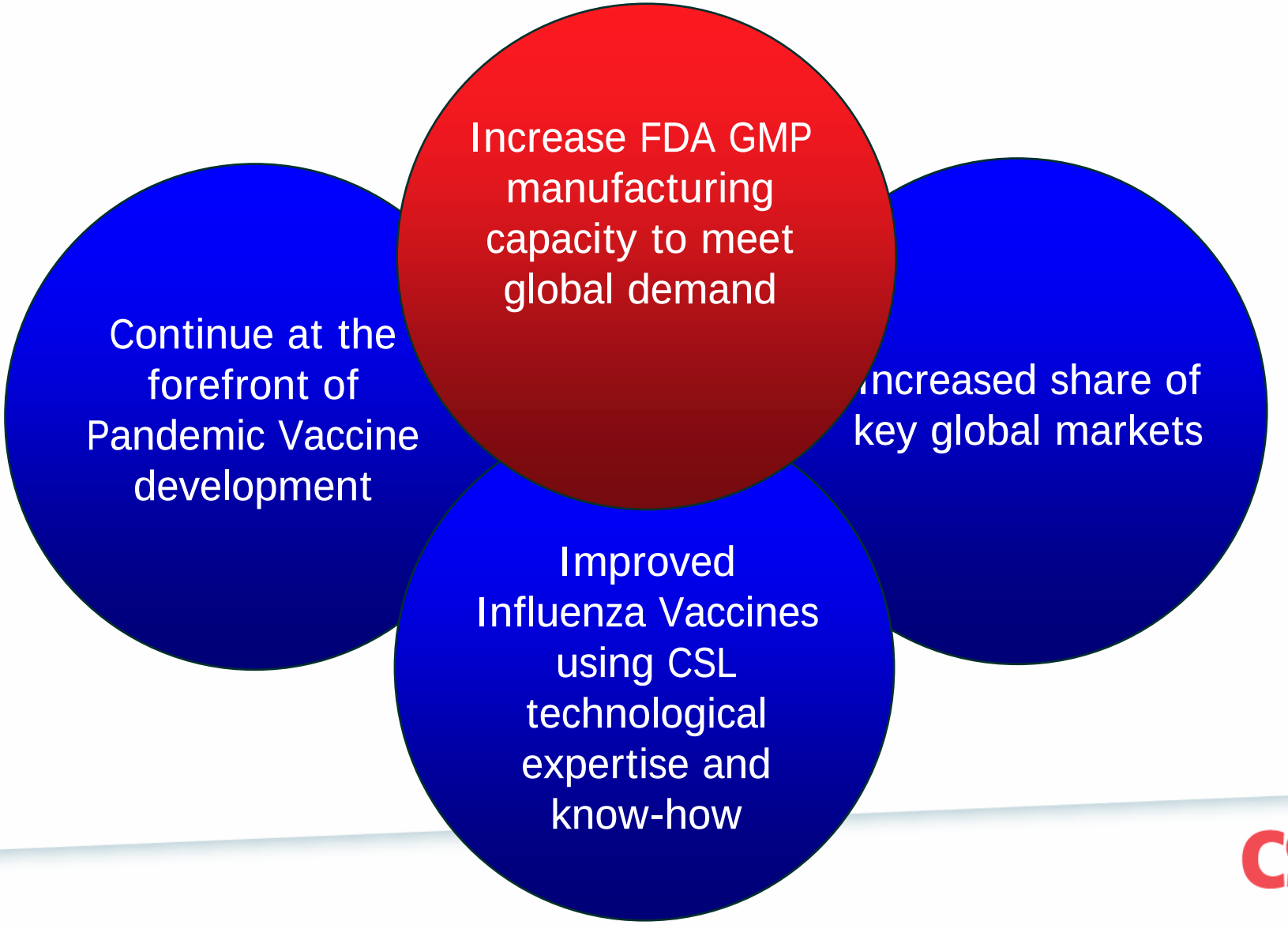
- Manufactured influenza vaccine since 1968
- Leading provider and sole manufacturer of flu vaccine in Southern Hemisphere
- CSL flu vaccines are licensed and sold in 16 countries worldwide

Buffer preparation area in CSL's new state-of-the-art influenza vaccine centre

Influenza Vaccine Strategy



Influenza Vaccine Strategy

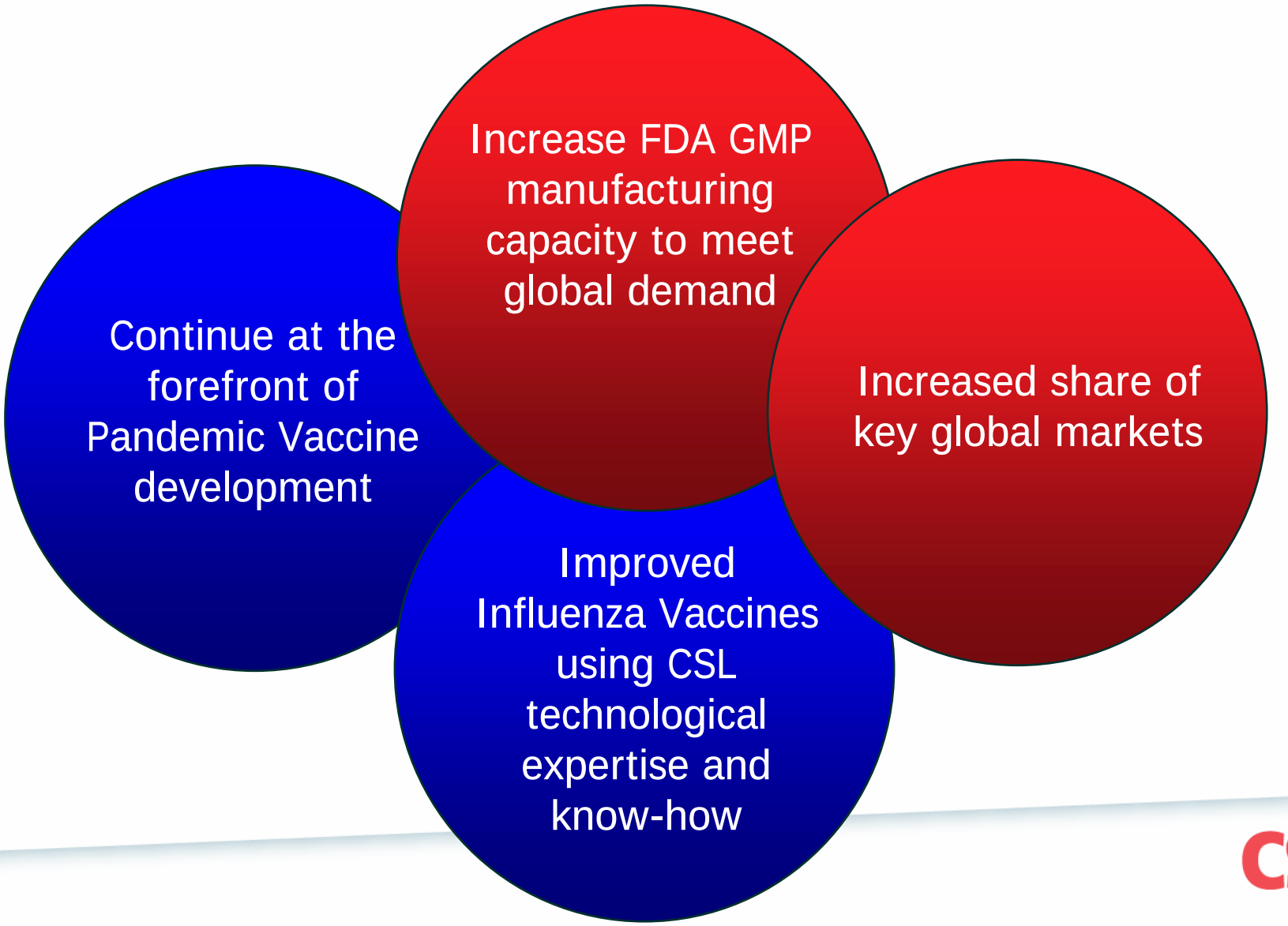


Influenza Vaccine Manufacturing Capacity

- Modern egg processing facility completed in 2004
- $80m investment to double vaccine capacity
  - Duplication of existing facility
  - NH capacity of ~40m doses

Egg harvesting machine in CSL's new state-of-the-art influenza vaccine centre

Influenza Vaccine Strategy



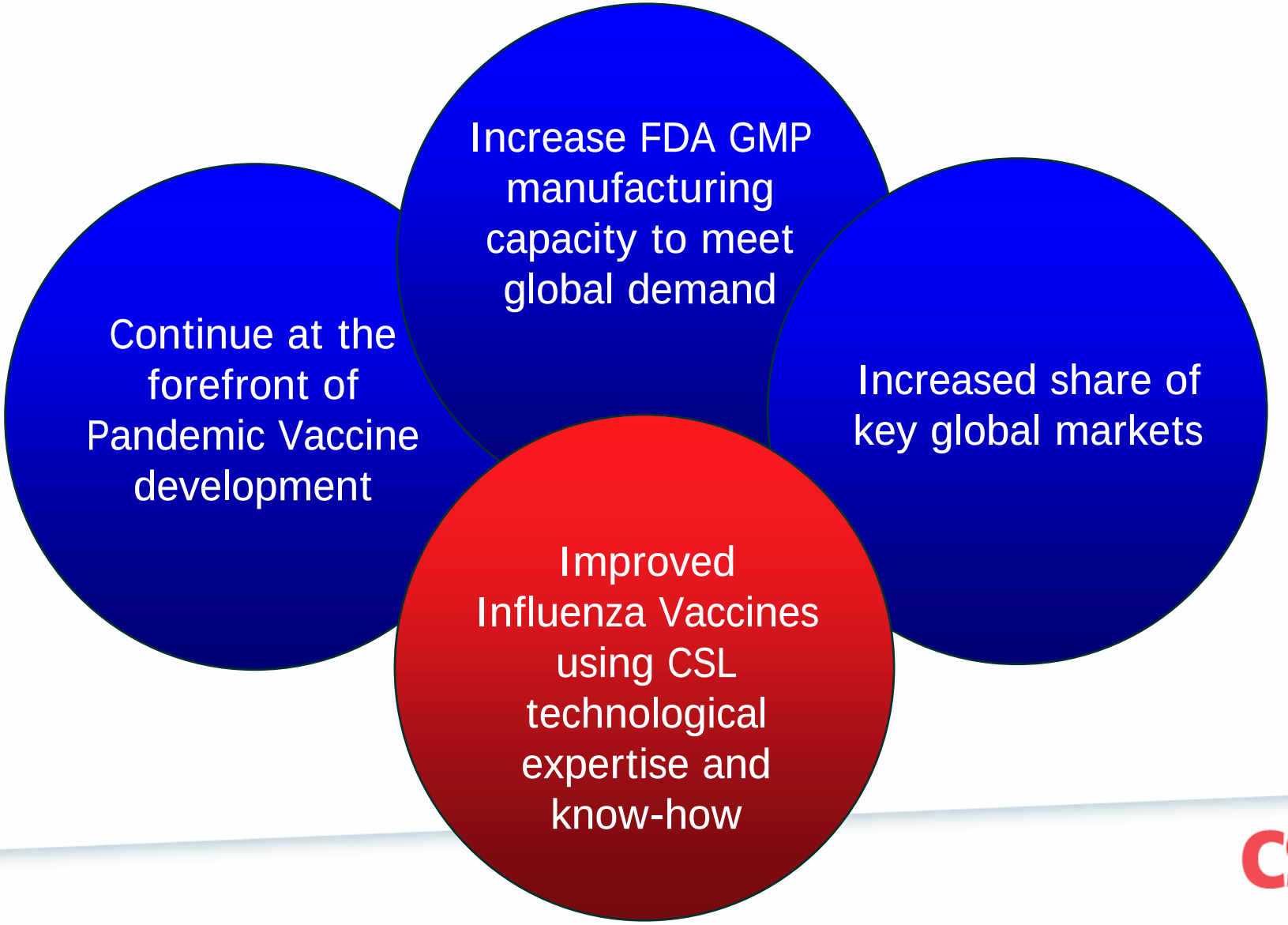
Global Influenza Vaccine Program

- Expand flu business
  - Enter the U.S., China and new markets in Europe
  - Meet regulatory and clinical requirements for each new market
  - Increase share of key global markets
- Utilise resources and capability of CSL Biotherapies to market and distribute vaccine

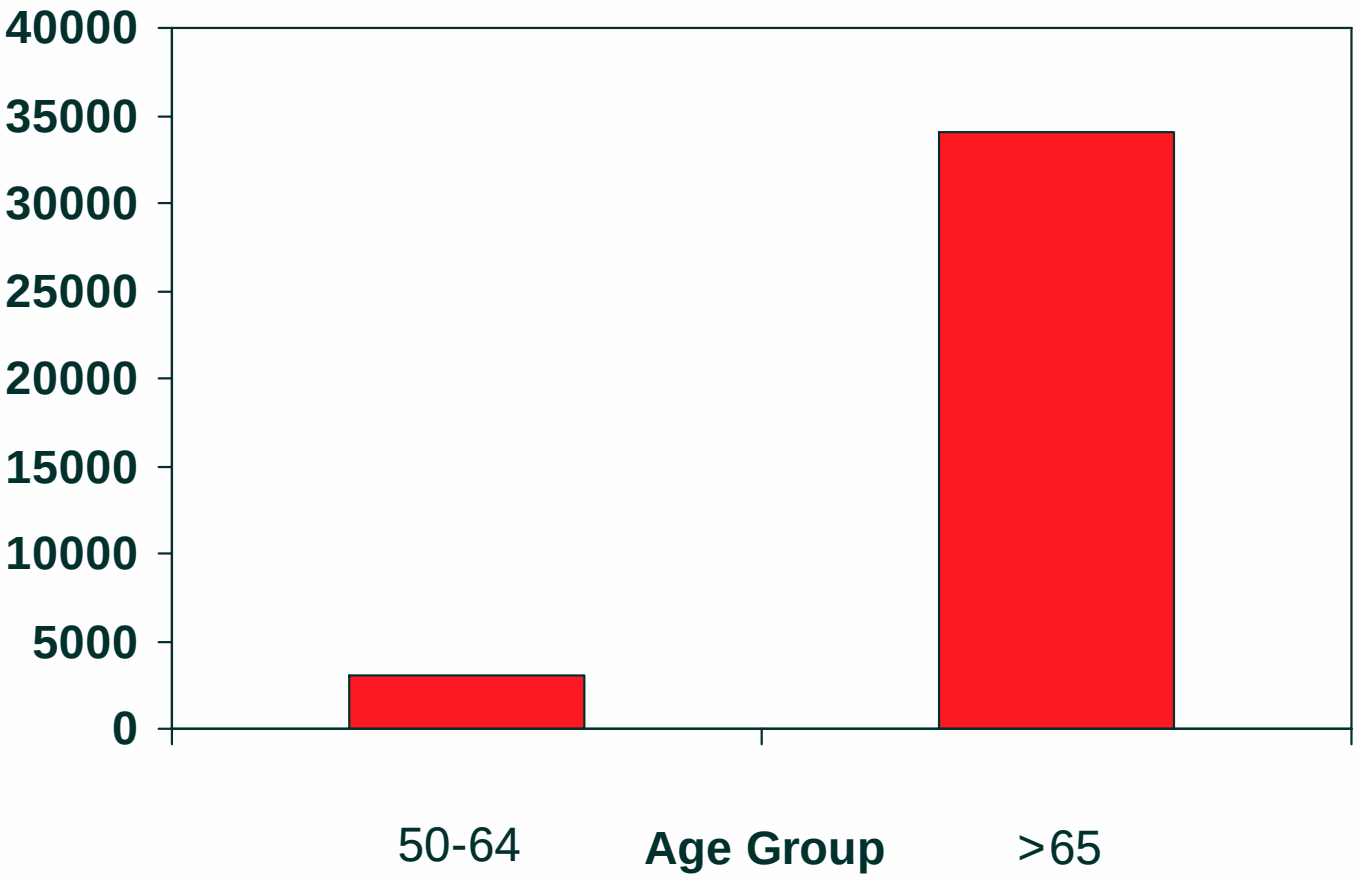
United States

- IND filed April 2006
  - Pivotal Clinical Trial completed
  - 1359 subjects recruited
  - Immunogenicity criteria met
- BLA submission end Q1 2007
- Launch 2007/08 winter season (contingent upon regulatory approval)

Influenza Vaccine Strategy



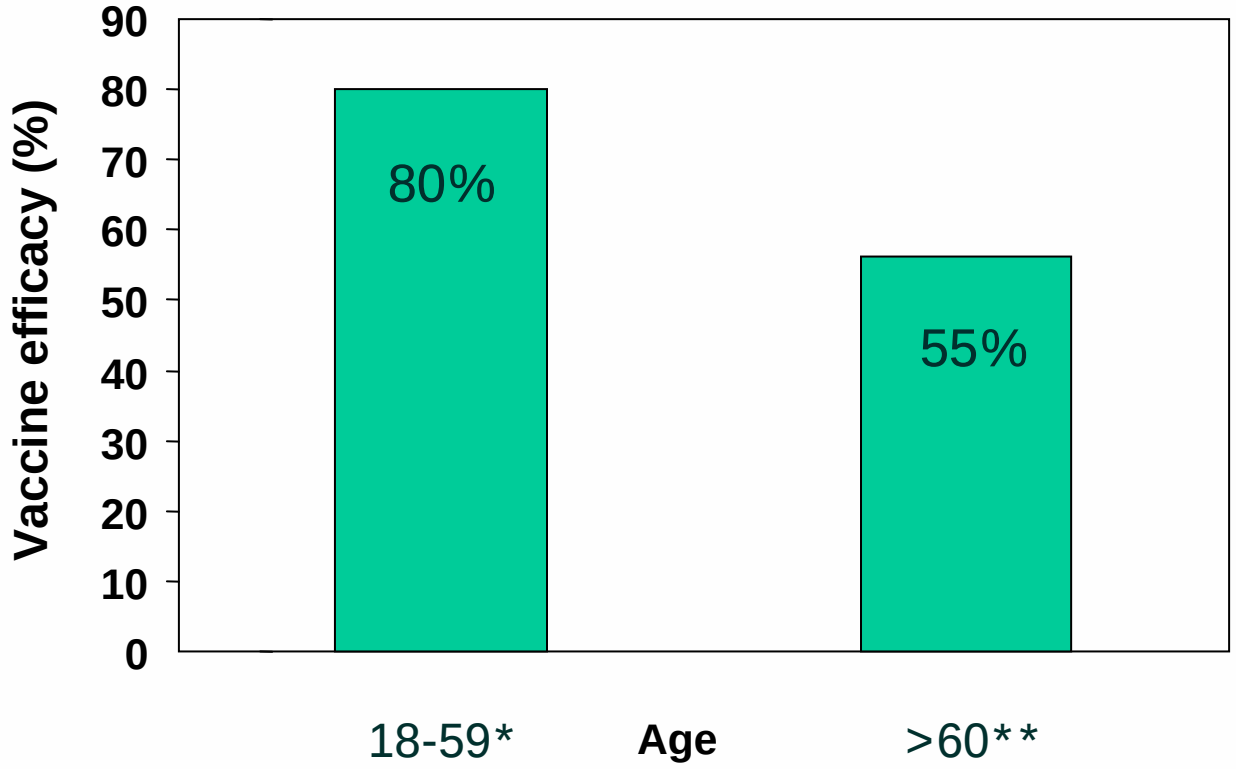
Annual Flu-Related Deaths - US



Elderly have 13-fold higher risk of death from flu than ages 50-64

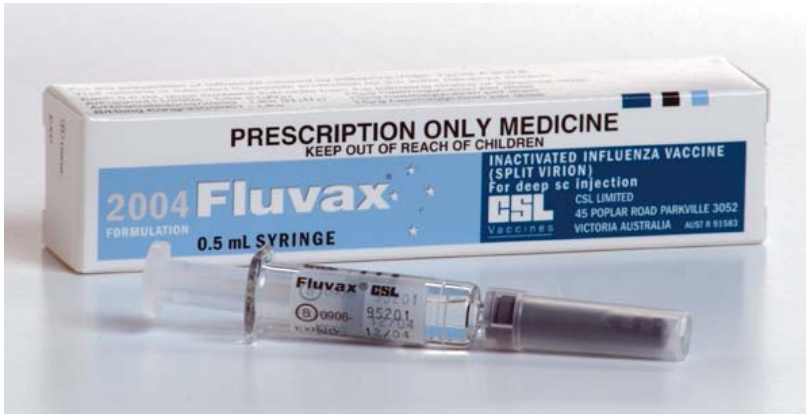
Source: CDC (www.cdc.gov)

Current Flu Vaccines Less Effective in Elderly



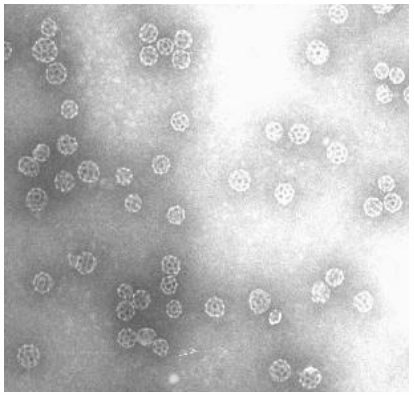
*Source: CDC (www.cdc.gov)
**Source: Govaert, JAMA, 1994

Influenza ISCOMATRIX ® Vaccine



Global presence & expertise

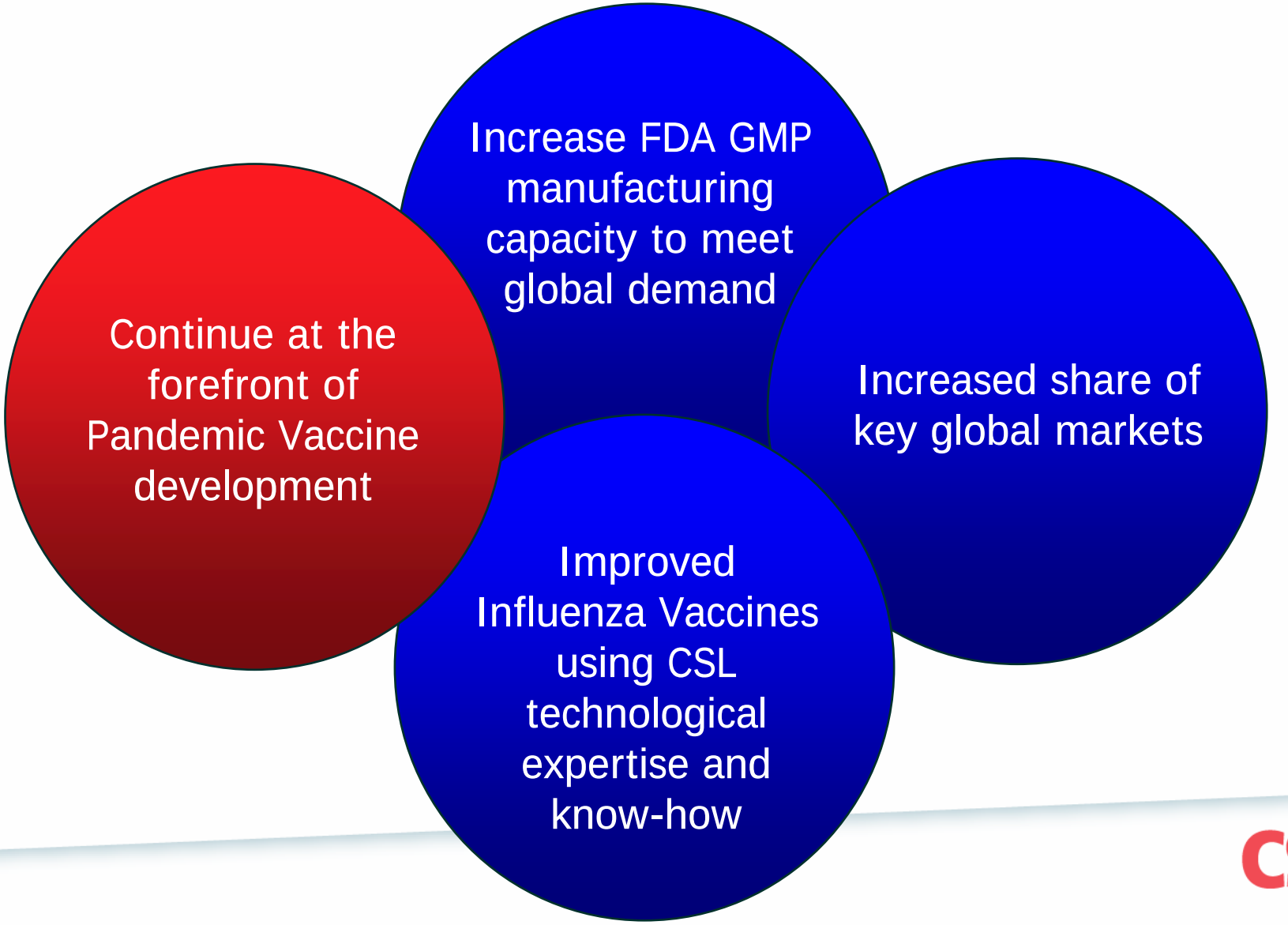
+



Proprietary ISCOMATRIX® adjuvant & expertise

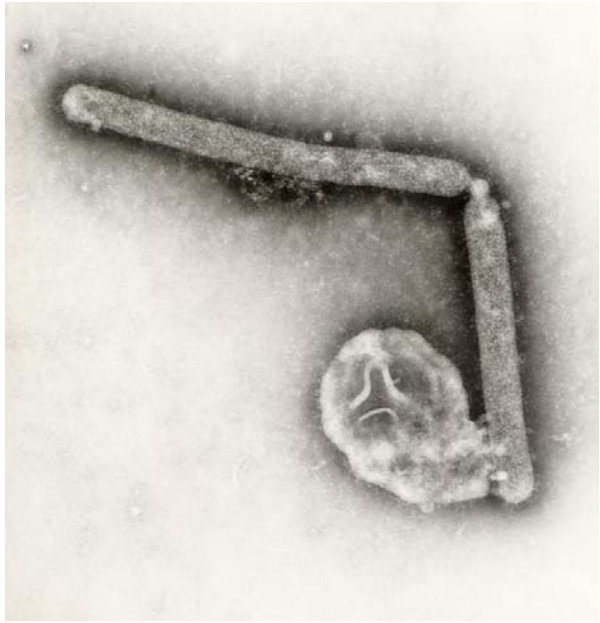
- Reduction of incidence of influenza-associated illness and mortality in people aged 65yrs and older
- Commence clinical program Q3 2007

Influenza Vaccine Strategy



Pandemic Vaccine Development

- Testing human immune response to avian influenza vaccine
- Using Aluminium adjuvant with long and safe history of use
- First Trial
  - Excellent safety and tolerability
  - Two doses of vaccine and an adjuvant required to achieve a satisfactory immune response

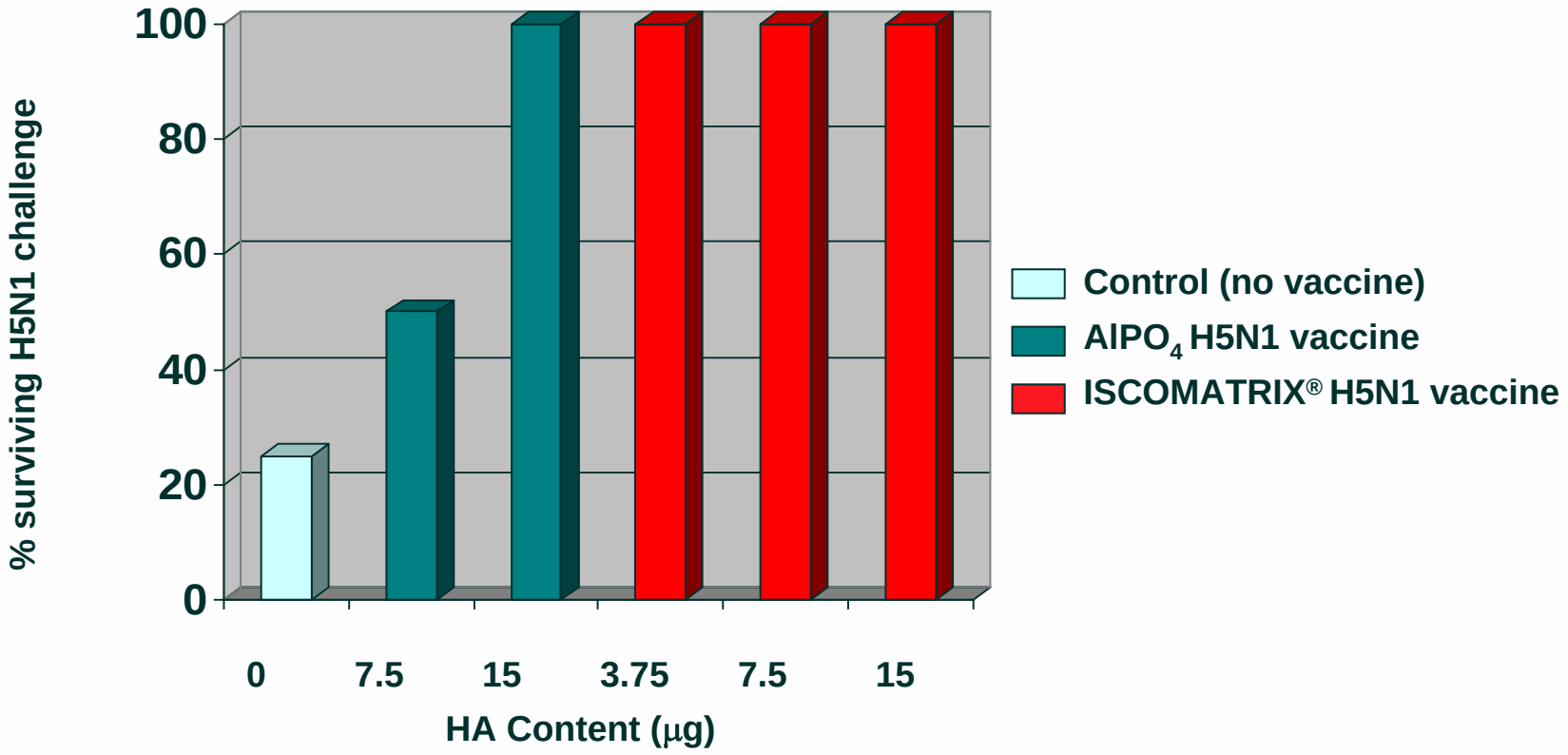


Transmission electron micrograph of 2 H5N1 virions. Source: CDC Public Health Image Library.

Pandemic Vaccine Development cont.

- Further trials to support registration of ‘prototype’ vaccine
  - Higher doses of antigen
  - Broader population base
- Drivers for approach
  - Generate understanding of immunogenicity and safety of range of antigen doses
  - Develop body of data to guide policy decisions

H5N1 Challenge in Ferrets using an ISCOMATRIX® H5N1 Vaccine*



* NHMRC Avian Influenza Pandemic Research Grant
Participants: UniMelb, CSIRO, WHO CC for Influenza, CSL Limited

ISCOMATRIX® H5N1 Vaccine

- Potential for:
  - Antigen Sparing
  - Increased duration of immune response
  - Cross reactivity with other H5N1 clades
- Clinical Development
  - Commence clinical program 2007
  - Assess range of antigen doses

Influenza Vaccine Program

- Expansion of business into key global markets
- Evaluation of improved influenza vaccines
- Development of pandemic influenza vaccines

Dr. Simon Green

General Manager

CSL Behring, GmbH

Marburg, Germany

Plasma R&D Centres of Excellence

Marburg GER

Haemophilia
Wound Healing
Specialty Products

Bern CH

Immunoglobulins
rHDL

Kankakee USA

Alpha-1 Proteinase Inh.

Broadmeadows AUS

Product Support
Technical Innovation

King of Prussia USA

US Clinical, Regulatory
& Pharmacovigilance

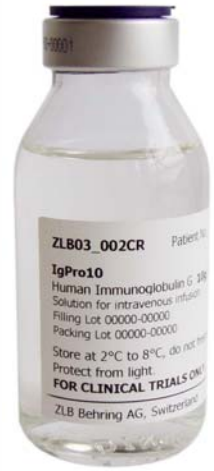
Tokyo JPN

JPN Clinical & Regulatory

Immunoglobulins

Clinical Phase I - Phase III	Regulatory Review	Approved
Liquid IVIG	12% Liquid	**11 Countries**
	10% Chrom	
Liquid SCIG		Vivaglobin®
Chrom SC		
HyperImmunes *HDN*	Rhophylac	**26 Countries**
New indication, ITP	Rhophylac	
		CytoGam

Liquid IVIG



Chromatographic 10%

- Clinical program based on PID and ITP
- BLA submitted Sept 06. Accepted for filing, Nov 06
- Global registration program to start in Jan, 2007

Sandoglobulin® Liquid 12%

- Successfully marketed in 11 European countries
- Registrations received in Canada & Australia
- BLA review process ongoing
- US focus likely to shift the high yielding chromatographic liquid

CSL™

Liquid Sub Cutaneous IgG

Vivaglobin®

- 16% liquid formulation
- Successfully marketed in 20 EU countries, USA and Canada for PID
- First subcutaneous product licensed in the USA
- Excellent feedback from patients – home therapy

Chromatographic SC

- High yielding process
- Phase III clinical trials commenced

HyperImmune Immunoglobulins

Rhophylac®

- Indicated for Haemolytic Disease of the Newborn
- Approved in 26 countries. 11 more countries in progress
- New indication: Chronic Immune Thrombocytopenic Purpura (ITP)
- BLA efficacy supplement for ITP accepted for filing by FDA, Aug 06

CytoGam®

- Cytomegalovirus (CMV) immune globulin
- Acquired from Medimmune, Dec 06
- Prophylaxis against CMV disease associated with transplantation of the kidney, lung, liver, pancreas and heart.

Haemophilia – Humate® P / Haemate® P

Needleless transfer device

Mix-2-Vials successfully launched

(Helixate, Beriate & Berinin)

Volume Reduction

Approved in 22 countries

Indication for vWD & Surgery

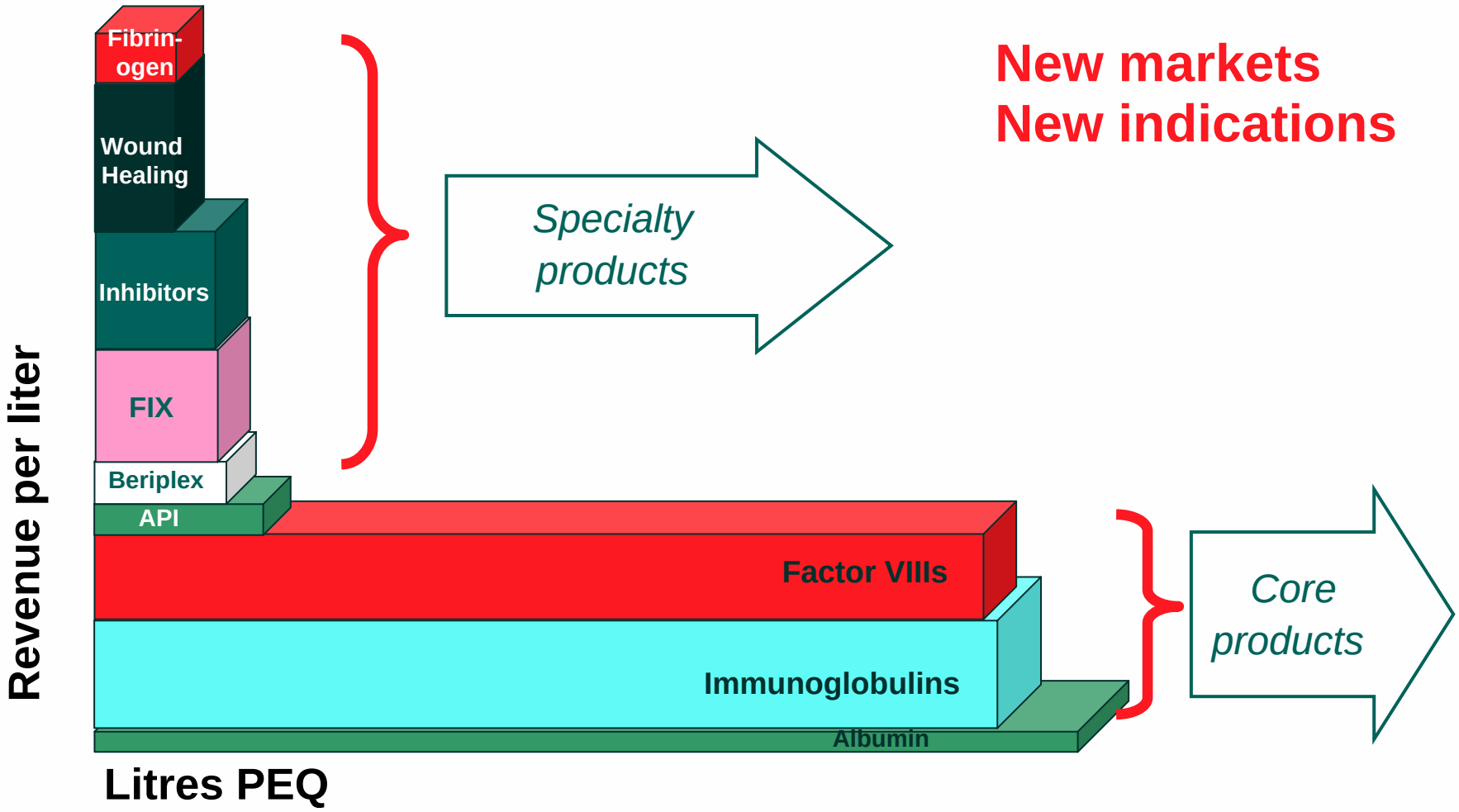
Humate® P

Interim label claim approved

BLA efficacy supplement submitted, Jun 06

2006 2007 2008

Opportunities for Growth



Specialty Products – New Markets

Beriplex® P/N

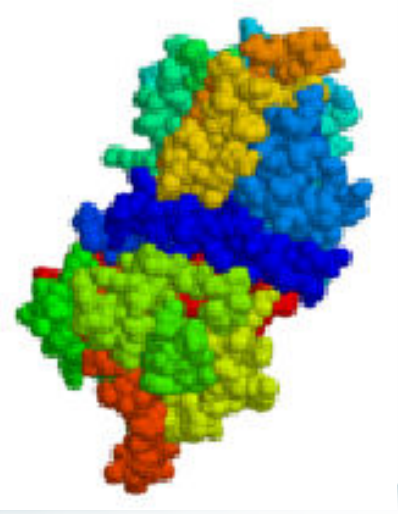
- Indicated for acquired bleeding deficiency (ie. Warfarin reversal)
- Expansion of European market
- Phase III clinical trial complete
- Regulatory process initiated

Berinert ® P

- C1 esterase inhibitor indicated hereditary angioedema
- Expansion into both USA and EU markets
- Phase III clinical trial ongoing

Zemaira ®

- Indicated for Alpha1 Proteinase Inhibitory Deficiency
- FDA Phase IV post approval commitment
- Clinical data to support European registration



Recombinant Antibody Portfolio

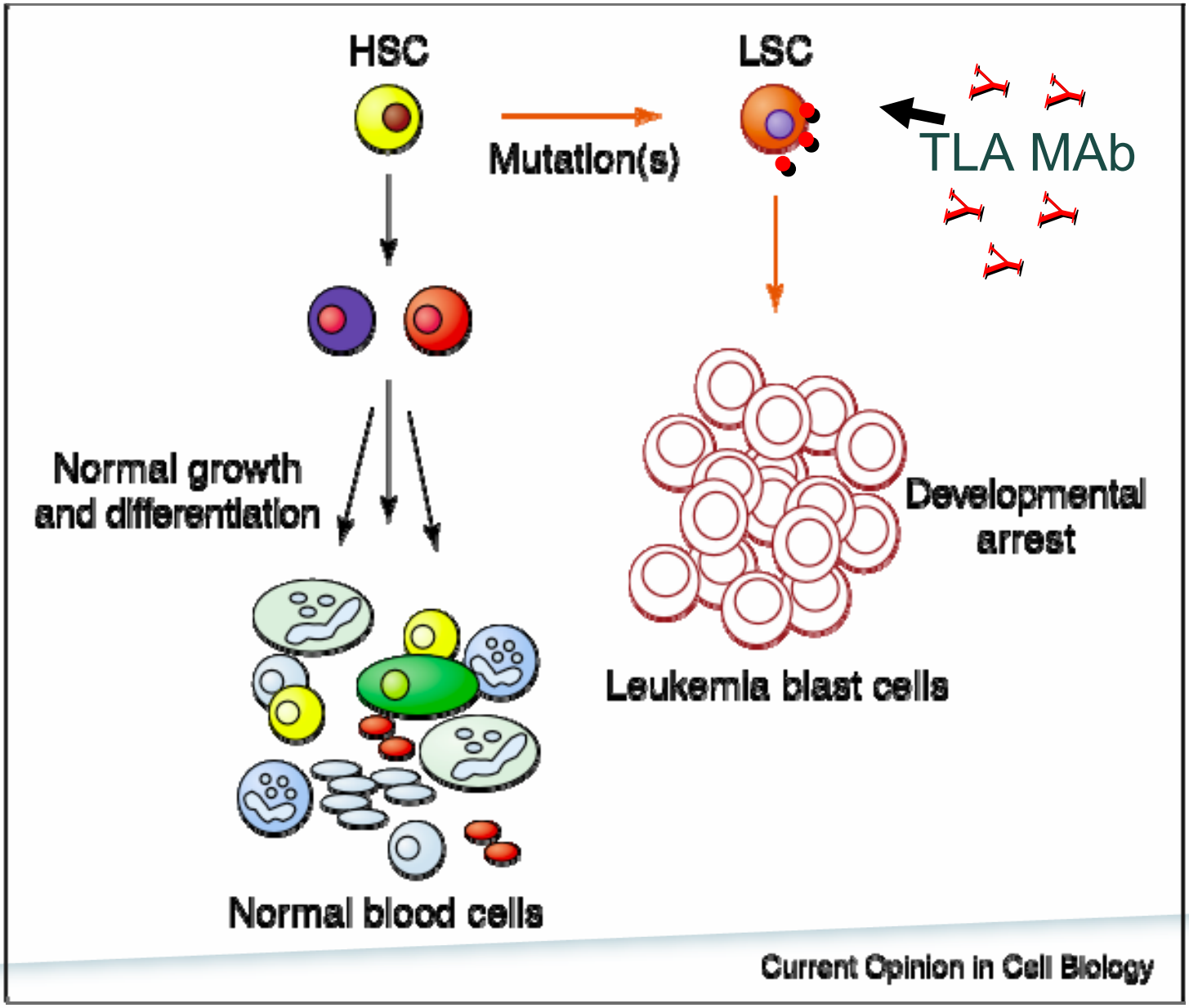
Therapeutic Leukaemia Antibody (TLA)

Therapeutic Leukaemia Antibody (TLA)

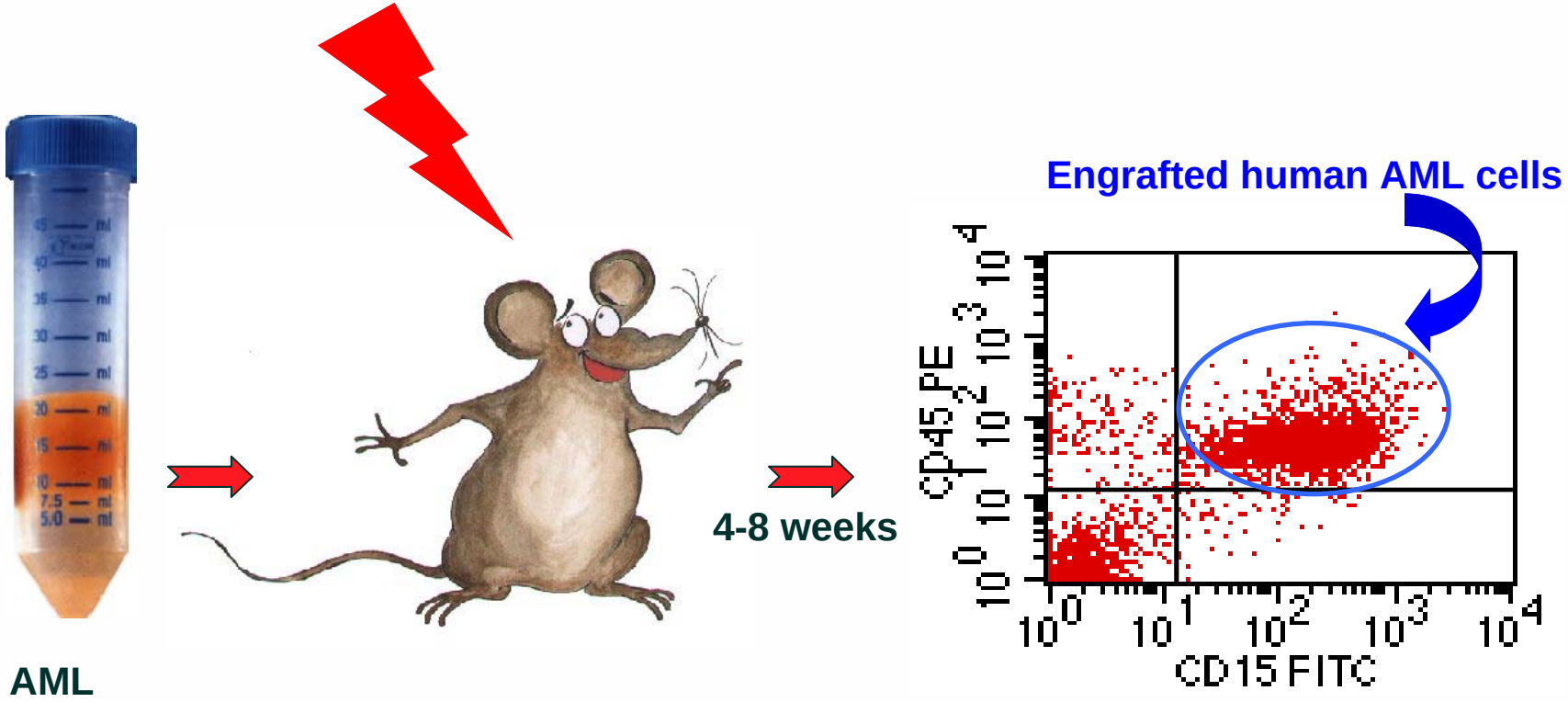
- **Acute Myeloid Leukemia**
- Anaemia, infection, bleeding
- US incidence 10,500
- 18% 5 year survival, often only months
- First line therapy chemo +/- BMT
- 80% relapse / refractory
- Limited treatment options

- IP from Australian academic collaborator
- Target is differentially expressed between leukaemia and normal blood cells
- Correlation with poor outcome
- Target common to all types of AML
- Parent antibody effective in disease models
- Human compatible antibody ready for AML patient clinical trial in 2007

TLA Therapeutic Concept



In vivo Leukaemia Assays



Engraftment: AML stem cells initiate human leukemia when transplanted into irradiated NOD/SCID mice. Quantitative assay for AML stem cells.

Status: Therapeutic Leukaemia Antibody

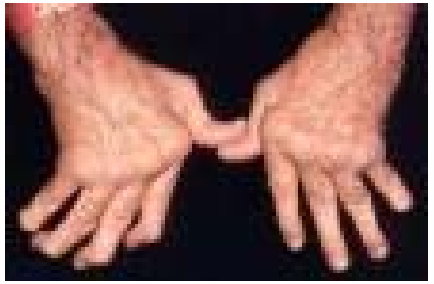
- Effective in models of leukaemia
- Antibody modified for human therapeutic use
- CHO cell line scale up completed
- Safety determined in primate toxicity studies
- IND filing completed
- Phase I clinical safety trial in AML patients aimed for 2007

GM-CSFr and IL13r MAbs

GM-CSFR – Rheumatoid Arthritis

Rheumatoid Arthritis (RA)

- Chronic inflammatory disease of the joints
- 2.4 million treatable RA patients in the US (2006)
- First line therapies include DMARDS such as methotrexate
  - 33-49% achieve ACR50
- Biological DMARDS
  - anti-TNF's (Enbrel, Remicade, Humira)
  - 50% achieve ACR50
- Market opportunity – anti-TNF inadequate responders

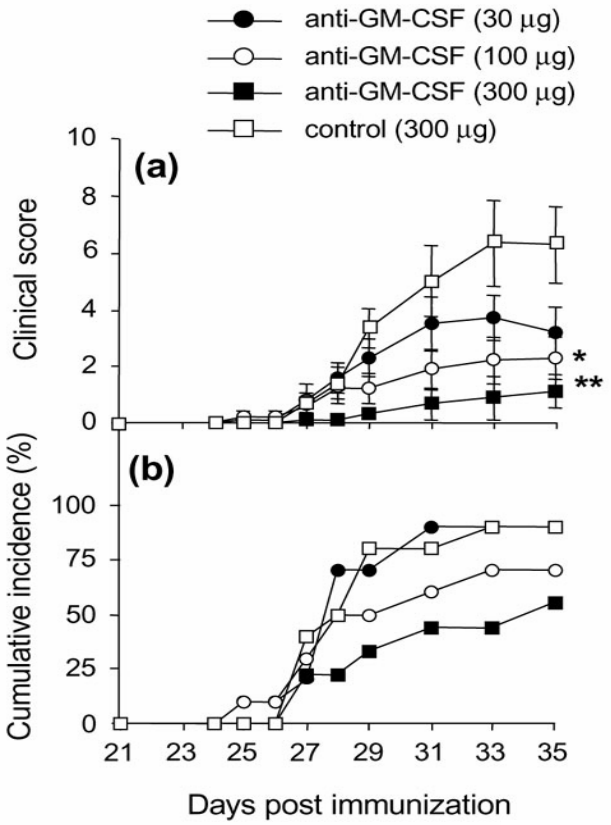


GM-CSFR – Rheumatoid Arthritis

GM-CSF and rheumatoid arthritis

In animal models of RA

- GM-CSF antibodies inhibit disease
  - inflammation and cartilage destruction
  - TNFα and IL-1β levels
- Animals genetically modified to lack GM-CSF are resistant to the development of RA
- GM-CSF administration exacerbates RA



From Cook *et al* Arthritis Res. 2001, 3:293-298

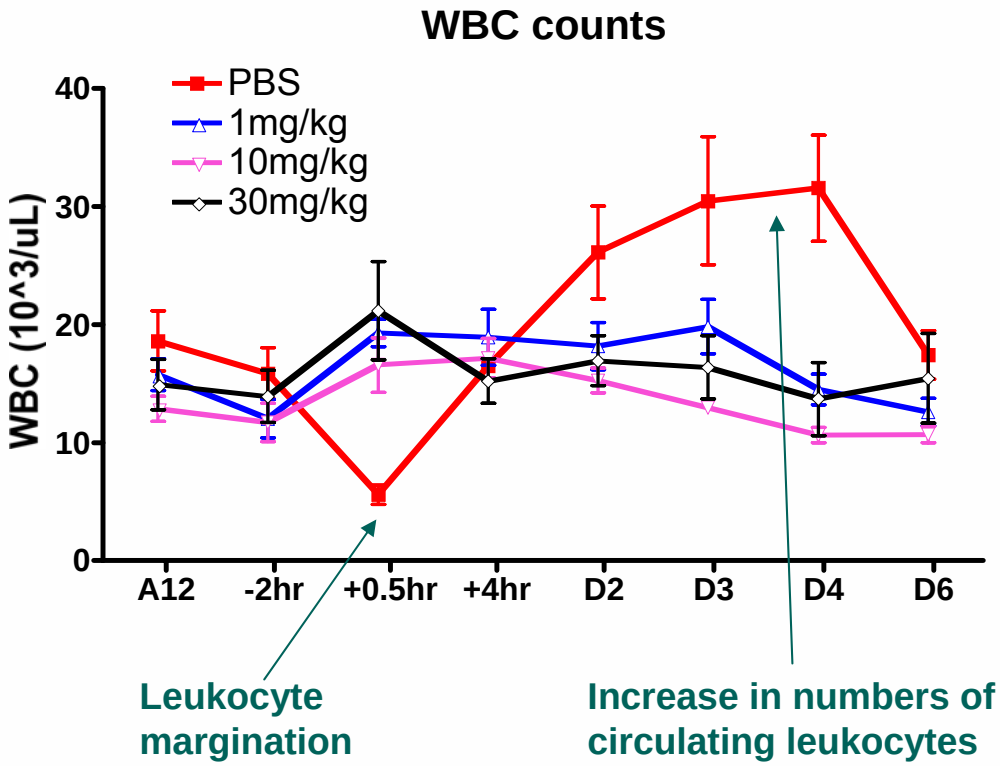
GM-CSFR – Rheumatoid Arthritis

A GM-CSFR antibody for the treatment of RA

- Zenyth holds granted target related IP
- Partnered with Cambridge Antibody Technology (Dec 01)
- CSL and CAT to share costs of drug development
- CAT Phage Display technology to generate human antibodies
- An optimised lead antibody has progressed into manufacturing and preclinical development (CAM-3001)

GM-CSFR – Rheumatoid Arthritis

CAM-3001 is a potent inhibitor of the response to GM-CSF in non-human primates



GM-CSFR – Rheumatoid Arthritis

CAM-3001 – a GM-CSFR antibody for the treatment of RA

- Antibody generation and optimisation completed
- Cell-line development / manufacturing in progress
- *In vivo* confirmation of antagonist activity completed
- Formal preclinical toxicology in progress
- Phase I clinical studies planned to commence mid-2007

IL-13R – Asthma

Asthma

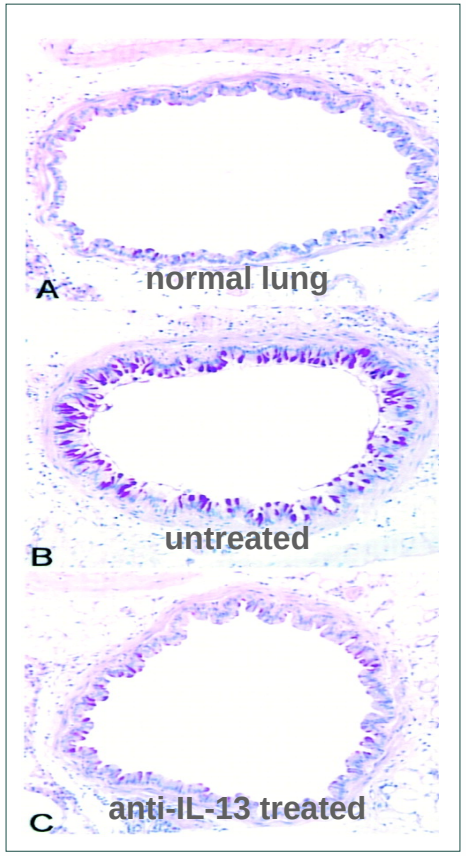
- Chronic inflammatory disease of the lungs
- Affects 20 million people in the US (2005), 5000 deaths annually
- First line therapies include β_2-agonists and inhaled corticosteroids
- New therapies
  - leukotriene receptor antagonists (Singulair)
  - biologicals (Xolair)
- Market opportunity – severe persistent asthma (5-10%)

IL-13R – Asthma

IL-13 and asthma

In animal models of asthma

- IL-13 antagonists inhibit disease
  - eosinophilic inflammation
  - airways hyperresponsiveness
  - mucus hypersecretion
- Animals genetically modified to lack IL-13 are resistant to the development of asthma-like pathology
- IL-13 administration induces asthma-like pathology



From Wills-Karp *et al*. 1998
Science 282:2258

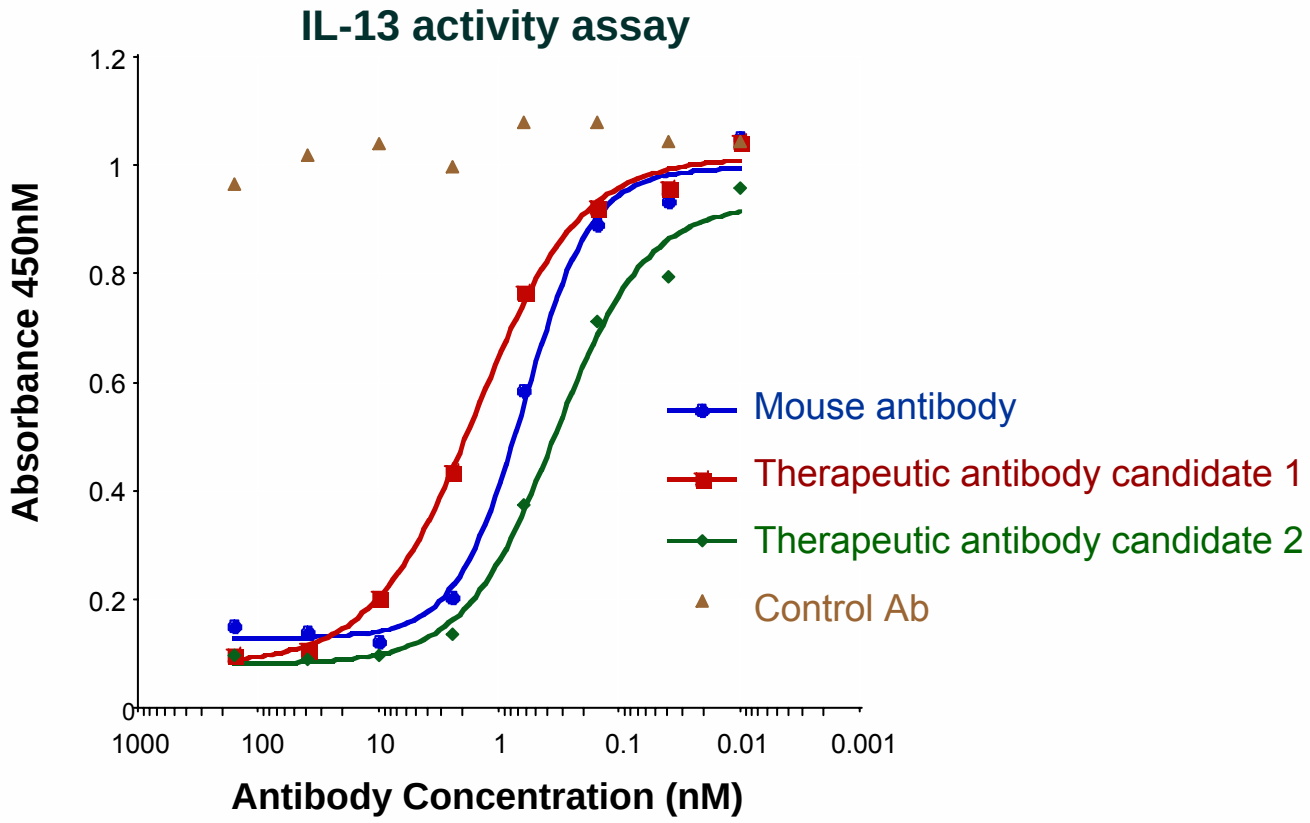
IL-13R – Asthma

An IL-13R antibody for the treatment of asthma

- Zenyth holds target related IP (WEHI, CRC-CGF)
- Licensed to Merck and Co., Inc in June 2003
- Zenyth / Medarex license agreement, May 2003
- An optimised lead antibody has been generated and progressed into development
- Further preclinical and clinical milestone payments plus royalties
- Future drug development costs to be met by Merck

IL-13R – Asthma

Antibodies directed against IL-13Rα1 are potent inhibitors of IL-13 activity



IL-13R – Asthma

An IL-13R antibody for the treatment of asthma

- Antibody generated and optimised
- Cell-line development / manufacturing underway
- Preclinical development in progress

SUMMARY / Q&A

ANDREW CUTHBERTSON

R&D Portfolio