R&D Briefing

December 10, 2009

Draft Agenda with timings
December 2009 R&D Briefing

830-9am		Sign in and coffee
9-905am	Welcome	Mark Dehring
905-930am	Introduction and highlights	Andrew Cuthbertson
930-10am	Plasma Replacement Therapies	Val Romberg
10-1015am	rCoagulation Products	
1015-1030am	Q&A	Val and Andrew
1030-1050am	Break	
1050-1110am	rHDL	Sam Wright
1110-1130am	Therapeutic proteins (rMAbs)	Andrew Nash
1130-1145am	News – Flu, IMX, Context	Andrew Cuthbertson
1145-noon	Summary highlights, Q&A	

Agenda December 2009 R&D Briefing

830am: Sign in and coffee

• Welcome	Mark Dehring
• Introduction and highlights	Andrew Cuthbertson
• Plasma Replacement Therapies	Val Romberg
• rCoagulation Products	
• Q&A	
• 20 Minute Break	
• rHDL	Sam Wright
• Therapeutic proteins	Andrew Nash
• Influenza vaccines	Andrew Cuthbertson
• Summary highlights, Q&A	

Noon: Finish

R&D Strategy

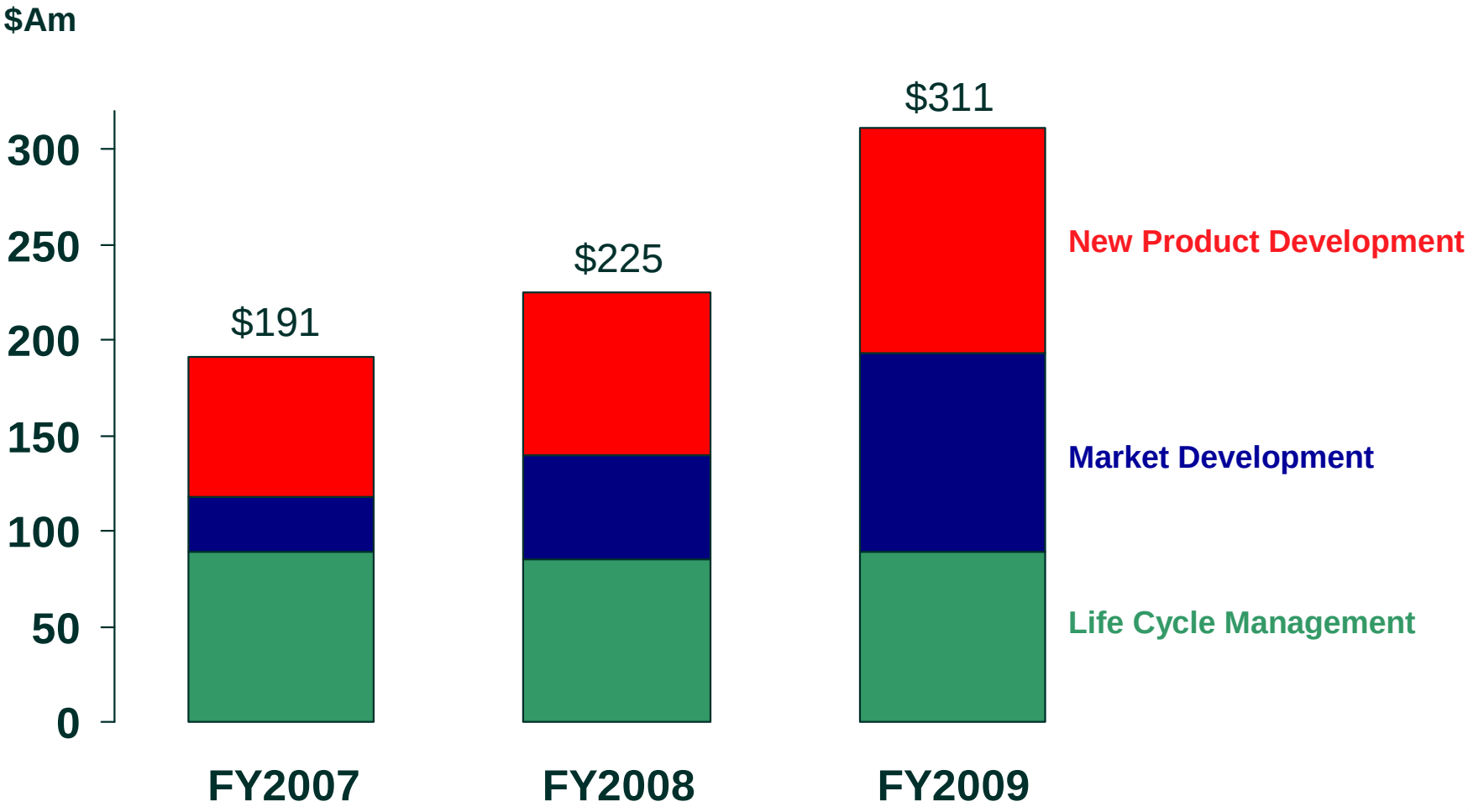
- Maintain commitment to extracting maximum value from existing assets and supporting and improving current products
- Develop new protein-based therapies for treating serious illnesses focusing on products that align with our technical and commercial capabilities

Dr Klaus Schmitt and laboratory assistant, Irina Steinbrecher carrying out a protein composition check on a sample of Haemocomplettan(r), one of the critical care therapies manufactured at CSL Behring's Marburg site.

R&D Integral to Company Strategy

R&D Investment

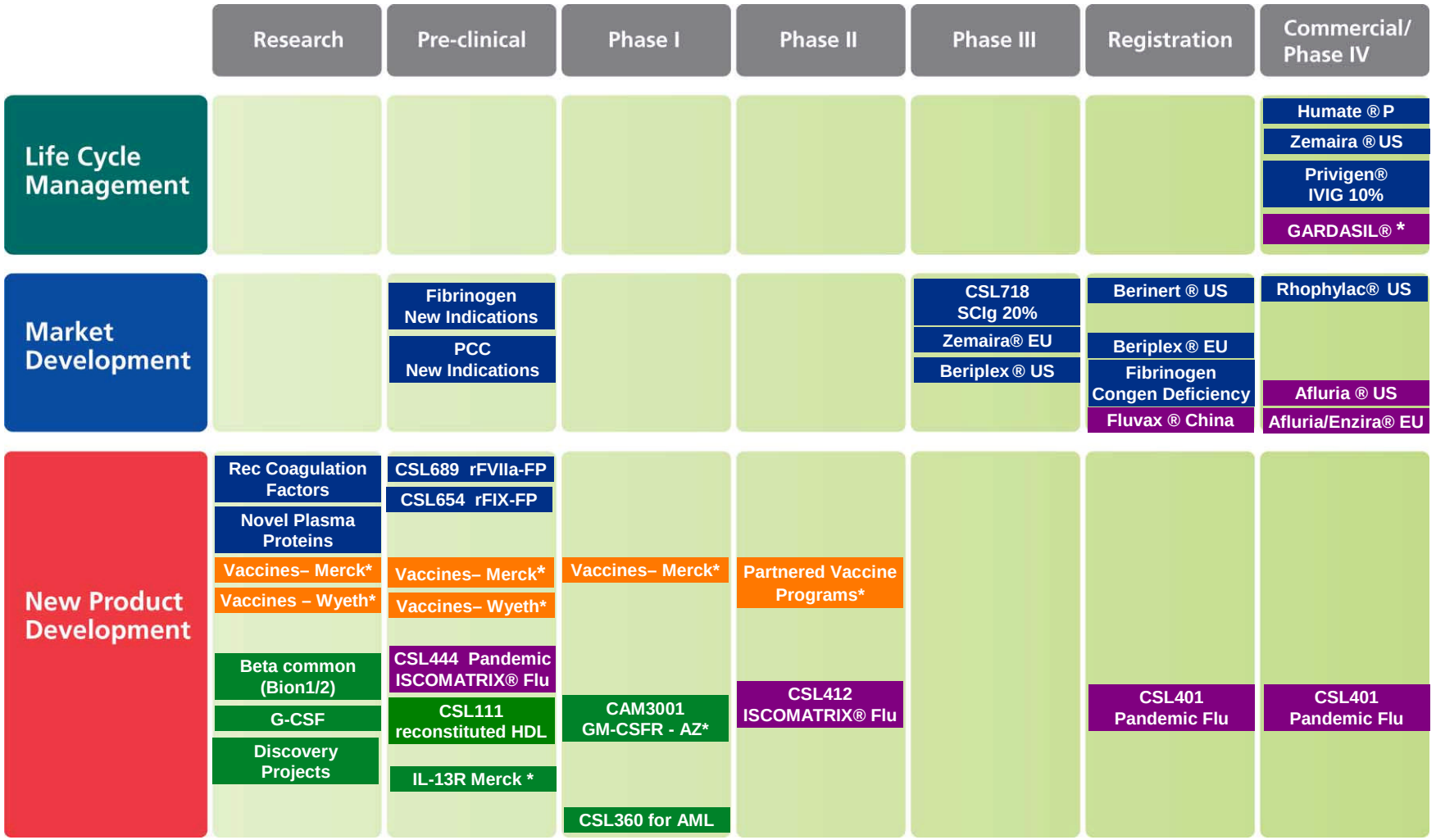
Growth in new product and market development



Focus Areas


Protein Replacement Therapies
Therapeutic Proteins
Immunomodulators/ Vaccines

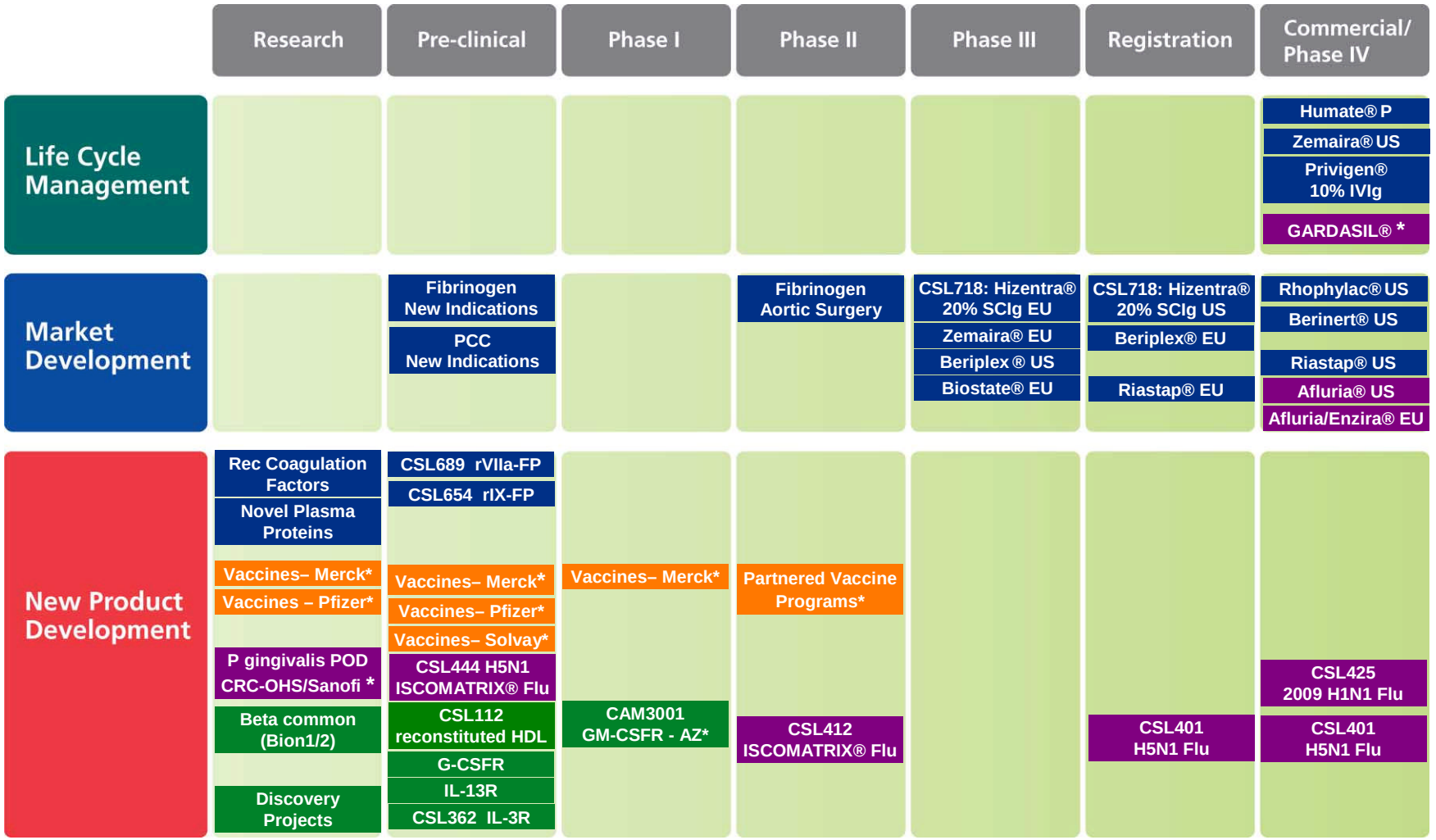
Global R&D Pipeline December 2008



Core Capabilities: Replacement Therapies | Vaccines | Immunomodulators | Therapeutic Proteins

* Partnered Projects

Global R&D Pipeline December 2009

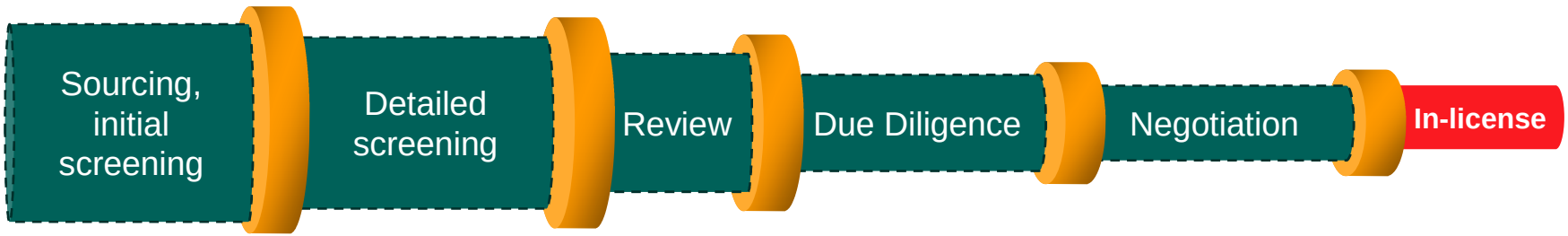


Core Capabilities: Replacement Therapies | Vaccines | Immunomodulators | Therapeutic Proteins

* Partnered Projects

Global R&D: Integrated R&D Facilities

Building Quality R&D Pipeline



GARDASIL® Update

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

- New indication: Adult Women
  - Approved in Australia for women up to 45 years of age in April 2009
  - Based on efficacy data
- Efficacy data in males 16-26 (reduction of external genital lesions) submitted to TGA Q1 2009, approved in the USA in Oct 2009
- Clinical studies:
  - Male efficacy study in AIN and anal cancer ongoing
  - Multivalent HPV vaccine underway with anticipated regulatory filing in 2012
- US patents

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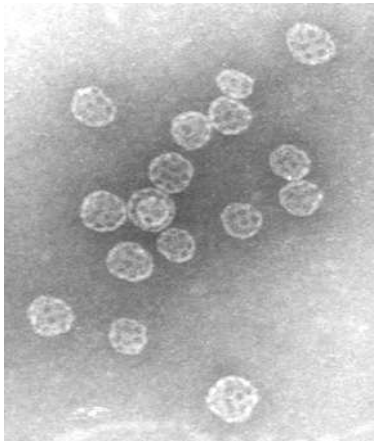
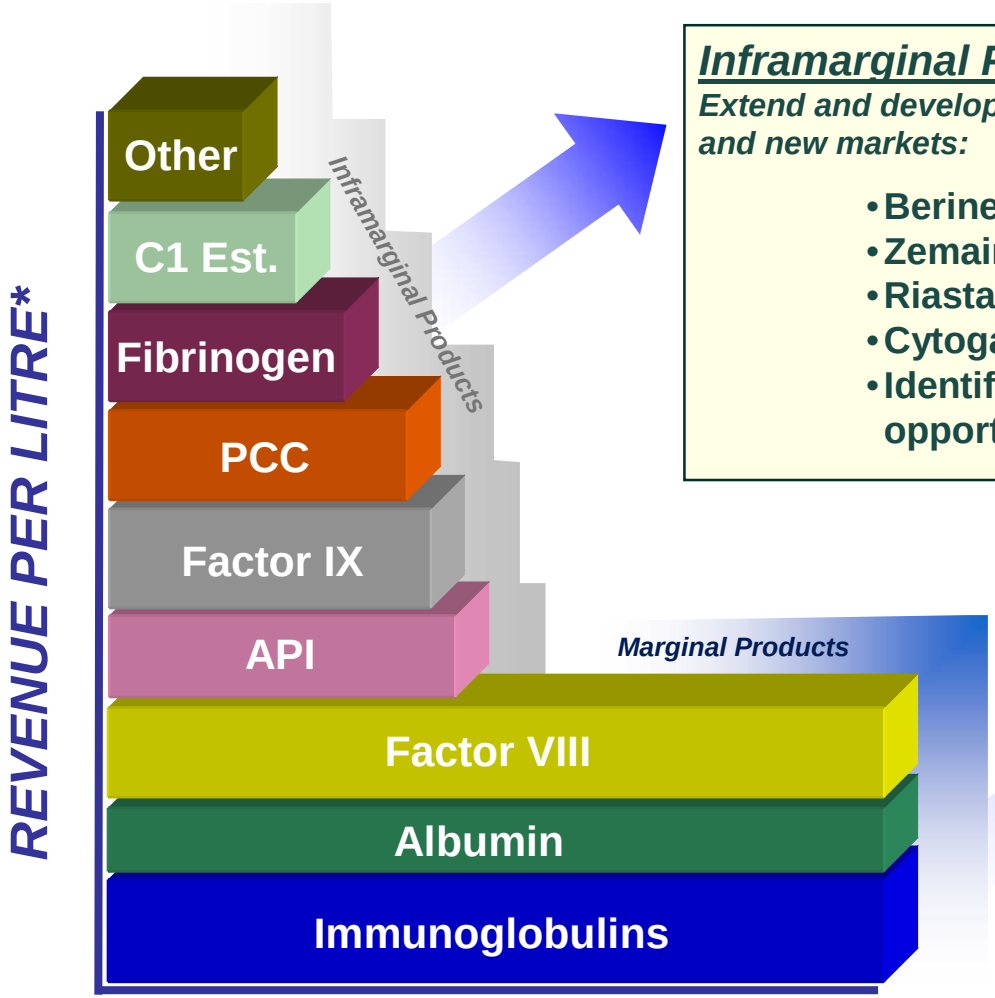
ISCOMATRIX® Adjuvant Update



- Merck
  - Alzheimer's study continuing
  - Broad interest in infectious diseases
- Pfizer
  - Wyeth License and Option Agreement
  - Further evaluation
- Solvay
  - License

Protein Replacement Therapies

Plasma Proteins Strategy



Inframarginal Products

Extend and develop new registrations and new markets:

- **Berinert® P/N**
- **Zemaira®**
- **Riastap®**
- **Cytogam®**
- **Identify new plasma-derived opportunities**

Marginal Products

Grow Marginal Product Franchises with a balanced litre strategy

- **IG Strategy: Transfer Carimune® markets to Privigen®, transfer Vivaglobin® markets to Hizentra®**
- **FVIII Strategy: Develop vWF globally and find long-term pdFVIII outlets**

*Illustrative, not to scale

Privigen

- Room Temperature stable IVIG
- New facility (IgLab) approved
  - FDA – 5-Mar-09
  - EMEA – 30-Mar-09
  - SwissMedic – 30-Apr-09
- IgLab2 comes on-line next year
- Additional registrations underway in 33 countries

privigen®
Human Normal Immunoglobulin
IVIG therapy made simple

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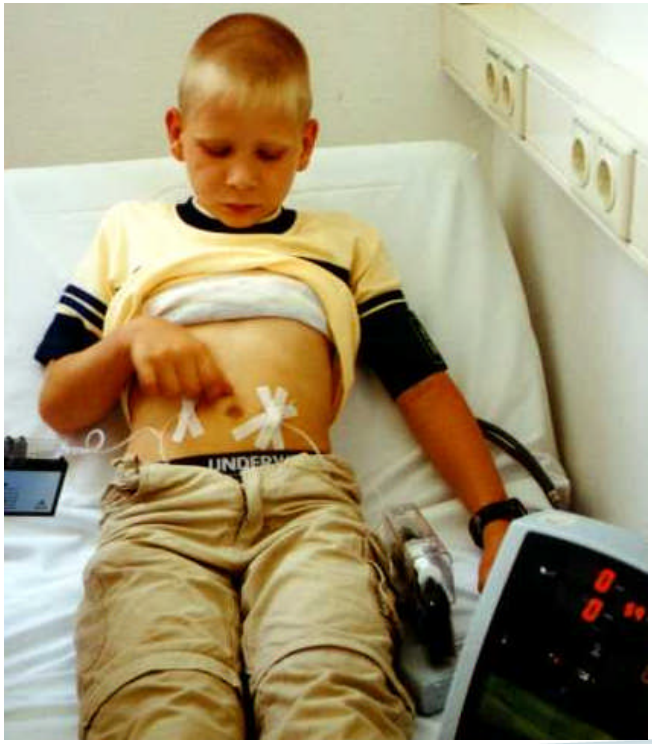
Hizentra (IgPro20)

- Only 20% SCIG in the clinic
- US submitted in April, Action date Q1 ‘10
- Phase III PID Europe study completed
  - EMEA submission planned for H1’10

Hizentra™
Immune Globulin Subcutaneous (Human)
20% Liquid



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Specialty Products – Market Expansion

- Cytogam
  - Transferring process to Bern
  - US FDA submission – mid ’10
- Zemaira
  - Phase III/IV enrollment on track
  - Trial results for EU licensure

CYTOGAM®
Cytomegalovirus Immune Globulin Intravenous (Human) (CMV-IVIG)

Zemaira®
alpha$_1$-proteinase inhibitor (Human)

CSL™

Specialty Products – Market Expansion

- Berinert
  - MRP completed 11-Dec-08, now approved in 23 EU countries
  - US FDA approved 9-Oct-09, only C1 esterase inhibitor approved for acute attacks of HAE.
  - Canada and Australia – application under review

BERINERT®
C1 Esterase Inhibitor, Human
Reliable Relief. On-Demand.

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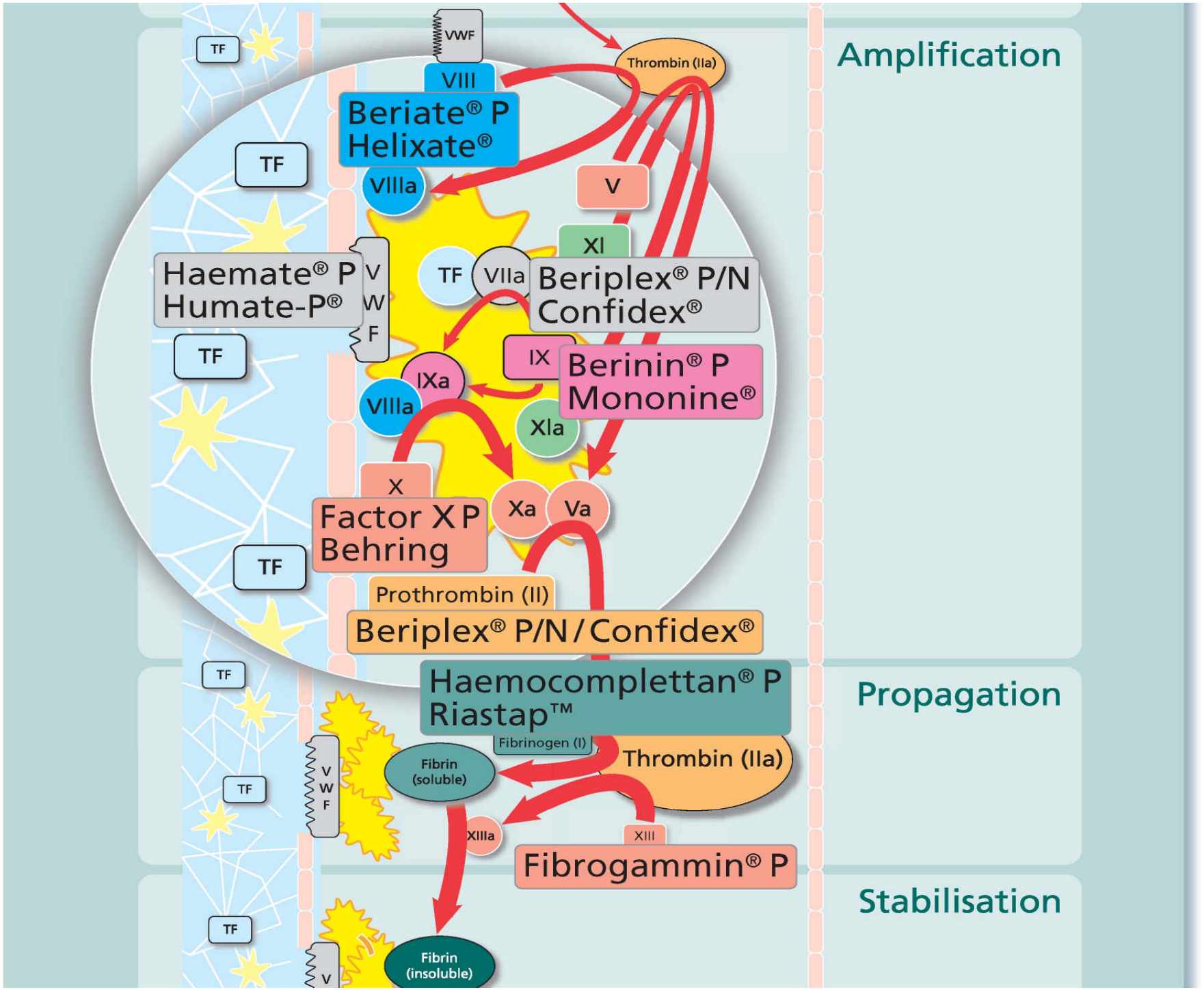
Amplification
Propagation
Stabilisation
TF
VWF
VIII
Thrombin (IIa)
Beriate® P
Helixate®
VIIIa
V
XI
Haemate® P
Humate-P®
V
W
F
TF
VIIa
Beriplex® P/N
Confidex®
IX
Berinin® P
Mononine®
IXa
VIIIa
XIa
X
Factor X P
Behring
Xa
Va
Prothrombin (II)
Beriplex® P/N / Confidex®
Haemocomplettan® P
Riastap™
Fibrinogen (I)
Fibrin
(soluble)
Thrombin (IIa)
XIIIa
XIII
Fibrogammin® P
Fibrin
(insoluble)

Specialty Products – Market Expansion

- Riastap
  - FDA approved 16-Jan-09
  - PEI approved 4-Dec-09
  - European approval anticipated in mid-2010

  - Only Fibrinogen approved in the US

RIASTAP™
Fibrinogen Concentrate
Strengthens clots. Speeds haemostasis.

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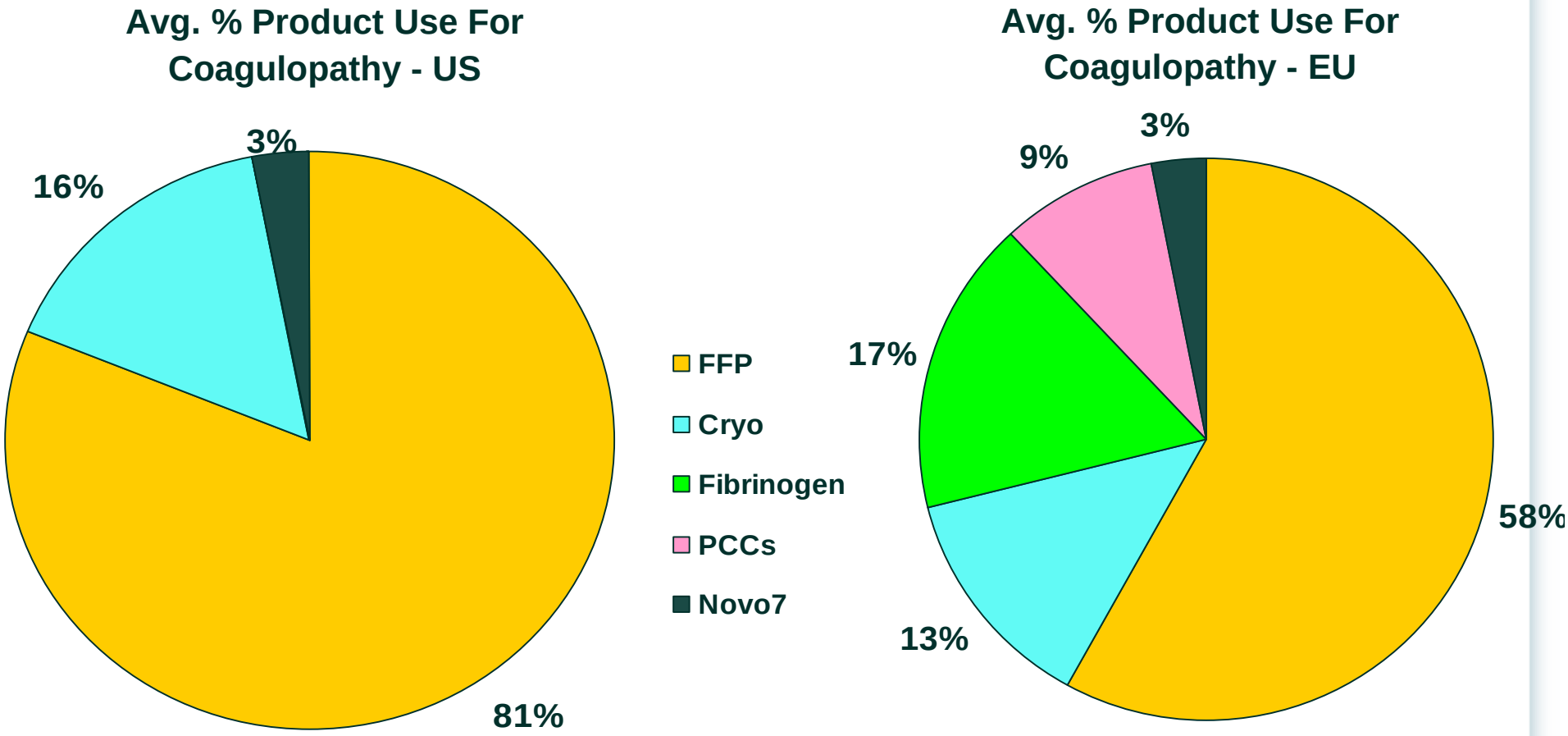
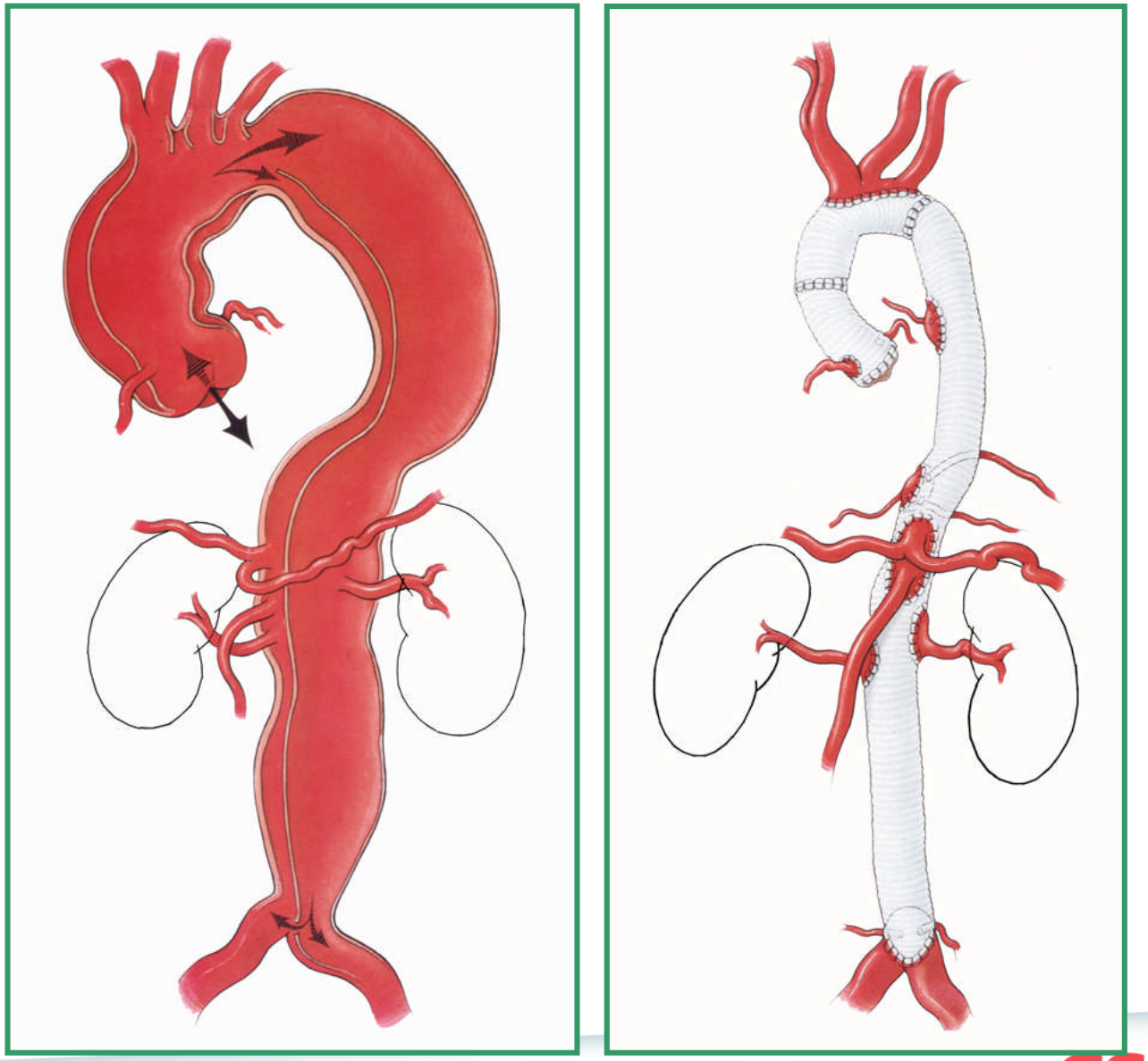
Estimated Product Use for Correction of Coagulopathy: Cardiac/CV

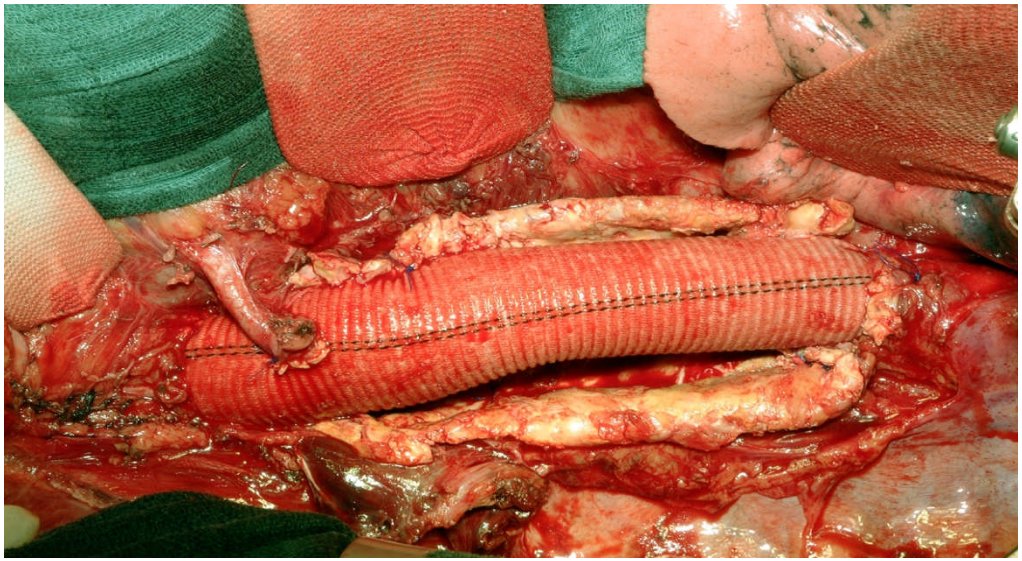


***Note**: Volumetric use ESTIMATES ONLY EXCLUDE other blood products such as RBCs, platelets, tranexemic acid etc*
***Sources**: US A/U Research, Resolutions, July 08, EU Prod Opp Assess, Ziment, July 08*

Fibrinogen in Aortic Surgery



Fibrinogen in Aortic Surgery



	Bleeding parameter OP + 24h				
Control group	**RBC**	**FFP**	**PC**	**Drain**	**Fibrinogen [mg]**
TAAA (retrospective) (n=12)	**4,1**	**9,1**	**3,2**	**1154**	**0**
	*	*	*	*	
Fibrinogen group					
TAAA (n=6)	**1,0**	**1,0**	**0,5**	**449**	**7833**

16.4 units : 2.5 units => Difference 13.9

Specialty Products – Market Expansion

- Beriplex P/N: Prothrombin Complex Concentrate (PCC) – combination of vitamin K dependant coagulation factors

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Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Regular Article

Prothrombin complex concentrate (Beriplex P/N) for control of bleeding after kidney trauma in a rabbit dilutional coagulopathy model ☆

Ingo Pragst, Franz Kaspereit, Bärbel Dörr, Gerhard Dickneite *

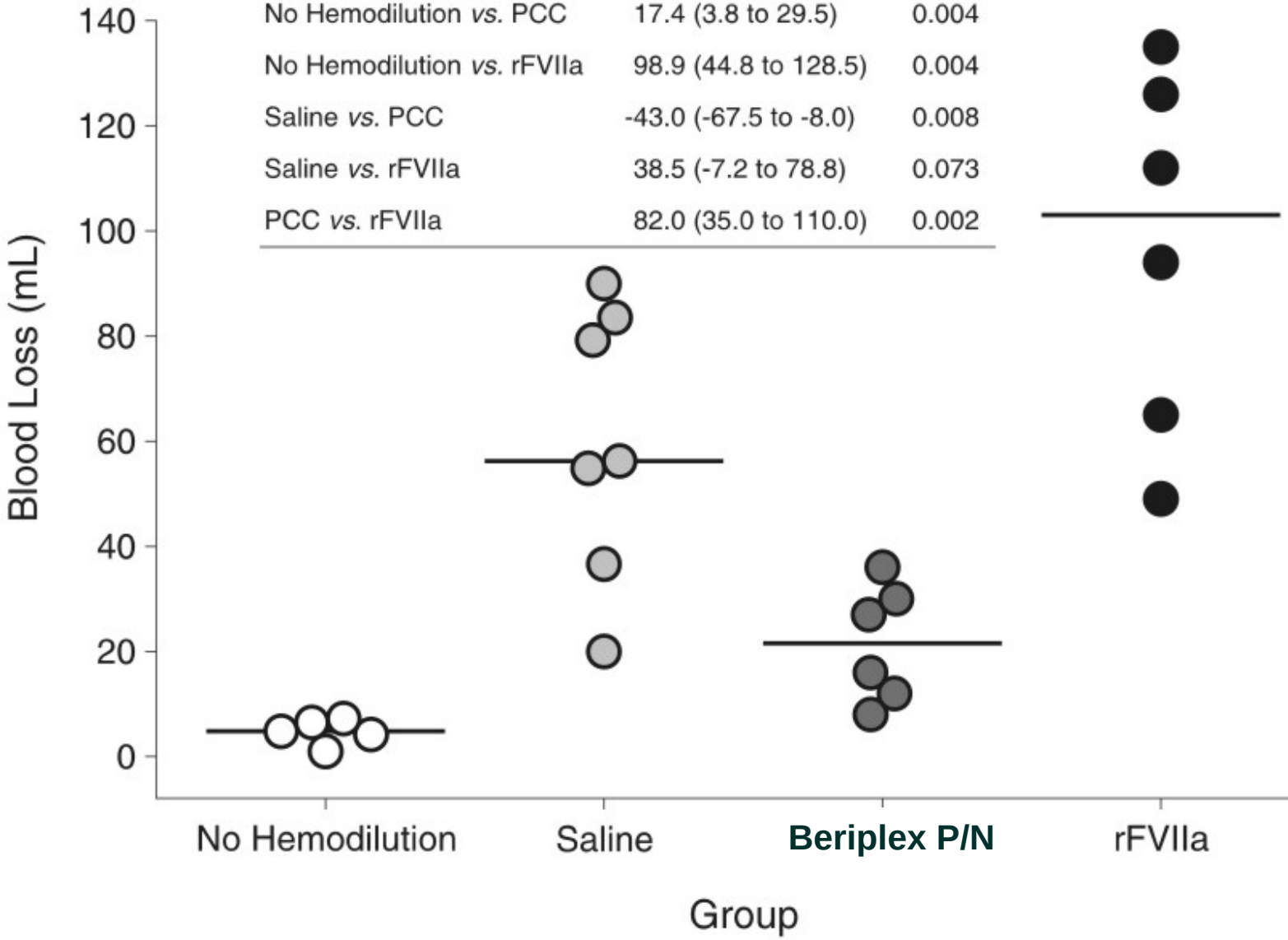
Department of Pharmacology and Toxicology, CSL Behring GmbH, Marburg, Germany

Pragst I, et al, Prothrombin complex concentrate (Beriplex P/N) for control of bleeding after kidney trauma in a rabbit dilutional coagulopathy model, Thromb Res (2009), doi:10.1016/j.thromres.2009.10.011

CSL

Blood Loss after Hemodilution

Comparison	Median Difference (CI)	p
No Hemodilution *vs.* Saline	52.0 (29.4 to 82.5)	0.003
No Hemodilution *vs.* PCC	17.4 (3.8 to 29.5)	0.004
No Hemodilution *vs.* rFVIIa	98.9 (44.8 to 128.5)	0.004
Saline *vs.* PCC	-43.0 (-67.5 to -8.0)	0.008
Saline *vs.* rFVIIa	38.5 (-7.2 to 78.8)	0.073
PCC *vs.* rFVIIa	82.0 (35.0 to 110.0)	0.002



Specialty Products – Market Expansion

Beriplex® P/N

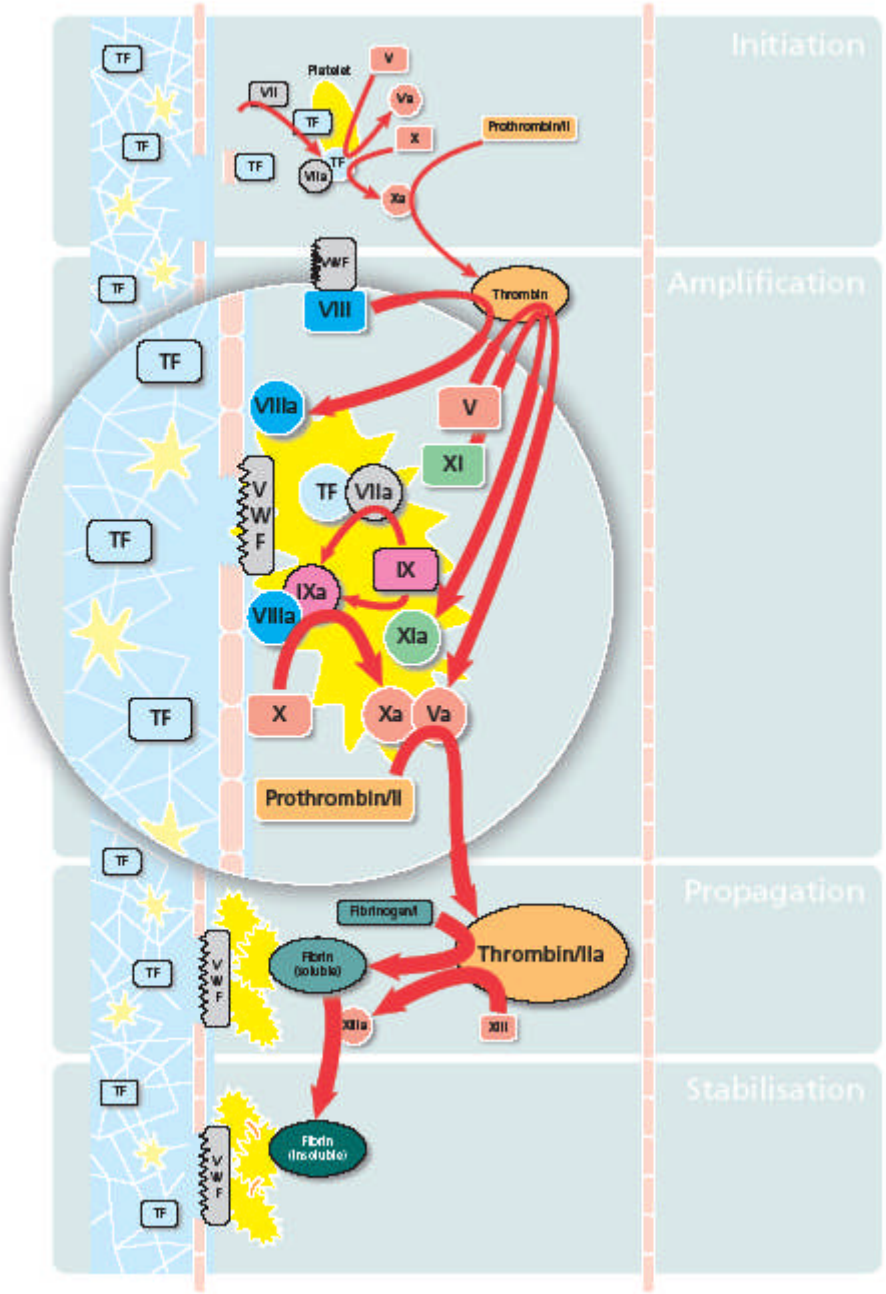
- Anticoagulant Reversal Trial is proceeding in both surgery and emergency bleeding
- Capacity expansion underway

vWF/FVIII

- Haemate® P / Humate-P® is the world's leading vWF/FVIII
- Biostate®
  - Compliments Humate-P®
  - Takes advantage of existing capacity, broadens use
  - Serves additional markets
  - Manufactured in Australia for export using CSL Behring cryo
  - Currently running a Hemophilia A (FVIII) and a von Willibrand's disease study for EU licensure

BIOSTATE®
Human Coagulation Factor VIII and Human VWF Complex

CSL™



Recombinant Coagulation Factors with extended half-life

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Half-life Improvement for Coagulation Products

Products with improved half-life will be beneficial to patients

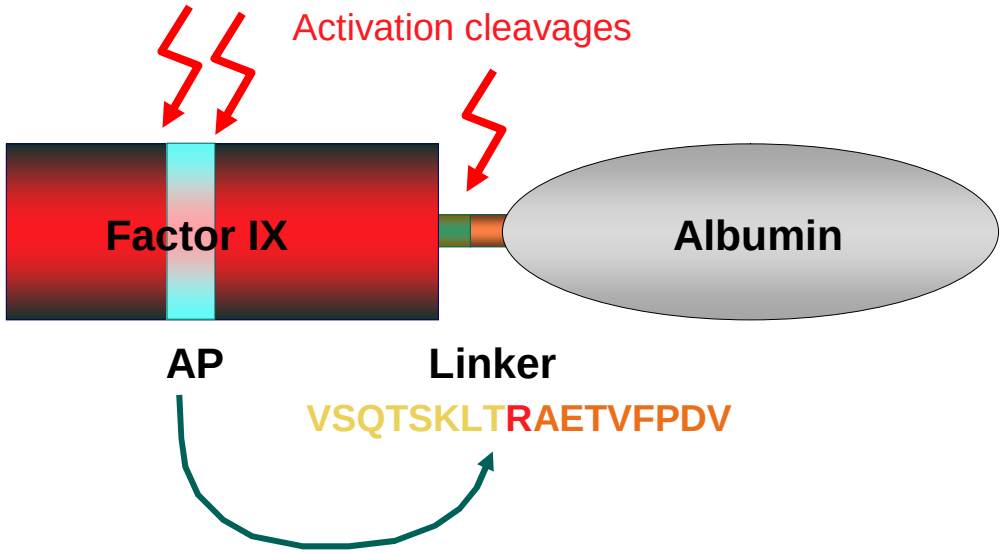
- Less frequent injections
- Improved compliance
- May enable prophylaxis

Albumin as a Carrier Protein

- Albumin has a naturally long half-life (~20 days)
- Highly abundant protein
- Proof of principle data for FVIIa and FIX

rIX-FP: advanced concept

- rIX-FP with proteolytically cleavable linker
  - Albumin fused to the C-terminus of FIX
  - Cleavable linker between FIX and albumin derived from FIX activation region



rIX-FP: half-life *in vivo* (FIX:Ag)

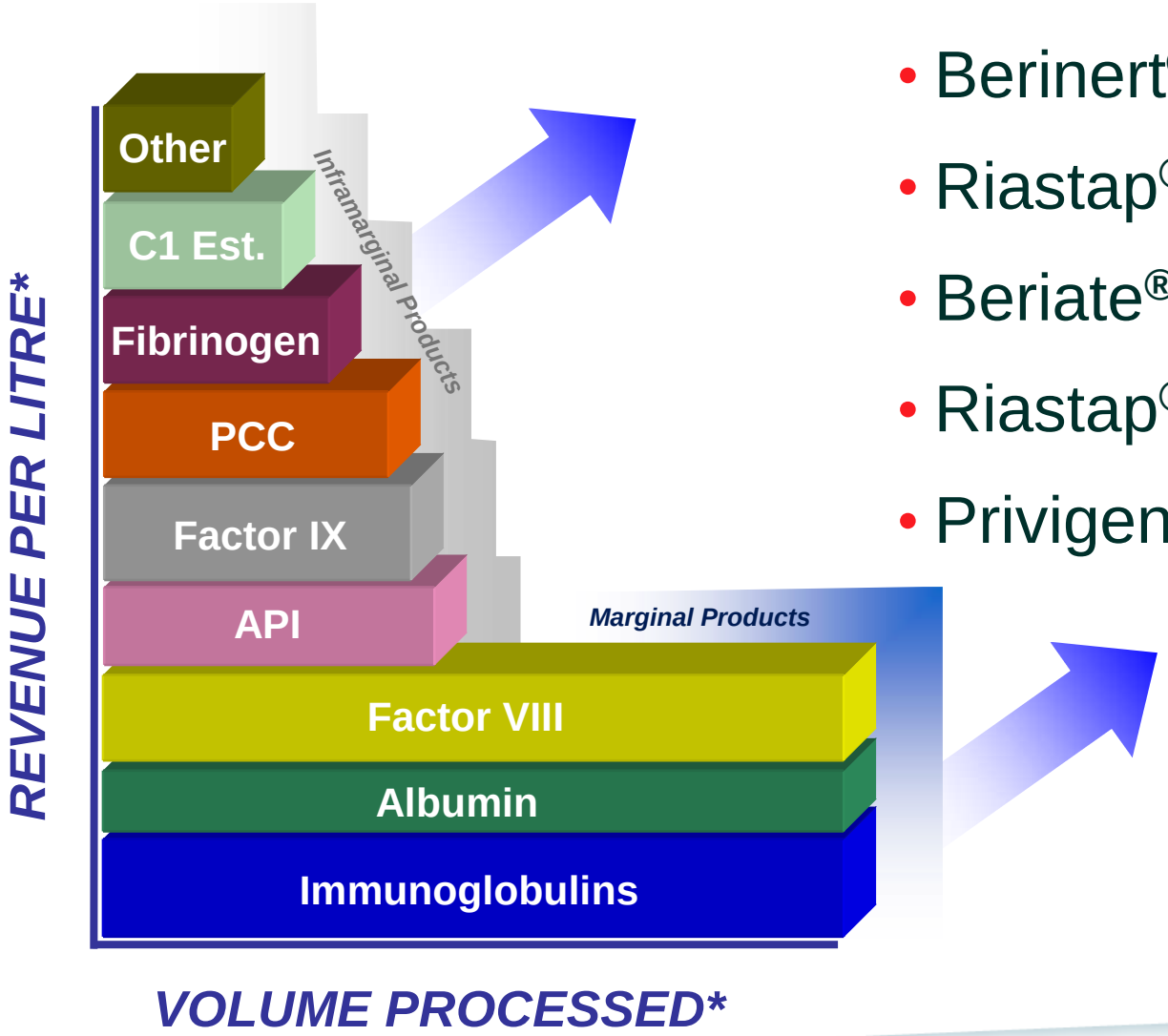
Product	Terminal half-life (h)			
	Rat	**Rat**	**Rabbit**	**Rabbit**
BeneFIX	4.7	5.1	9.9	8.6
rIX-FP (HEK)	8.5		27.7	
rIX-FP (CHO)		10.4		33.9
Ratio rIX-FP/BeneFIX	1.8	2.0	2.8	3.9

- **rIX-FP has an improved half-life**

Recombinant Coagulation Factors: next steps

- Toxicology is underway
- Planning for start of clinical studies in the next year
- rVIIa-FP is following shortly behind

Plasma Products Approved in the Last Year



- Berinert® P/N in the EU
- Riastap® in the US
- Beriate® in Russia
- Riastap® in Germany
- Privigen® Plant

*Illustrative, not to scale

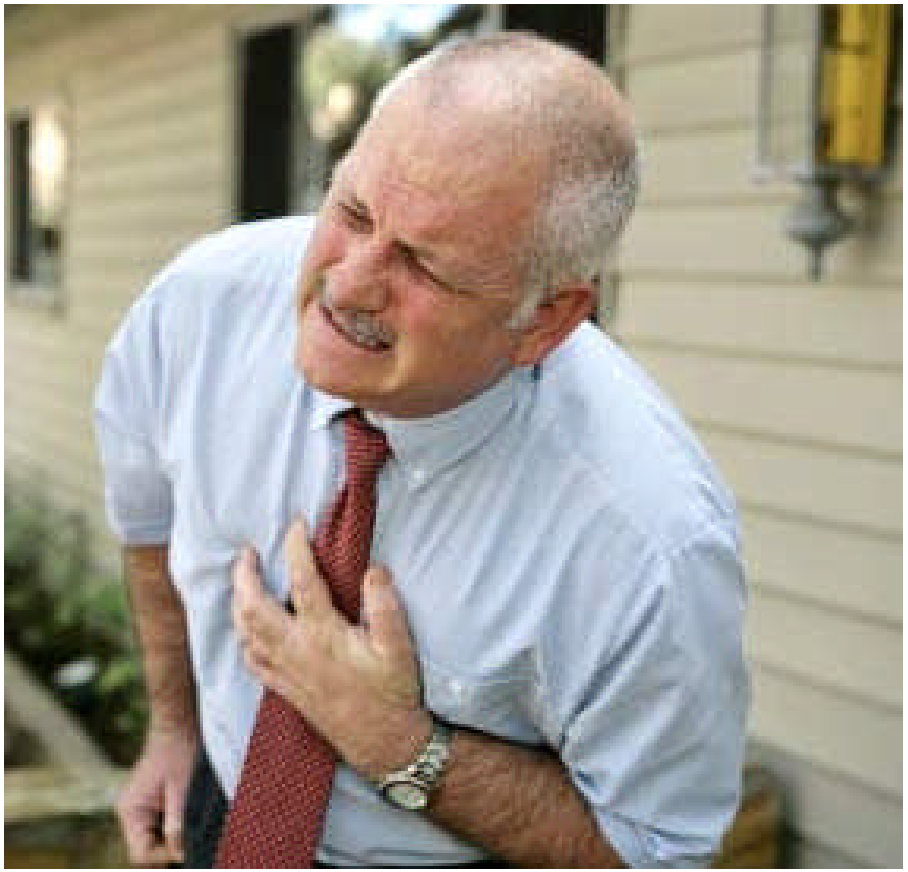
Q&A

Break

CSL112:

Reconstituted HDL for treatment of ACS

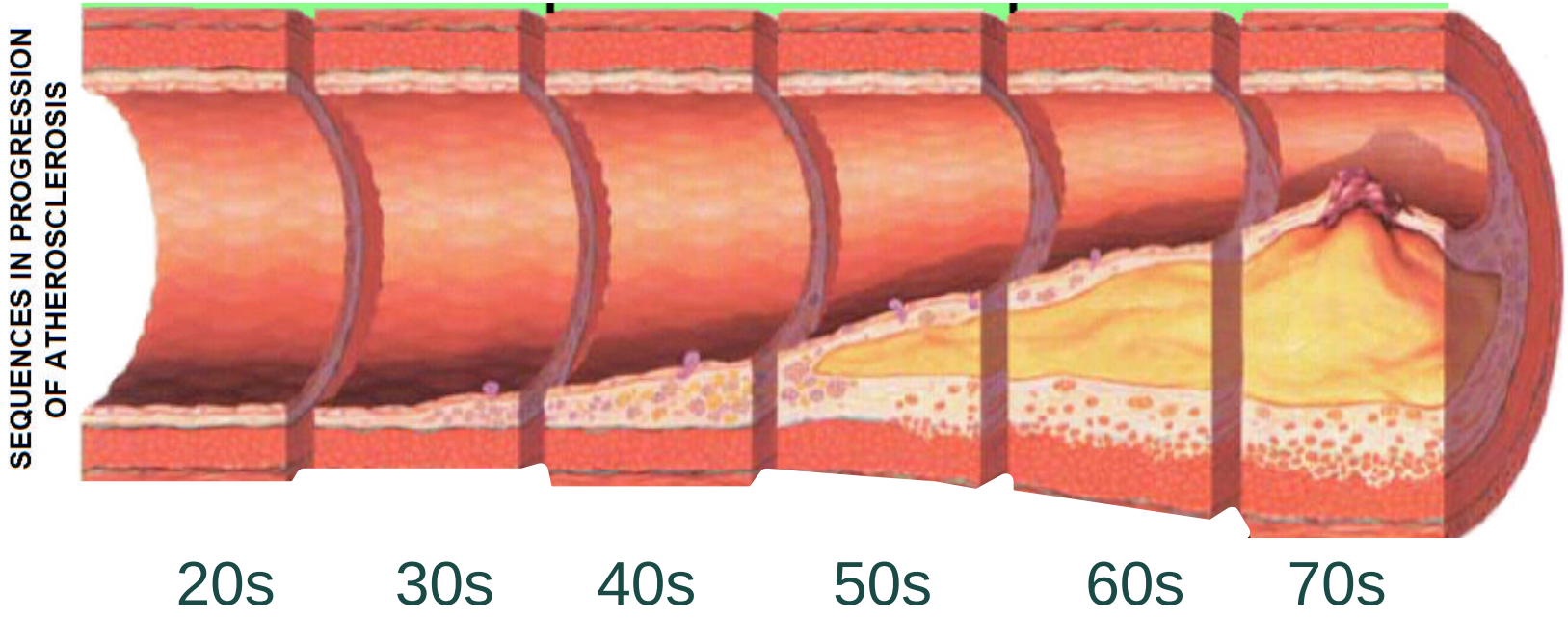
Coronary Heart Disease: Unmet Medical Need



- Leading cause of death in men and women
- 1,255,000 new or recurrent coronary attacks annually
- 450,000 deaths
- $165 Bn annual direct costs

(Figures for USA)

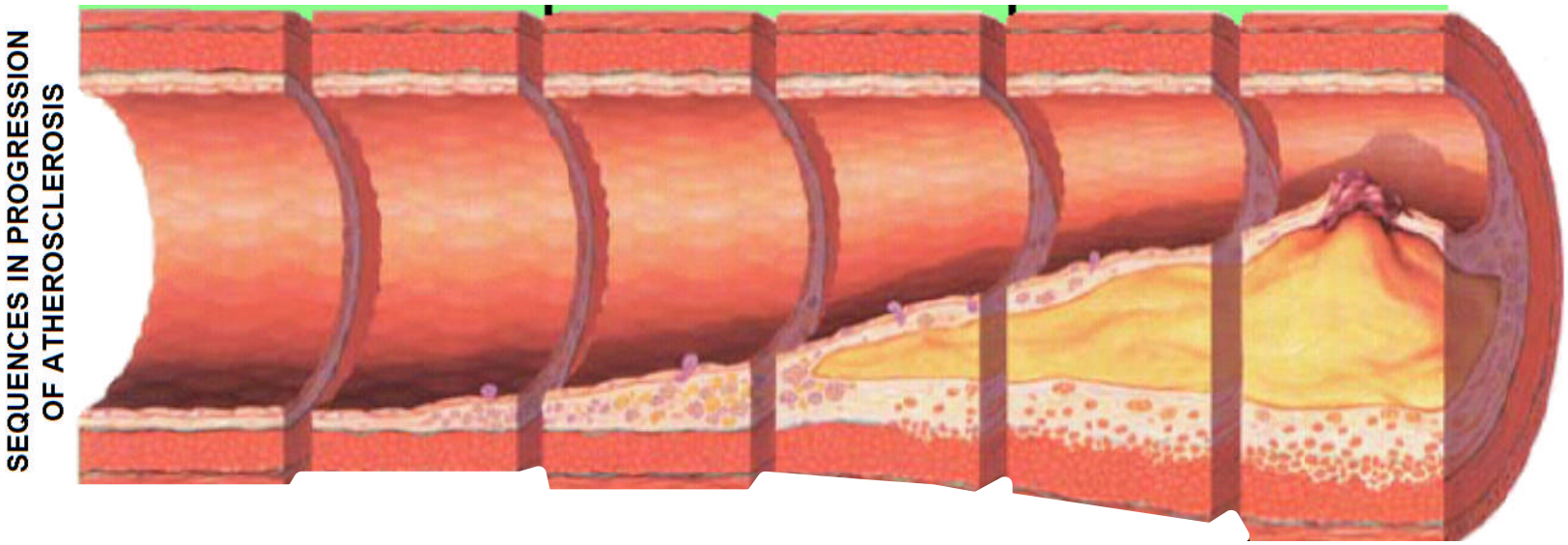
Coronary Heart Disease is caused by buildup of cholesterol in the artery wall



- **Cholesterol is carried to plaque by LDL (bad cholesterol)**

- **Cholesterol is carried away from plaque by HDL (good cholesterol)**

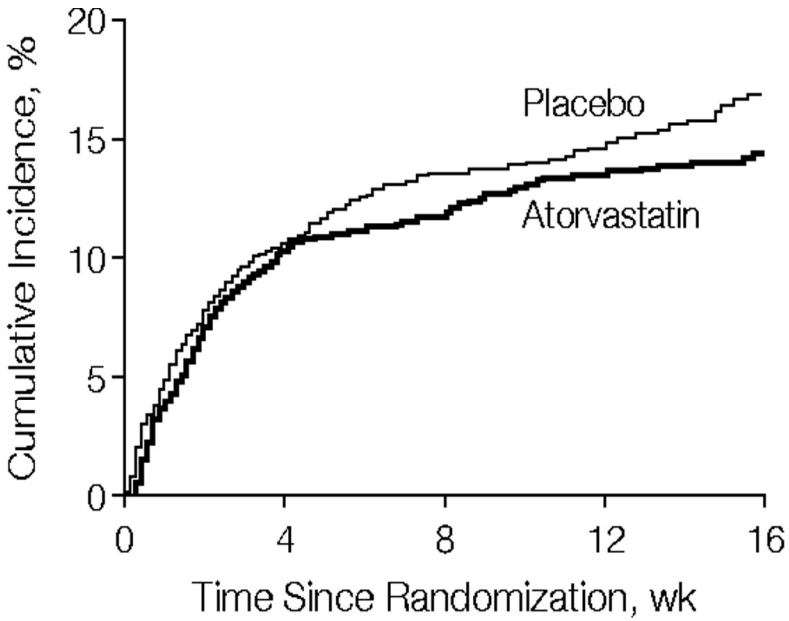
The Medical Hypothesis We Will Test



CSL112: Acute treatment for acute coronary syndrome

- Short series of IV infusions immediately after ACS
- Seek to reduce recurrent events in months following ACS
- Product niche distinct from statins, other oral anti-hyperlipidemics

Modest effect of statins in ACS



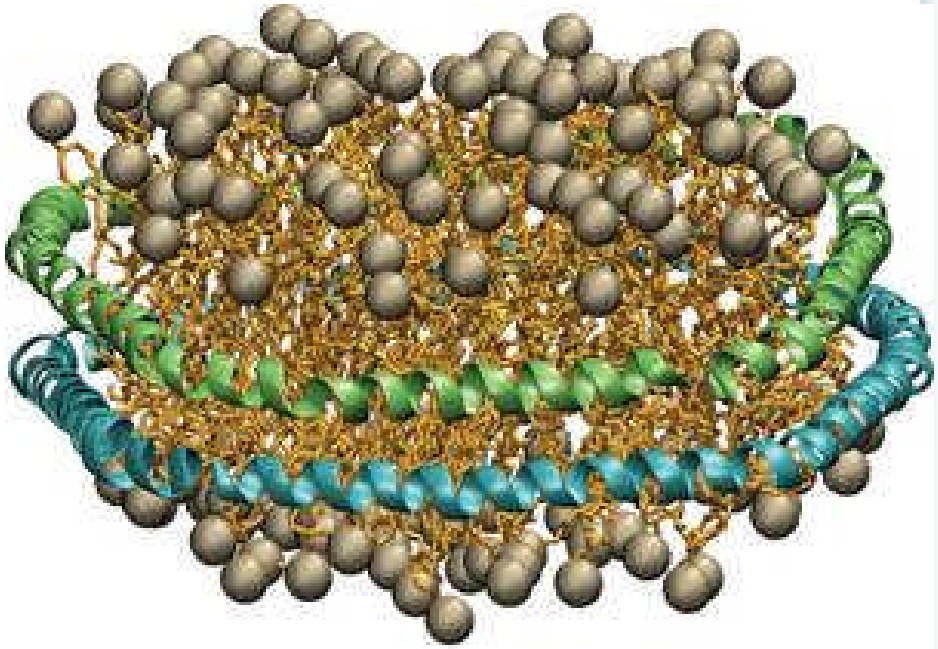
Schwartz, G. G. et al. JAMA 2001;285:1711

Long history of HDL infusion reducing atheroma burden

- 1989: infusion of HDL reduced rabbit athero
- Repeated in rabbits and mice
- 1990s: transgenic studies showed ApoAI to be the active agent

Manufacturing reconstituted HDL: a strength of CSL

- Step 1. purify ApoA-I, the dominant protein of HDL, from a waste fraction of plasma
- Step 2: pasteurized apoA-I is then combined with phosphatidyl choline to form HDL
- Prototype formulation termed CSL111

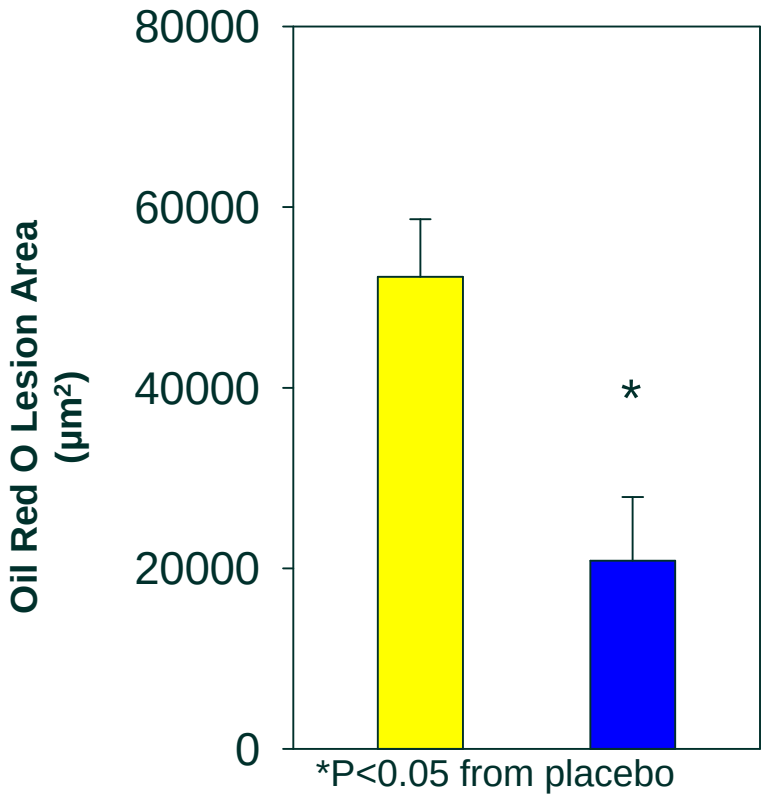


Reconstituted HDL

CSL111 reduced atheroma in man

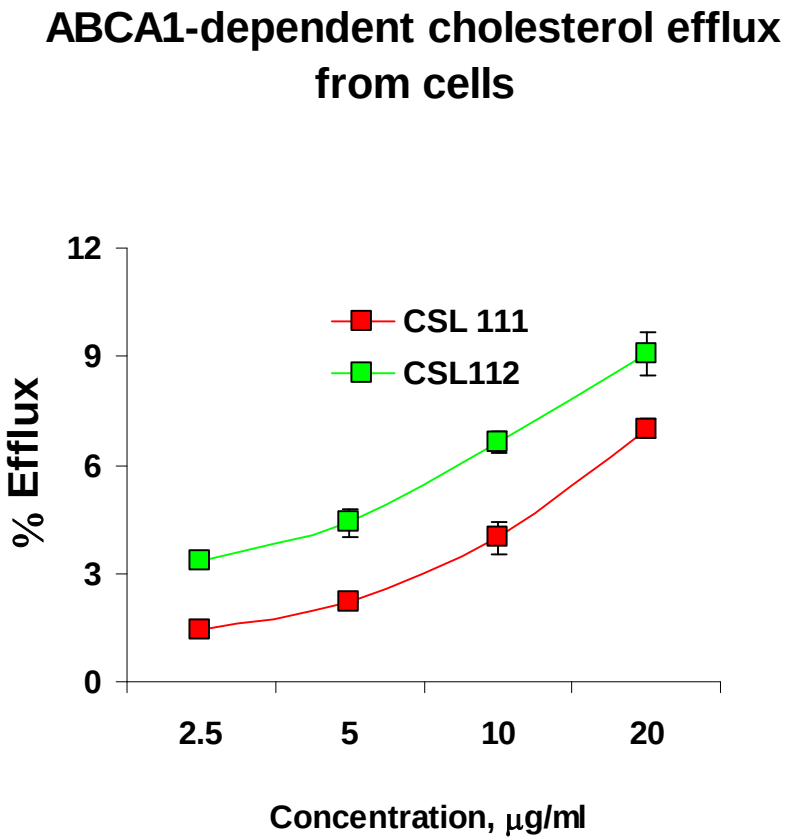
- Four infusions of our prototype, CSL111, reduced the volume of coronary atheroma in ERASE (JAMA 2007)
- Single infusion of CSL111 reduced plaque lipid >60% in femoral arteries (Circ. Res. 2008)

Reduction of plaque lipid by CSL111



CSL112: Formulated to optimize efficacy in ACS

- Prototype CSL111 was formulated before modern understanding of cholesterol transport
  - ABCA1, a cellular “pump,” transports cholesterol to HDL
- CSL112 optimized to receive cholesterol from ABCA1



CSL112: Formulated to optimize safety

- Laboratory indices of liver function were dose-limiting with CSL111 in the ERASE trial
- Animal studies suggest hepatic effects derive from excipients used to formulate CSL111
- CSL112 was reformulated to reduce excipients
- Animal data suggests > 3-fold reduction in hepatic effects of CSL112 vs CSL111

Development plans for CSL112

- Preclinical safety studies in progress
- Phase 1 anticipated to begin in 2010
  - Safety, PK, biomarkers
  - ABCA1-dependent cholesterol efflux
- Phase 2: biomarkers to determine optimal dosing
- Phase 3 will demonstrate clinical benefit in ACS patients

Focused efforts on Coronary Heart Disease at CSL

- New personnel hired to reinforce expertise in CV drug development including
  - Chuck Shear (former Vice President; Cardiovascular, Metabolic and Endocrine Disease Development, Pfizer)
  - Sam Wright (former Vice President, Cardiovascular Basic Head, Merck)
- Elite group of expert advisors recruited

Therapeutic Protein Portfolio

Early clinical / preclinical projects

Therapeutic Proteins: project updates

Early clinical projects

- CAM3001, anti-GM-CSFRα, rheumatoid arthritis
- CSL360, anti-IL-3Rα, acute myeloid leukemia

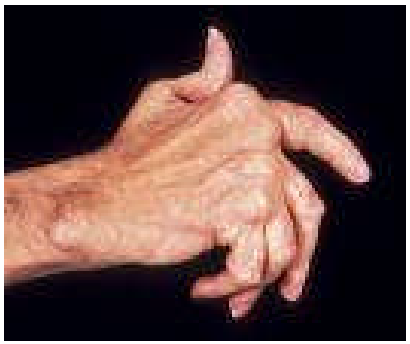
Preclinical research projects

- periodontal disease vaccine

CAM3001 (GM-CSFRα) – Rheumatoid Arthritis

Rheumatoid arthritis

- common chronic inflammatory disease of the joints
- market opportunity – DMARD / biological DMARD inadequate responders



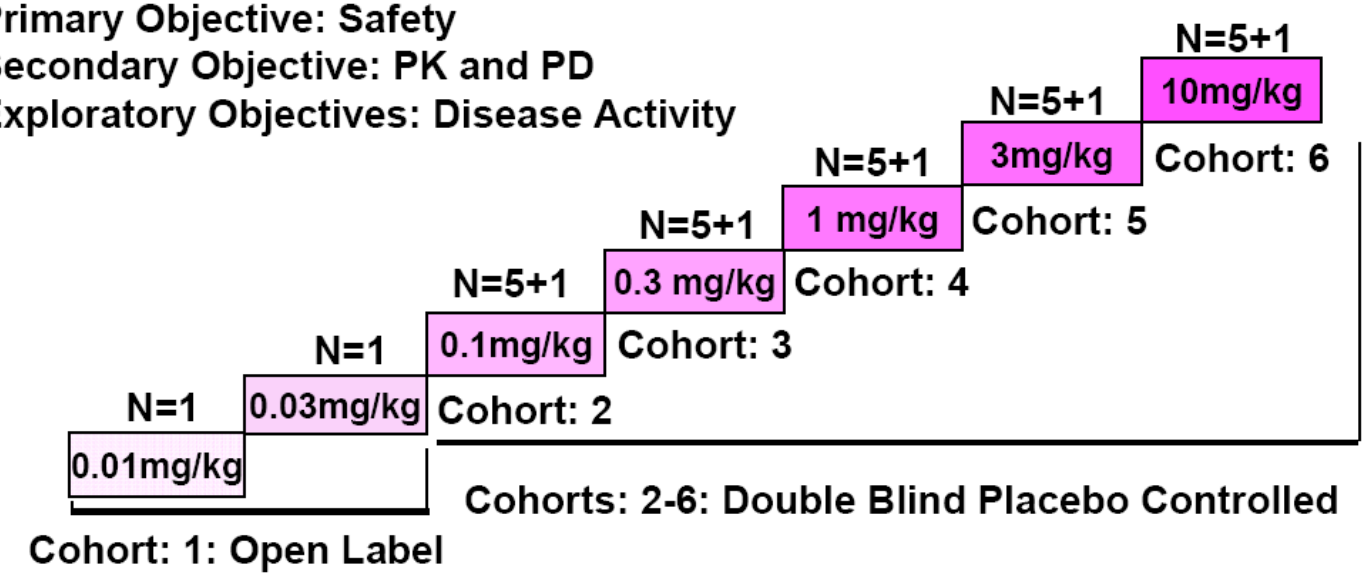
CAM3001

- fully human mAb targeting the GM-CSFRα
- licensed to MedImmune / AstraZeneca
- CSL to receive milestones and royalties
- CAM3001 Phase I study in RA patients complete
- study results presented at ACR meeting, October 2009
- phase II study to commence 2010

CAM3001 (GM-CSFRα) – Rheumatoid Arthritis

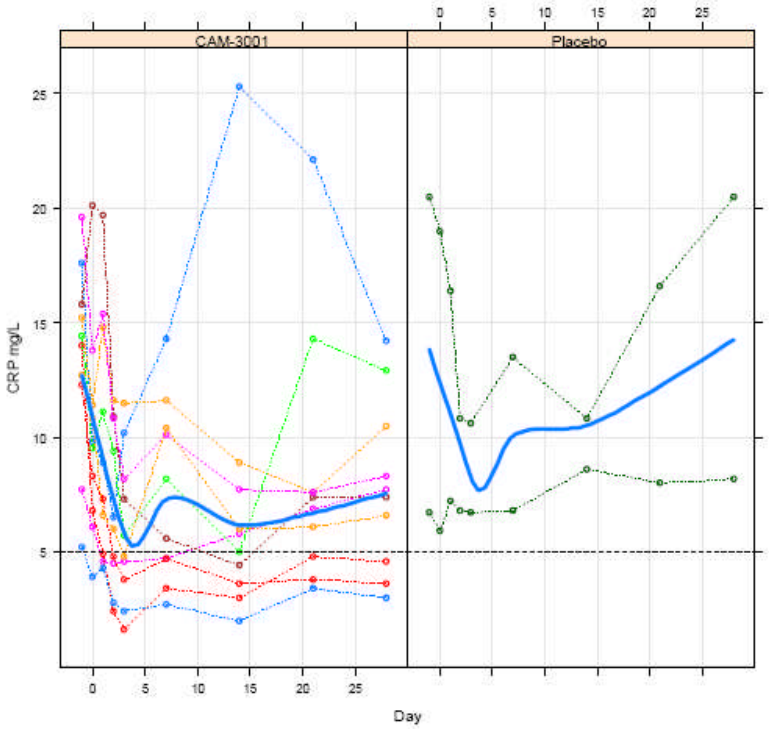
- Double-blind, placebo-controlled, 5:1 randomization CAM-3001:placebo
- Single ascending doses intravenously once, with 6-month follow-up
- 32 male and female subjects with adult onset RA ≥ 6 months
  - Functional capacity class I, II, or III
  - Stable on standard-of-care medication Methotrexate ≥ 3 months
  - DAS ≤ 4.8

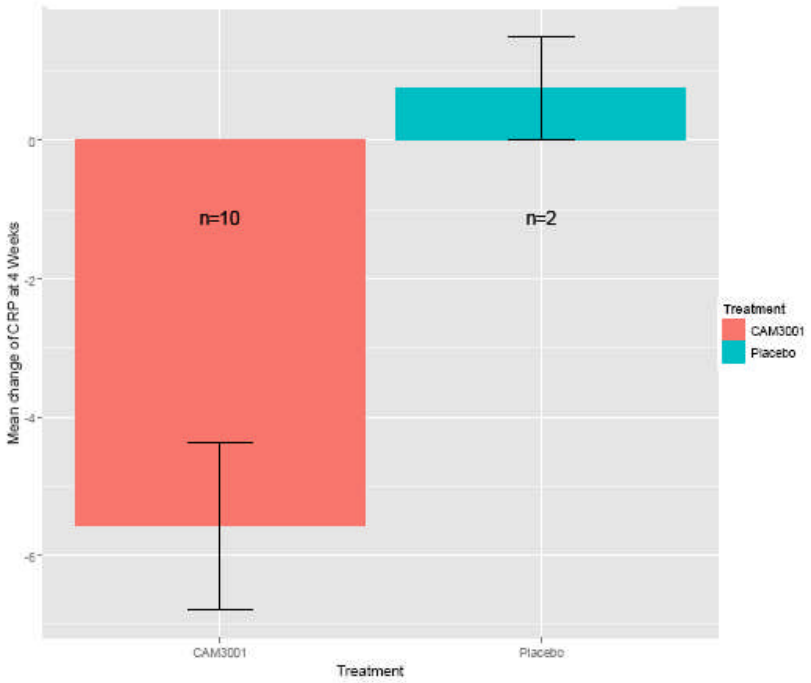
- **Primary Objective: Safety**
- **Secondary Objective: PK and PD**
- **Exploratory Objectives: Disease Activity**



* MedImmune, ACR 2009

CAM3001 (GM-CSFRα) – Rheumatoid Arthritis





- The study population had low disease activity at baseline
- 63% of patients had normal Acute Phase Reactants at the study entry
- Of the 10/27 subjects treated with CAM-3001 who had high ESR (≥ 20 mm/hr) at baseline, ESR was normalised in 9 of them after treatment

* MedImmune, ACR 2009

CAM3001 (GM-CSFRα) – Rheumatoid Arthritis

Summary of Phase I study

- at single i.v doses up to 10mg/kg CAM3001 had an acceptable safety profile supporting further clinical development
- PK analyses were consistent with an 'antigen sink' and a half-life of 11-21 days at 3 and 10 mg/kg doses, respectively
- anti-CAM3001 antibodies not detected in any subject
- effects observed on acute phase reactants and disease activity, 4 weeks following a single infusion are encouraging with respect to effect and duration on RA symptoms

- **the efficacy and safety profile of repeat administrations of CAM3001 will be formally assessed in a Phase II study commencing in 2010**

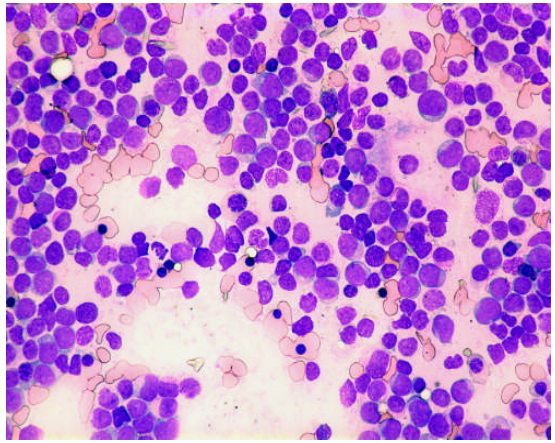
* MedImmune, ACR 2009

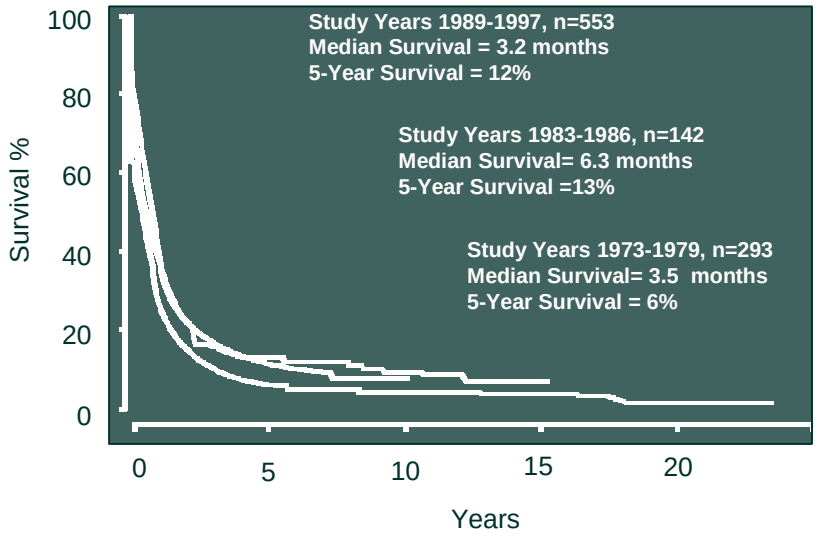
CSL360 (IL-3Rα) - AML

Acute myeloid leukemia (AML)

- most common acute leukaemia in adults
- incidence increases with age
- untreated AML fatal (3-4 months)
- chemotherapy → 50-75% CR
  ~70% will relapse

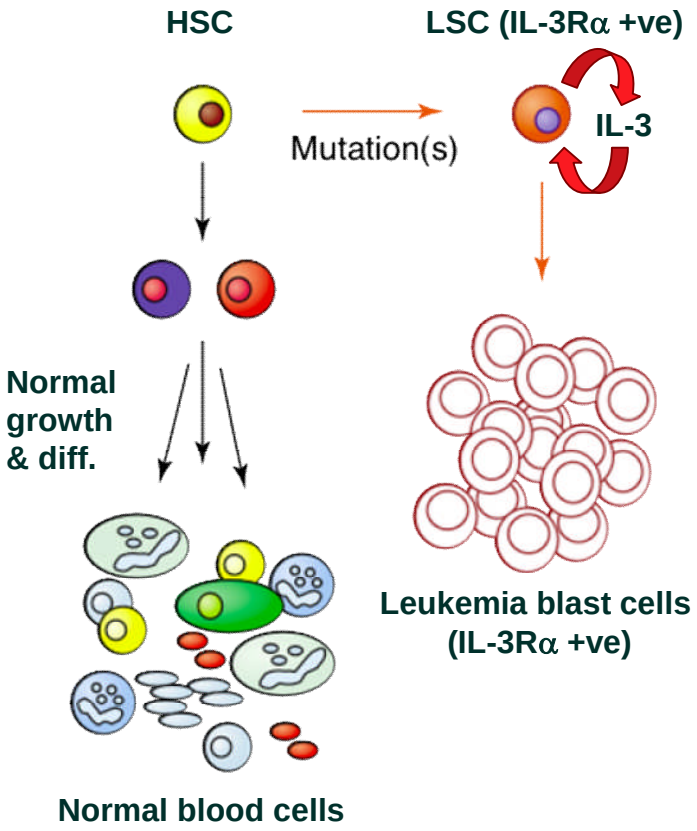
- 5 year OS = 21% (2008)
  - <55 yrs ~40%
  - 55 - 65 yrs <10%
  - >65 yrs <5%

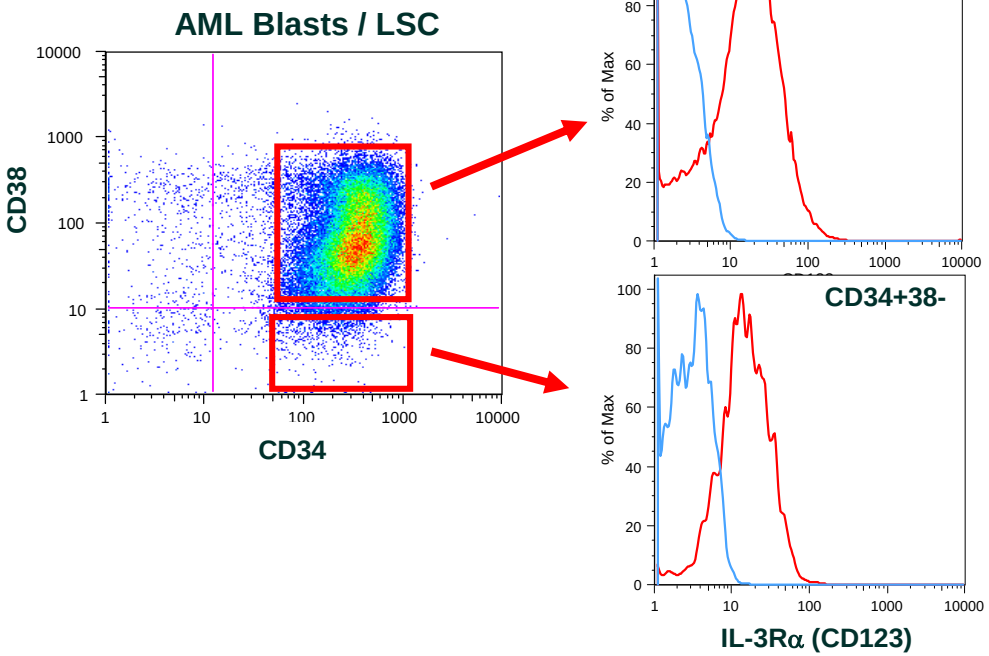




CSL360 (IL-3Rα) - AML

Targeting the IL-3Rα for the treatment of AML



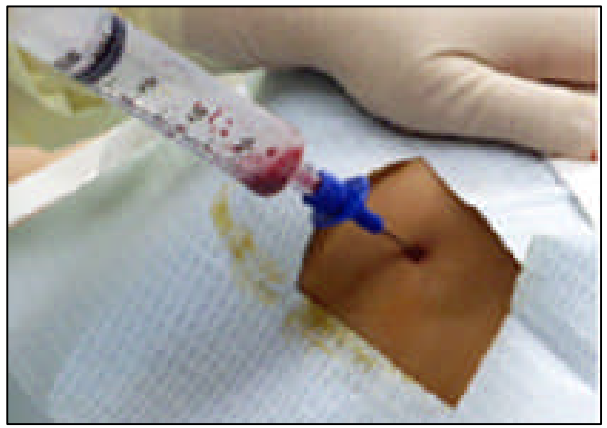


CSL360 (IL-3Rα) - AML

FIH, Phase 1 Study of CSL360 in AML Patients

CSL360:

- chimeric IgG1 mAb targeting IL-3Rα



Primary objectives:

- safety and tolerability of escalating doses
- PK; immunogenicity

Secondary objectives:

- MTD (if exists within range)
- anti-leukaemic activity (clinical response rate)
- biological effect on CD123+ LSC and blasts
- biologically effective dose & schedule

CSL360 (IL-3Rα) - AML

Phase I study design:

- patients with relapsed, refractory or high-risk AML
- standard "3 + 3" cohort, Phase 1 design
- 5 sequential, escalating dose level cohorts:

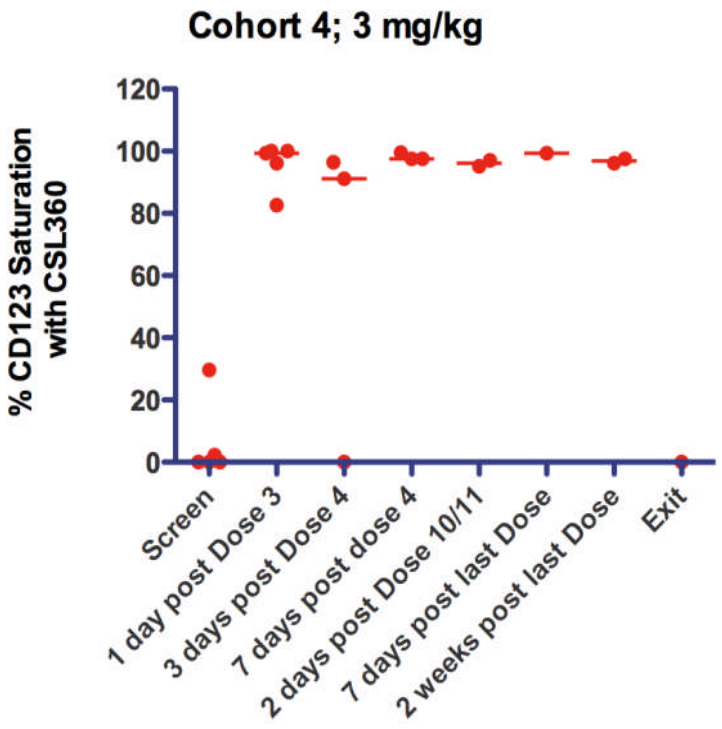
  0.1, 0.3, 1.0, 3.0, and 10.0 mg/kg; weekly IV dosing
- expansion of 10.0 mg/kg dose level cohort (N=18)

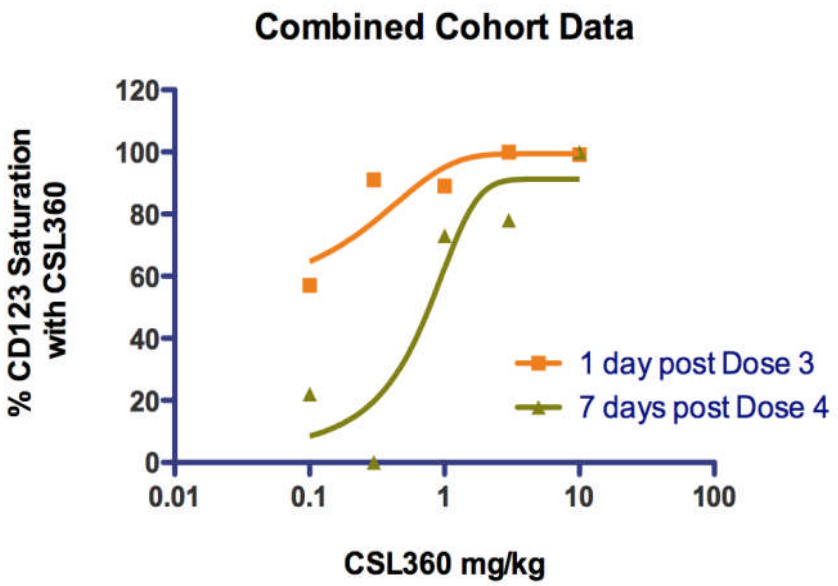
Correlative research / Biological assays to determine:

- expression of the target (CD123) and binding of CSL360 to target cells ✔
- ex vivo effect of the drug on AML proliferation / survival ✔
- ex vivo effect of drug on IL-3 signaling ✔
- effect of the drug on AML stem and blast cell numbers X

CSL360 (IL-3Rα) - AML

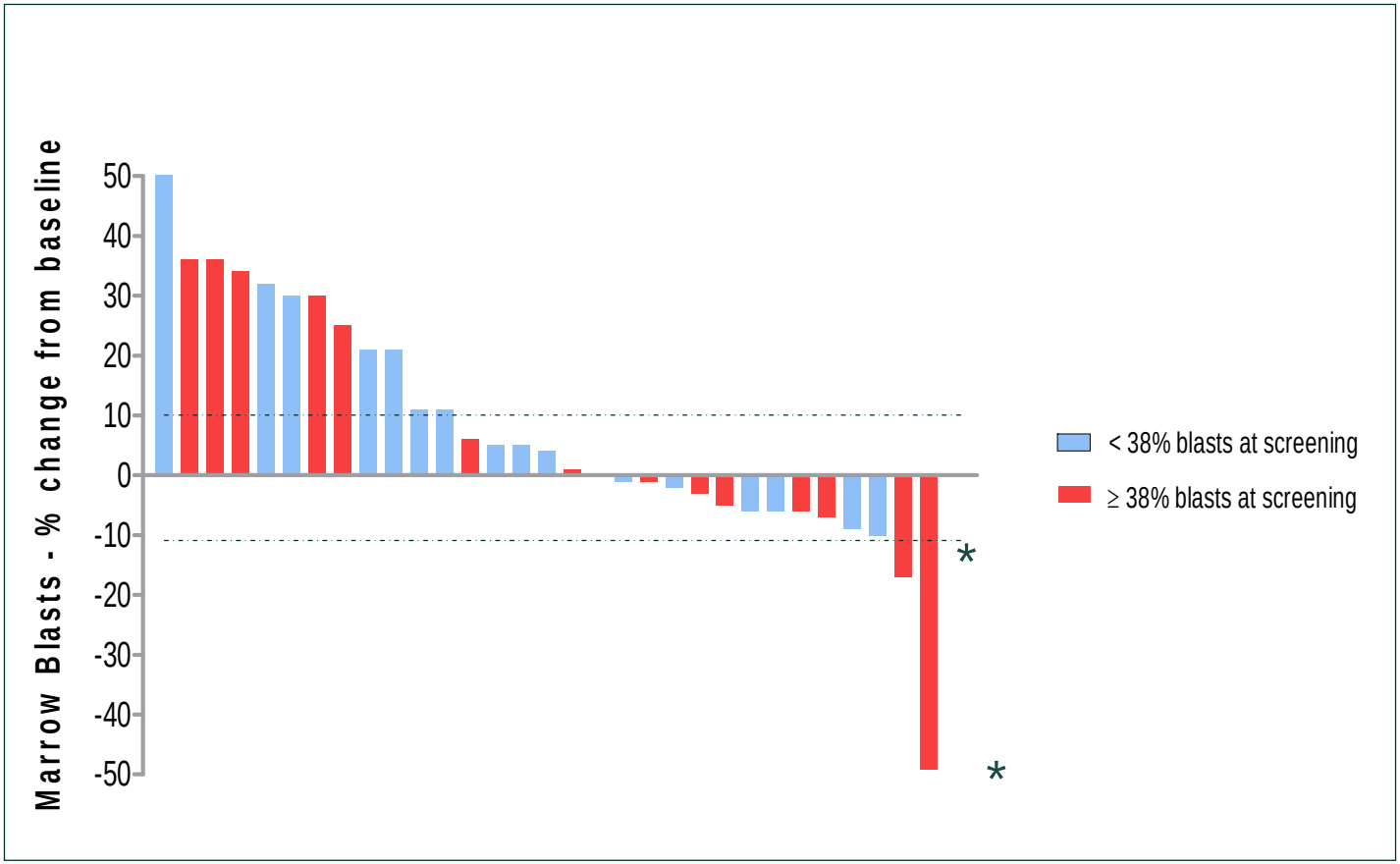
Dose-dependent Saturation of CSL360 Binding on PB and BM Blasts





CSL360 (IL-3Rα) - AML

Clinical outcome: % Change in Bone Marrow Blasts from Baseline

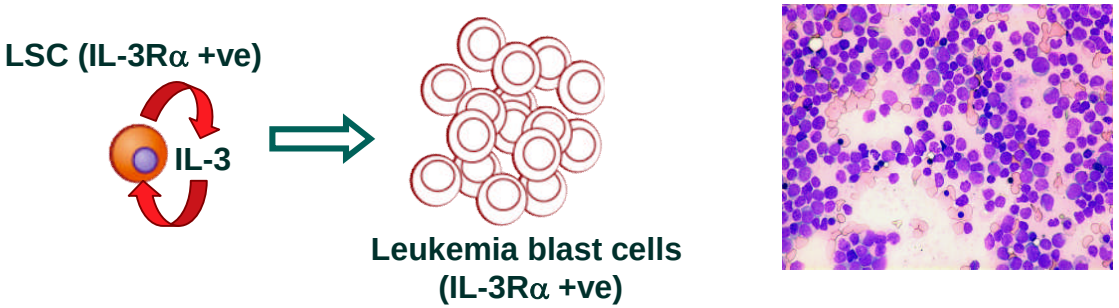


All Patients with at least 2 BM blast Measures; n=30

CSL360 (IL-3Rα) - AML

Summary of Phase I study:

- successful targeting of IL-3Rα with CSL360
- effective blockade of IL-3 binding & ex-vivo response
- evidence that leukaemia blasts and LSC survive
- **blocking IL-3 signalling alone, does not provide a therapeutic effect in these patients**



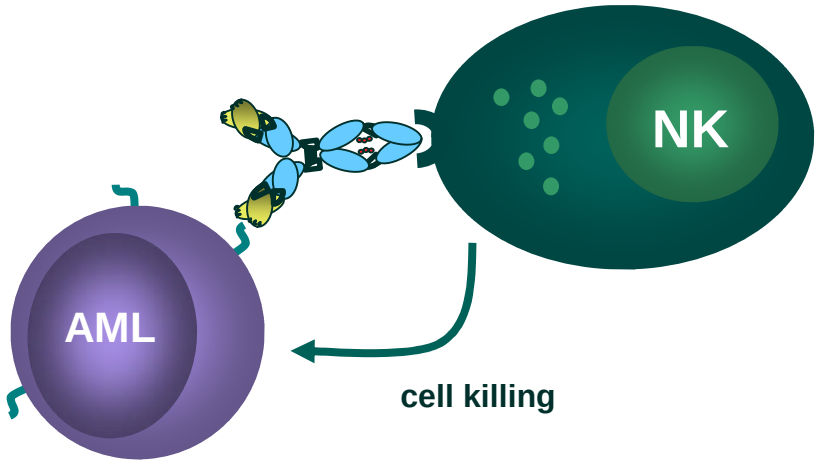
Conclusion:

- the IL-3R represents an excellent target - **therapeutic mAbs will need to be optimised for tumour cell killing**

CSL362 (IL-3Rα) - AML

CSL362 – a second generation mAb targeting the IL-3Rα

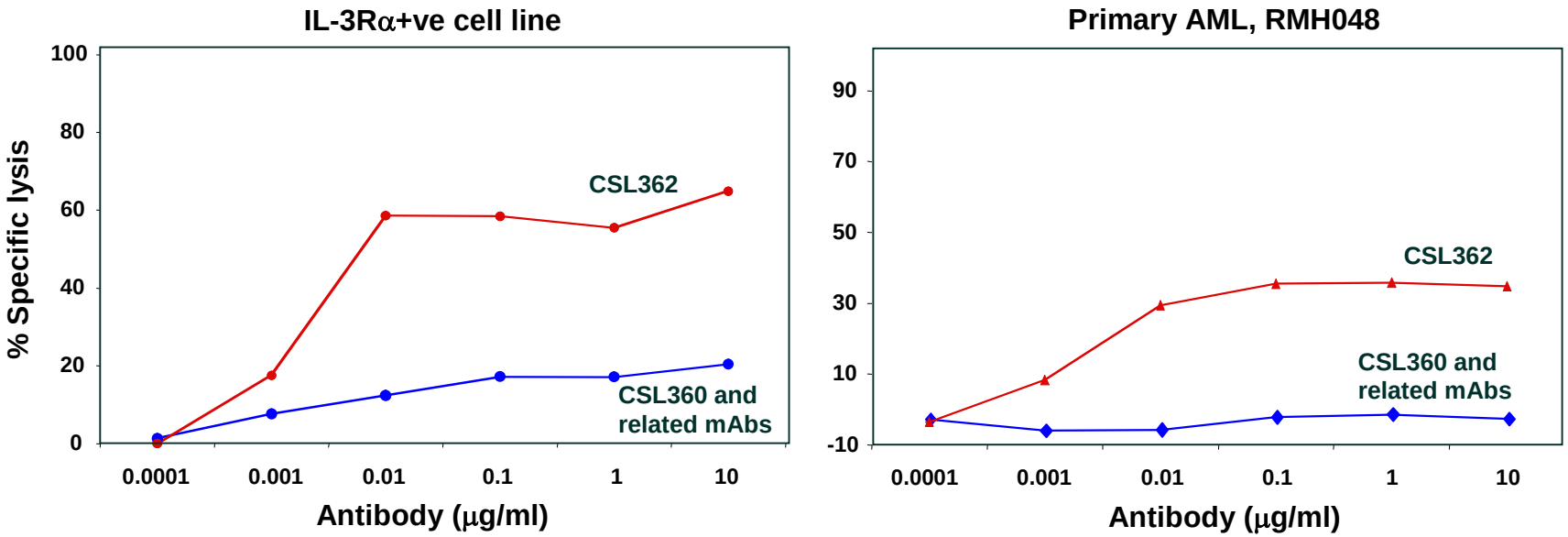
- retains the ability to potently inhibit IL-3 activity
- humanised for reduced immunogenicity
- optimised for enhanced tumour killing activity
  - proprietary technologies



CSL362 (IL-3Rα) - AML

CSL362 – a second generation mAb targeting the IL-3Rα

- enhanced *in vitro* killing of tumour cell lines and primary AML cells
- enhanced *in vivo* killing of transplanted primary AML cells



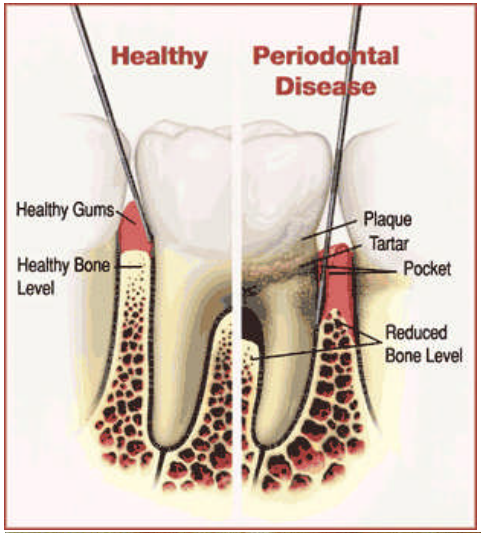
- CSL362 progressing towards formal preclinical studies

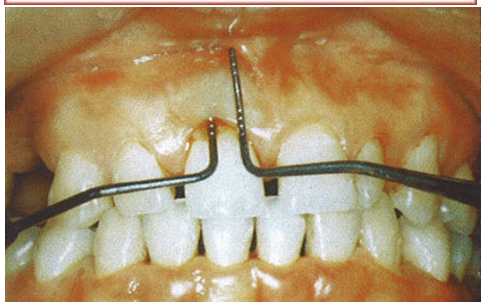
Periodontal disease vaccine

Periodontal disease

- Chronic inflammation of gum tissue - periodontitis
- Tissue and bone destruction, tooth loss
- Treatment
  - scaling and root planing
  - 17 million treatments in US pa ($6b)
  - recurrence common
- Several bacterial species
  - *P. gingivalis* “necessary cause”
- Epidemiological studies link periodontitis with systemic disease
  - cardiovascular diseases
  - oropharyngeal and pancreatic cancers
  - diabetes - pre-term birth and low birth weight

Probe measures the pocket between the tooth and the gums - healthy pocket measures 3mm or less and does not bleed.



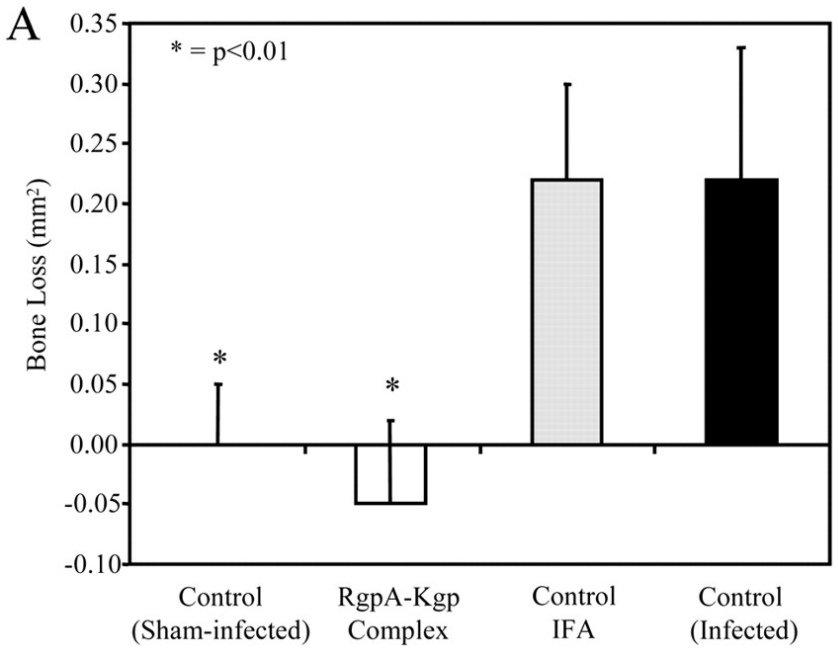


Periodontal disease vaccine

- CSL and The University of Melbourne Dental School have been involved in a long term collaboration dating the from early–mid 90's
  - substantial portfolio of IP

Mouse model of P.gingivalis mediated periodontal disease

- prophylactic model, oral infection, assess bone (maxillae) loss
- complex, proteins and peptides protective
- O'brien-Simpson *et al*., J. Immunol. 175:3980, 2005



Periodontal disease vaccine

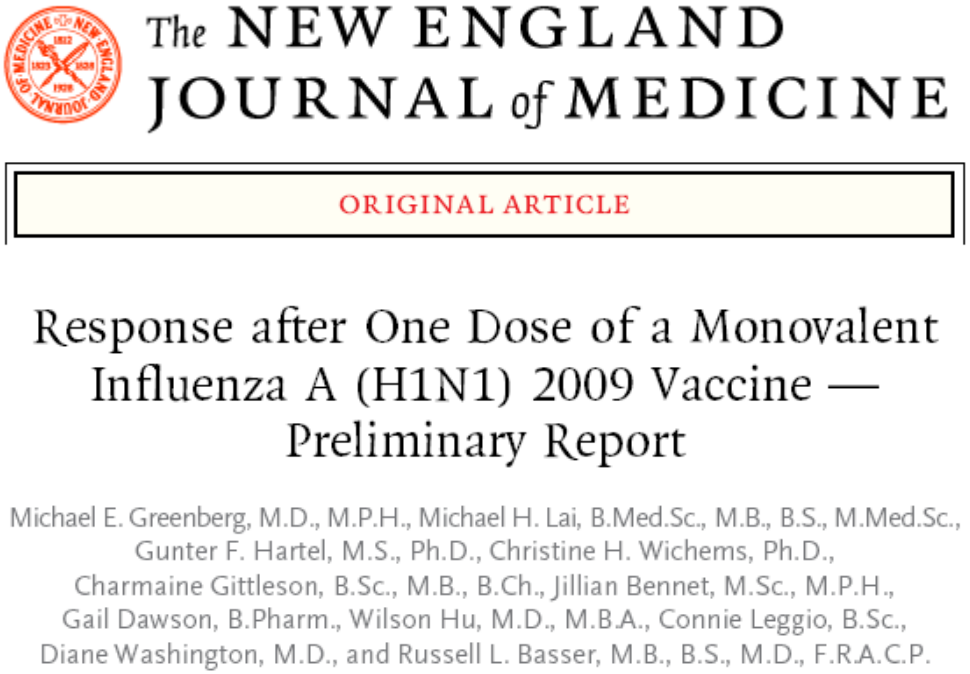
- Research and development of a therapeutic vaccine for the treatment of periodontal disease

Collaboration partners

- CRC for Oral Health Science
  - successful rebid July 09, $32m funding over 9 years from Jan 2010
- CSL Limited
  - CSL a major industry participant in the CRC with rights in the area of vaccine development
- **Sanofi Pasteur**
  - **leading global manufacturer of vaccines**
  - **CSL and Sanofi have entered into a research agreement**
  - **option to an exclusive worldwide license**

Influenza Vaccines

Publications



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Response after One Dose of a Monovalent Influenza A (H1N1) 2009 Vaccine — Preliminary Report

Michael E. Greenberg, M.D., M.P.H., Michael H. Lai, B.Med.Sc., M.B., B.S., M.Med.Sc., Gunter F. Hartel, M.S., Ph.D., Christine H. Wichems, Ph.D., Charmaine Gittleson, B.Sc., M.B., B.Ch., Jillian Bennet, M.Sc., M.P.H., Gail Dawson, B.Pharm., Wilson Hu, M.D., M.B.A., Connie Leggio, B.Sc., Diane Washington, M.D., and Russell L. Basser, M.B., B.S., M.D., F.R.A.C.P.

Pandemic (H1N1) 2009 Influenza Vaccine

- *Findings: A single 15 mcg dose is highly immunogenic in adults. Safety & tolerability consistent with seasonal flu.*
- *Published 10 Sept 09*

Seasonal Influenza

- Nolan et al. (2009) Safety and immunogenicity of an inactivated thimerosal-free influenza vaccine in infants and children. Influenza and Other Respiratory Viruses

Clinical Studies

- *Dosing for all influenza clinical trials now complete:*
  - *22,175 participants recruited at 115 sites in 3 countries, in 20 months (between 25 February 08 to 21 October 09)*

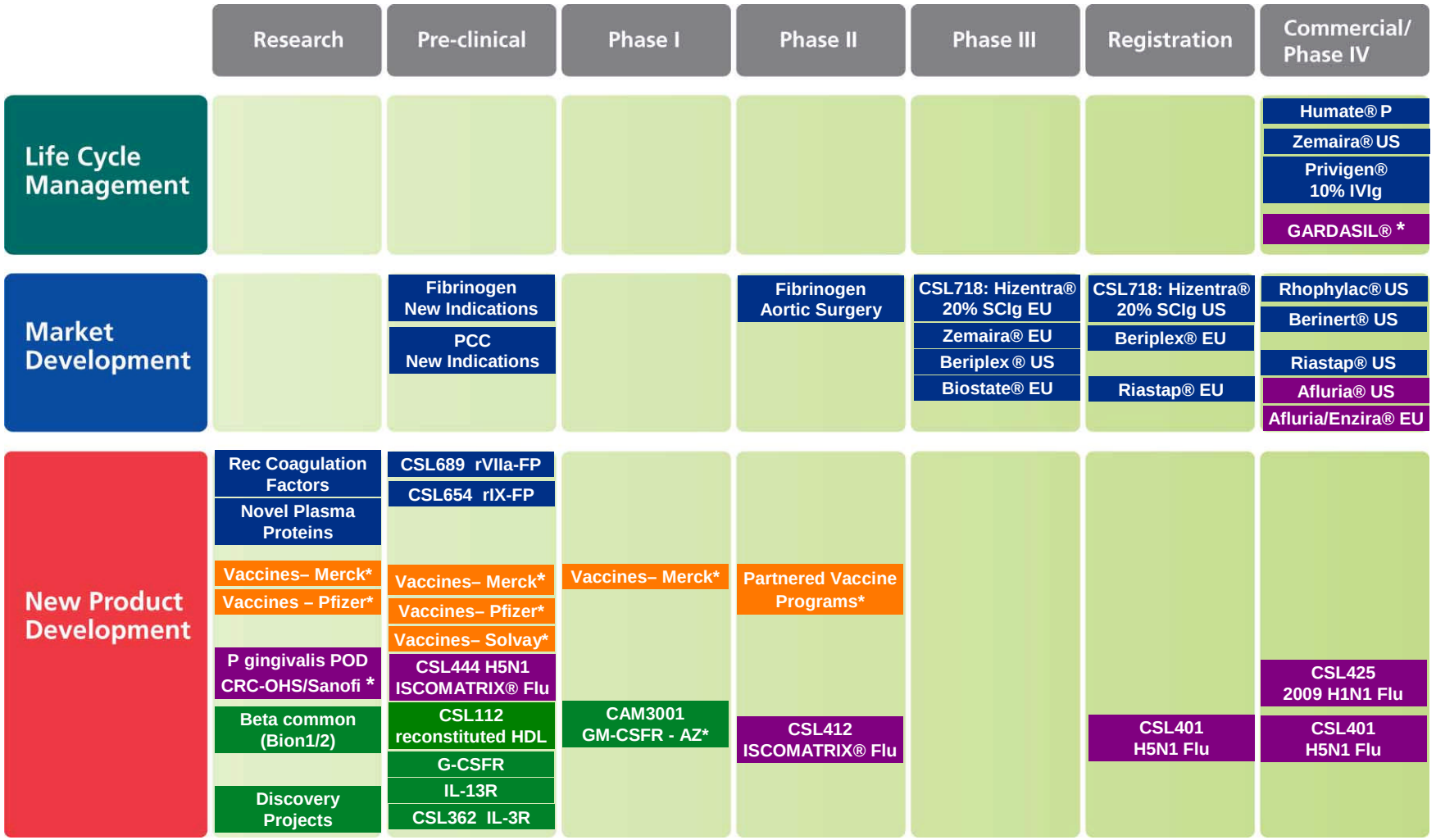
- Afluria® Seasonal Influenza Vaccine (USA)
  - 4 post-marketing commitment studies
  - On track to meet FDA deadline of 30 June 2010

- Pandemic (H1N1) 2009 Influenza Vaccine
  - 4 studies: paediatric & adult in Australia & USA

New Registrations

- USA
  - FDA approved Influenza A (H1N1) 2009 Monovalent Vaccine for 18 years and over – 15 September 09
  - FDA approved Afluria ® / Influenza A (H1N1) 2009 Monovalent Vaccine for 6 months to 17 years – 10 November 09
- Australia
  - TGA approved Panvax® H1N1 Vaccine for 10 years and over – 18 September 09
  - TGA approved Panvax H1N1 Junior® influenza vaccine for 6 months to 3 years – 3 December 09
- Other Pandemic (H1N1) 2009 Influenza Vaccine Approvals
  - Singapore – 9 October 09
  - Germany – 27 November 09
  - WHO – 1 December 09

Global R&D Pipeline December 2009



Core Capabilities: Replacement Therapies | Vaccines | Immunomodulators | Therapeutic Proteins

* Partnered Projects

Q&A