

# R&D Briefing

December 8, 2011

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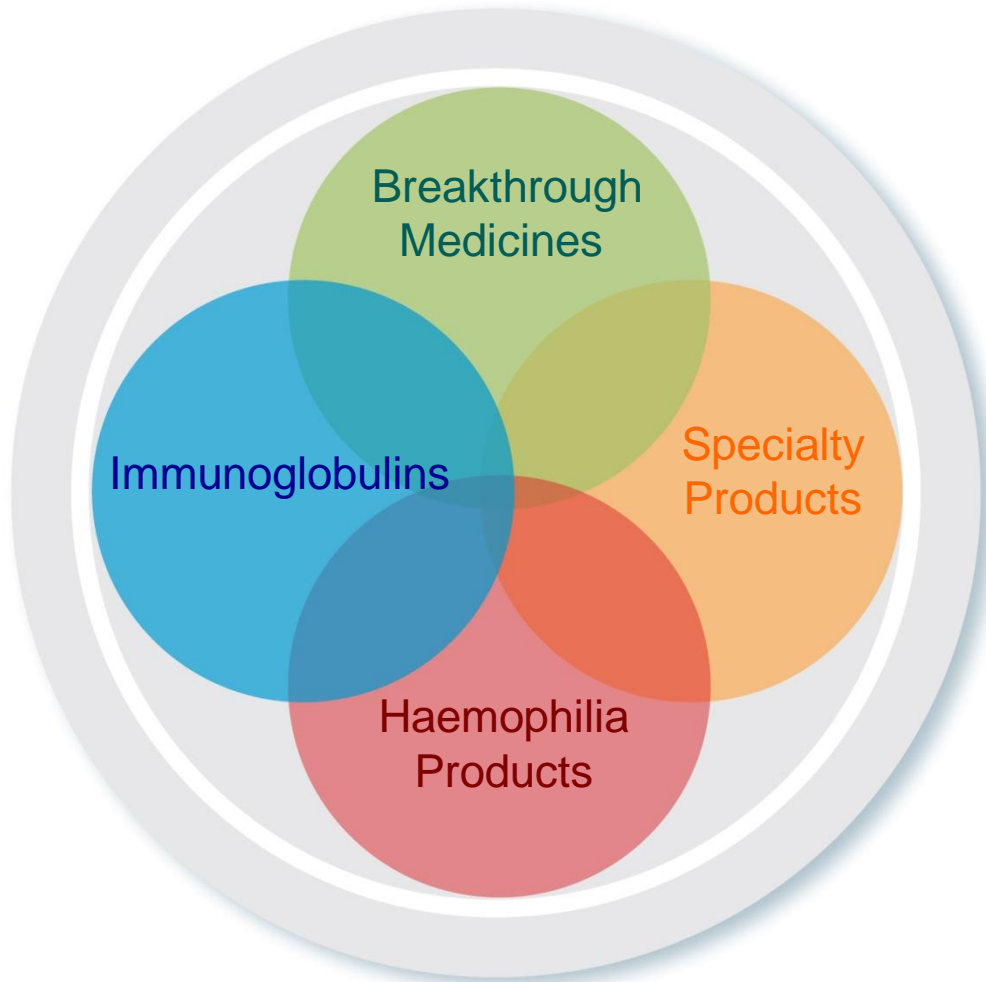
# Agenda December 2011 R&D Briefing

## 8.30am: Sign in and coffee

- Welcome Mark Dehring
- Introduction & Highlights Andrew Cuthbertson
- Immunoglobulins
- Specialty Bleeding Products
  - Clinical Development Russell Basser
  - Commercial Opportunities Ingolf Sieper
- Q&A and Break
- Coagulation/Haemophilia
  - New Product Development Val Romberg
  - Commercial Opportunities Ingolf Sieper
- Licensing Andrew Cuthbertson
- Summary
- Q&A

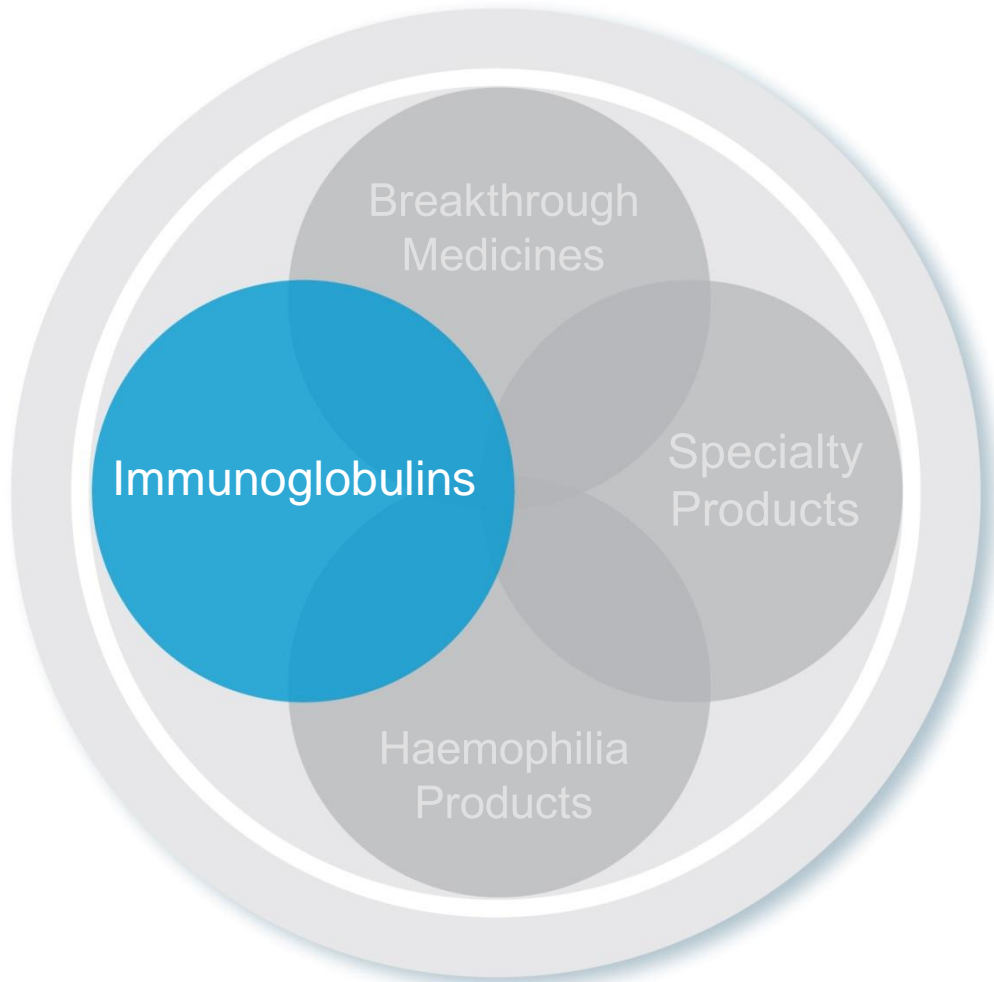
# Introduction and Highlights

# CSL 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

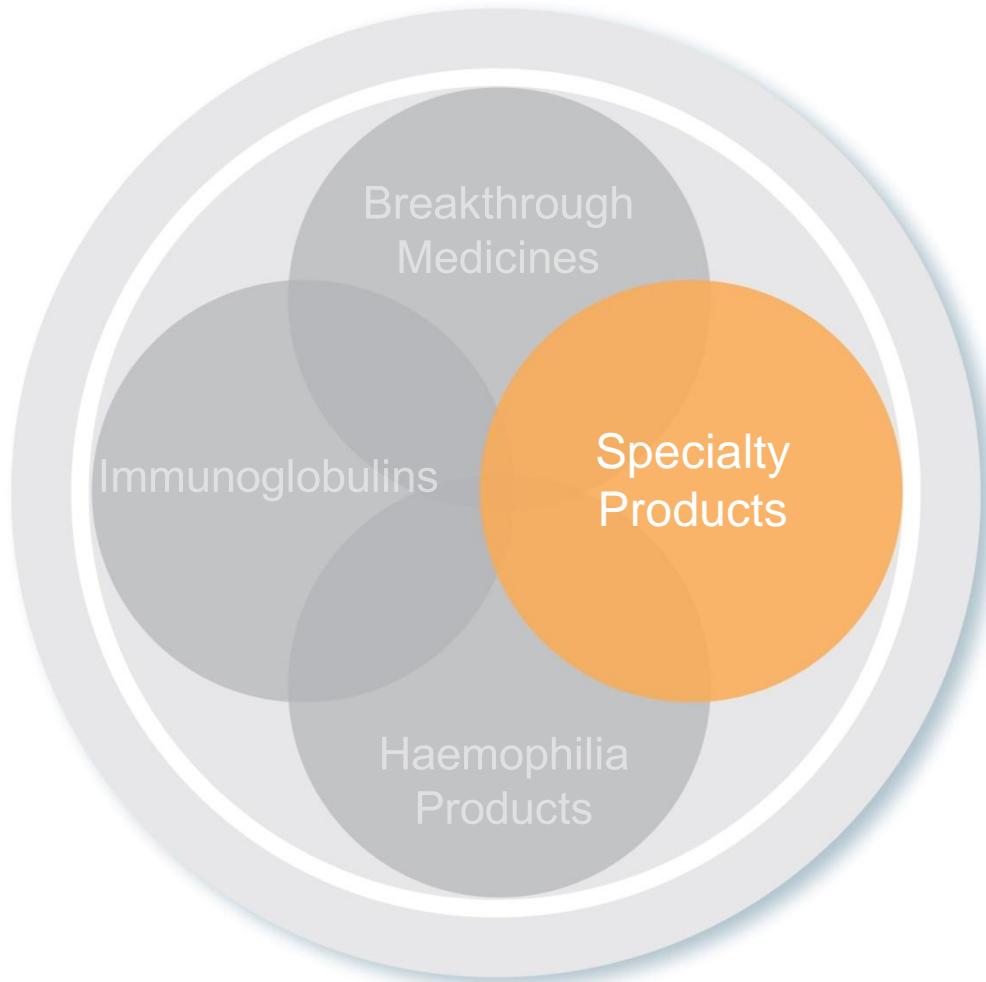
# Immunoglobulins Strategy



Supporting and enhancing current portfolio

- Patient convenience
- Yield
- Label
- Formulation science

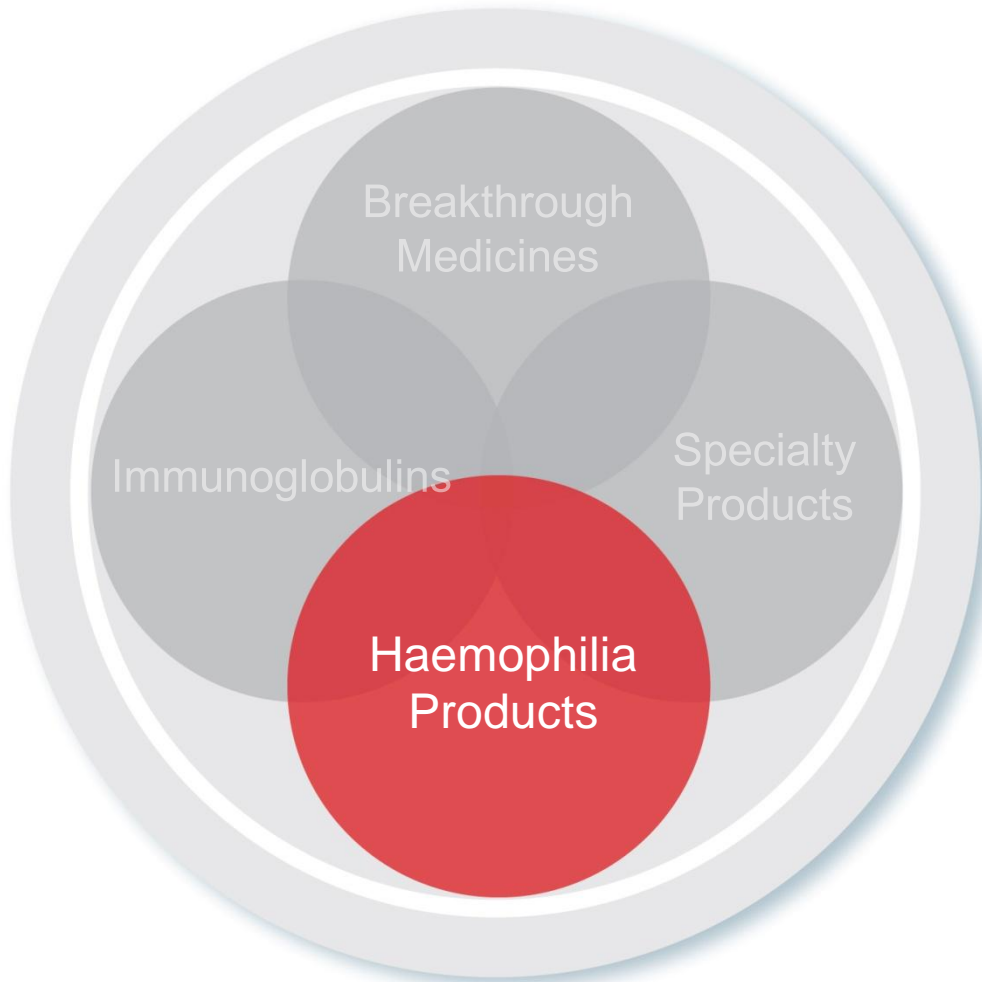
# Specialty Products Strategy



Expanding use of specialty plasma products through:

- New markets
- Novel indications
- Novel modes of administration

# Haemophilia Strategy

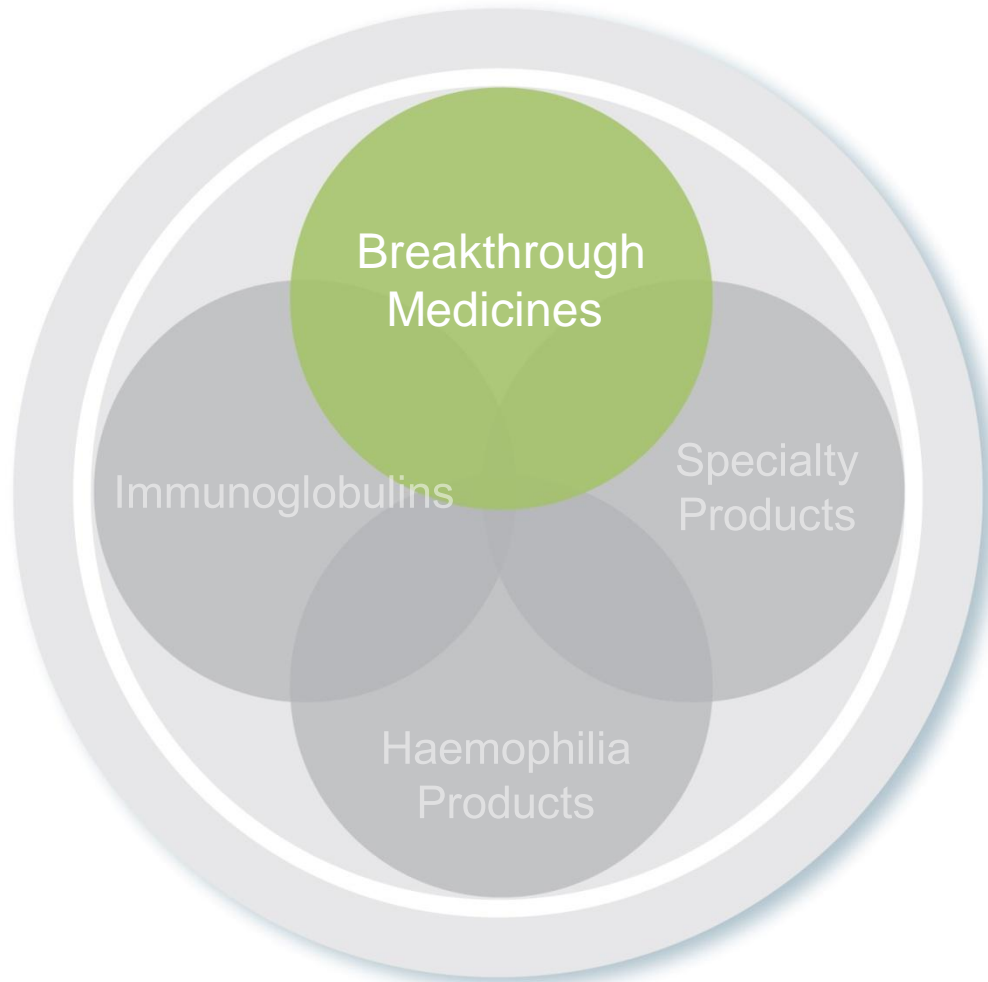


Supporting and enhancing portfolio and developing new products

- Plasma products
- Recombinant analogs
- Coagulation research



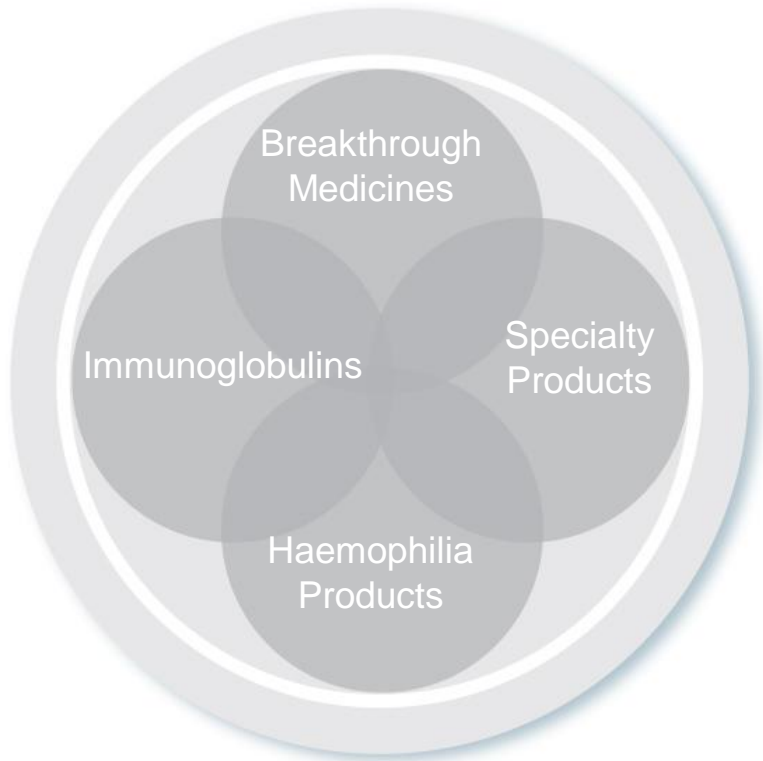
# Breakthrough Medicines Strategy



Developing new protein-based therapies

- Significant unmet need
- Multiple indications

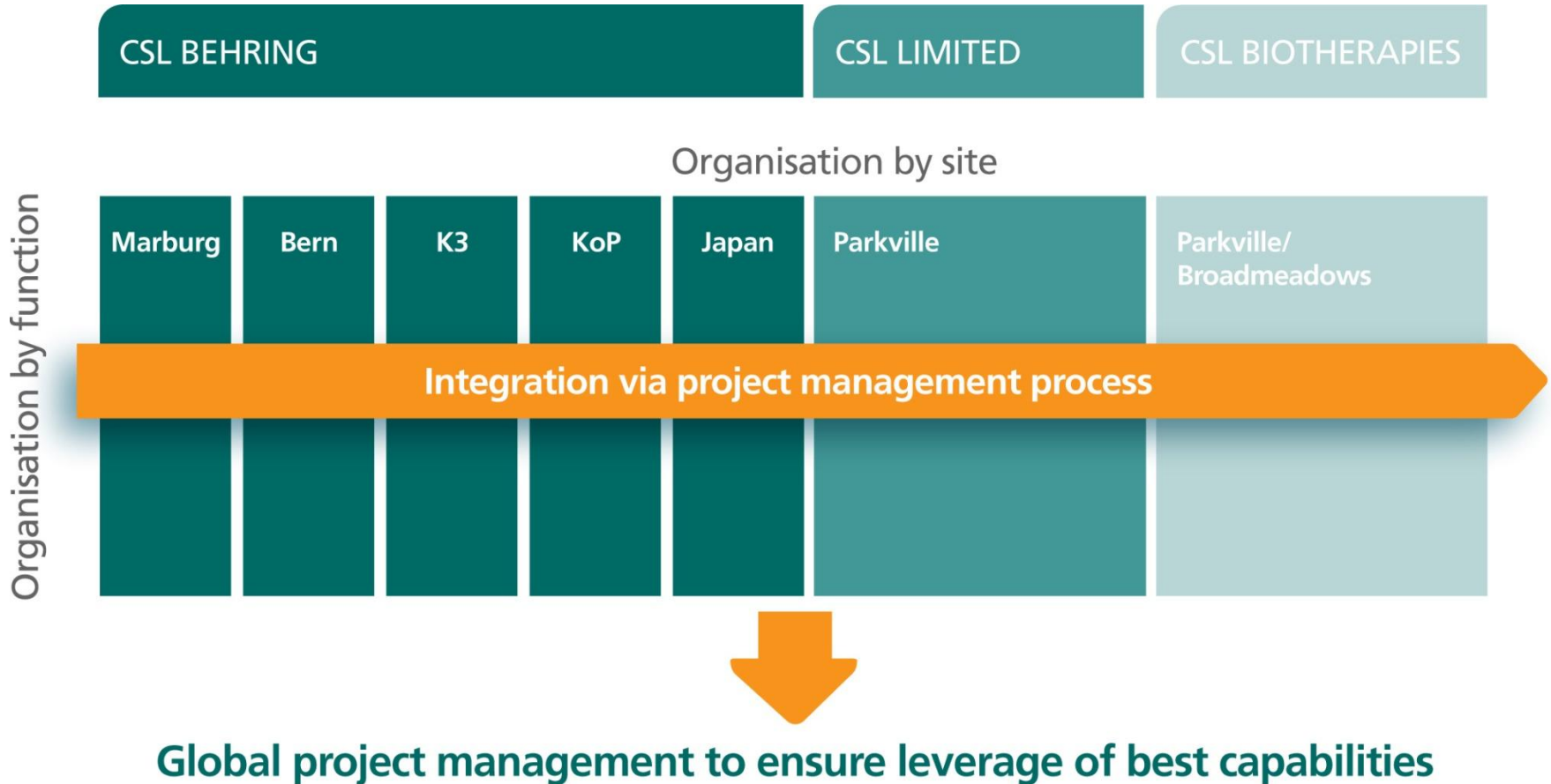
# Licensing Strategy



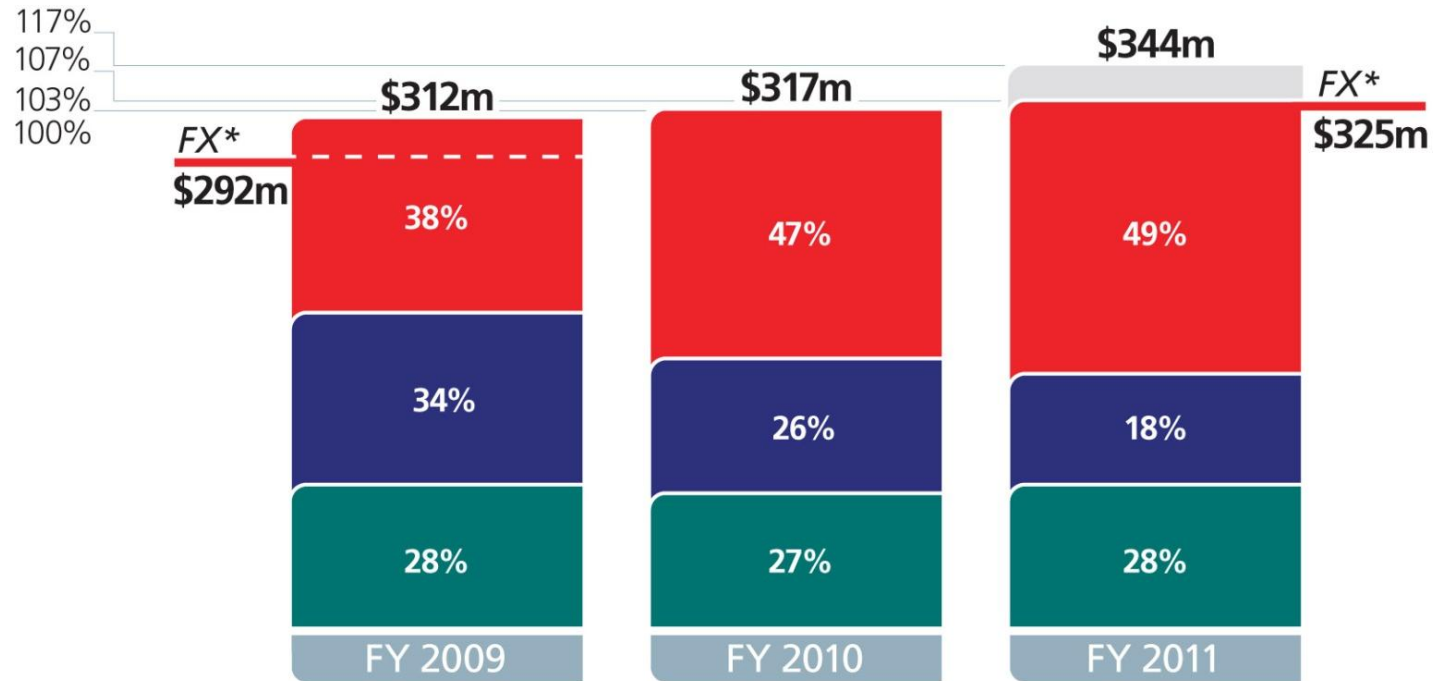
Optimise value of IP Portfolio and assets

- Partner high opportunity products
- Continue broad licensing strategy for ISCOMATRIX® adjuvant

# Leveraging Global Capabilities



# R&D Investment



Life Cycle Management

Market Development

New Product Development

\*Foreign currency impact using FY2010 exchange rates

# Global R&D Pipeline

December 2010

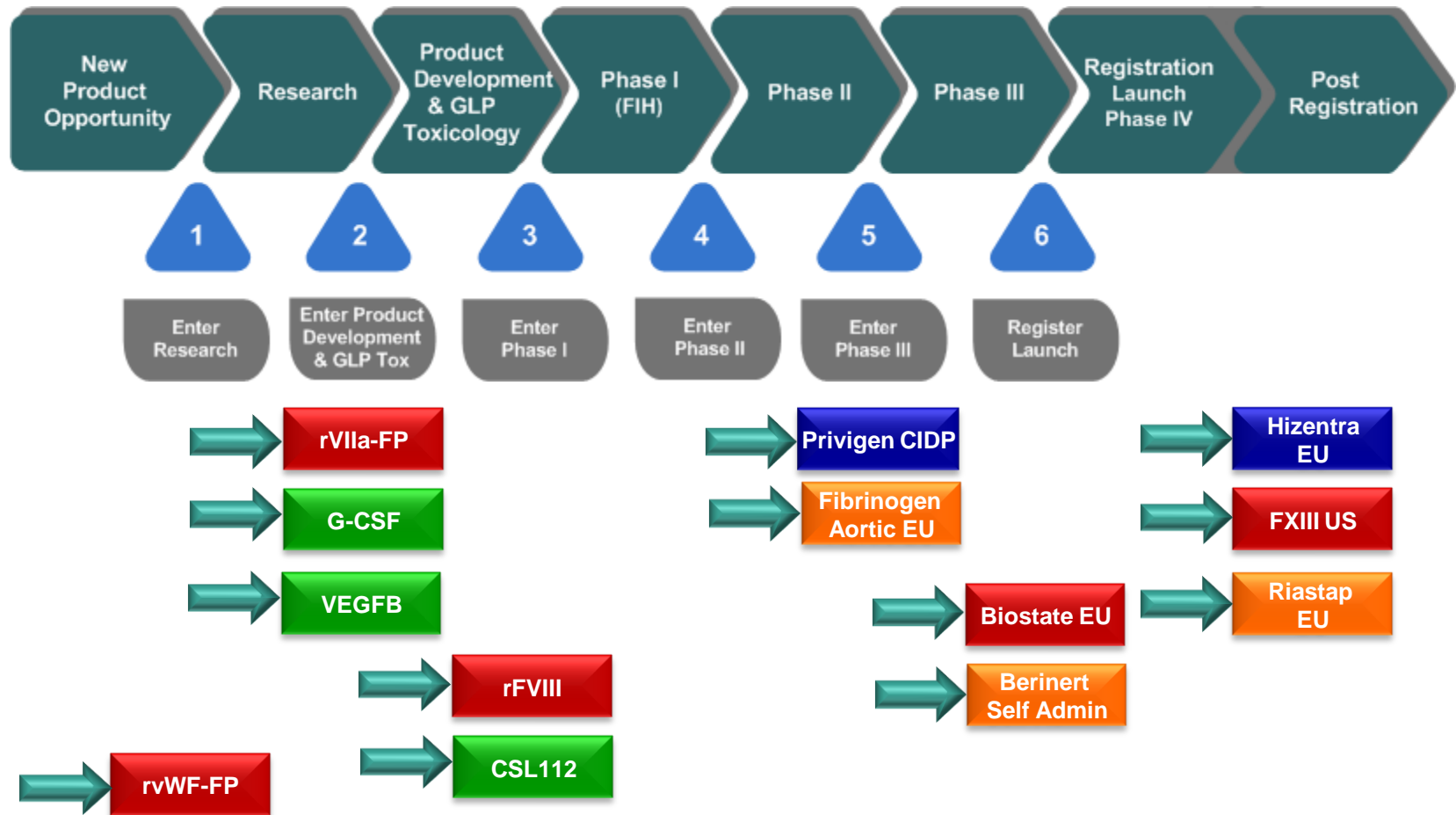


Core Capabilities



\* Partnered Projects

# Progress through Stage Gates in 2011





Core Capabilities



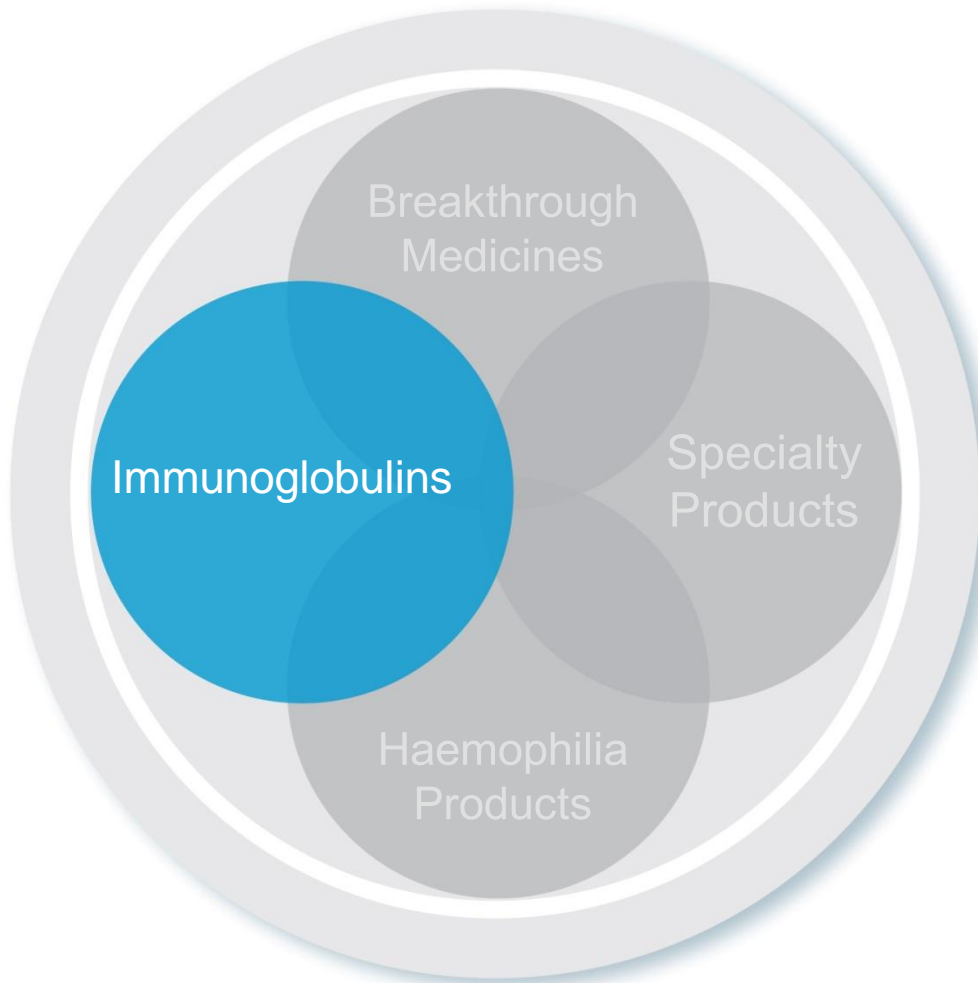
\*Partnered Projects

#LCM includes direct post marketing commitments as well as pathogen safety, capacity expansions, yield improvements, new packages and sizes for all registered products

# Immunoglobulins



# Immunoglobulins



Supporting and enhancing current portfolio

- Patient convenience
- Yield
- Label
- Formulation science

Key Focus

- Hizentra<sup>®</sup>
- Privigen<sup>®</sup>

The first 20% high concentration low volume SCIG for convenient self administration providing steady-state Ig levels and an established long-term safety record with chronic administration

## Global Introductions Continue

- Launched in US since 2010
- In 2011, broader approvals in EU and Canada
- Japan Phase III licensing study complete



## Exploring Chronic Use of Hizentra in Immunomodulation

- Pursuing SCIG for the treatment of CIDP
- Anticipated study initiation in 2012

The first and only 10% liquid intravenous immunoglobulin (IVIg) therapy that is proline stabilised with room temperature storage up to 36 months

## Building Capacity to Address Patient Needs Globally

- IgLab Module2 on-line increasing capacity
- Privigen approved in US, Europe, South America with additional country registrations underway

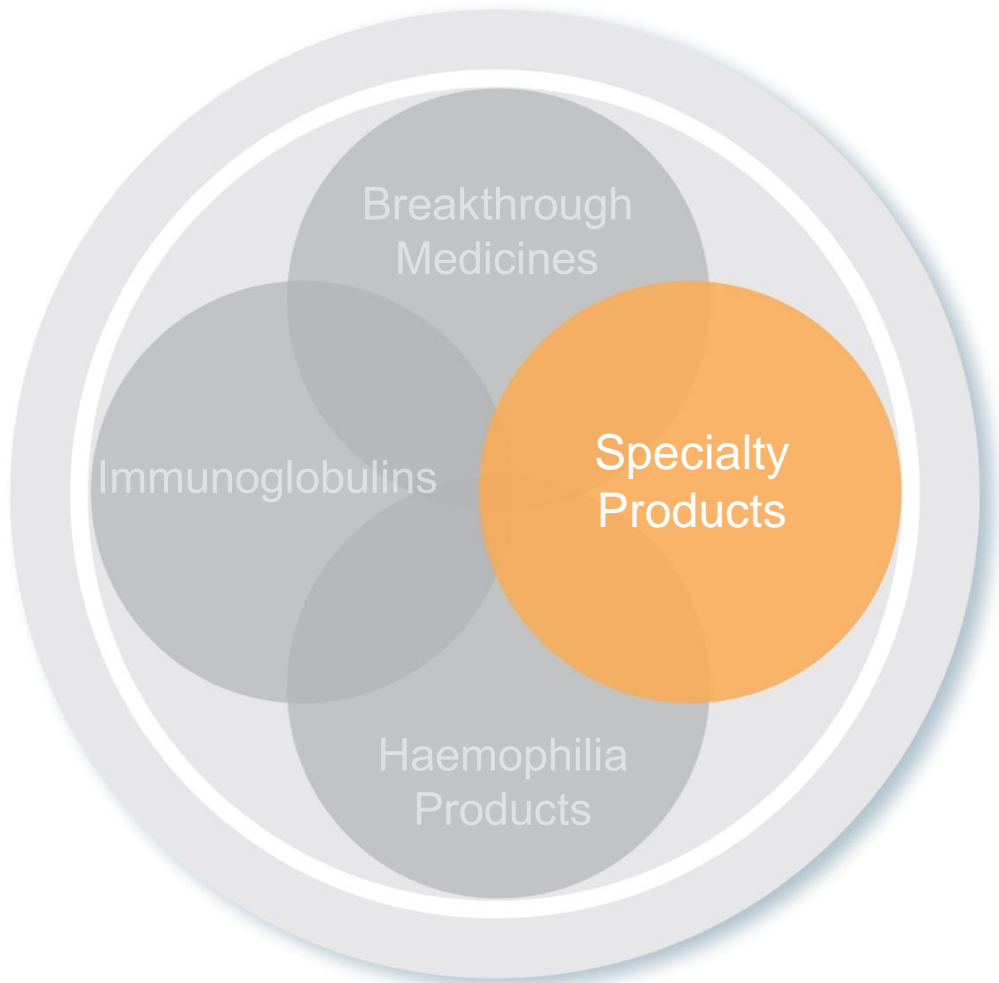
## Strengthening Presence in Neurology Market

- Phase III study in CIDP conducted in Europe
- LPLV Completed Nov 2011
- Anticipate filing in EU in Q2 2012



# Specialty Products

# Specialty Products



Expanding use of specialty plasma products

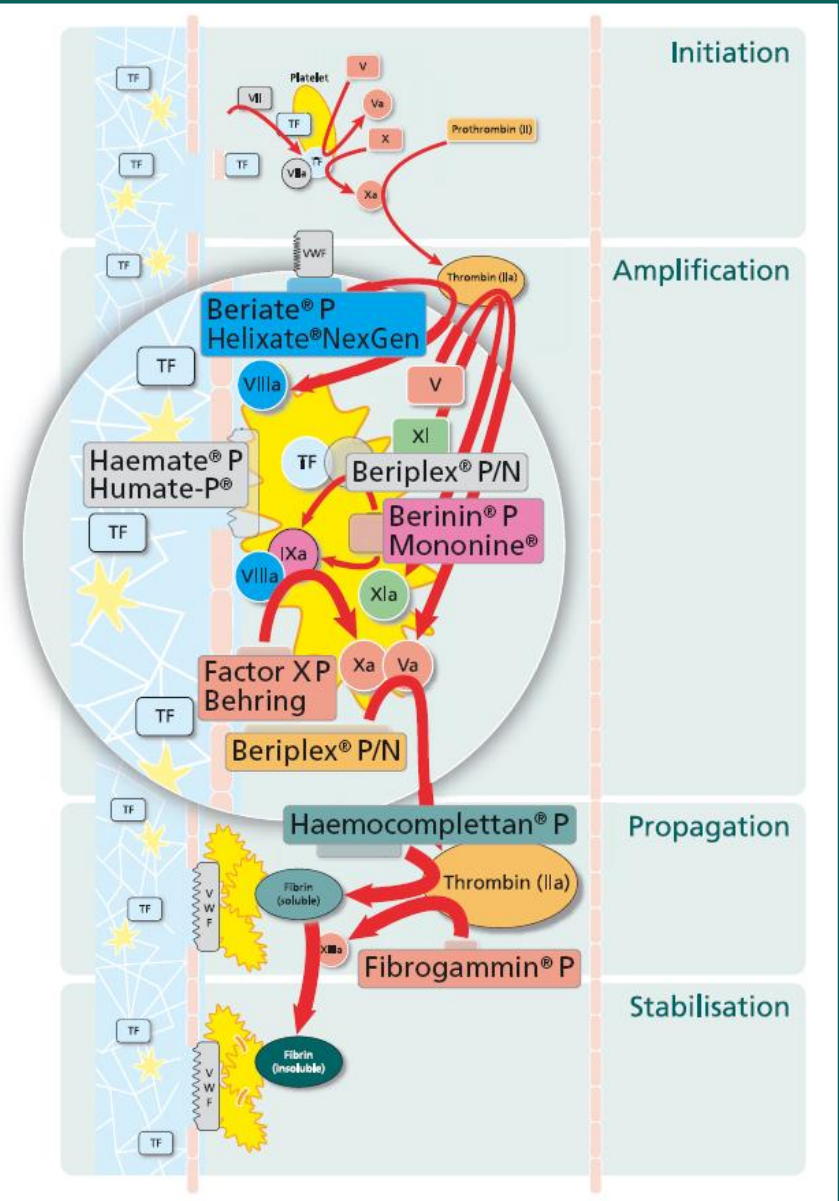
e.g.

- Berinert<sup>®</sup>
- Beriplex<sup>®</sup>
- Riastap<sup>®</sup>
- Zemaira<sup>®</sup>

Key Focus

- Acquired bleeding
  - Perioperative bleeding

# Correcting problems that lead to bleeding



# Acquired Bleeding Disorders

- Coagulation factor deficiencies can occur because of drugs, surgery, trauma, liver disorders, other diseases
- Current treatment options
  - Traditional blood products – platelets, fresh frozen plasma (FFP), cryoprecipitate
  - Specific factor concentrates such as those in CSL portfolio
- Limitations with traditional approaches
  - Sensitivity reactions
  - Large volume
  - Time taken to administer
  - Storage not straightforward
  - Consume a lot of donated blood
  - Limited lifespan

Fibrinogen  
(Riastap™ / Haemocomplettan®)  
for Complex Cardiac Surgery



# Fibrinogen in cardiopulmonary bypass surgery

- Coagulation factors are consumed → bleeding



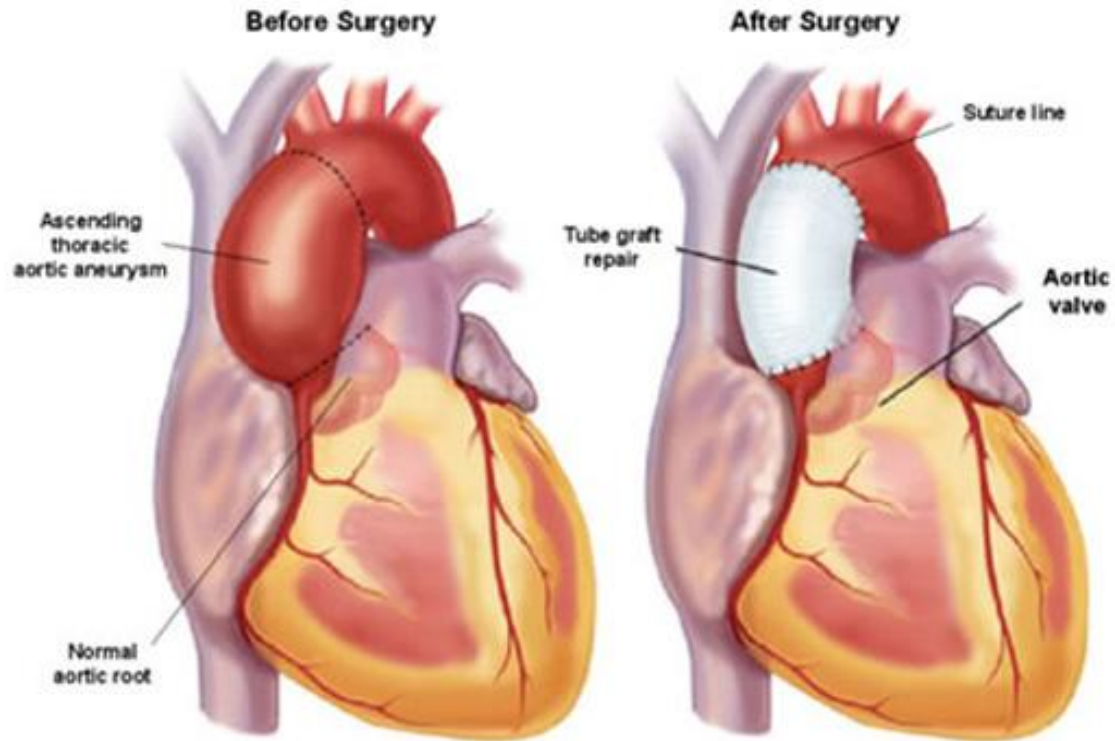
# Hannover proof-of-concept study in aortic repair

- Fibrinogen reduced proportion of patients requiring transfusion

Administration of donated blood products	Proportion of subjects	
	<b>Fibrinogen</b> (N = 29)	<b>Placebo</b> (N = 31)
No	45%	0%
Yes	55%	100%

p<0.0001

# Complex Cardiac Surgery



# Fibrinogen Development

- Europe / Global
  - *Peri-/post-operative control of coagulopathic bleeding*
  - REPLACE Phase III study
    - 200 subjects – sites initiated December 2011
    - Aim to file label extension H2 2013
- US
  - *Coagulopathic bleeding related to complex cardiac surgery*
  - Dose-finding required by FDA
  - Considering options for broader indication

# Beriplex<sup>®</sup> to Reverse Anti-coagulation

# Challenges with anti-coagulation

- Anti-coagulants used to prevent clotting for people who are at risk
  - Vitamin K antagonists (ie warfarin) - most commonly prescribed
  - New generation products now being approved around the world
    - Specific for FXa, FIIa
- Potential problems
  - Bleeding can occur related to excessive anti-coagulation
  - Need to urgently reverse if trauma, surgery immediately required
  - ~3M people currently on warfarin in the US
    - ~100K patients in need of urgent reversal annually

# What is Beriplex<sup>®</sup>?



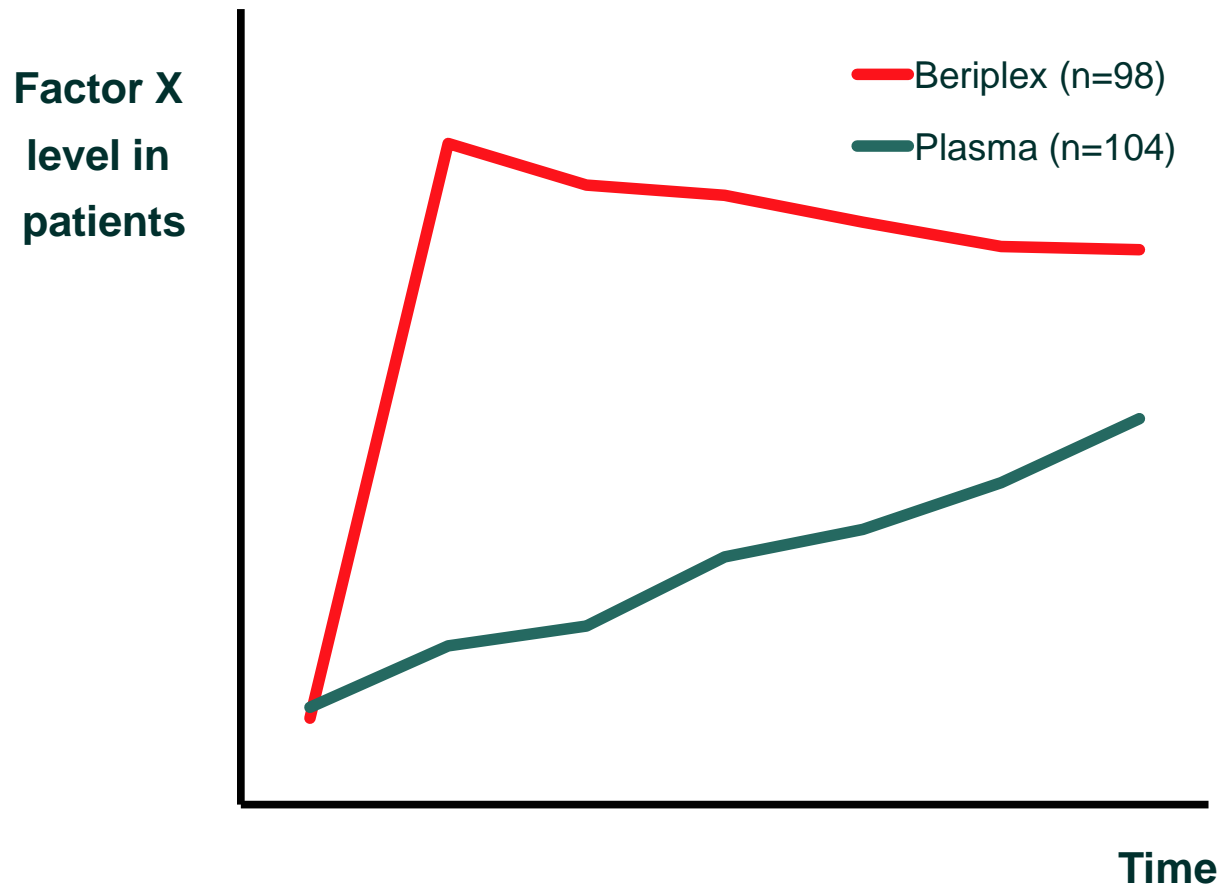
- Prothrombin Complex Concentrate = PCC
  - vitamin K-dependent coagulation factors (FII, FVII, FIX, FX)
  - 2 viral inactivation steps
- Specific antidote to vitamin K antagonists
  - new anti-coagulants?
- Used in Europe for >10 years with excellent safety record
- Current program
  - Expand geographical usage
  - Evaluate potential for correcting bleeding due to new anti-coags

# Program to licence Beriplex<sup>®</sup> in US

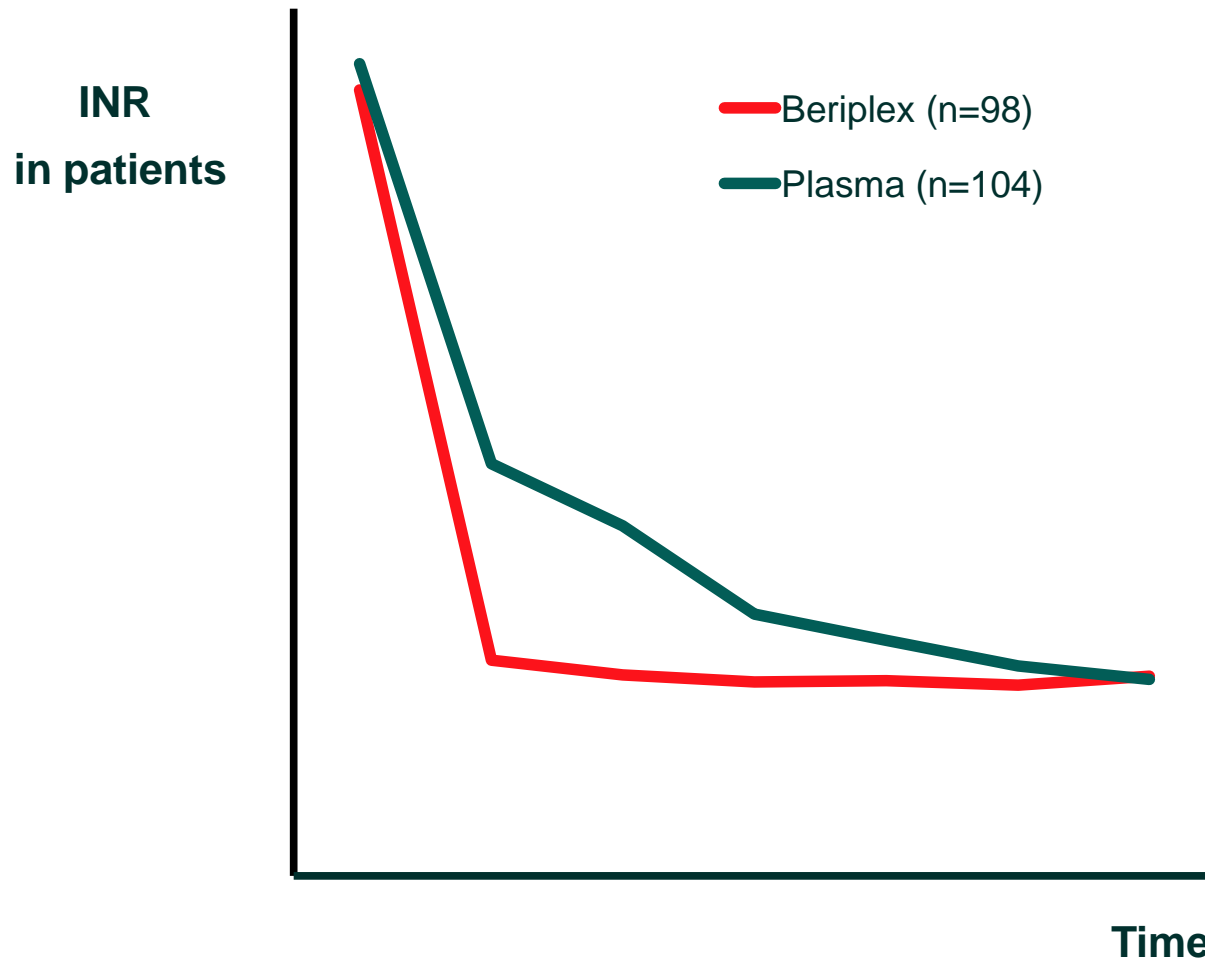
- Seeking approval for use of Beriplex<sup>®</sup> to reverse the effects of vitamin K antagonists for
  - Bleeding related to over-anticoagulation
  - Patients needing surgery
- 2 large randomised, controlled clinical trials
  - Bleeding study completed
  - Surgical study due to be completed mid 2012
- BLA submission planned for Q1 2012



# Effects of Beriplex<sup>®</sup> on specific clotting factor levels in Bleeding Study

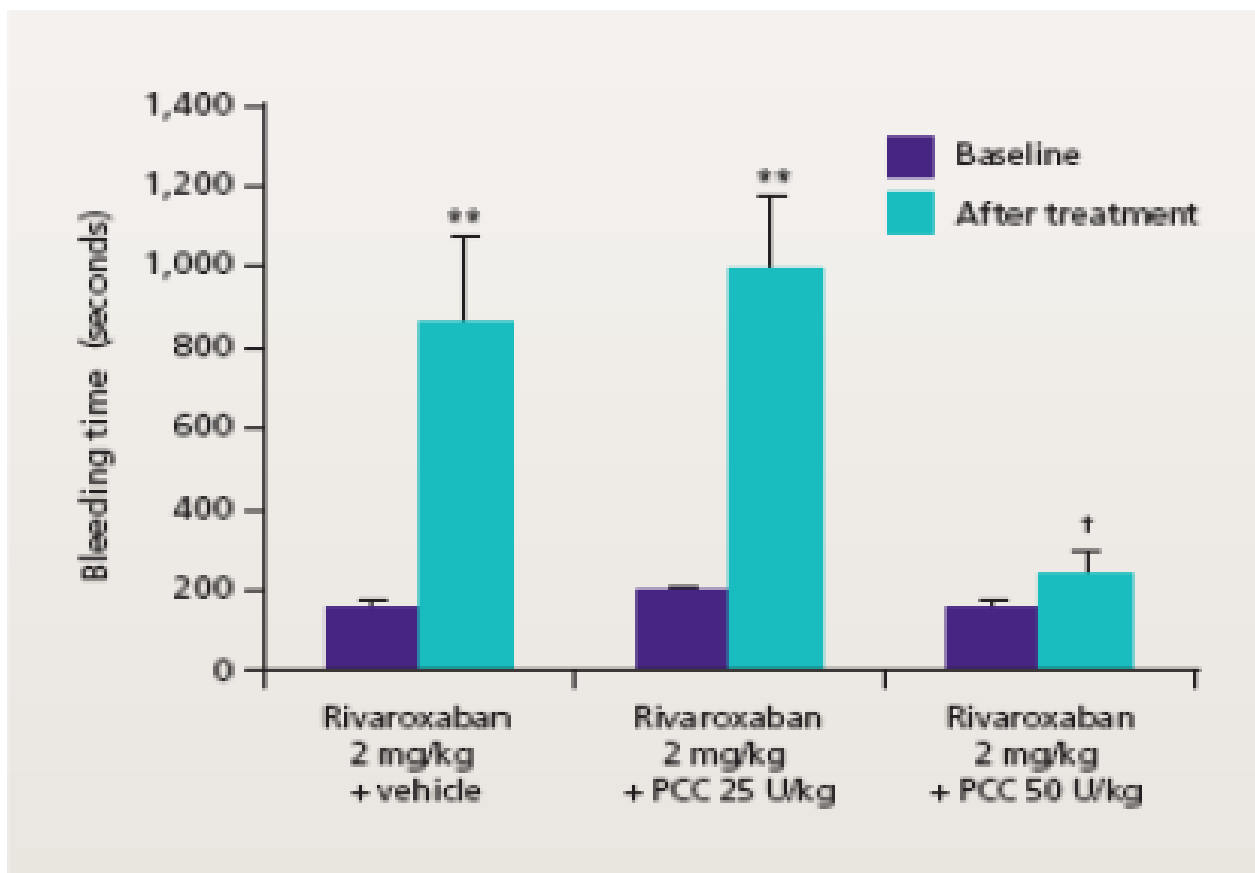


# Effects of Beriplex<sup>®</sup> on bleeding test in Bleeding Study



# Potential of Beriplex<sup>®</sup> for bleeding related to new anti-coagulants

*Preclinical data – rat bleeding model*



# Globalisation of Perioperative Bleeding (POB)

# Surgical or Coagulopathic Bleeding?



... in some cases a combination of both !!!

# What is the Challenge?

**BOF Syndrome!**

# BOF Syndrome



# Coagulation Cascade

## Intrinsic System

PL → XII → XI

IX

## Extrinsic System

VII ← TTPL

VIII

X

V

II

Stabilized through FXIII

Fibrinogen


Fibrin



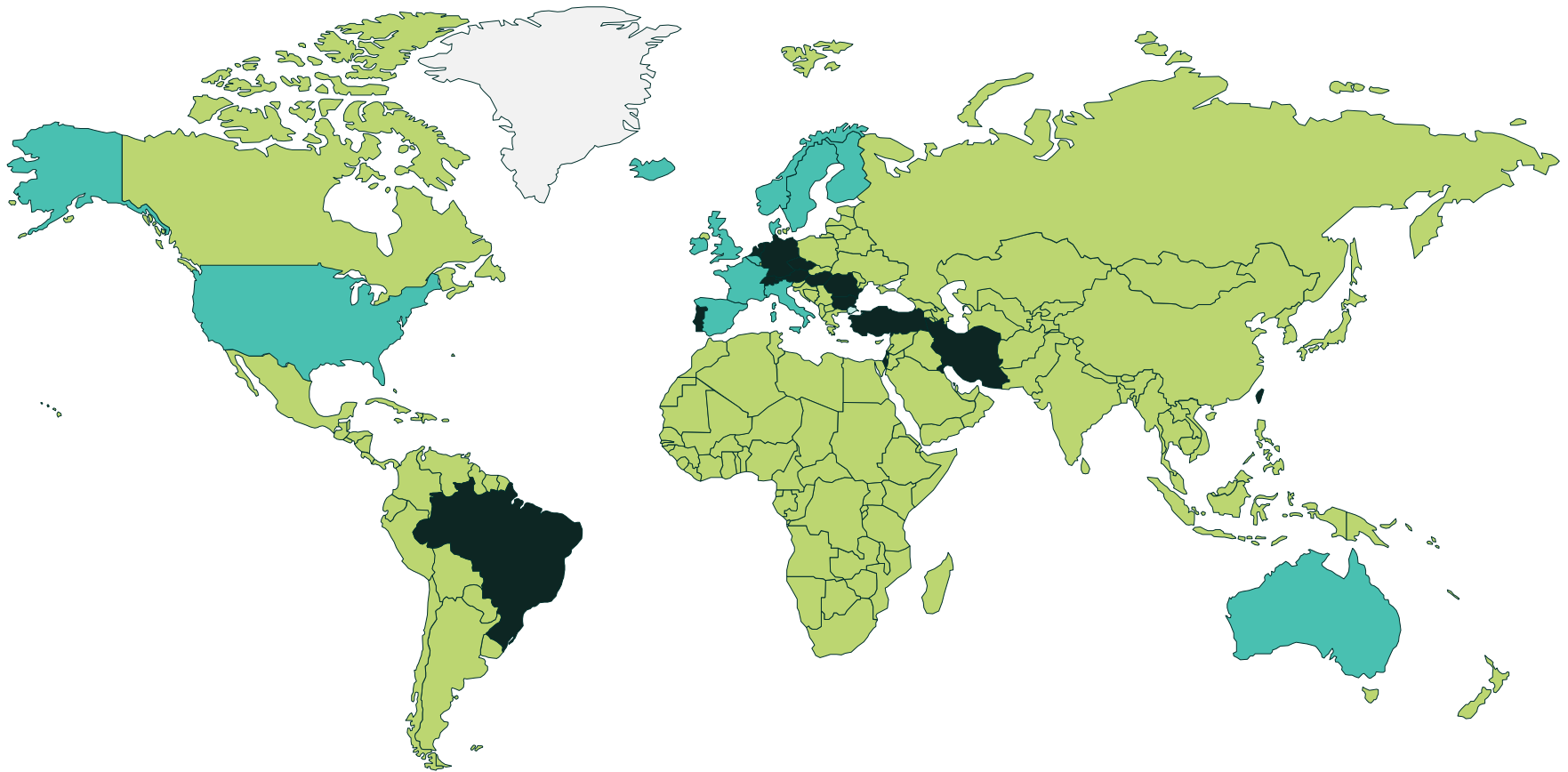
# Treatment Paradigm in Central Europe

- Given the order of factor deficiency in coagulopathic bleeding
  - **First:** Fibrinogen deficiency
    - First line – RiaStap when confirmed fibrinogen deficiency
  - **Second:** Impaired thrombin generation
    - First line – Beriplex P/N after fibrinogen normalisation and confirmation of impaired thrombin generation
  - **Subsequently:** Impairment of fibrinolysis post-surgery
    - First line –Fibrogammin >12 – 24 hours post-surgery

# Short-Term Strategy to Accelerate the Global Penetration of POB

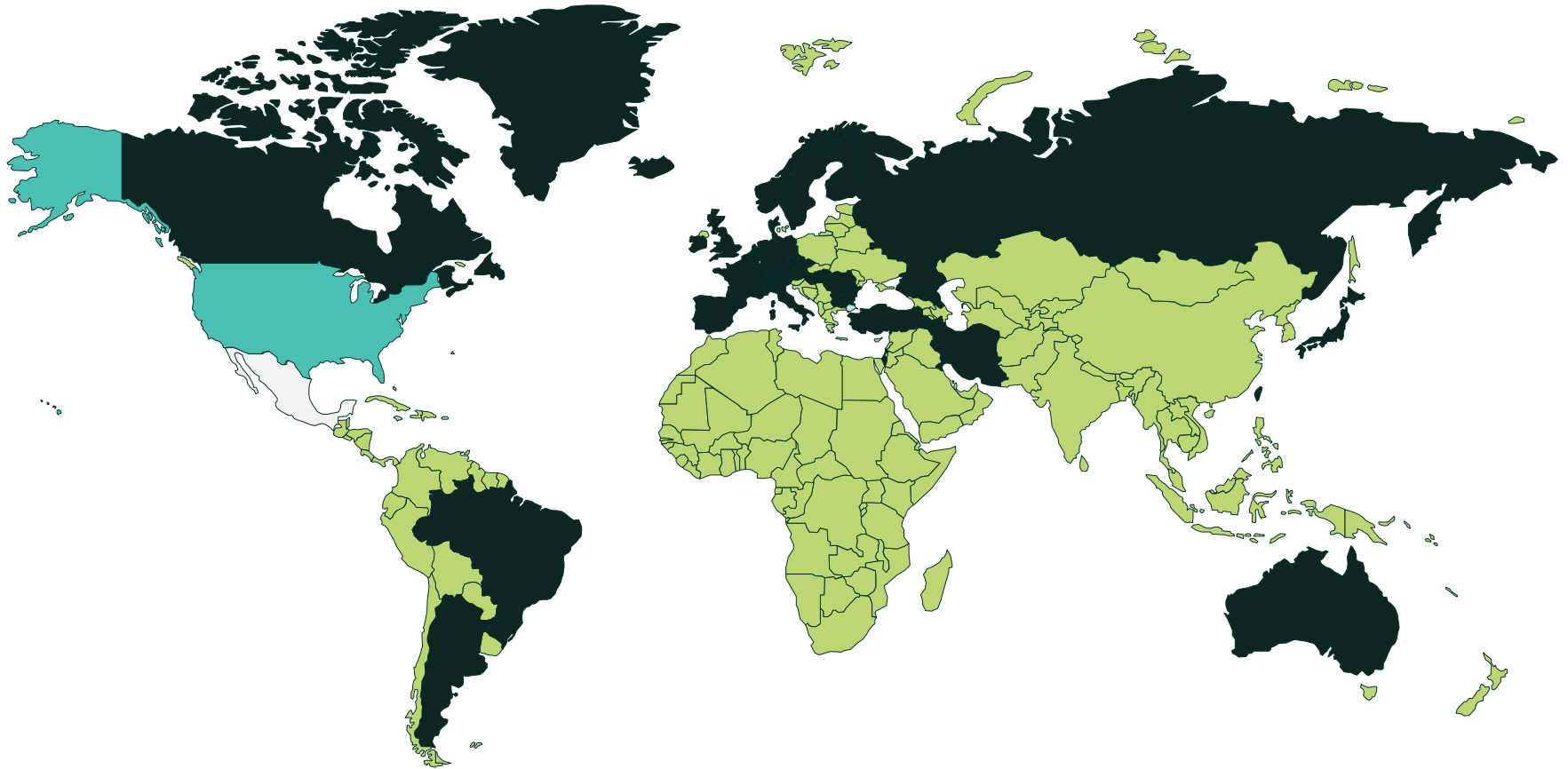
- Actively participate in ISICEM, WCA, EACTA, ESA
- Post partum hemorrhage guideline roundtables
- Grow in regions
  - Dedicated sales force
  - Education  100 roundtables
- Expand web presence
  - ISICEM supported medical education
  - *Allaboutbleeding* website

# Fibrinogen Registration Status 2011/12



	Acquired Indication	Austria, Brazil, Bulgaria, Czech Republic, Germany, Hungary, Iran, Israel, Kuwait, Netherlands, Portugal, Romania, Switzerland, Taiwan, Turkey
	Congenital Indication	Australia, Belgium, Denmark, Finland, France, Iceland, Ireland, Italy, Norway, Slovakia, Spain, Sweden, United Kingdom, USA

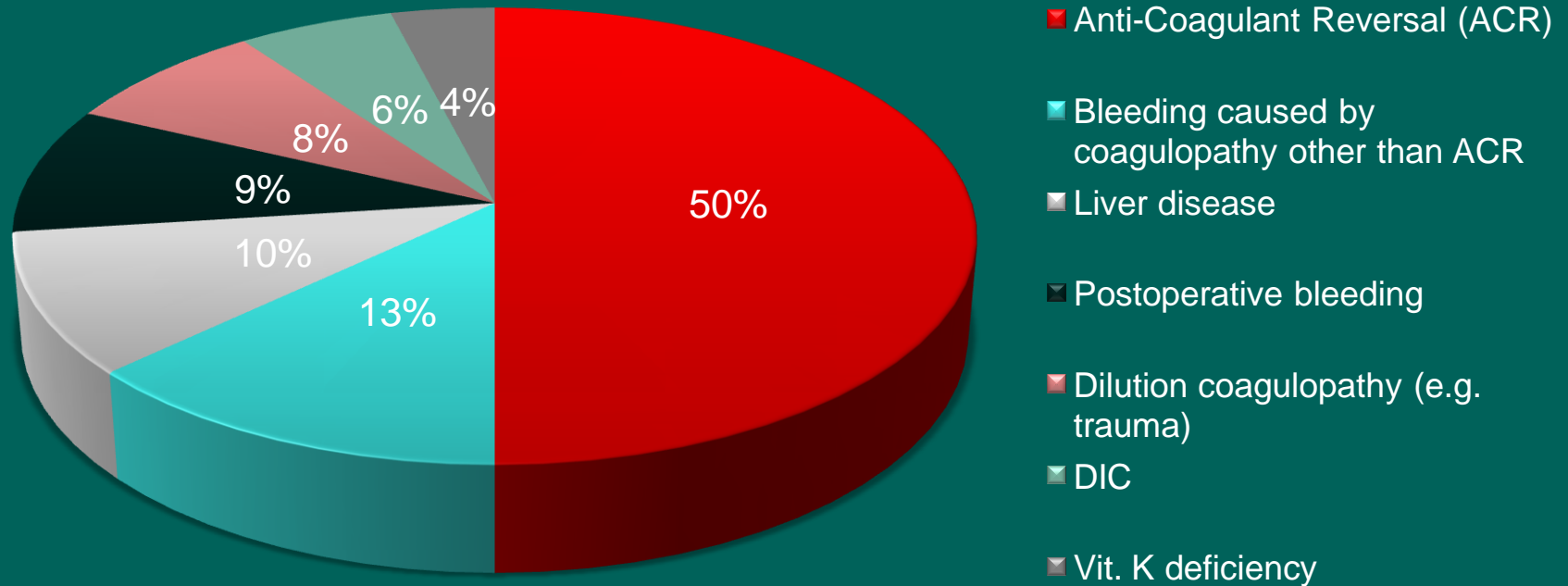
# Target Fibrinogen Registration Status 2015/16



Acquired Indication	Argentina, Austria, Australia, Belgium, Brazil, Bulgaria, Canada, Czech Republic, Denmark, Finland, France, Germany, Hungary, Iceland, Iran, Ireland, Israel, Italy, Kuwait, Netherlands, Norway, Portugal, Romania, Spain, Russia, Slovakia, Sweden, Switzerland, Taiwan, Turkey,
Congenital Indication	USA , Mexico

Beriplex®

# Main Indications for Beriplex<sup>®</sup>/PCC



Source: CSLB CEU PCC Market Research 2009

# Indications for Beriplex<sup>®</sup> US

- Two indications

1. Bleeding

- For the treatment of acute major bleeding resulting from an acquired deficiency of vitamin K-dependent coagulation factors and proteins C and S due to Vitamin K antagonist (warfarin) therapy

2. Surgery

- For the replacement of vitamin K-dependent coagulation factors and proteins C and S in patients on Vitamin K antagonist (warfarin) requiring emergency surgery or invasive intervention

# Primary Target Customer Segments

**ER Physicians, Nurses**

Need safe, cost effective treatments that rapidly resolve acute bleeding episodes

**Transfusion Medicine**  
Blood Bankers / Hematologists

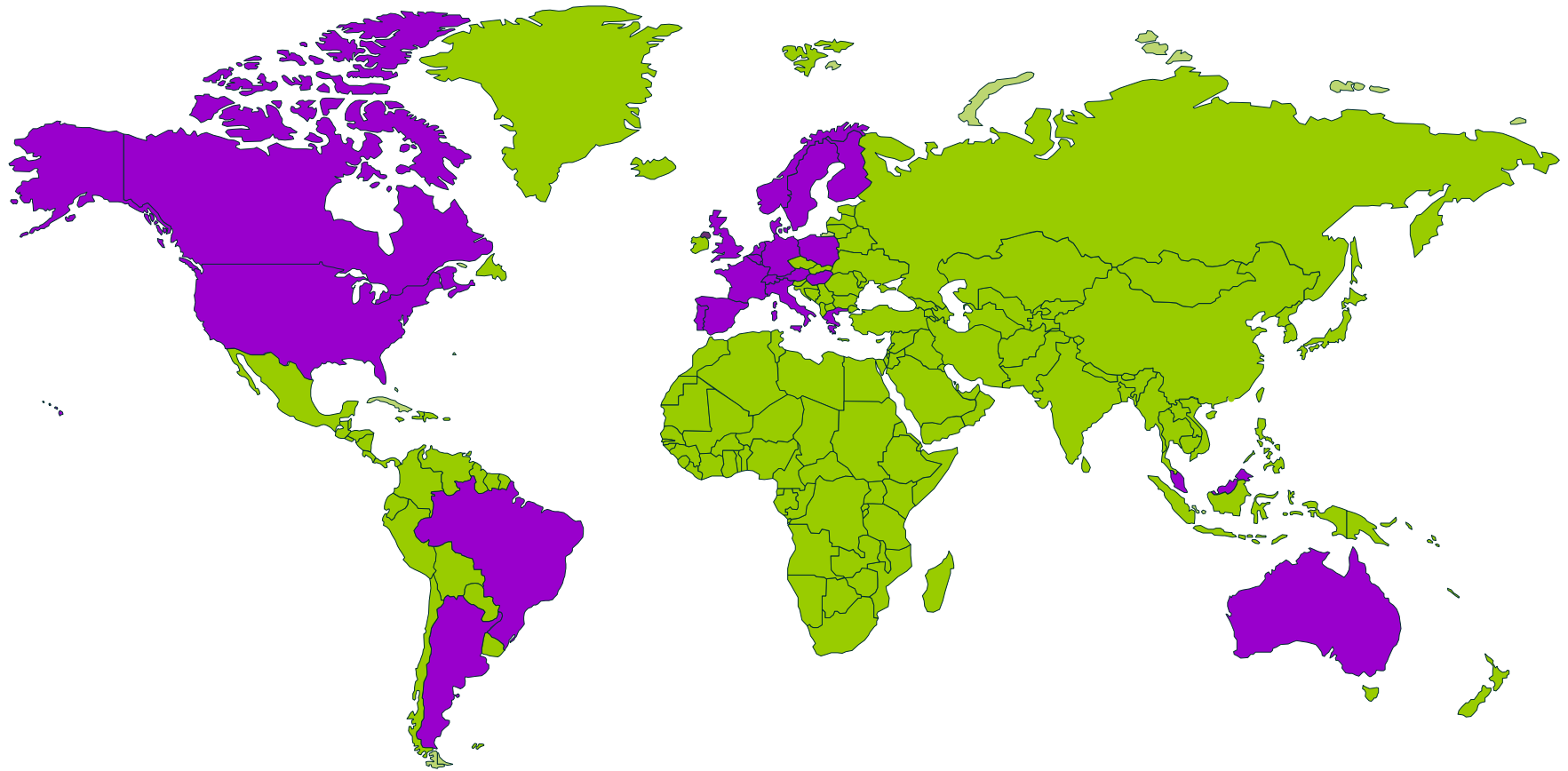
Need treatments that satisfy hospital physicians needs while helping them effectively manage the utilisation of blood products



**Pharmacists**

Need cost effective treatments to manage pharmacy budget while satisfying the needs of hospital physicians



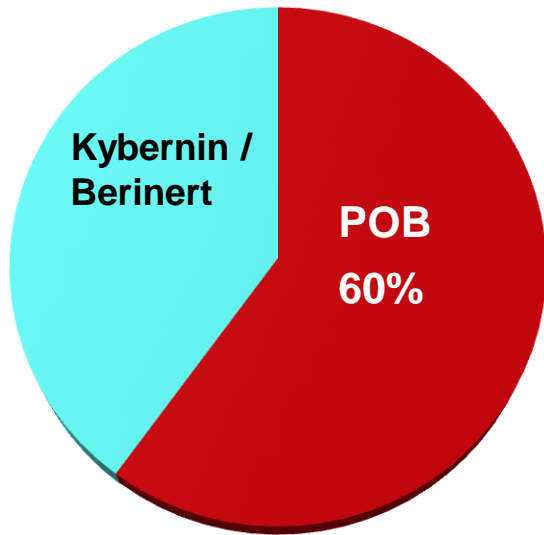
# Beriplex<sup>®</sup> Registration Status 2012



	registered/launched	Argentina, Australia, Austria, Belgium, Brazil, Canada, Finland, France, Germany, Great Britain, Greece, Hong Kong, Hungary, Italy, Luxembourg, Malaysia, Netherlands, Norway, Poland, Portugal, Spain, Sweden, Switzerland, Taiwan, United States
		

# Summary Commercial Opportunity POB

**Specialty Critical Care**  
**FY11 \$367m**



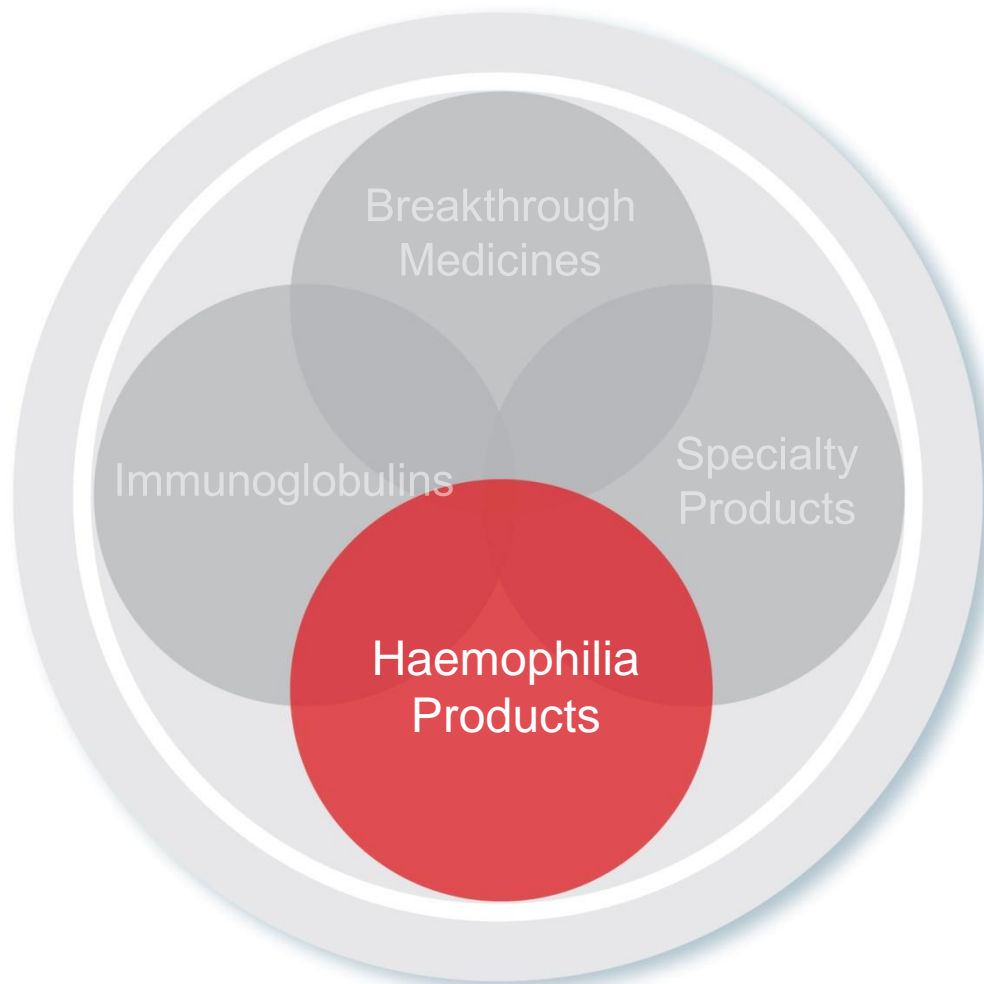
- Perioperative Bleeding
  - PCC: Beriplex<sup>®</sup>
  - Fibrinogen: Riastap<sup>®</sup>/Haemocomplettan<sup>®</sup>
  - FXIII: Fibrogammin<sup>®</sup>/Corifact<sup>®</sup>
- Treatment paradigm for POB has shifted in Central Europe
- Rest of Europe has started to follow
- In terms of registration we are 3+ years ahead
- Growth Potential POB
  - ~20% per annum mid-term

# Q&A

Break

# Haemophilia Products

# Haemophilia



Supporting and enhancing portfolio and developing new products

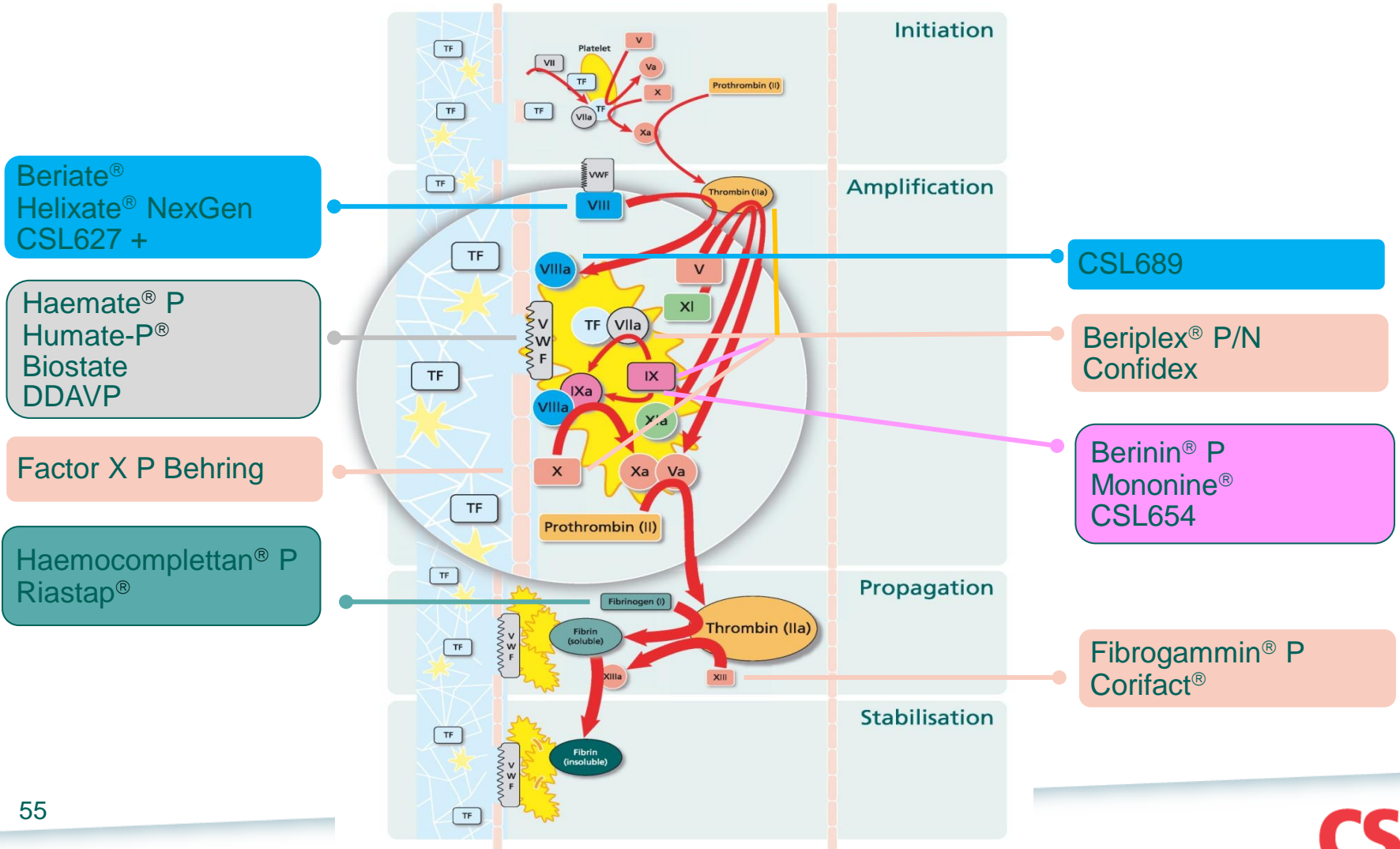
- Plasma products
- Recombinant analogs
- Coagulation research

## Key Focus

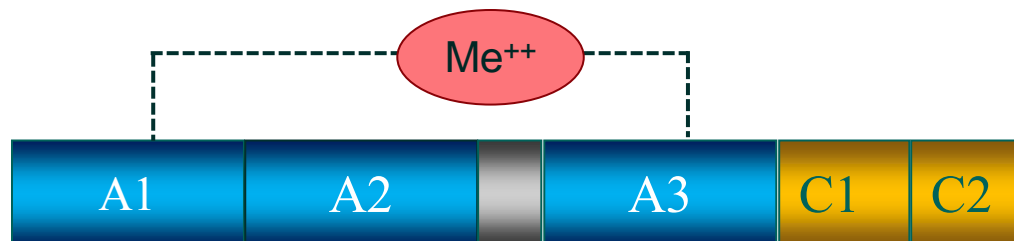
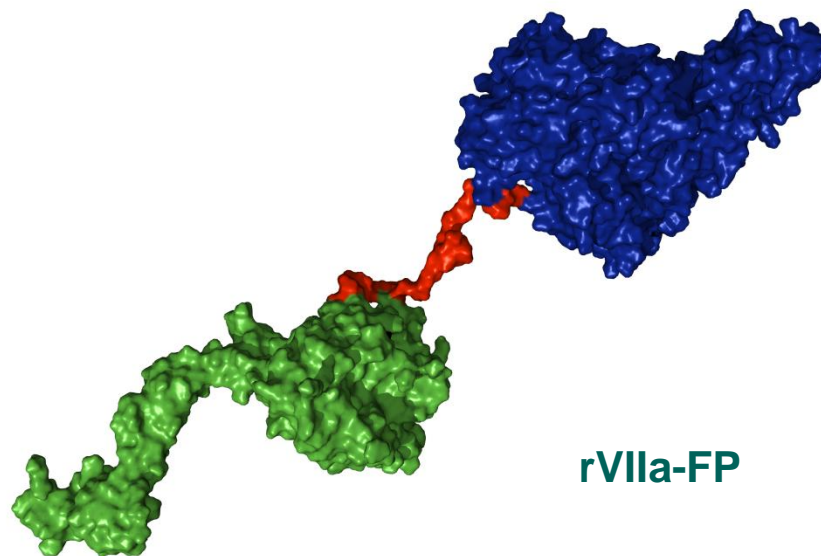
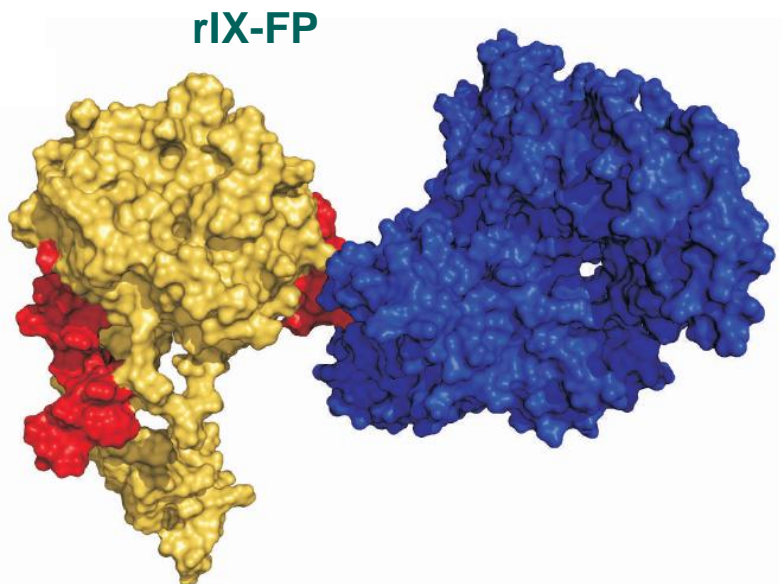
- Long acting rIX-FP
- Long acting rVIIa-FP
- rVIII-Single Chain
- Research into long acting rvWF-FP

# Coagulation Cascade

Not all products are licensed in all countries



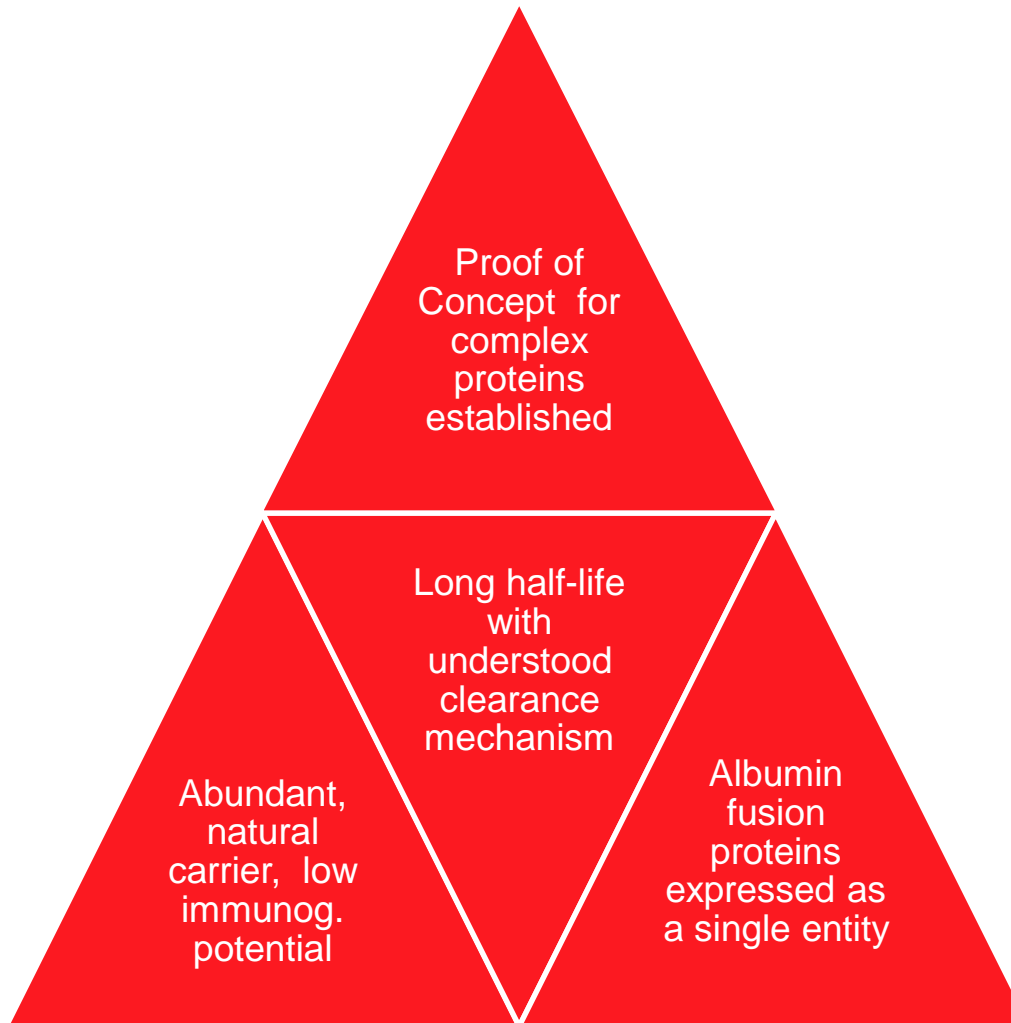
# Innovations in Coagulation



rVIII-SingleChain



# Albumin Fusion Technology



# Recombinant Albumin Fusion Proteins

- **rIX-FP (CSL654)**

- Recombinant fusion protein linking coagulation factor IX with albumin

- **rVIIa-FP (CSL689)**

- Recombinant fusion protein linking coagulation factor VIIa with albumin

- **Rational design to optimise efficacy**

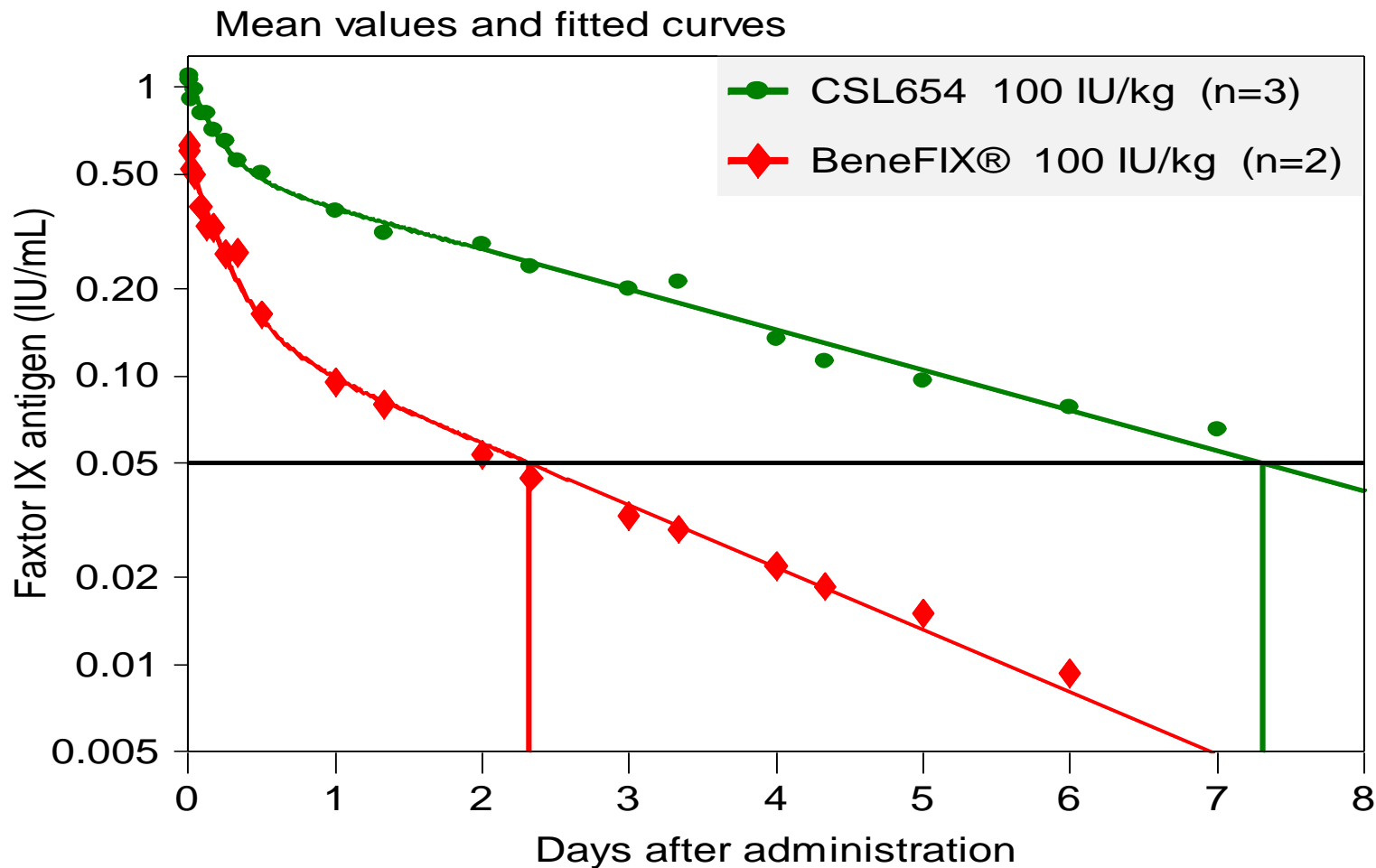
- Designed to maintain molecular activity
- Optimised to minimise immunogenicity
- Demonstrated by *in vitro* / *in vivo* testing

# Development of rIX-FP, CSL654

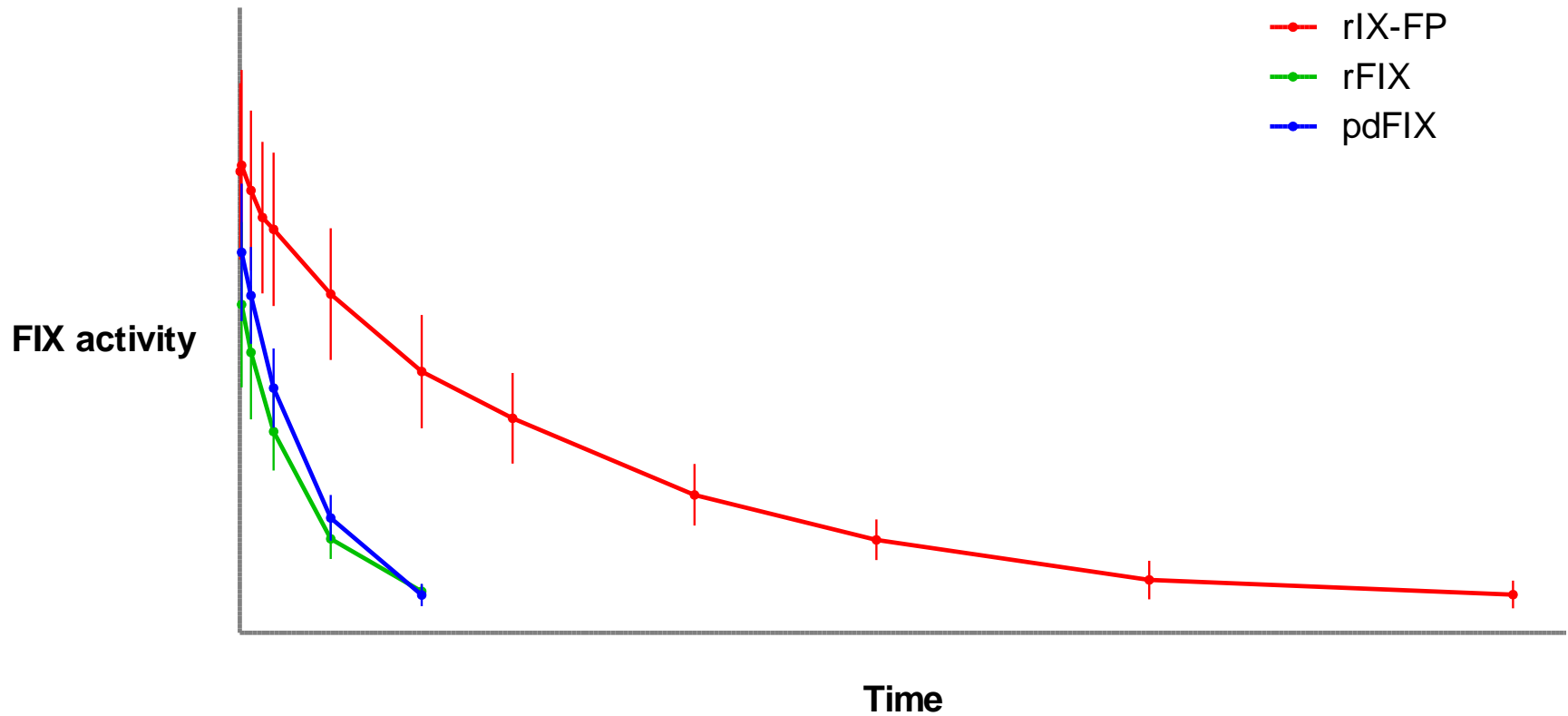
- Completed discussions with EMA, PEI and FDA
  - Agreement for clinical program and criteria for licensure
  - Paediatric Investigational Plan agreed
- Phase I PK study completed and results to be presented at GTH\* in February
- Phase I/II prophylaxis and on-demand study recruitment complete
- Phase II/III study commencing early 2012

\*German Society of Thrombosis and Haemostasis

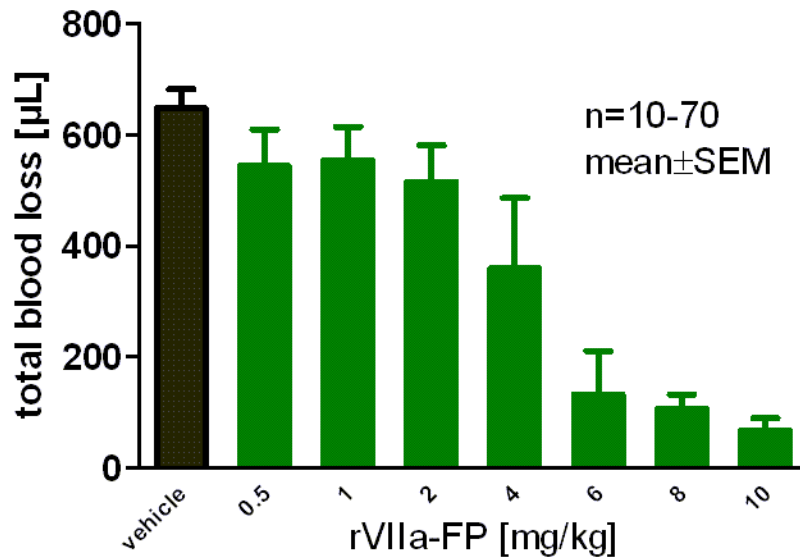
# rIX-FP has a half life ~3x longer than BeneFIX in haemophilia B dogs



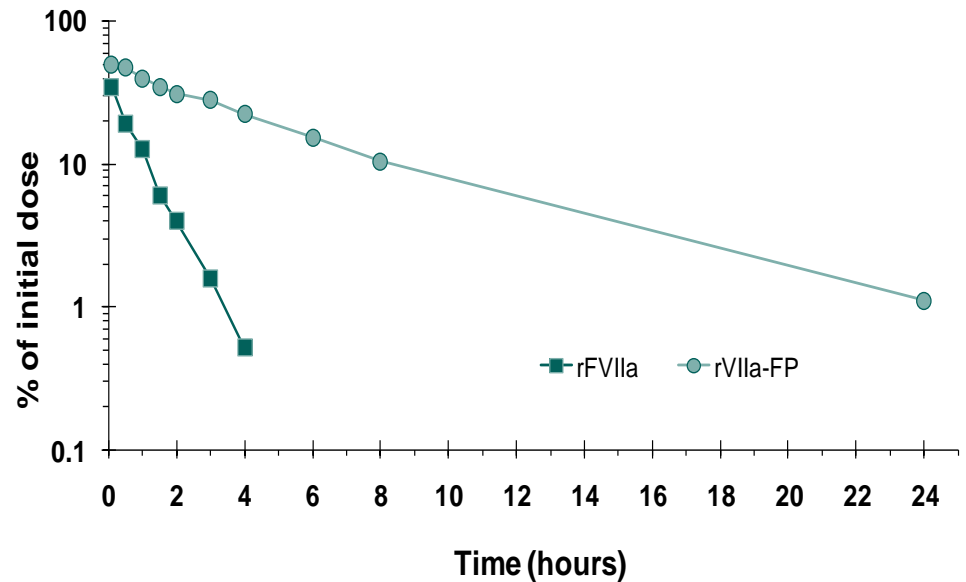
# rIX-FP Activity in Haemophilia B Patients



# rVIIa-FP is active and has a half life ~6 times longer than FVIIa



Weimer et. al. rVIIa albumin fusion



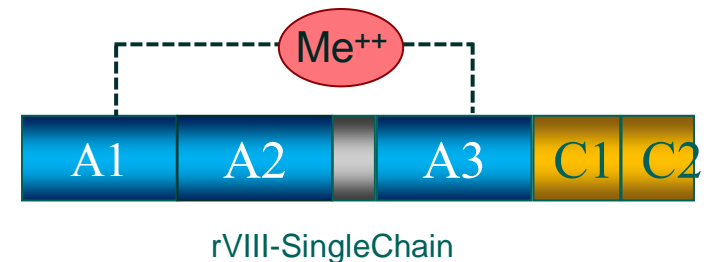
→ rVIIa-FP has an improved half-life in rat model

# Recombinant Albumin Fusion Proteins Summary

- **Significant half-life extension demonstrated**
  - Pre-clinical studies in rats, rabbits and monkeys
    - rIX-FP ~3 to 4-fold
    - rVIIa-FP ~8 to 10-fold
- **Both proteins designated Orphan Medicinal Products in Europe**
- **Stage of development**
  - **rIX-FP:** Phase I PK trial complete and data being evaluated  
Presentation of Phase I data at GTH\* Congress Feb 2012  
Phase I/II on-going
  - **rVIIa-FP:** Pharmacology and toxicology studies completed
  - **rvWF-FP:** Research program for long acting vWF initiated

# rVIII-SingleChain: approach for improved FVIII

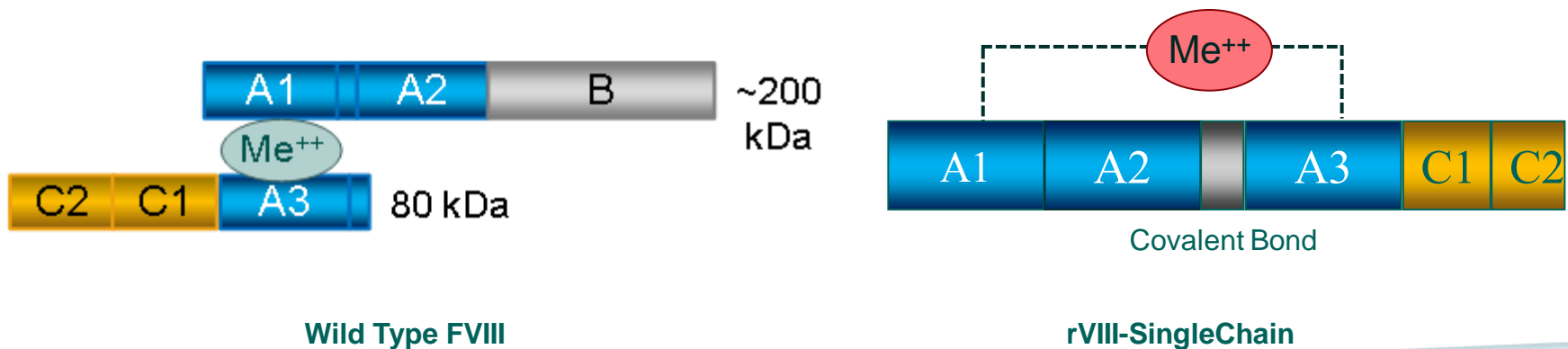
- **FVIII's physiological partner in plasma is von Willebrand factor (VWF)**
  - The FVIII/VWF complex plays an important role in the physiological activity and clearance of FVIII
  - *Aim: Improve binding to VWF*
- **FVIII is an unstable molecule in the manufacturing environment**
  - Potential for dissociation which leads to loss of procoagulant activity of FVIII
  - *Aim: Improve molecular stability*
- **Appropriate molecule originated by SK Chemicals**



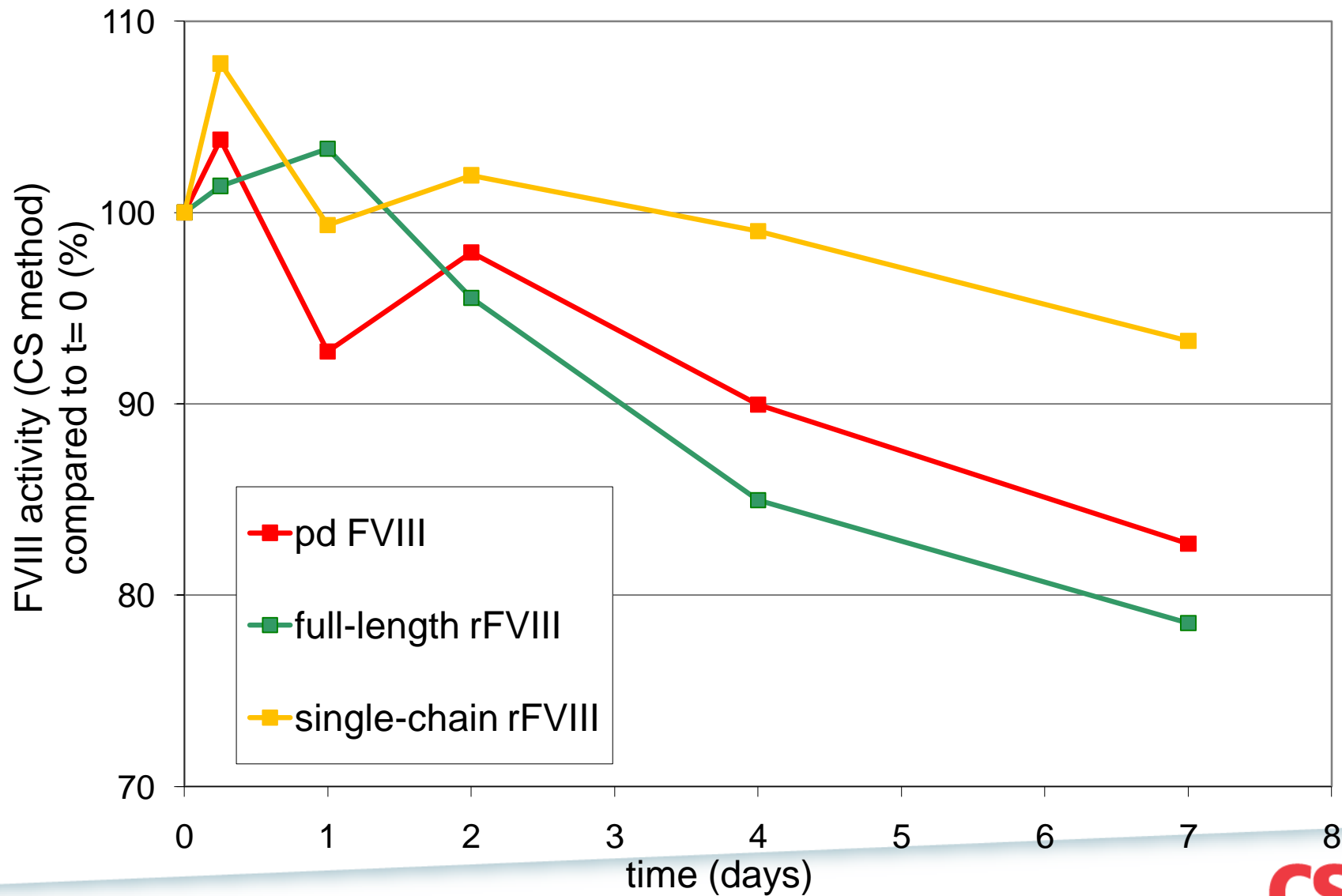


# rVIII-SingleChain (CSL627)

- **Increased heavy/light chain stability**
  - Covalent linkage between heavy and light chain
  - Expressed as a recombinant single-chain FVIII
  - Enhanced molecular integrity
- **Very strong affinity to von Willebrand factor (VWF)**
  - Faster and more efficient binding to VWF

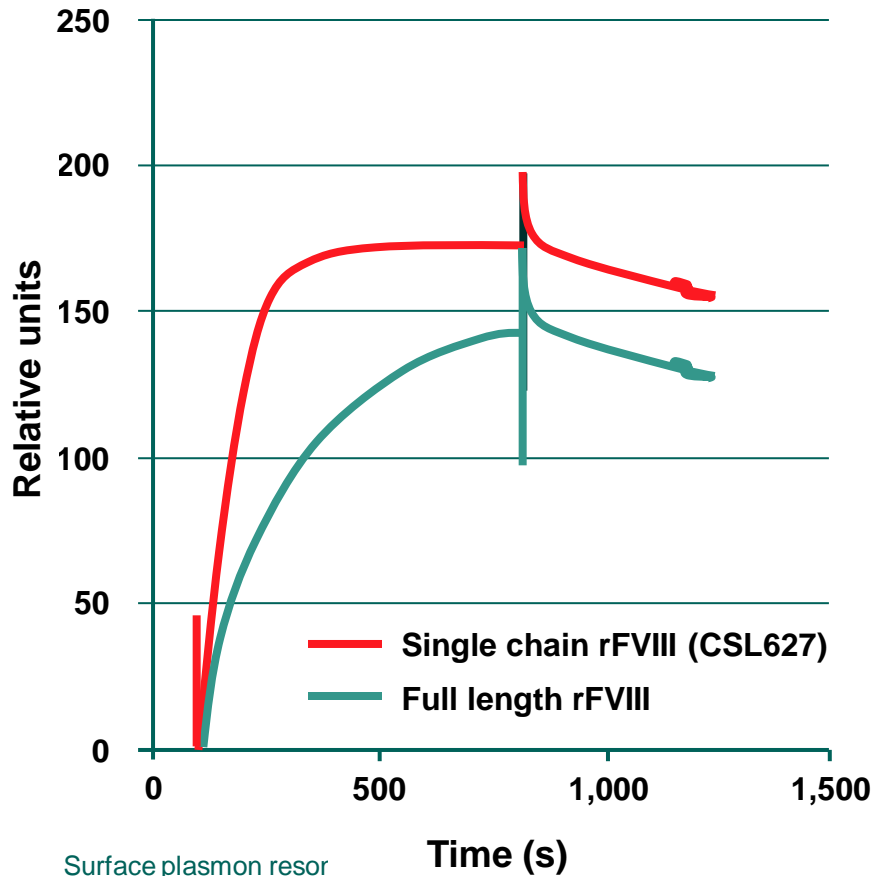


# Short-term reconstituted stability at 25°C



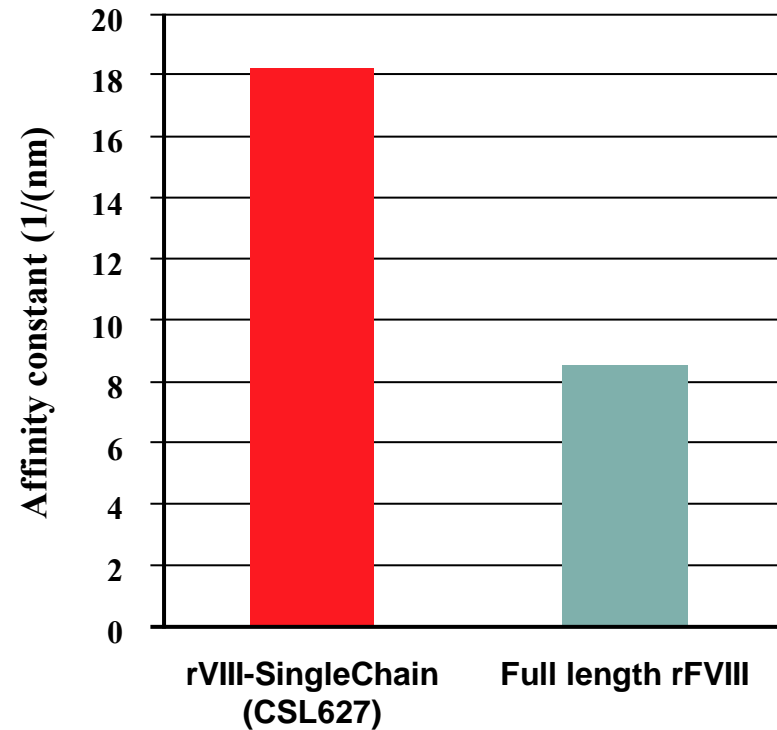
# rVIII-SingleChain: high affinity for vWF

## Binding to plasma-derived (pd) VWF



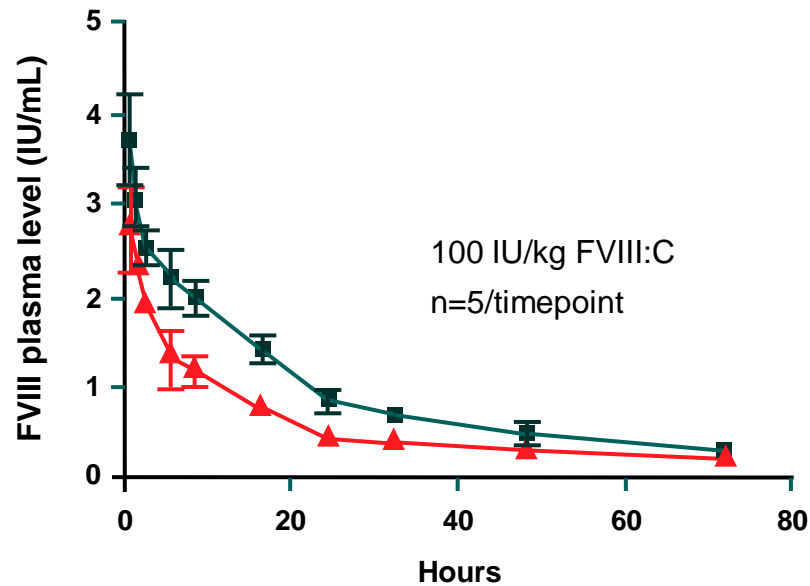
Surface plasmon resor  
CSL Behring. Data on file

## Comparison of VWF affinity constants

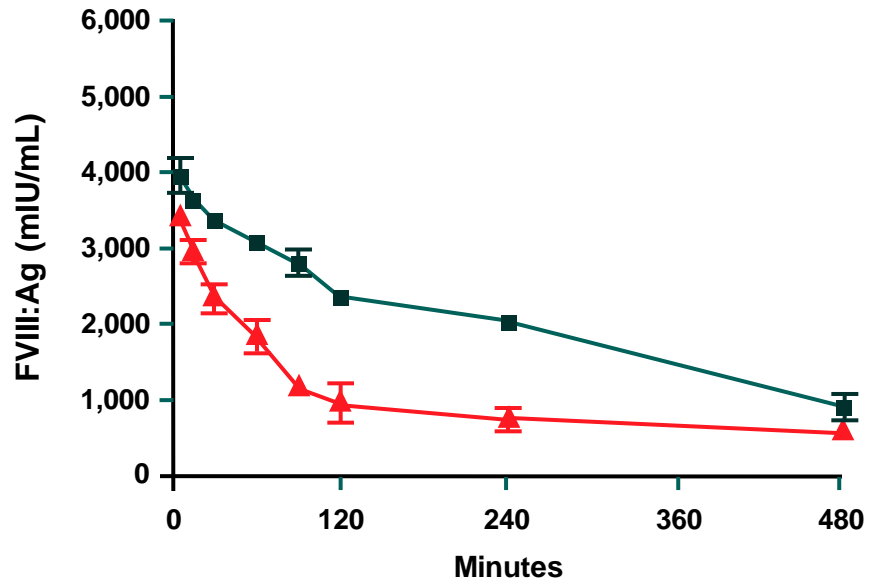


# rVIII-SingleChain: PK properties in mice and rats

## PK in haemophilia A mice



## PK in rats



■ rVIII-SingleChain (CSL627)  
▲ Full length rFVIII

# rVIII-SingleChain: PK parameters in cynomolgus monkeys

	<b>Single chain rFVIII (CSL627) (250 IU/kg)</b>	<b>Full length rFVIII (250 IU/kg)</b>
AUC (h*IU/mL)	101.7	67.2
C <sub>max</sub> (IU/mL)	10.7	11.19
Clearance (mL/kg/h)	2.0	3.4
T <sub>1/2</sub> β (h)	9.7	6.8

CSL Behring. Data on file

# Development of rVIII-SingleChain, CSL627

## Progress to date

- Completed discussions with EMA, PEI and FDA
  - Agreement for phase I/III clinical program and criteria for licensure
  - Paediatric Investigational Plan agreed
- Toxicology completed
- Phase I study sites initiated
- Phase III component to commence within 15 months

# rVIII-SingleChain: Summary

## **Novel single chain rFVIII molecule which demonstrates:**

- Very high binding affinity to VWF
- Improved stability after reconstitution
- Comparable haemostatic efficacy to full length rFVIII in FVIII deficient mice

## **Advanced status of development**

- Pharmacology and toxicology studies completed
- Animal PK studies show promising results
- Phase I/III clinical trial sites initiated



CSL Behring. Data on file

# Commercial Opportunities and Activities



# Haemophilia General Market Trends

- Market growth

- \$7-8Bn market and growing
- The rate of prophylaxis in adults and children is increasing
- Weight gain across the population increases the weekly dose
- Increased life expectancy of people with haemophilia leads to higher use in surgery and age related complications
- Geographic expansion

- Therapy type

- Treatment categories remain “plasma derived” and “recombinant”
- Within recombinant segment a category with improved PK parameters will establish itself. This opens an opportunity for differentiation

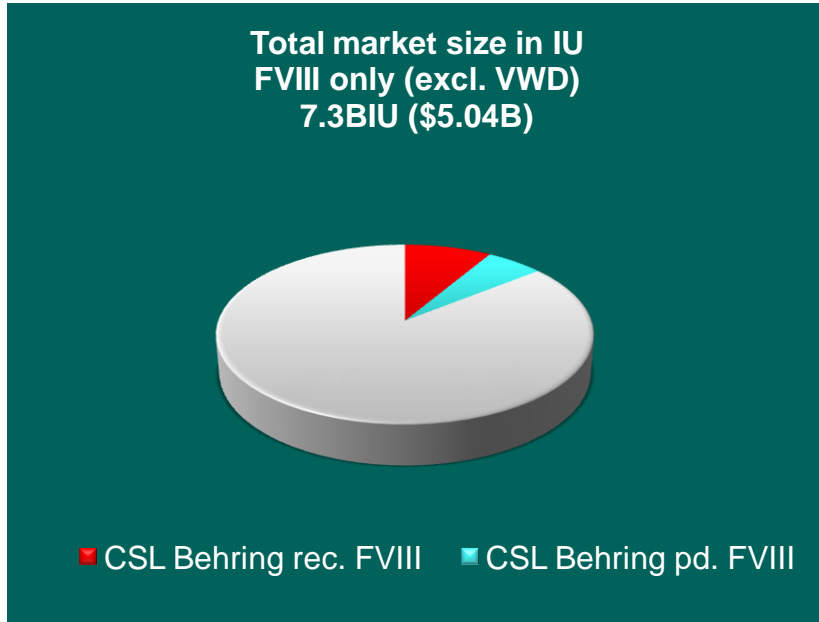
# CSL Haemophilia Portfolio Overview

	Haemophilia A	Haemophilia B	VWD	FVIII/ FIX Inhibitors	
				Bleed Management	ITT
Plasma-derived	Beriate® Monoclate-P®	Mononine® Berinin®	Biostate® Haemate® P Humate-P®	-	Haemate® P Biostate®
Recombinant	Helixate®				
Recombinant Bio-Better					
Recombinant Half life extended					

# CSL Haemophilia Portfolio Overview

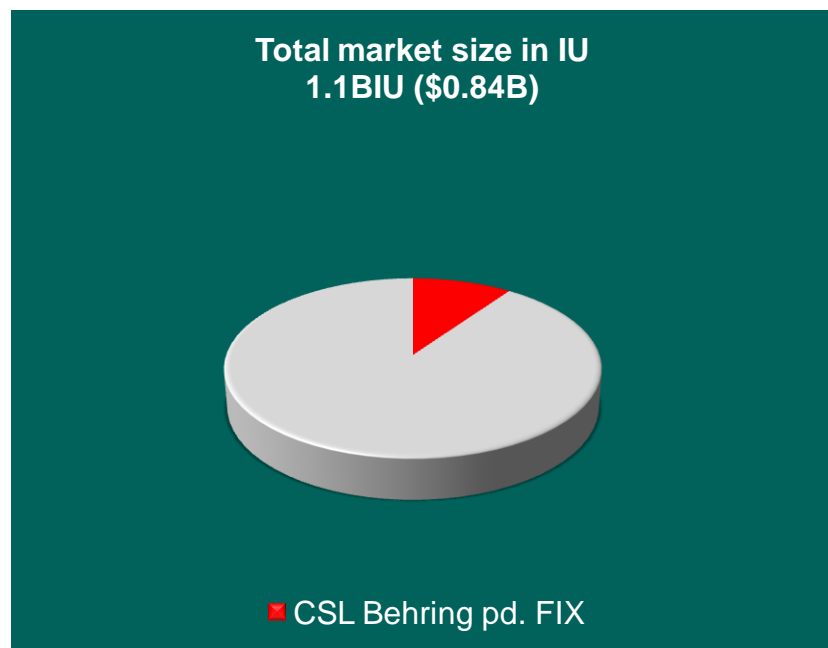
	Haemophilia A	Haemophilia B	VWD	FVIII/ FIX Inhibitors	
				Bleed Management	ITT
Plasma-derived	Beriate® Monoclate-P®	Mononine® Berinin®	Biostate® Haemate® P Humate-P®	-	Haemate® P Biostate®
Recombinant	Helixate®				
Recombinant Bio-Better	<b>CSL627</b> <b>rVIII-SC</b>				
Recombinant Half life extended		<b>CSL654</b> <b>rIX-FP</b>	<b>Research</b> <b>rvWF-FP</b>	<b>CSL689</b> <b>rVIIa-FP</b>	

# Status of Haemophilia A Products



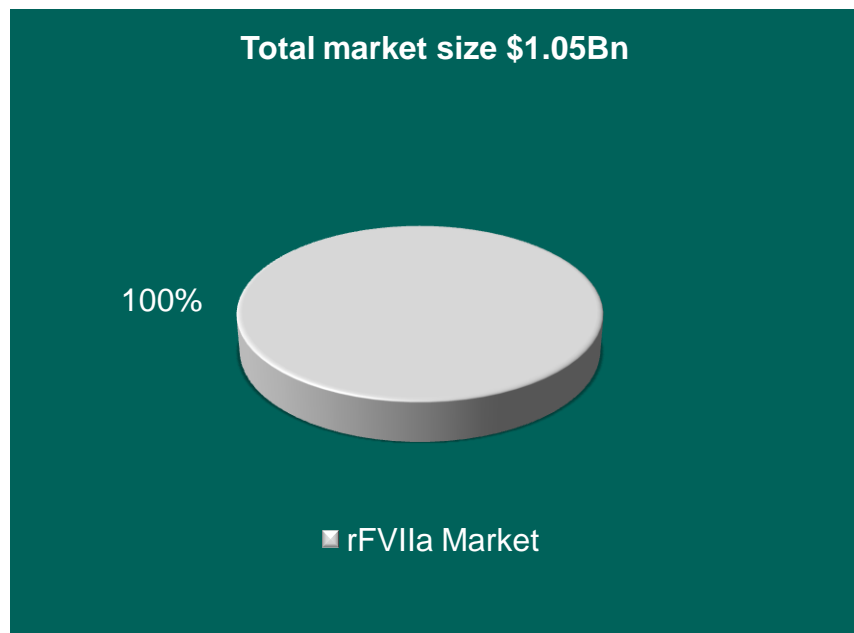
- Growing Market
- CSL market leader in plasma derived products
- Significant opportunity to grow our own rFVIII

# Status of Haemophilia B Products



- Anticipated \$1Bn market in next 4-5 years
- In longer term 2/3 of market likely to shift to half life extended products
- CSL has the potential to be a major player

# Status of Haemophilia Inhibitor Bleeding: rFVIIa



- Only bleeding management
- Most of the market likely to shift to extended half life products
- CSL is developing a potentially very competitive product

# Product Features

# CSL654 (rIX-FP) Features



Attribute	Ideal TPP*	CSL654 (rIX-FP)
Range of vials	Wide	✓
Human protein in manufacturing/ formulation process?	No	✓
Animal protein in purification process?	No	✓
Half life extension technology	Low immunogenicity	✓
PK: Half life extension	> three fold	✓✓
PK: Recovery	> 1.2 (IU/mL)/(IU/kg)	✓
Cell line	CHO	✓
Reconstitution volume	Low	✓
Reconstitution device	Simple, needle-free	✓

\*Target Product Profile



# CSL689 (rVIIa-FP) Features



Attribute	Ideal TPP	CSL689 (rVIIa-FP)
Range of vials	Wide	✓
Animal / Human protein in manufacturing/ formulation process?	No	✓
Half life extension technology	Low immunogenicity	✓
PK: Half life extension	> 6 fold	✓✓
Cell line	CHO	✓
Reconstitution volume	Low	✓
Reconstitution device	Simple, needle-free	✓

\*Target Product Profile

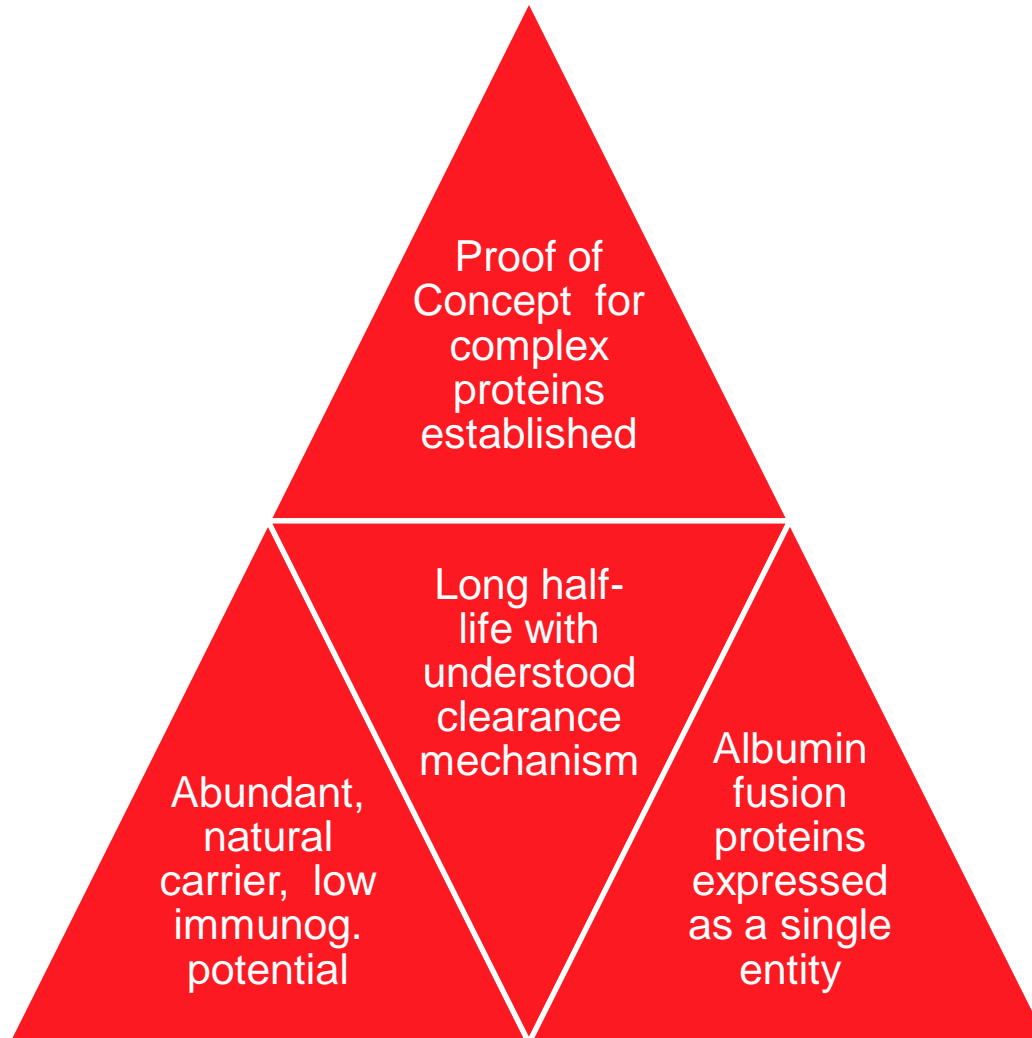
# CSL627 (rVIII-SingleChain) Features



Attribute	Ideal TPP	CSL627
Range of vials	Wide	✓
Human protein in manuf. / formulation proc?	No	✓
Animal protein in purification proc?	No	✓
Chain	One	✓
Binding to VWF	High affinity	✓
BDD	Yes (yield)	✓
PK: Half life extension	3 fold extension	Approx. 1.3 times
Cell line	CHO	✓
Immunogenicity risk	Low	✓
Reconstitution volume	Low	✓
Reconstitution device	Simple, needle-free	✓

\*Target Product Profile

# Advantages of Albumin as a Fusion Partner



# CSL654 (rIX-FP) & CSL689 (rVIIa-FP)

## Scientific Edge

Improved  
half life,  
extended  
dosing  
interval

rAlbumin as  
fusion  
platform

Precise  
engineering  
of specially  
designed  
linker



# Scientific Edge: rIX-FP Prophylactic Dosing Interval

- Standard dosing      2  $\Rightarrow$  3 x per week










MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED
									

- CSL654 dosing      1 x per 1  $\Rightarrow$  2 week




MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE	WED
									

# Scientific Edge: rVIIa-FP Prophylactic Dosing Interval

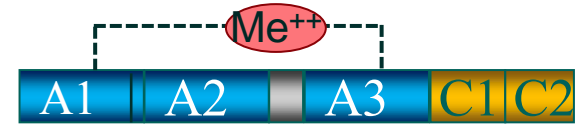
- Standard dosing

MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE
								

- CSL689 dosing      2 ⇨ 3 x per week

MON	TUE	WED	THU	FRI	SAT	SUN	MON	TUE
								

# CSL627 (rVIII-SingleChain)



Covalent bond



Commercial  
Edge

Scientific Edge

Improved  
financial  
contribution

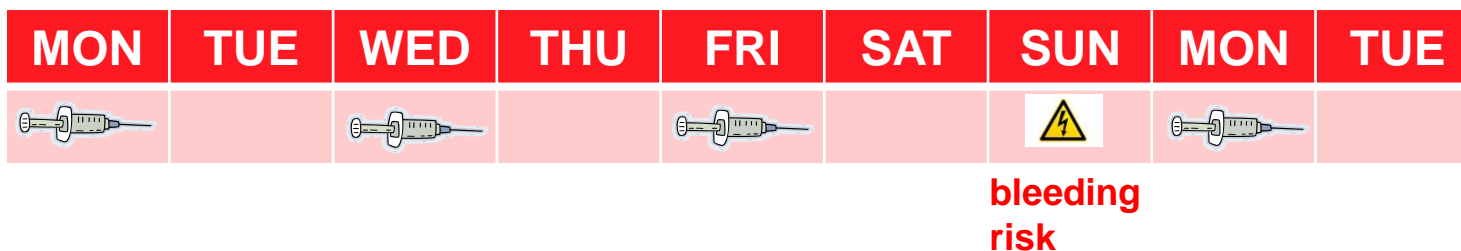
High VWF  
affinity

Improved  
molecular  
stability

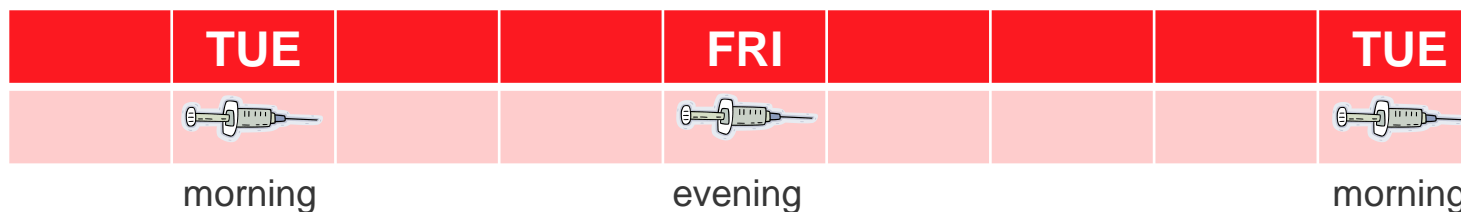
Opportunity for Extended  
Dosing Interval

# Scientific Edge: rVIII Prophylactic Dosing Interval

- Standard dosing



- Alternative dosing



- CSL627 will be tested in both dosing regimens



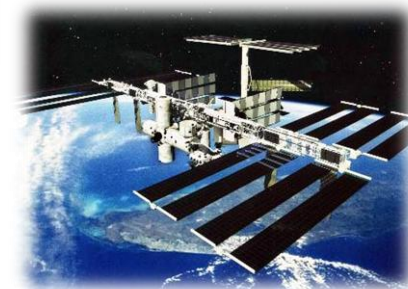
# Rec. Coag Portfolio Summary

## 2015

- **CSL654 (rIX-FP)**
  - Recombinant fusion protein genetically linking coagulation factor IX with recombinant human albumin

## 2016

- **CSL627 (rVIII-SingleChain)**
  - Recombinant single - chain factor VIII



## 2017

- **CSL689 (rVIIa-FP)**
  - Recombinant fusion protein genetically linking coagulation VIIa with recombinant human albumin

# Sharing our Results

**rIX-FP**  
Innovations in Coagulation rIX-FP:  
Recombinant fusion protein linking coagulation factor IX with albumin

Biologics for Life™ CSL Behring

Biologics for Life™ CSL Behring

**Pioneering Designs for Recombinant Coagulation Factors**

- **rIX-FP**  
recombinant fusion protein linking coagulation factor IX with albumin.
- **rVIIa-FP**  
recombinant fusion protein linking coagulation factor VIIa with albumin.
- **rFVIII**, unique single chain design

Please talk to your CSL Behring representative about opportunities to join our clinical program.

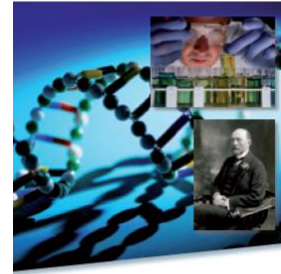
Factors for Life™

**Factors for Life™**  
Our Commitment: A Broad Range of Products for the Treatment of Rare Bleeding Disorders

Biologics for Life™ CSL Behring

## Advancing Research for More than One Century

- Focus on Safety: First Effectively Virus Inactivated Factor VIII
- Broad Range of Products for the Treatment of Rare Bleeding Disorders
- Advancing Therapy: Half Life Extension of Recombinant FVIIa by Fusion to Albumin



**Innovations in Coagulation:**  
Prolonged Half-Life of Recombinant Factor VIIa by Fusion to Albumin (rVIIa-FP)

Biologics for Life™ CSL Behring

**rIX-FP**  
Innovations in Coagulation  
Recombinant fusion protein linking coagulation factor IX with albumin

Biologics for Life™ CSL Behring

**rIX-FP**  
Innovations in Coagulation  
Slide Kit

Biologics for Life™ CSL Behring

**Factors for Life™**  
Our Commitment: A Broad Range of Products for the Treatment of Rare Bleeding Disorders

Biologics for Life™ CSL Behring™



**Innovations in Coagulation II:**  
Prolonged Half-Life of Recombinant Factor IX by Novel Fusion Concept to Albumin (rIX-FP)

Biologics for Life™ CSL Behring



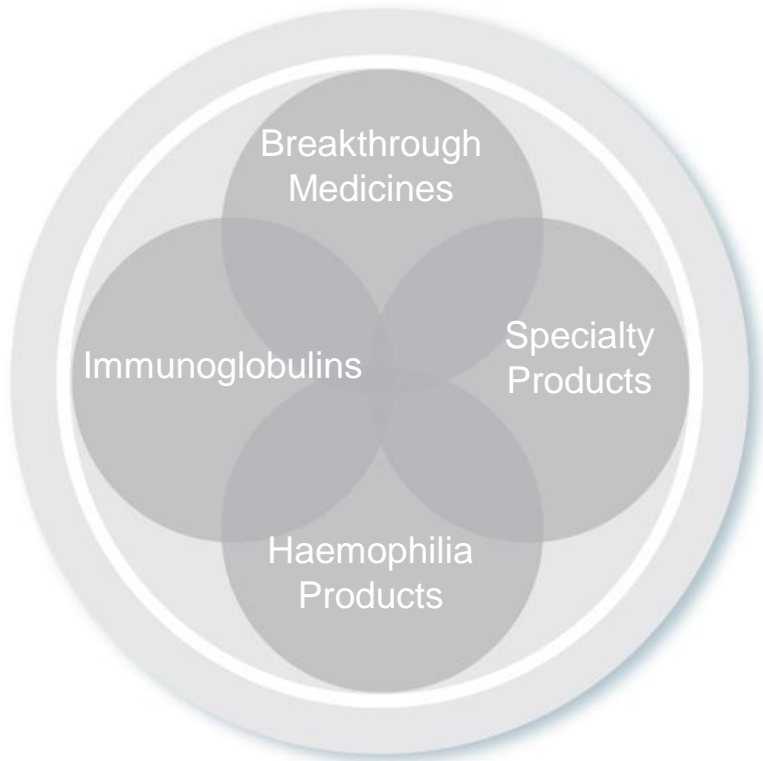
# Summary Commercial Opportunities Haemophilia Products

- \$7-8Bn market and growing
- Significant upside potential by entering new markets
- New CSL product portfolio meets/exceeds the “ideal” TPP
- “Albumin” technology provides a strong competitive edge
- CSL has one of the most experienced commercial organisations in the coagulation business, with a proven track record in Haemophilia and other coagulation related disorders like POB

# Licensing and Collaborations

# Licensing

Optimise value of IP Portfolio and assets



- Partner high opportunity products
  - GARDASIL<sup>®</sup> IP
  - GM-CSFR $\alpha$  (Medi/AZ)
  - Periodontal disease (Sanofi)
- Continue broad licensing strategy for ISCOMATRIX<sup>®</sup> adjuvant

# GARDASIL®

## Impact of Australian HPV Vaccination Program

- Significant reduction in genital warts and high grade abnormalities<sup>1,2</sup>

## Long term protection

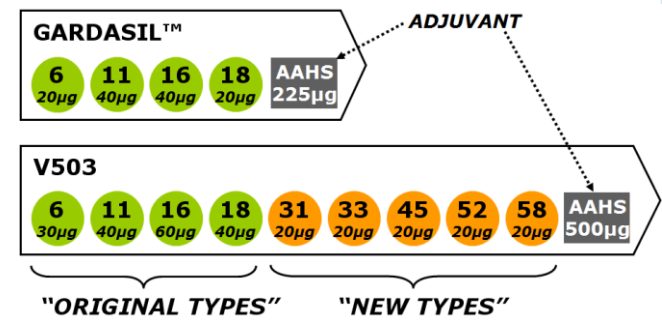
- Studies indicate no break through disease 6 & 7 yrs post immunisation

## Male clinical data

- Efficacy against external genital lesions established
- Efficacy against anal disease under review by the TGA (approved in US & Canada)

## V503: 9-Valent HPV Vaccine

- Pivotal efficacy study completed (N=14,000)
- Anticipated global regulatory filings mid 2012



# CAM3001 / Mavrilimumab

## Rheumatoid arthritis

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



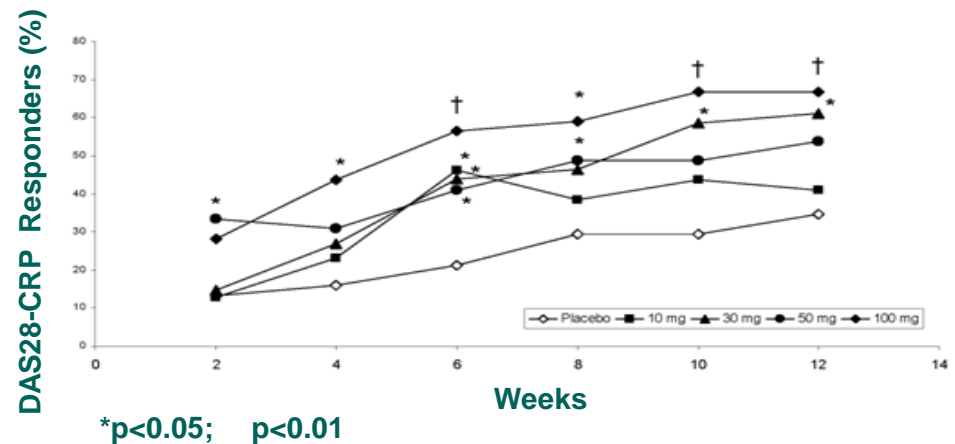
## CAM3001

- fully human mAb targeting the GM-CSFR $\alpha$
- licensed to MedImmune / AstraZeneca
- CSL to receive milestones and royalties
- phase II study commenced in 2010
- study results presented at ACR meeting, October 2011

# Mavrilimumab Phase IIa Study

- 3 mnth sequential ascending dose study, dosing every 2nd wk
- 233 subjects with active RA
- Mavrilimumab showed a rapid (< 2 wks) and significant clinical effect compared with placebo, especially in the higher (100 mg) dose cohort
- Clinical activity maintained at 12 wks
- Short-term safety profile to support further clinical development

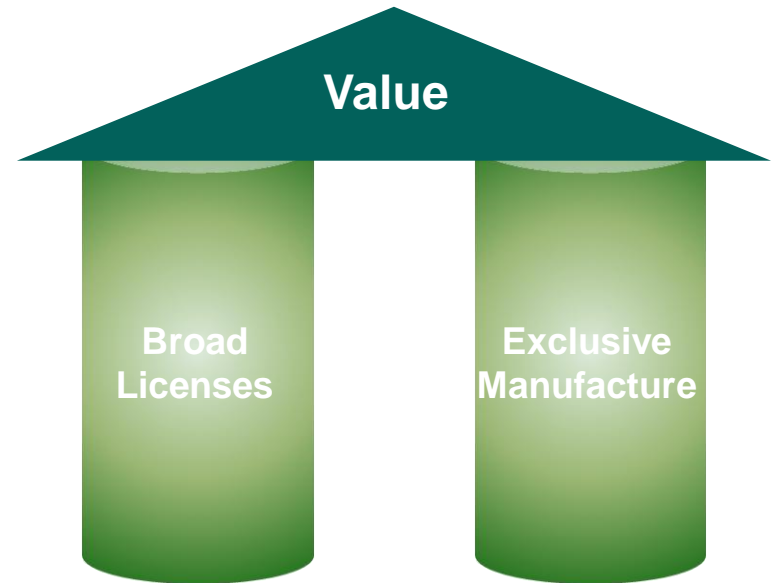
Proportion of subjects achieving a change of 1.2 from baseline DAS28-CRP





# ISCOMATRIX® Adjuvant Partnering Activities

- Major partners continue to advance vaccine development programs using ISCOMATRIX® adjuvant
- Merck
  - Additional field
  - Progressing new program into clinic
- Pfizer
  - Program in GLP tox study
- ~40 fields across all partners



# NIH Multi-site CMV Trial



- CMV infection is the leading known cause of birth abnormalities in developed countries
  - 1-2% of pregnant women are infected with CMV
  - Total live births per year with CMV disease in US >6,000
- Partnership with US National Institutes of Health (NIH) to determine efficacy of CMV immunoglobulin in preventing mother to baby transmission
  - Large multi-site clinical trial involving >150,000 women commencing December 2011
  - CSL donating Cytogam<sup>®</sup>, the only registered CMV immunoglobulin in the US.
  - Primary analysis expected 2016



# Summary



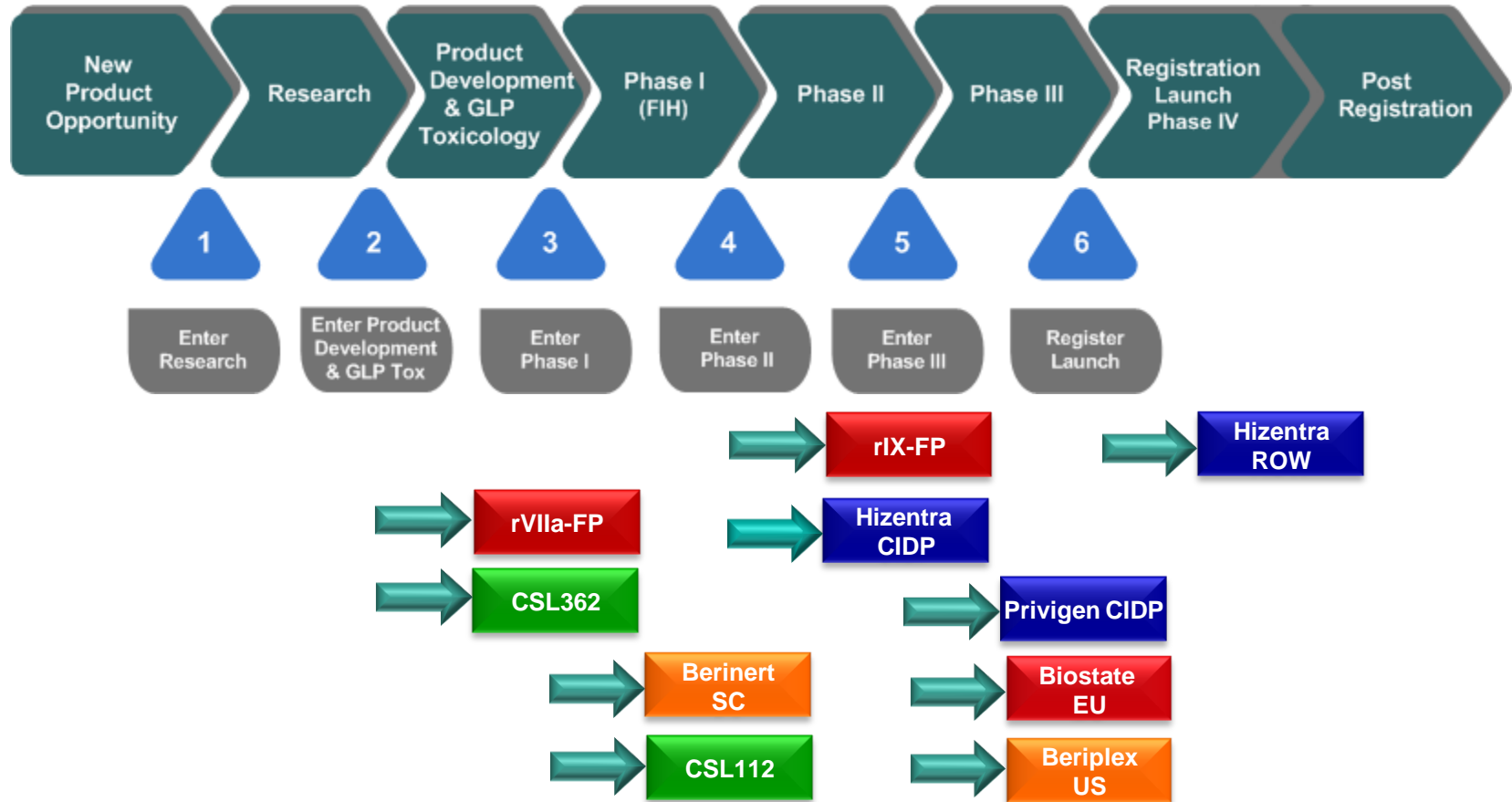
Core Capabilities



\*Partnered Projects

#LCM includes direct post marketing commitments as well as pathogen safety, capacity expansions, yield improvements, new packages and sizes for all registered products

# Expected Progress in next 12 Months



# Short to Mid-term Target Launch Dates

2012	2013	2014	2015	2016
	Biostate EU		CSL654 rIX-FP	CSL627 rFVIII
Beriplex® US Bleeding		Fibrinogen Aortic Surgery	Zemaira® EU	Berinert® SC
Berinert® Self Admin		Beriplex® US Surgical		
Hizentra® EU	Privigen®CIDP EU			Hizentra® CIDP

Core Capabilities

Immunoglobulins

Haemophilia

Specialty Products

Breakthrough Medicines

Vaccines & IP

\*Partnered Projects

\*Calendar Years

# Q&A