# **R&D Investor Briefing**

#### December 5, 2017





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# **Introduction and Highlights**

Professor Andrew Cuthbertson AO R&D Director and Chief Scientist



## Agenda

- Welcome
- Introduction and Highlights
- Research
- Early Development
- Immunoglobulins, Haemophilia and Specialty Products
  - Clinical Development
  - Commercial Opportunities
- Q&A
- Break –
- Transplant and Breakthrough Medicines (CSL112)
  - Clinical Development
  - Commercial Opportunities
- Summary
- Q&A

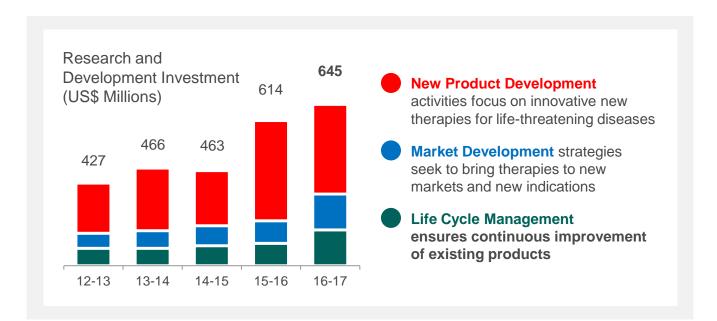
Mark Dehring Andrew Cuthbertson Andrew Nash Charmaine Gittleson

Bill Mezzanotte Bill Campbell

Bill Mezzanotte Bill Campbell Andrew Cuthbertson



#### **Commitment to Research and Development**



R&D investment ~10-11% global revenue

#### **Key Past Launches from R&D Portfolio**

	2006	2007	> 2008	2009	2010	2011	2012	2013	> 2014	2015	2016	2017
<u>5</u>		GLOBIN <sup>®</sup> PHYLAC <sup>®</sup>	• PR	<b>IVIGEN</b> ®	• HIZ	ZENTRA®	)		/IGEN® P (EU)		lg IsoLo	0 <sup>®</sup>
Specialty		NRA® (US) PLEX® (EU			• BERII • RIAS	NERT® (U STAP®	S) • CORIF#	• KCEN ACT®	TRA® (U	·	SPREEZ/ EGARDA	
Haem									ENTO® (E	IDELVIC	DN® ● STYLA® (	•
Vaccines	• GARE	DASIL®	(		A® H1N1				Fl	URIA® QI\ LUCELVA FLUAD® (	X® ●	

### **Leveraging Global Capabilities**



### **R&D Portfolio – December 2016**

	RESEARCH	PRE-CLINICAL	PHASE I	PHASE II	PHASE III	REGISTRATION	COMMERCIAL / PHASE IV
							Immunoglobulins
Life Cycle							Haemophilia
Management <sup>#</sup>							Specialty Products
							Influenza Vaccine
	PCC New Indications	C1-INH New Indications			HIZENTRA <sup>®</sup> CIDP	PRIVIGEN <sup>®</sup> CIDP US	VONCENTO <sup>®</sup> VWD EU
Market		Fibrinogen New Forms			PRIVIGEN <sup>®</sup> Japan	KCENTRA <sup>®</sup> Japan	RESPREEZA® EU/US
Development		Haptoglobin /Hemopexin			HIZENTRA <sup>®</sup> IIM		
					CSL842 C1-INH Transplant		
	Next Gen Ig Formulations	CSL626 D'D3 LA rVIII	CSL689 rVIIa-FP Congen Def	CSL689 rVIIa-FP Inhibitors		AFSTYLA <sup>®</sup> Europe	IDELVION <sup>®</sup> US, EU, Japan
	Rec Coagulation Factors	CSL334 IL-13R* ASLAN	CSL640 rIX-FP subct	Mavri GM-CSFR-AZ*		AFLURIA <sup>®</sup> QIV 5-17 US, AUS	AFTSYLA® US
New Product Development	P. gingivalis/POD OH- CRC	CSL346 Anti-VEGFB	CSL312 Anti-FXIIa	CSL362 IL-3R AML Janssen			AFLURIA <sup>®</sup> QIV 18+ US & AUS
	Discovery Projects		CSL324 Anti-G-CSFR	CSL112 apo-Al			FLUAD <sup>®</sup> TIV 65+ US
							FLUCELVAX <sup>®</sup> QIV 4+ US

Core Capabilities: Immunoglobulins | Haemophilia | Specialty Products | Breakthrough Medicines | Vaccines & IP

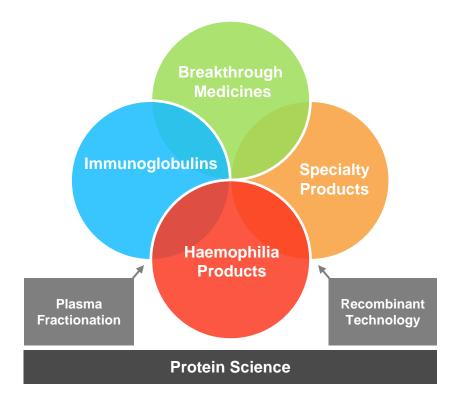
\*Partnered Projects

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



#### Global

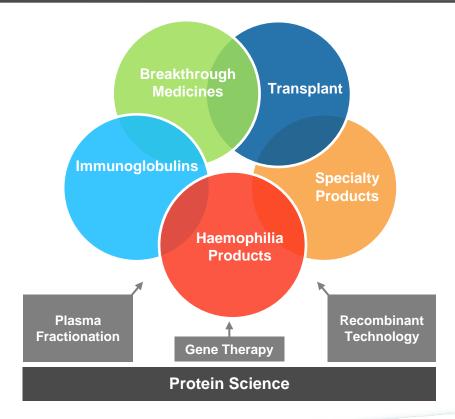
#### **CSL Behring Protein Therapeutics Platform**





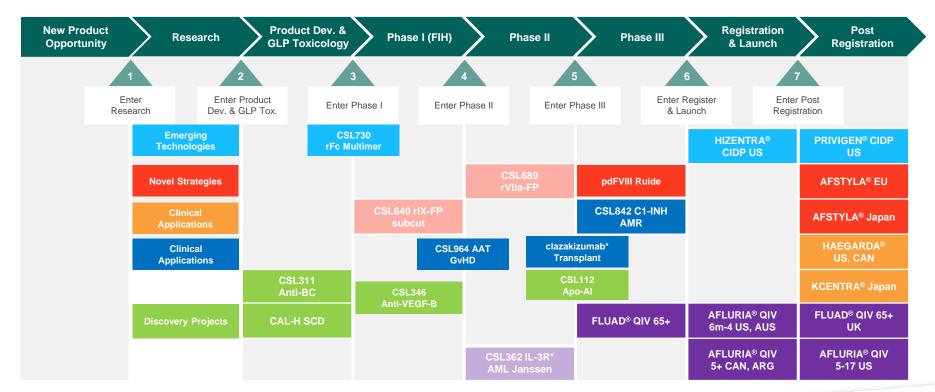
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## **Evolving Therapeutics Platform**





#### **Progress Through Stage Gates in 2017**



Core Capabilities: Immunoglobulins | Haemophilia | Specialty Products | Breakthrough Medicines | Vaccines & IP | Transplant

\*Partnered Projects

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## **R&D Portfolio – December 2017**

	RESEARCH	PRE-CLINICAL	PHASE I	PHASE II	PHASE III	REGISTRATION	COMMERCIAL / PHASE IV
	Clinical Applications	C1-INH New Indications			PRIVIGEN <sup>®</sup> Japan	HIZENTRA <sup>®</sup> CIDP	PRIVIGEN <sup>®</sup> CIDP US
		Fibrinogen New Formulations			HIZENTRA® IIM		KCENTRA® Japan
Life Cycle		Haptoglobin/ Hemopexin		CSL964 AAT GvHD		HAEGARDA <sup>®</sup> EU	HAEGARDA <sup>®</sup> US
Management / Market		CSL640 rIX-FP subct			PRIVIGEN <sup>®</sup> CIDP Japan	AFLURIA <sup>®</sup> QIV 5-17 AUS	FLUAD® TIV 65+ US, UK
Development					CSL842 C1-INH AMR		FLUCELAX <sup>®</sup> QIV 4+ US
							AFLURIA® QIV 5-17 US
	Emerging Technologies	CSL730 rFc Multimer			clazakizumab* Transplant		<b>IDELVION</b> ®
	Novel Strategies	CSL626 D'D3 LA rVIII	CSL312 Anti-FXIIa	Mavri GM-CSFR-AZ*	pdFVIII Ruide		<b>AFSTYLA®</b>
New Product	Discovery Projects	CSL334 IL-13R* ASLAN	CSL324 Anti-G-CSFR				
Development	<b>Clinical Applications</b>	CSL311 Anti-BC	CSL346 Anti-VEGF-B		CSL112 apo-Al		
		P. gingivalis/POD* OH-CRC					

Core Capabilities: Immunoglobulins | Haemophilia | Specialty Products | Breakthrough Medicines | Vaccines & IP | Transplant

12 \*Partnered Projects



## **Research Portfolio and Technologies**

Dr Andrew Nash Senior Vice President, Research



## **Research Organisation & Portfolio**

Coordinated global project portfolio

Immunoglobulins	Haemophilia	Specialty Products	Breakthrough Medicines	Transplant
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- Hub (Bio21, Parkville) & spoke model
- Bio21 expansion to be completed Feb 2018
- Research capabilities: plasma & recombinant proteins, gene and cell-based therapies







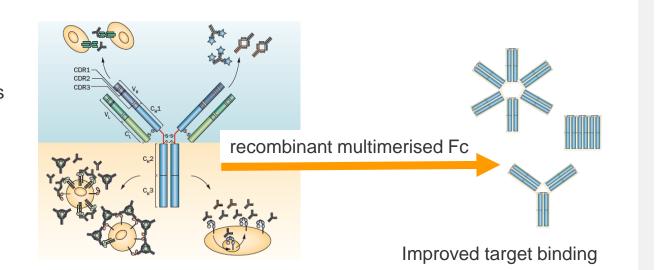
Bio21 expansion



## **Recombinant Fc Multimer – CSL730**

Fab regionImmune deficiencies

Fc regionAutoimmune conditions

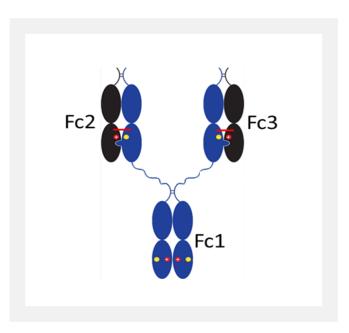




## **Recombinant Fc Multimer – CSL730**

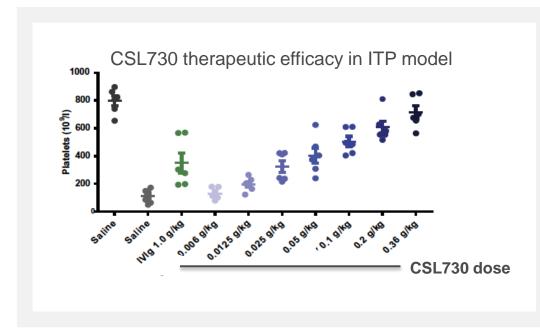
#### **CSL / Momenta Collaboration**

- First-in-class recombinant Fc multimer targeting Fcγ receptors
- Exclusive Research Collaboration and License Agreement
  - Development and commercialisation of the Fc multimer M230/CSL730
  - Research & development of additional Fc multimers
- Momenta has elected to co-fund development of CSL730





## **Recombinant Fc Multimer – CSL730**



- Non-clinical safety toxicity data supports commencement of FIH studies
- Phase I study (healthy volunteers) planned to commence Q1 2018
- Phase Ib proof of mechanism study anticipated for 2019



## **Calimmune Technology**

- Acquisition of California based biotechnology company
  - Performance based milestones
- Gene / cell based therapy, rare genetic disorders
  - ex vivo Lenti virus transduction of hematopoietic stem cells (HSC's)
- Calimmune differentiating technology:



Cytegrity Lentivirus Manufacturing

 stable & scalable GMP compliant system



Select+ In Vivo Selection Tool

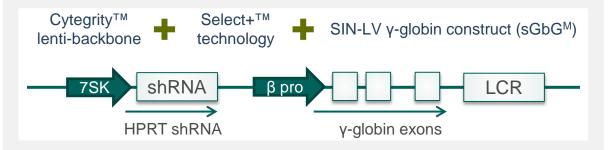
- drives engraftment with lower intensity conditioning
- significantly reduced burden on patient

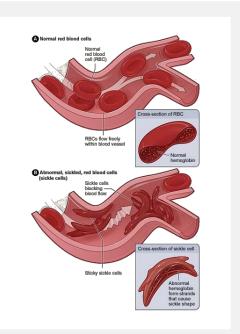


## Calimmune – CAL-H Program

#### **Sickle Cell Disease**

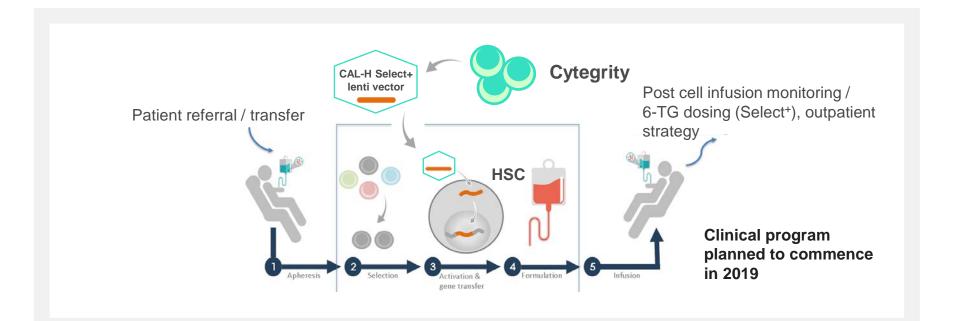
- Group of disorders caused by abnormal beta-globin gene resulting in sickled red cells
- Average life expectancy in the developed world is 40 60yrs
- High unmet need
- Total SCD patients: 155,000 (US + 5EU)





CAL-H program aims to provide sufficient functional globin gene to prevent sickling

## **Calimmune – CAL-H Program**



Range of further opportunities beyond SCD

# **Early Development Portfolio**

Dr Charmaine Gittleson Chief Medical Officer



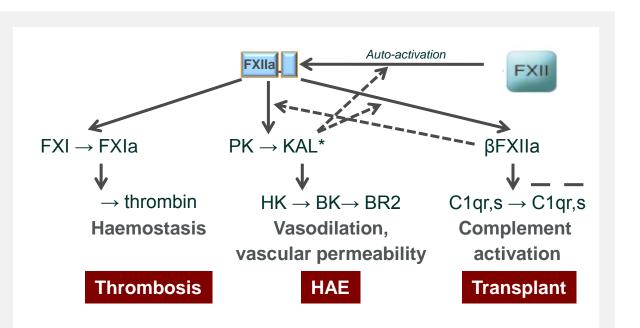
## **Early Development Portfolio**

- Portfolio of preclinical and early-mid stage clinical opportunities consistent with CSL commercial objectives
- Delivery of high quality candidates for clinical development



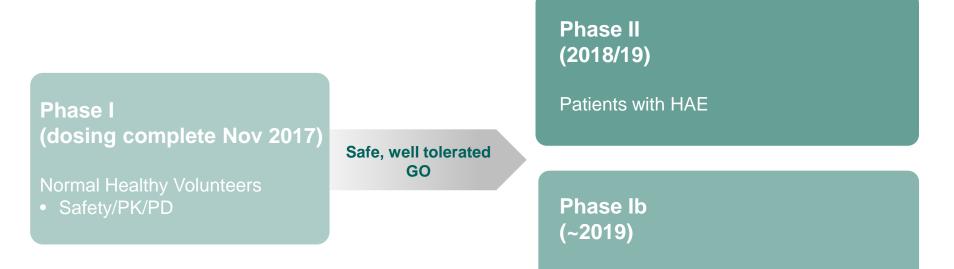
## **CSL312 – HAE and Thrombosis**

- Targeting FXIIa represents a novel approach to the treatment of hereditary angioedema and contact activated thrombosis
- Efficacy in multiple animal models and translational studies





## **CSL312 – HAE and Thrombosis**



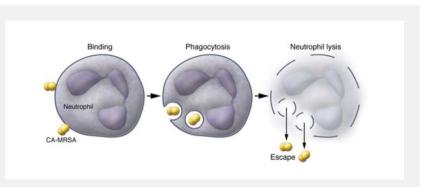
#### First in Human Phase I study

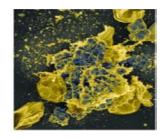
- Single doses administered
- Confirmed CSL312 safe and well tolerated with good bioavailability

Proof of mechanism in thrombosis

## **CSL324 Anti-G-CSF Receptor Antibody**

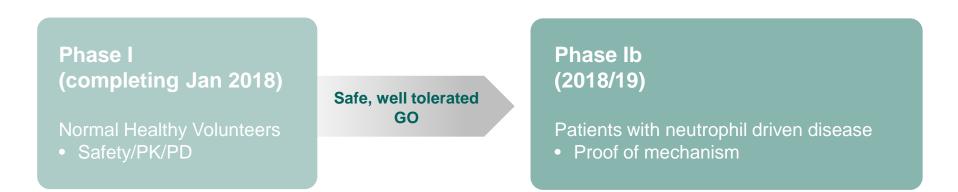
- White blood cells (neutrophils) contribute to protective mechanism against infections
- Neutrophil numbers and activity under control of Granulocyte Colony Stimulating Factor (G-CSF)
- Excessive activated neutrophils, in absence of infection, cause chronic severe inflammatory diseases
- Blocking G-CSF could decrease unwanted effects of excessive neutrophils, possibly ameliorate chronic inflammatory diseases







### **CSL324 Anti-G-CSF Receptor Antibody**



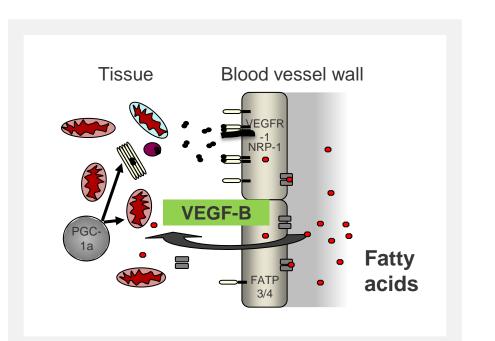
#### First in Human Phase I study

- Single and multiple doses administered; dosing completed
- Confirmed CSL324 can block receptors and lower neutrophil counts



## **CSL346 Anti-VEGF-B Antibody**

- Free fatty acids (FFA) in diet support normal energy requirements in skeletal muscle, heart and kidney
- VEGF-B controls FFA movement into tissues
- Excess fatty acid uptake causes:
  - Reduced glucose utilisation, insulin resistance and diabetic complications
  - Toxic fat accumulation in vital organs (liver, kidney)
- Blocking VEGF-B action may help prevent or treat effects of excess FFA





### **CSL346 Anti-VEGF-B Antibody**

#### Phase I

Normal Healthy Volunteers

- Safety/PK/PD
- Started November 2017

Safe, well tolerated GO

#### Phase lb

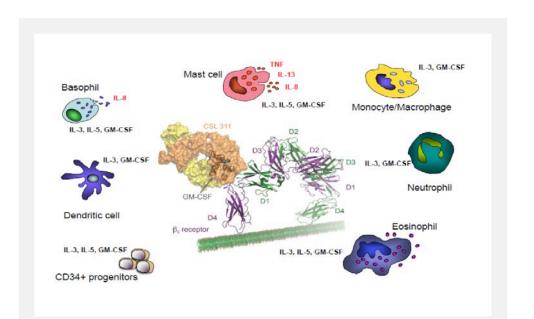
Patients with metabolic disorders

- Proof of mechanism
- Study anticipated for 2019



## CSL311 – Anti-Beta Common

- Central receptor (Beta Common) involved in stimulating immune modulating cells
- Increased activation in Auto-immunity, Allergy and Inflammation
- Blocking Beta Common (CSL311) and down regulating cells may ameliorate disease
- CSL311 blocks activity of GM-CSF, IL-3 and IL-5
- CSL311 inhibits activity of myeloid cells from normal and diseased tissue
  - FIH targeted for calendar year 2019



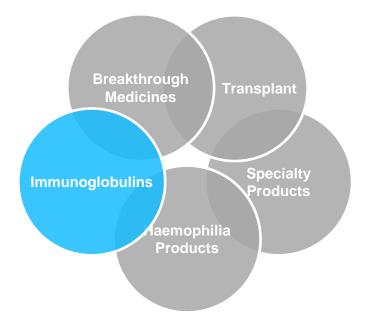


# Immunoglobulins, Haemophilia and Specialty Products

Dr Bill Mezzanotte Senior Vice President, Clinical Development



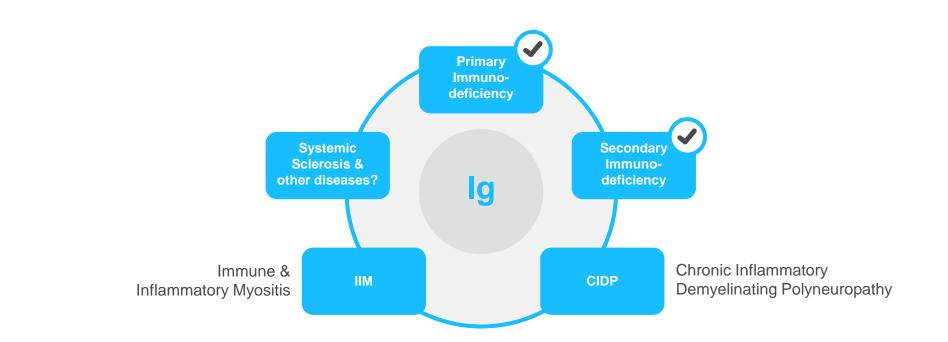
#### Immunoglobulins



- Maintaining leadership position through focus on:
  - New Indications
  - Geographic expansion
  - Delivery options
- Key Focus:
  - HIZENTRA<sup>®</sup>
  - PRIVIGEN®

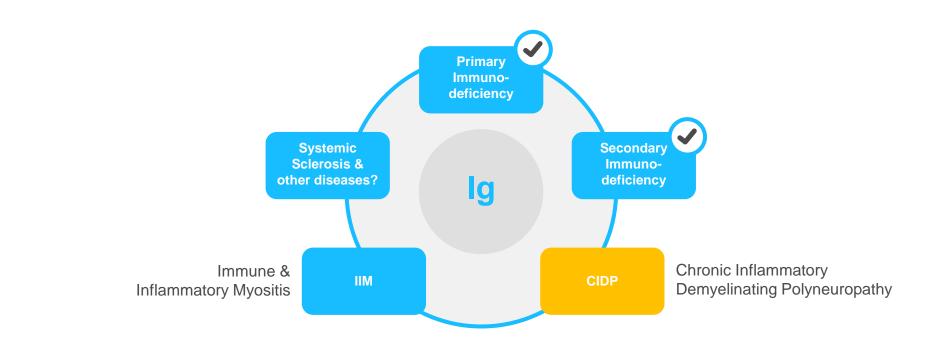


#### Impact of Ig (IV & SC) in Rare Diseases



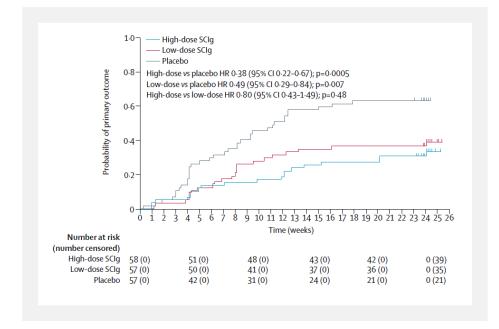


#### Impact of Ig (IV & SC) in Rare Diseases





#### PATH: SCIg (HIZENTRA®) Provides Effective Prophylaxis for CIDP Patients



- PATH study the largest controlled CIDP study ever performed
- Investigated multiple doses
- Disease control demonstrated in patients previously treated with IVIG

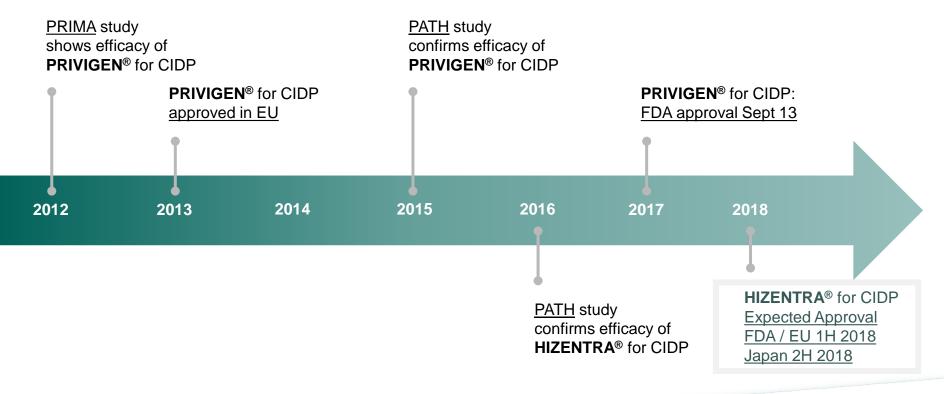


van Schaik et al; Lancet Neurology – Nov 17

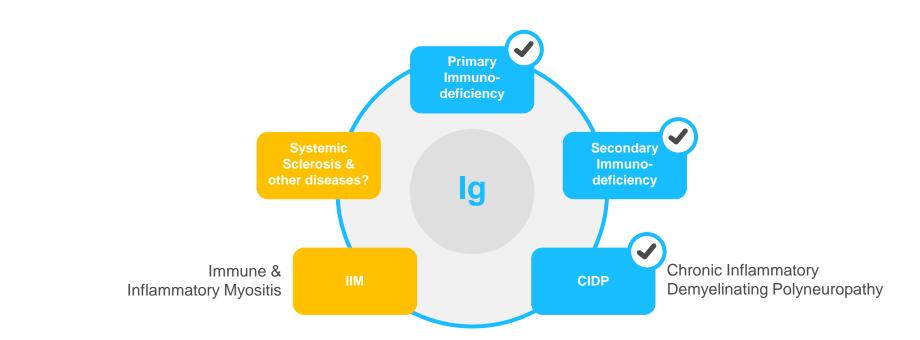
### IV and SC Ig are Effective Treatments for CIDP

- In the **PRIMA trial** 
  - 61% of patients responded to PRIVIGEN<sup>®</sup>; 50% after the first dose
  - Almost 50% of IVIG-naïve patients responded to PRIVIGEN<sup>®</sup>
- In the PATH study
  - 81% patients on high dose and 67% on low dose of HIZENTRA<sup>®</sup> remained relapse free (after initial PRIVIGEN<sup>®</sup> stabilisation)
  - All efficacy outcomes showed clinically relevant improvements
- PRIVIGEN<sup>®</sup> & HIZENTRA<sup>®</sup> :
  - Improve multiple measures of CIDP disease activity
  - Are well tolerated by patients with CIDP

#### **Milestones in Ig Development for CIDP**

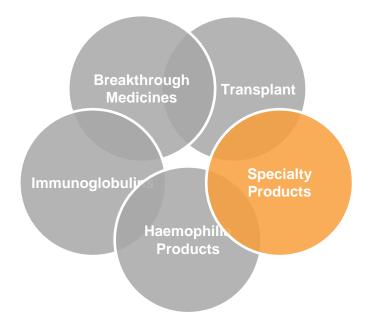


#### Impact of Ig (IV & SC) in Rare Diseases



- Proposed Ig IIM with Unique Study Design to start 2018
- Health Authority (FDA, EMEA, PMDA) interactions 1Q 2018

# **Specialty Products**



- Leveraging high quality broad product portfolio through:
  - New markets
  - Novel indications
  - Novel modes of administration
- Key Focus:
  - HAEGARDA<sup>®</sup>/BERINERT<sup>®</sup>
  - KCENTRA<sup>®</sup>/BERIPLEX<sup>®</sup>
  - ZEMAIRA<sup>®</sup>/RESPREEZA<sup>®</sup>

### **Hereditary Angioedema (HAE)**

- Hereditary angioedema (HAE) is a disorder that results in recurrent attacks of severe swelling
- All body sites are associated with impairment and patients are impacted during and between attacks
- Most severe are laryngeal attacks which can require emergency interventions to protect the airway





COMP

#### **Demonstrating the Unique Benefit of HAEGARDA®**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prevention of Hereditary Angioedema Attacks with a Subcutaneous C1 Inhibitor

Median Attack Rate Reduction: 95% 4 HAE attack/month (median) 3 2 0 Placebo 60 IU/kg

100 8.9 28.9 75 Severe 68.9 Moderate 17.8 50 Mild Unknown severity 25 40.0 22.2 No attack 0 60 IU/kg CSL830 Low-volume Placebo

**CSL830 Reduces Severity of Attacks** 

• Approval in US & Canada; approval pending EU



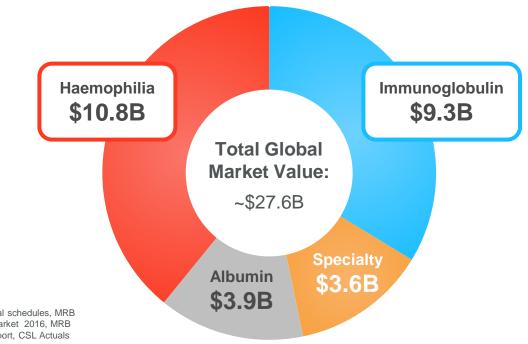
# **Commercial Market Overview**

Mr Bill Campbell Executive Vice President & Chief Commercial Officer



#### Global

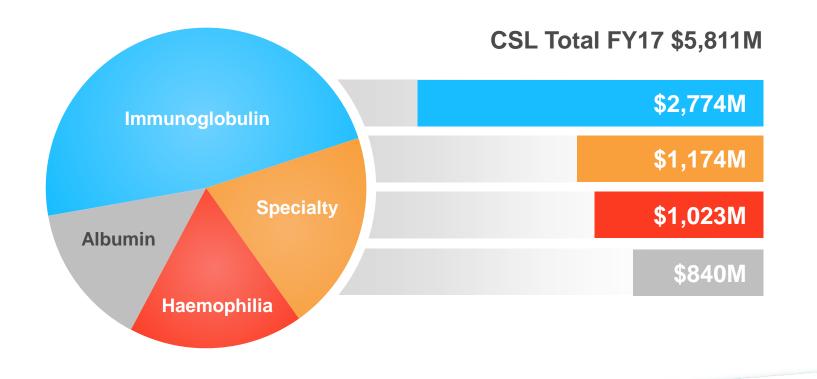
#### **Targeted Protein Therapeutic Market**



**Sources:** Company annual reports/financial schedules, MRB global Coagulation Factors Concentrate Market 2016, MRB WW Plasma Fractionation Market 2015 report, CSL Actuals FY17.



#### **CSL** Portfolio





# **Commercial / R&D Partnership**

- Integrated strategy teams
- Coordinated New Product Development / Market preparation
- Disciplined launch preparation & execution



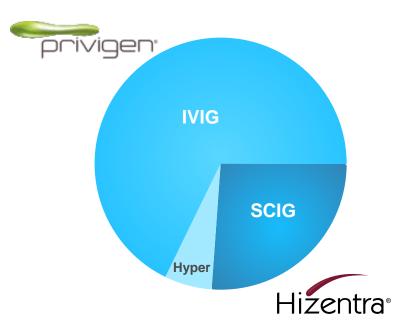
Multiple high value product launches:		
2013	KCENTRA®	
2016	IDELVION <sup>®</sup> & AFSTYLA <sup>®</sup>	
2017	HAEGARDA®	
2018	HIZENTRA <sup>®</sup> CIDP (pending approval)	

#### Foundational products plus new launches will continue to fuel significant growth

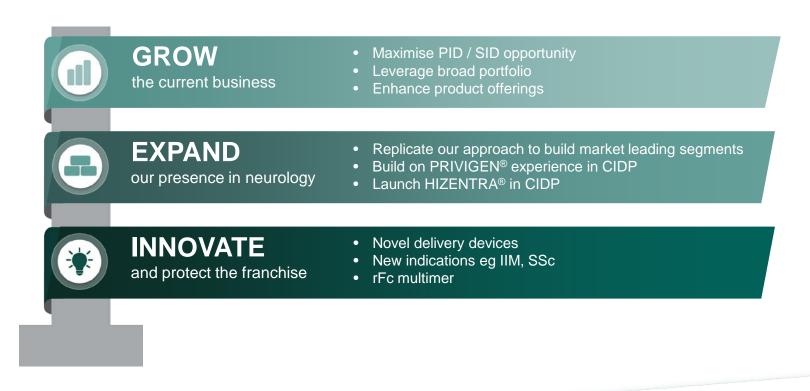


#### **CSL's Global Performance**

- CSL FY17 Sales \$2,774 M
- Significant growth opportunity
  - Per capita use varies widely
  - Core areas PID / SID
  - Neurology
  - New indications
- Continued acceptance, growth & patient benefits of SCIG



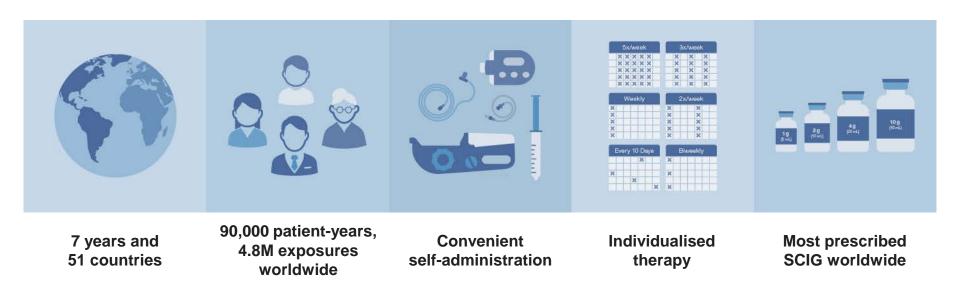
#### **Immunoglobulins: Category Leadership**





#### **HIZENTRA®: Innovator, Market Leader**

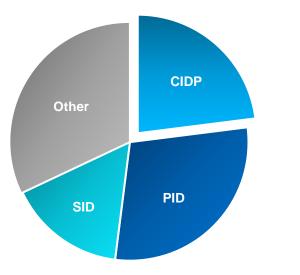






#### **CIDP – Growing Area of Focus**

#### **Global IG volume by indication**



- ~23% of all IG usage globally
- Growing market segment
- Many unmet needs remain



Sources: Data on File – US, 5EU, Japan.

#### **HIZENTRA®** addresses unmet needs in CIDP therapy





#### Unmet Needs

IVIG improves CIDP symptoms but many patients experience "wear off" with IVIG therapy



Steady state IG levels for continuous control



IVIG therapy difficult for patients with poor venous access



Hizentra therapy does not require venous access



Many patients on IVIG suffer from systemic effects like nausea and headache

4 fold lower systemic AE rates than IVIG



Majority of patients receive IVIG at infusion centers

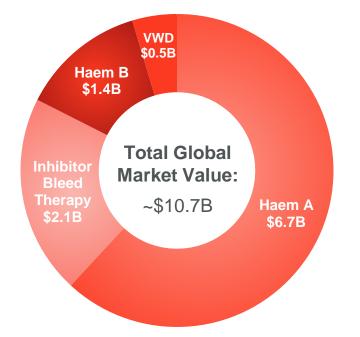
Increased independence and flexibility (time/site/frequency)

HIZENTRA® was preferred by 3X as many patients as IVIG



#### **Global Market**

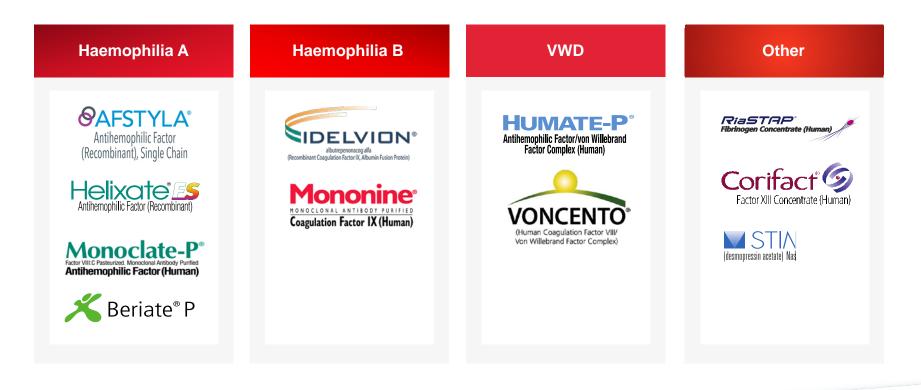
- Highly competitive Haem A market space
- Rapid transition of Haem B category
- Major advancements in patient care
- 75% of patients with bleeding disorders are under/untreated



**CSL** 

**Sources:** Company annual reports/financial schedules, based on 2017 data, MRB Global Coagulation Factors Concentrate Market 2016, CSL Actuals FY17.

### **Coagulation Portfolio**





### **Transforming Care of Haemophilia B Patients**

#1 "Switch to" brand providing highest factor levels for the longest period of time

1 <sup>st</sup> Haemophilia therapy with up to 14-day dosing	Long-lasting protection with high trough levels	Excellent efficacy
UP TO <b>14-DAY</b> DOSING	14 DAYS <b>ABOVE 13%</b> WITH 75 IU/KG	ZERO BLEEDS MEDIAN ASBR
Greater freedom from infusions	Ability to live a more normal life	Protection from bleeds





"All my IDELVION<sup>®</sup> patients were on prophylaxis previously with BeneFIX... they were very interested in having less frequent infusions."

- Hematologist, HTC

"

"This is not something I would associate with another FIX. It's higher than Alprolix, and, from a physician's perspective **the most important thing is that a patient not bleed.**"

– Hematologist, MD

"I mean, it's very impressive. Once we get to 21%, you know the patient is very well-protected. **Seven-day dosing** – **there's nothing not to like about this.**" – *HTC MD* 

"About half of my Alprolix patients have switched to IDELVION<sup>®</sup> now. I expect more will do the same." – Hematologist, MD



## **Transition to New Products in Haemophilia B**



#### US QTR pre US 15 mths Germany 13 launch post launch mths post launch ■ IDELVION ■ Alprolix ■ Other

#### Patient switches %

- Demand exceptionally strong
  - Capturing ~2/3 of patient switches
- Ongoing launch
  - Launched in 12 countries
  - First hemophilia product in Japan
  - France, Spain, Greece, Poland, Portugal, Israel, Canada, Australia, New Zealand and others still to come
- Extension Study
  - Clinically meaningful efficacy using 21 day regimen



#### **Accelerating AFSTYLA® Adoption**

**ØAFSTYLA**°

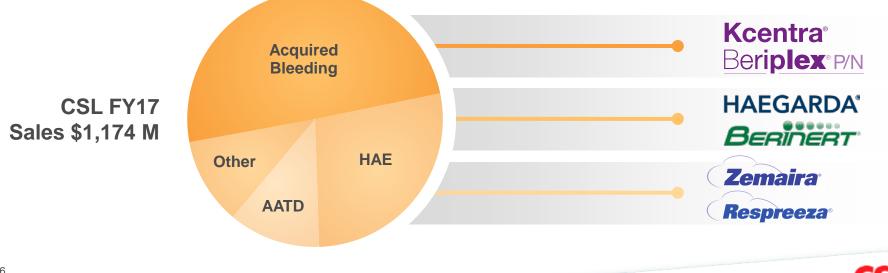
Proven long-lasting bleed protection with a unique single-chain design

Higher binding affinity to vWF	Long-lasting protection with high trough levels	Excellent efficacy	Individualised dosing
<b>3X HIGHER</b> COMPARED TO OCTOCOG ALFA	ABOVE 1.9% WITH 2X/WEEK DOSING	ZERO BLEEDS MEDIAN ASBR	2X WEEKLY AVAILABLE
Extended time in circulation	Ability to live a more normal life	Protection from bleeds	Flexible dosing – 2x or 3x weekly



#### **CSL's Global Performance**

- Specialty portfolio growth FY17 +20%
  - KCENTRA<sup>®</sup> / BERIPLEX<sup>®</sup> +35%; BERINERT<sup>®</sup> +31%
- HAEGARDA<sup>®</sup> US launch & rapid acceptance
- Often under or misdiagnosed



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#### **US Anti-Coagulation Market**

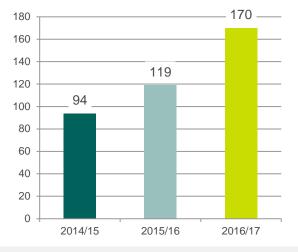
# PRADAXA SAVAYSA 0% 4% ELIQUIS 25%

US Demand (IU) 180 160 140 119 120 94 100 80 60 40 20 0 2014/15 2015/16 2016/17

#### Japan

- Launch Sep 2017
- Fast formulary acceptance
  - **Over 300** \_ hospitals

Continued Growth Opportunities for Kcentra<sup>®</sup>



# **Kcentra**<sup>®</sup>

Specialty



HAEGARDA®

# **Specialty Products – HAEGARDA®**

- Product launched July 2017
- 7 year orphan exclusivity
- 95% reduction in HAE attacks
- >99% reduction in the need for rescue medication
- First and only subcutaneous formulation
- Strong patient, physician and provider engagement







"

"I haven't had a single attack since starting the HAEGARDA® study in 2015!"	"This is the <b>longest period in my life having</b> <b>gone without a single attack</b> since my very first one at age 13."
"I choose not to suffer, and HAEGARDA <sup>®</sup> gives me that choice."	"I feel like I am finally a <b>participant in my own life!</b> "
"The patient is just giddy."	"It is, hands down, the easiest medication I've had to administer that <b>ACTUALLY works.</b> "

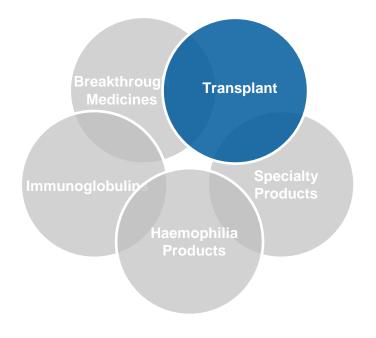


# Transplant and Breakthrough Medicines (CSL112)

Dr Bill Mezzanotte Senior Vice President, Clinical Development



## Transplant



- Developing CSL and other novel therapies with potential to improve transplant outcomes:
  - Significant unmet need
- Key Focus:
  - C1 inhibitor (C1-INH) / BERINERT®
  - Alpha1 anti-trypsin (AAT) / ZEMAIRA<sup>®</sup>
  - Anti-IL-6 / clazakizumab\*
  - CSL312 (anti-FXIIa mAb)
  - CSL324 (anti-G-CSFR mAb)

\*Partnered project

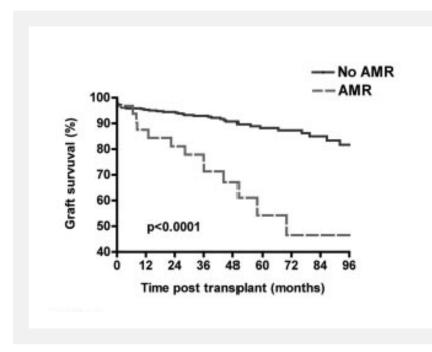
### Solid Organ Transplant (SOT): Unmet Medical Need

Before Transplantation		During Transplantation	After Transplantation
Patient & Donor	Donor Organs	Patient	Patient
Organ Availability and Patient-Donor Matching	Organ Viability and Donor Management	Ischemia-Reperfusion Injury and Consequences	Transplant Rejection
Donor-specific antibody reduction; increased access to transplantation	Improving organ utilisation and reducing ischemic injury prior to transplant	Reducing IR-related injury and its consequences – e.g. Primary Graft Dysfunction (PGD) & Delayed Graft Function (DGF)	Improving Treatment & Prevention of Antibody Mediated Rejection
	ole Organs ilable	Graft St	urvival

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More Viable Organs Available Graft Survival			

# Antibody Mediated Rejection (AMR) in Kidney Transplantation

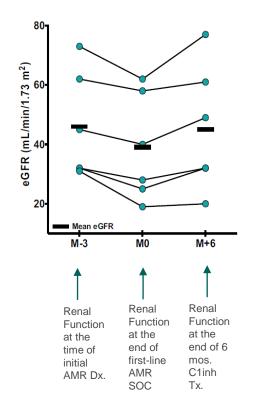


J Am Soc Nephrol 2010 Aug; 21(8): 1398–1406

The kidney is the most commonly transplanted solid organ

- AMR occurs in up to 5-10% of transplants acutely and up to 30% chronically
- AMR is marked by declining renal function and is associated with lower graft survival
- Patients with donor-specific antibodies are denied transplant due to the risk for AMR

#### Long Term C1 INH Administration Stabilises Graft Function in AMR Patients Unresponsive to Standard of Care

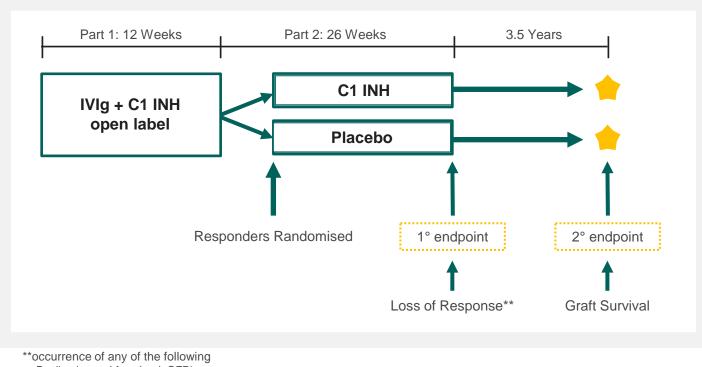


In a pilot study 6 patients with AMR, unresponsive to standard of care, were treated with C1 INH and had improved renal function (estimated Glomerular Filtration Rate, eGFR) at 6 months

Viglietti et al., Am J of Transplantation 2016



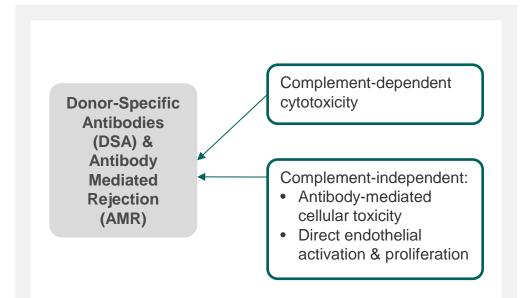
#### CSL842 C1-INH to prevent recurrent AMR: Randomised, Placebo-controlled Withdrawal



- Decline in renal function (eGFR)
- Allograft failure
- Subject death

7

#### **Complement Dependent & Independent Pathways Involved in AMR**



#### Potential Benefits of Anti-IL6 therapy in AMR:

- Reducing DSA production
- Reducing DSA mediated injury to allograft
- Pilot study demonstrated blocking IL-6 stabilises renal function and prolongs graft survival\*

\*Choi et al Am J Transplantation 2017



# **Vitaeris and CSL Strategic Collaboration**

- Vitaeris Inc.
  - clazakizumab (anti-IL6 mAb) in clinical development
  - Successful FDA Type C Meeting
- Anticipated dosing in AMR patients in 2018
- CSL Vitaeris Strategic Collaboration
  - Collaboration and purchase option agreement to expedite the development of clazakizumab
  - Exclusive Option to acquire company at later date with data readout
  - CSL with Board Observer & Director seats, Member of Scientific Advisory Board





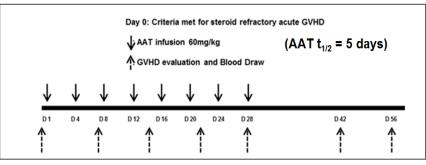
#### **Unmet Medical Need in Graft versus Host Disease (GvHD)**

- Incidence and mortality
  - Hematopoietic Stem Cell Transplant (HSCT) is a common effective therapy for many lifethreatening malignant and non-malignant diseases
    - Autologous Patient's own cells
    - Allogenic Donor cells
  - ~50-60% of Allogeneic HSCT develop acute Graft versus Host Disease (GvHD) despite prophylaxis
  - GvHD is a common cause of morbidity & mortality in HSCT
    - Therapies are often ineffective or cause severe immunosuppression
    - Survival is 30% for Grade III and 10% for Grade IV
  - Pathophysiology of GvHD in HSCT may be addressed by immunomodulatory effects of Alpha 1 Anti Trypsin (AAT)



#### Clinical Data: Treatment of Steroid-Refractory GvHD with AAT

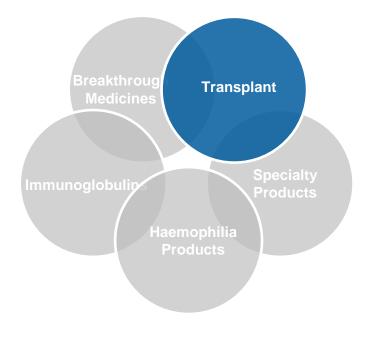
- ZEMAIRA® (AAT) Mangenau, ASBMT 2016
  - 40 Patients with Steroid refractory aGVHD
  - Open label AAT 60mg/kg twice weekly x 4 weeks
  - Overall response rate (ORR) 65%
    - 35% Complete Response
  - Sustained responses 73% at Day 60
  - Well tolerated with low rates of infection



- Proposed AAT GvHD Study
  - Anticipated study start in 2018
  - Final design pending ongoing regulatory discussions



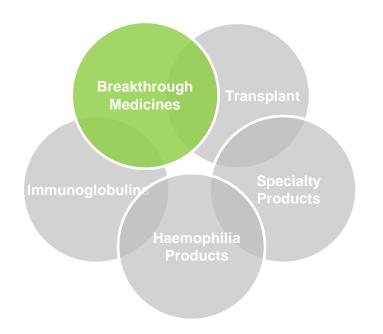
## Transplant



- Developing CSL and other novel therapies with potential to improve transplant outcomes:
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#### **Breakthrough Medicines**

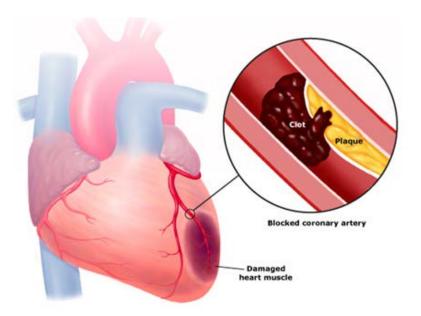


- Leveraging clinical and technical insight in developing novel protein-based therapies:
  - Significant unmet need
  - Multiple indications
- Key Focus:
  - CSL112 (ApoA-I)
  - CSL312 (anti-FXIIa mAb)
  - CSL324 (anti-G-CSFR mAb)
  - CSL346 (anti-VEGF-B mAb)
  - CSL311 (anti-BC mAb)



## Cardiovascular Disease (CVD) - High Unmet Medical Need

- CVD remains leading cause of death globally
- In the US alone, 800,000 acute MIs occur each year
- Survivors remain at high risk for early recurrent CV events
- Among high-risk populations:
  - 14% recurrence in year one
  - of these ~70% within first 90 days
- Reducing the risk of early recurrent events represents a significant unmet need



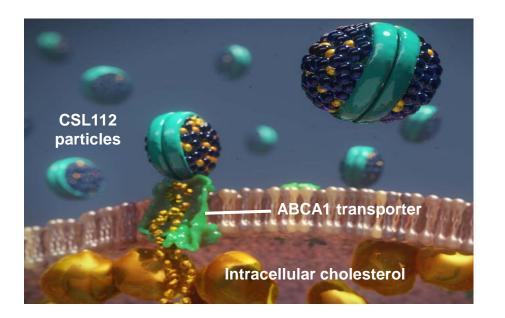
# **Cholesterol Efflux With CSL112 (apolipoprotein A-I)**

Apolipoprotein A-I (ApoA-I) is the primary component of HDL ("good cholesterol") and responsible for cholesterol efflux capacity (CEC)

 HDL levels & CEC are inversely correlated with atherosclerotic heart disease

#### CSL112:

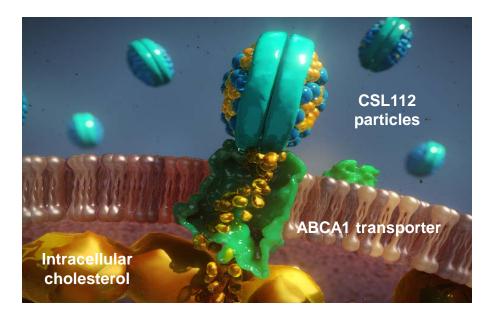
- purified ApoA-I from human plasma
- increases CEC, particularly ABCA1dependent CEC
- unique compound





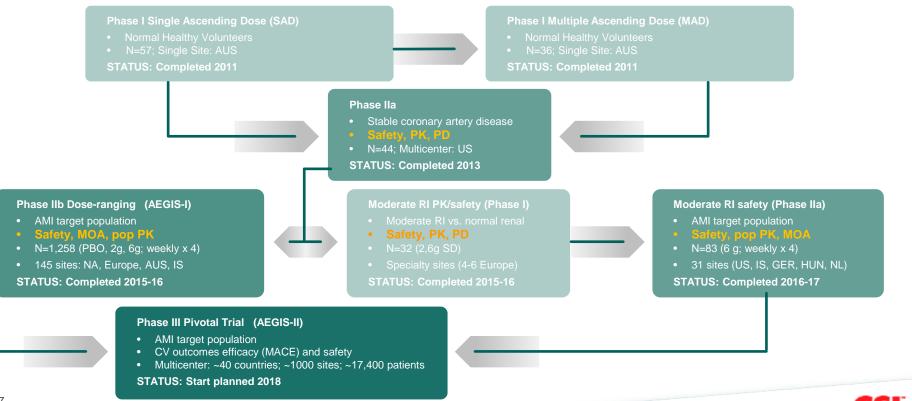
# **CSL112 Hypothesis**

- CSL112 will be safe and well tolerated
- CSL112 will enhance cholesterol efflux capacity (CEC)
- CSL112 will acutely stabilise atherosclerotic plaques and prevent subsequent major adverse cardiovascular events (MACE) in the early, highest risk period (unique treatment period)





#### CSL112: Clinical Path to Phase III – Safety & Mechanism of Action



#### No Safety Concerns in Patients with Moderate Renal Impairment

	Number of subjects with data	Number of subjects with events, n (%) n'			
Renal SAEs					
CSL112 6g (N=52)	52	1 (1.9%) 1			
Placebo (N=28)	28	4 (14.3%) 5			
Acute Kidney Injury (AKI) Events					
CSL112 6g (N=52)	50	2(4.0%)2			
Placebo (N=28)	28	4 (14.3%) 4			

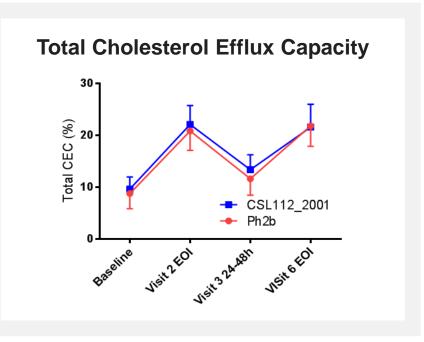
Low incidence of renal events across CSL112 and placebo

Safety data are consistent across:

- Degree of renal impairment: (eGFR 30- <45 ml/min) versus (eGFR 45 <60ml/min)
- Presence or absence of antidiabetic therapy

Results support including patients with moderate renal impairment into Phase III (AEGIS II)

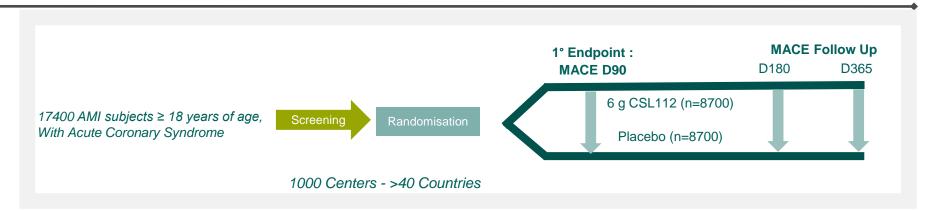
#### CSL112 raises Cholesterol Efflux to a similar extent in Patients with and without Moderate Renal Impairment



- At the end of infusion time points, the relative increases in CEC and ABCA1 dependent CEC were similar in both studies
- These efflux results are encouraging as patients with moderate renal impairment tend to experience a greater number of MACE events



# Phase III (AEGIS-II): Study Design



- Enriched Study Population: Multi-vessel coronary artery disease and at least one of the following:
- Age >65
- History of MI
- Diabetes mellitus
- Peripheral artery disease (PAD)
- Registry data confirms enriched AEGIS-II population is associated with high early recurrent event rate and supports our trial assumptions



## Phase III (AEGIS-II)

#### **Designed with Health Authority Input**

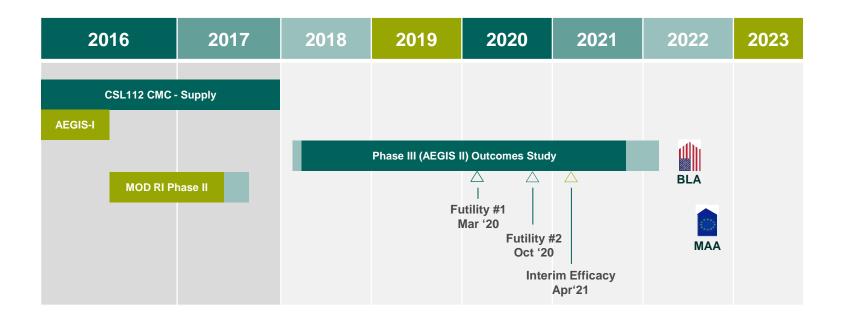


#### **Designed with International Trialists**





### **CSL112 Program Timeline**





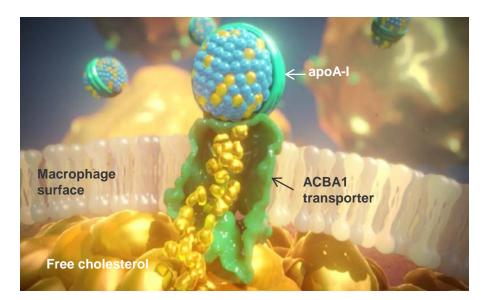
# **Breakthrough Medicines Commercial Opportunities**

Mr Bill Campbell Executive Vice President & Chief Commercial Officer



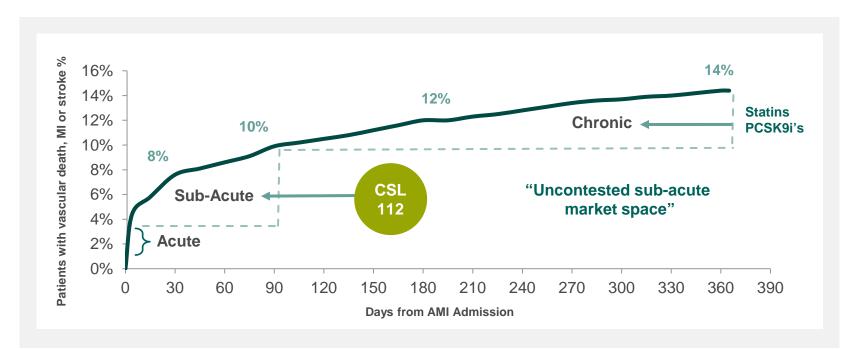
## **CSL112 to Address High Unmet Medical Need**

- CVD remains leading cause of death globally
- In the US alone, 800,000 acute MIs occur each year
- Survivors remain at high risk for early recurrent CV events:
- Among high-risk populations:
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- Reducing the risk of early recurrent events represents a significant unmet need



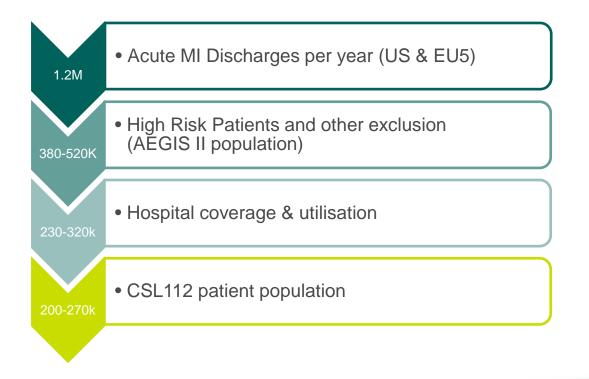


### **AEGIS-II** Population – High Early Recurrent Event Rate



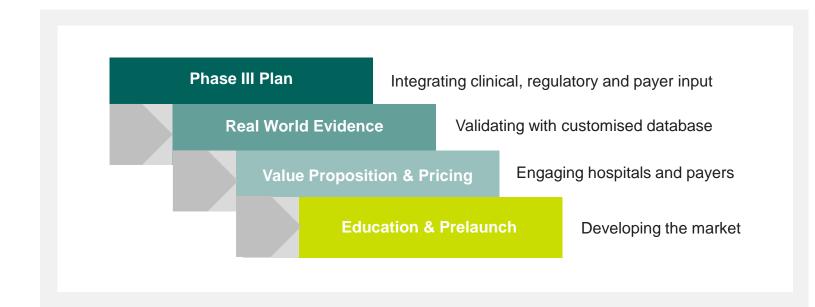
US AMI Registry/Symphony Health Claims Database N=75,758 (AEGIS-II eligible);2012-2015

## **Significant Opportunity in Sub Acute Space**





## **CSL112 Strategic Commercial Activities**





# Seqirus R&D

Professor Andrew Cuthbertson AO R&D Director and Chief Scientist



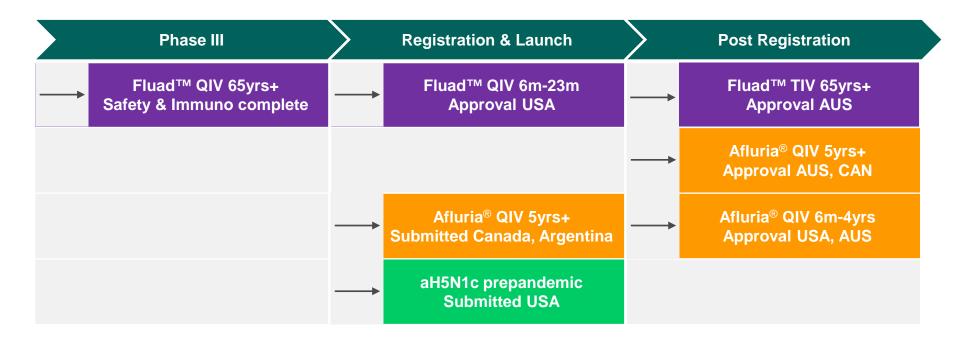
# Highlights of 2017



- FLUAD<sup>™</sup>
  - Approved in UK, strong recommendation for people 65yr and older
  - Holly Springs approved by FDA as a MF59 manufacturing and FLUAD fill-finish site
- aQIV
  - Submission for paediatric indication USA (end December)
- AFLURIA<sup>®</sup> QIV
  - 5 years+
    - Approved USA
    - Submitted Australia, Canada, Argentina, Sth Korea
  - 6 months to 4 years
    - Pivotal trial completed confirms improved safety profile of product
    - Submitted USA, AUS
- FLUCELVAX® QIV
  - FDA approval and first commercial manufacture of H3N2 using cell-based seed
  - Manufactured volumes more than quadrupled to 21m doses

# **Planned Milestones During 2018**





NB: plan to increase QIVc volumes by further 20%







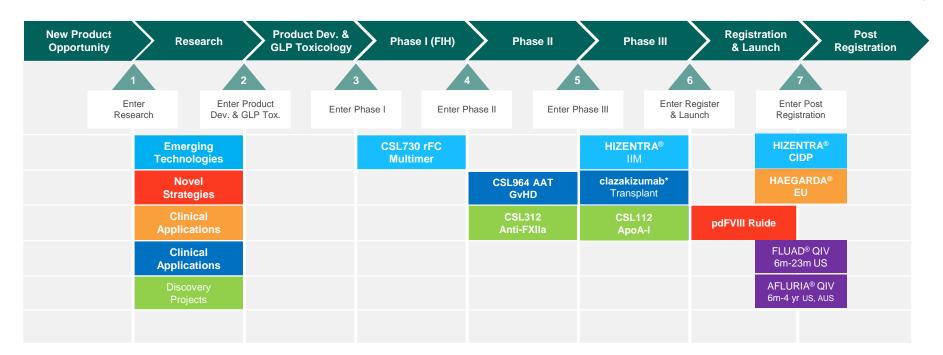
# **R&D Portfolio – December 2017**

	RESEARCH	PRE-CLINICAL	PHASE I	PHASE II	PHASE III	REGISTRATION	COMMERCIAL / PHASE IV
Life Cycle	Clinical Applications	C1-INH New Indications			PRIVIGEN <sup>®</sup> Japan	HIZENTRA <sup>®</sup> CIDP	PRIVIGEN <sup>®</sup> CIDP US
		Fibrinogen New Formulations			HIZENTRA® IIM		KCENTRA® Japan
		Haptoglobin/ Hemopexin		CSL964 AAT GvHD		HAEGARDA <sup>®</sup> EU	HAEGARDA® US
Management / Market		CSL640 rIX-FP subct			PRIVIGEN <sup>®</sup> CIDP Japan	AFLURIA <sup>®</sup> QIV 5-17 AUS	FLUAD <sup>®</sup> TIV 65+ US, UK
Development					CSL842 C1-INH AMR		FLUCELAX <sup>®</sup> QIV 4+ US
							AFLURIA® QIV 5-17 US
	Emerging Technologies	CSL730 rFc Multimer			clazakizumab* Transplant		<b>IDELVION</b> ®
	Novel Strategies	CSL626 D'D3 LA rVIII	CSL312 Anti-FXIIa	Mavri GM-CSFR-AZ*	pdFVIII Ruide		AFSTYLA®
New Product Development	Discovery Projects	CSL334 IL-13R* ASLAN	CSL324 Anti-G-CSFR				
	<b>Clinical Applications</b>	CSL311 Anti-BC	CSL346 Anti-VEGF-B		CSL112 ApoA-I		
		P. gingivalis/POD* OH-CRC					

Core Capabilities: Immunoglobulins | Haemophilia | Specialty Products | Breakthrough Medicines | Vaccines & IP | Transplant



# **Expected Progress in Next 12 Months**



Core Capabilities: Immunoglobulins | Haemophilia | Specialty Products | Breakthrough Medicines | Vaccines & IP | Transplant

# **Significant Target Launch Dates**

2017	2018	2019	2020-2023
PRIVIGEN <sup>®</sup> CIDP US	HIZENTRA <sup>®</sup> CIDP US/EU	PRIVIGEN <sup>®</sup> CIDP Japan	Hizentra <sup>®</sup> IIM
		PRIVIGEN <sup>®</sup> PID/SID Japan	
		HIZENTRA® CIDP Japan	
AFSTYLA <sup>®</sup> EU/Japan		pdFVIII Ruide	
CSL830 HAEGARDA <sup>®</sup> US	CSL830 EU		
KCENTRA <sup>®</sup> Japan			
			CSL112 ApoA-I
AFLURIA <sup>®</sup> QIV 5-17yr US	AFLURIA <sup>®</sup> QIV 6m-4yr US	AFLURIA <sup>®</sup> QIV 6m-5yr AUS	
	AFLURIA <sup>®</sup> QIV 5-17yr AUS	QIV EU	
	FLUAD <sup>®</sup> QIV 6m-23m US		
			CSL842 C1-INH AMR
			clazakizumab* Transplant

Core Capabilities: Immunoglobulins | Haemophilia | Specialty Products | Breakthrough Medicines | Vaccines & IP | Transplant



# **2017 Highlights**

Immunoglobulins	<ul> <li>PRIVIGEN<sup>®</sup> CIDP approved in US</li> <li>HIZENTRA<sup>®</sup> CIDP accepted for review by US FDA and EMA</li> <li>Momenta collaboration to develop CSL730 (rFC Multimer)</li> </ul>
Specialty Products	<ul> <li>HAEGARDA<sup>®</sup> results in 95% reduction in HAE attacks and &gt;99% reduction in rescue mediation and new standard of care for HAE</li> <li>HAEGARDA<sup>®</sup> registered and launched in the US</li> </ul>
Haemophilia	<ul> <li>IDELVION<sup>®</sup> dosage extension study supports 21 day regimen</li> <li>AFSTYLA<sup>®</sup> registered in EU, Japan and Australia</li> </ul>
Transplant	<ul> <li>CSL842 (C1INH) Phase III study in kidney AMR commenced</li> <li>Strategic collaboration and option agreement with Vitaeris to develop clazakizumab (anti-IL6 MAb) as a therapeutic option for AMR</li> </ul>
Breakthrough Medicines	<ul> <li>Data supports decision to proceed to CSL112 (Apo A-1) Phase III study (AEGIS-II)</li> <li>CSL346 (anti-VEGF-B) Phase I study commenced</li> <li>Completion of CSL312 (anti-FXIIa) HAE Phase I study</li> <li>Acquisition of Calimmune platform gene therapy technology and CAL-H SCD program</li> </ul>
Licensing & Vaccines	<ul> <li>AFLURIA<sup>®</sup> QIV registered in US in 5+ yrs; 6mnths-4yrs trial completed</li> <li>FLUAD<sup>®</sup> registered in UK, strong recommendation for people 65yr and older</li> </ul>





# **Further Information**

#### **Presentation Playback**

A webcast of the presentation can be accessed in the investors section of the CSL website. Contact: maria.pikos@csl.com.au

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