

CSL Limited  
45 Poplar Road Parkville  
Victoria 3052 Australia

T +613 9389 1911  
F +613 9389 1434  
www.csl.com.au



# ASX Announcement

**For immediate release**

4 December 2019

## **ANNUAL RESEARCH AND DEVELOPMENT INVESTOR BRIEFING**

Melbourne, Australia – CSL (ASX:CSL; USOTC:CSLLY)

Please find attached the presentation and an accompanying media release ahead of CSL's Annual Research and Development Investor Briefing being held today at 9am ADST.

The briefing will be webcast and can be accessed in the "Investor" section of CSL's website ([www.CSL.com](http://www.CSL.com)).

A handwritten signature in blue ink that reads 'F Mead'.

Fiona Mead  
Company Secretary

### **For further information, please contact:**

#### **Investors:**

**Mark Dehring**  
VP Investor Relations  
P: +61 3 9389 3407  
E: [mark.dehring@csl.com.au](mailto:mark.dehring@csl.com.au)

**Bernard Ronchi**  
Senior Manager, Investor Relations  
P: +61 3 9389 3470  
E: [bernard.ronchi@csl.com.au](mailto:bernard.ronchi@csl.com.au)

#### **Media:**

**Jemimah Brennan**  
Head of Communications, Asia Pacific  
P: +61 412 635 483  
E: [jemimah.brennan@csl.com.au](mailto:jemimah.brennan@csl.com.au)

**Christina Hickie**  
Senior Manager, Communications  
P: +61 429 609 762  
E: [christina.hickie@csl.com.au](mailto:christina.hickie@csl.com.au)



# R&D Investor Briefing

December 4, 2019

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### Forward looking statements

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After struggling for years to get an accurate diagnosis, hereditary angioedema (HAE) patient Kathrin Schoen is working to ensure the next generation of patients doesn't have to wait so long.

# Introduction

## William Mezzanotte, M.D.

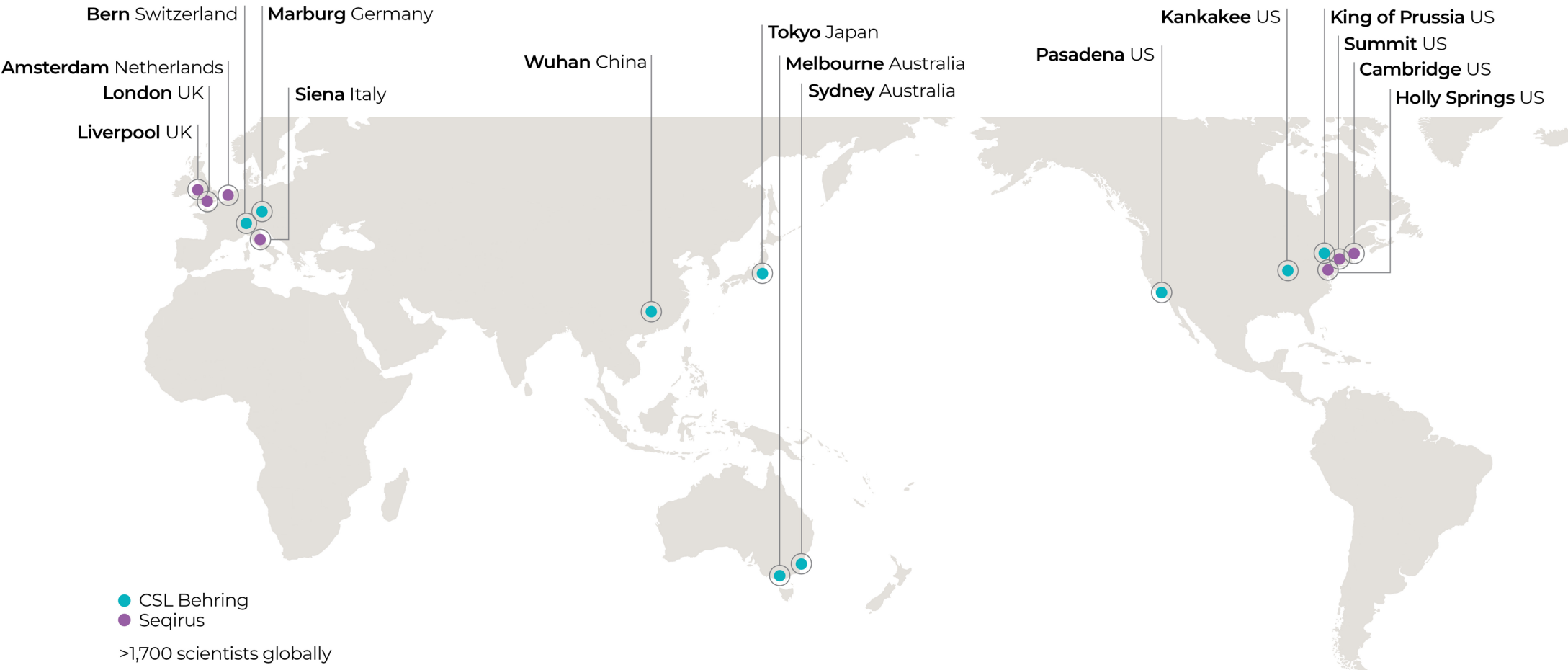
Executive Vice President, Head of Research and Development  
CSL Behring



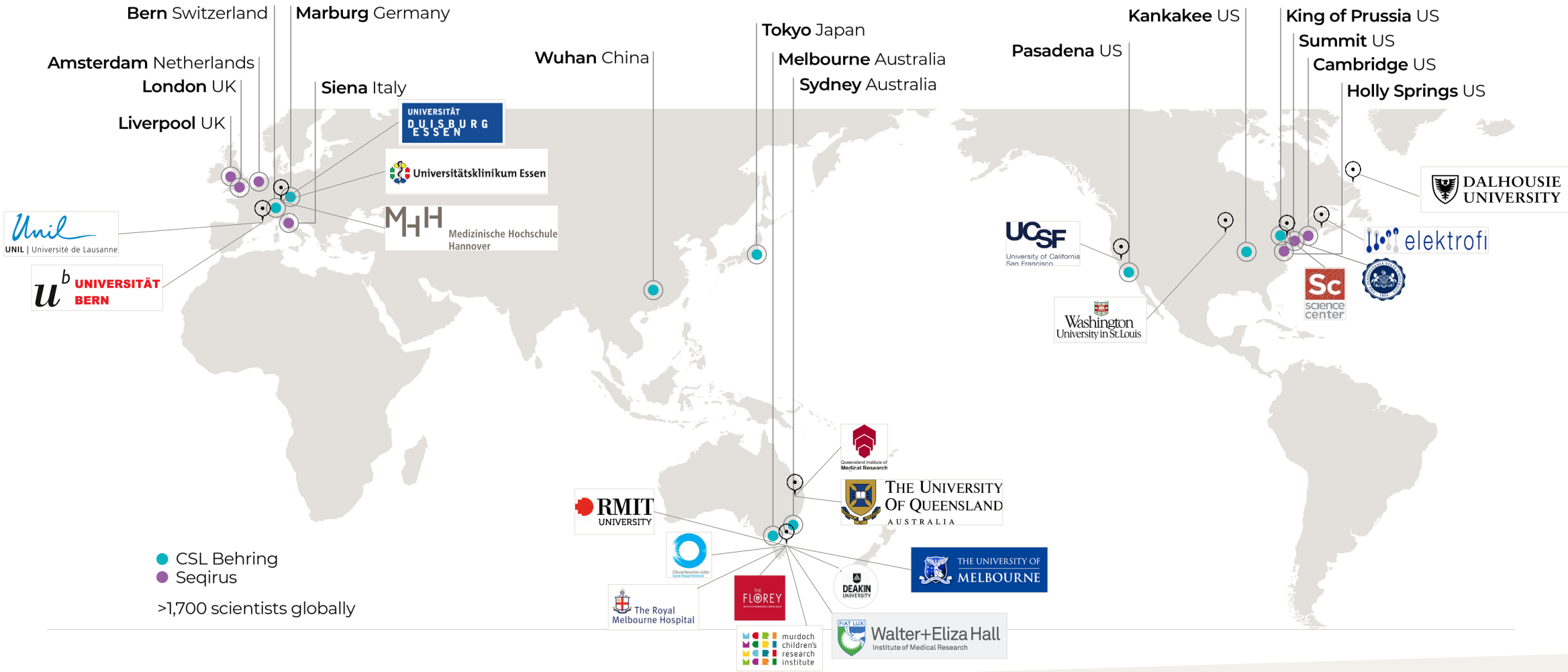
# Agenda

<b>Welcome</b>	<i>Mark Dehring</i>
<b>Introduction</b>	<i>Bill Mezzanotte</i>
<b>Research, Gene and Cell Therapy</b>	<i>Andrew Nash</i>
<b>Clinical Development Part 1</b>	<i>Diana Lanchoney</i>
<b>Commercial Part 1</b>	<i>Bill Campbell</i>
<b>Panel Q&amp;A Session</b>	
<b>Break</b>	
<b>Commercial Part 2</b>	<i>Bill Campbell</i>
<b>Seqirus</b>	<i>Russell Basser</i>
<b>Clinical Development Part 2 and Summary</b>	<i>Bill Mezzanotte</i>
<b>Panel Q&amp;A Session</b>	

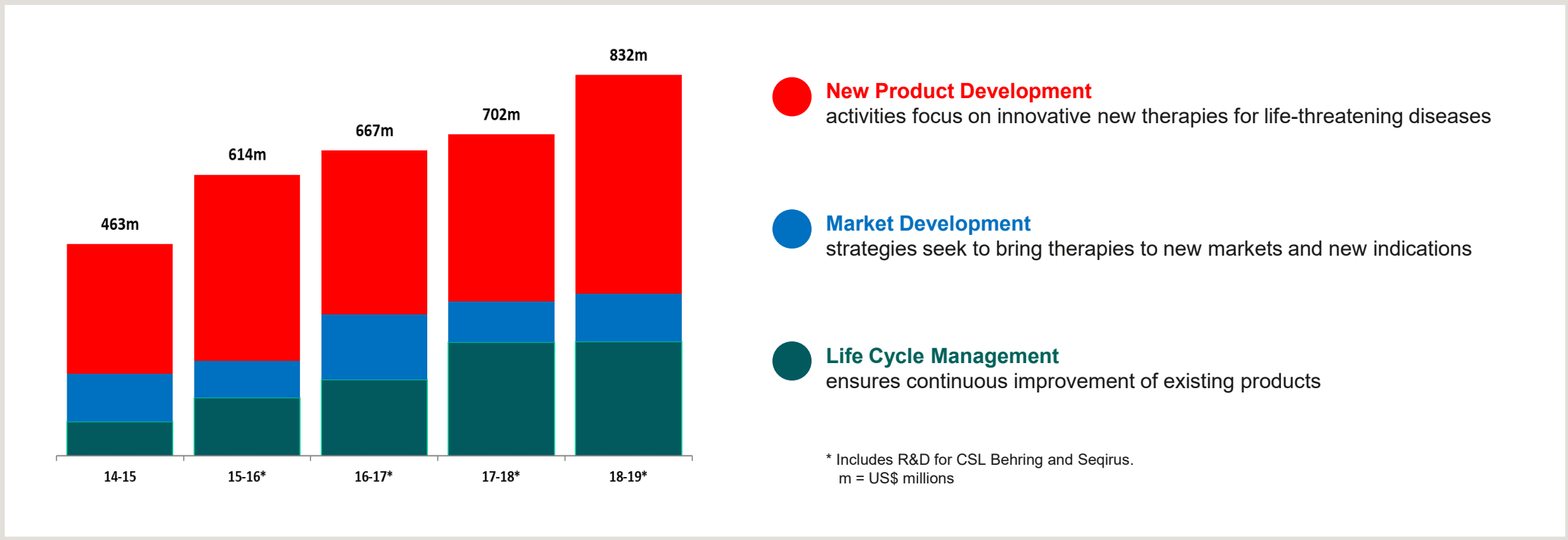
# Global Research and Development Footprint



# Global Collaborations for Innovation Access



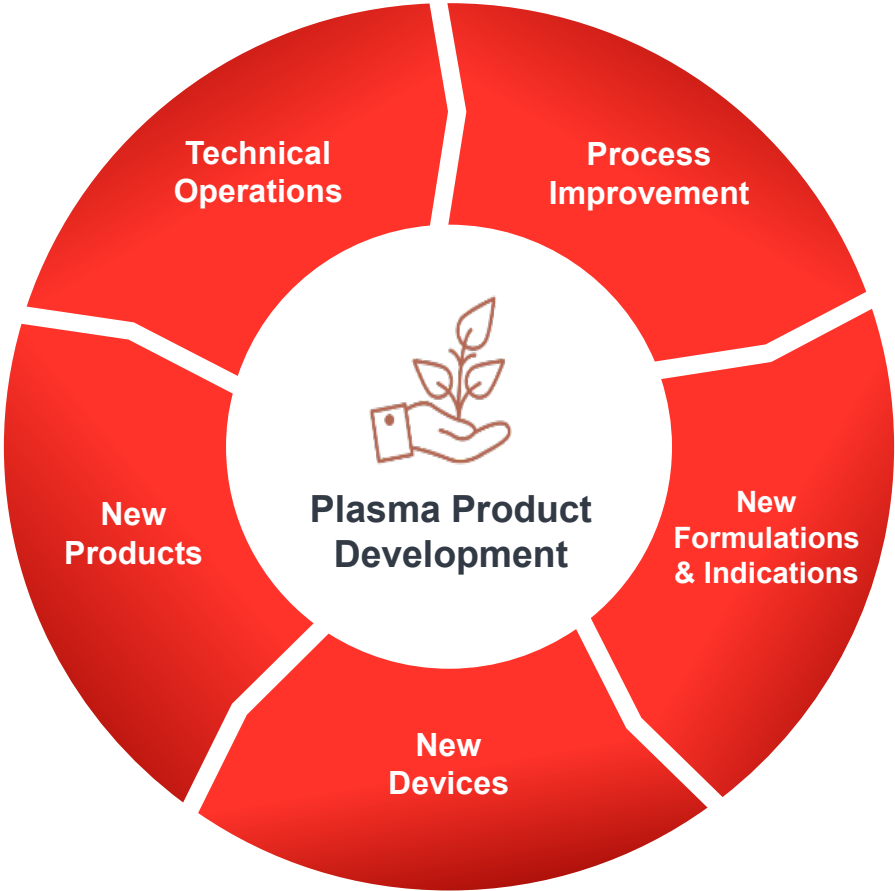
# Commitment to Research and Development



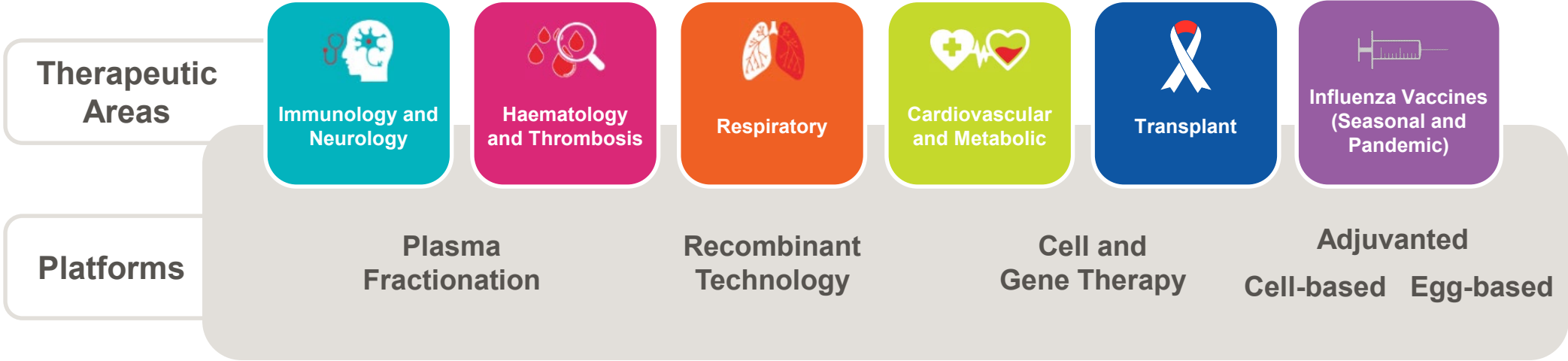
R&D investment ~10-11% global revenue



# Active R&D Support for Growth in Plasma Business



# Focus Through Our Therapeutic Areas and Platforms



# R&D Portfolio – December 2018

PRE-CLINICAL	PHASE I	PHASE II	PHASE III	REGISTRATION	POST-REGISTRATION
CSL200 (CAL-H)SCD	CSL730 rFc Multimer	CSL312 Anti-FXIIa HAE	PRIVIGEN® PID Japan	PRIVIGEN® CIDP Japan	CSL830 C1-INH Subcut EU
CSL889 Hemopexin SCD	CSL324 Anti-G-CSFR	Mavrilimumab GM-CSFR	HIZENTRA® IIM	HIZENTRA® CIDP Japan	PRIVIGEN® CIDP US
CSL787 Nebulised Ig	CSL346 Anti-VEGF-B		CSL630 pdFVIII Ruide	FLUCELVAX® QIV 9yrs+ EU	HIZENTRA® CIDP
CSL311 Anti-Beta Common	CSL334 IL-13R		CSL112 ApoA-I	AFLURIA® QIV 6M-4yrs AUS	HAEGARDA® US
P. gingivalis/POD			Clazakizumab		IDELVION®
			CSL842 C1-INH rAMR		AFSTYLA®
			CSL964 GvHD Prevention		KCENTRA® Japan
			FLUAD® QIV 65yrs+		FLUAD® aTIV 65yrs+
			Pre-Pandemic Vaccine (aH5N1c)		FLUCELVAX® QIV 4yrs+ US
					AFLURIA® QIV 6M+ US

▼ Partnered Projects

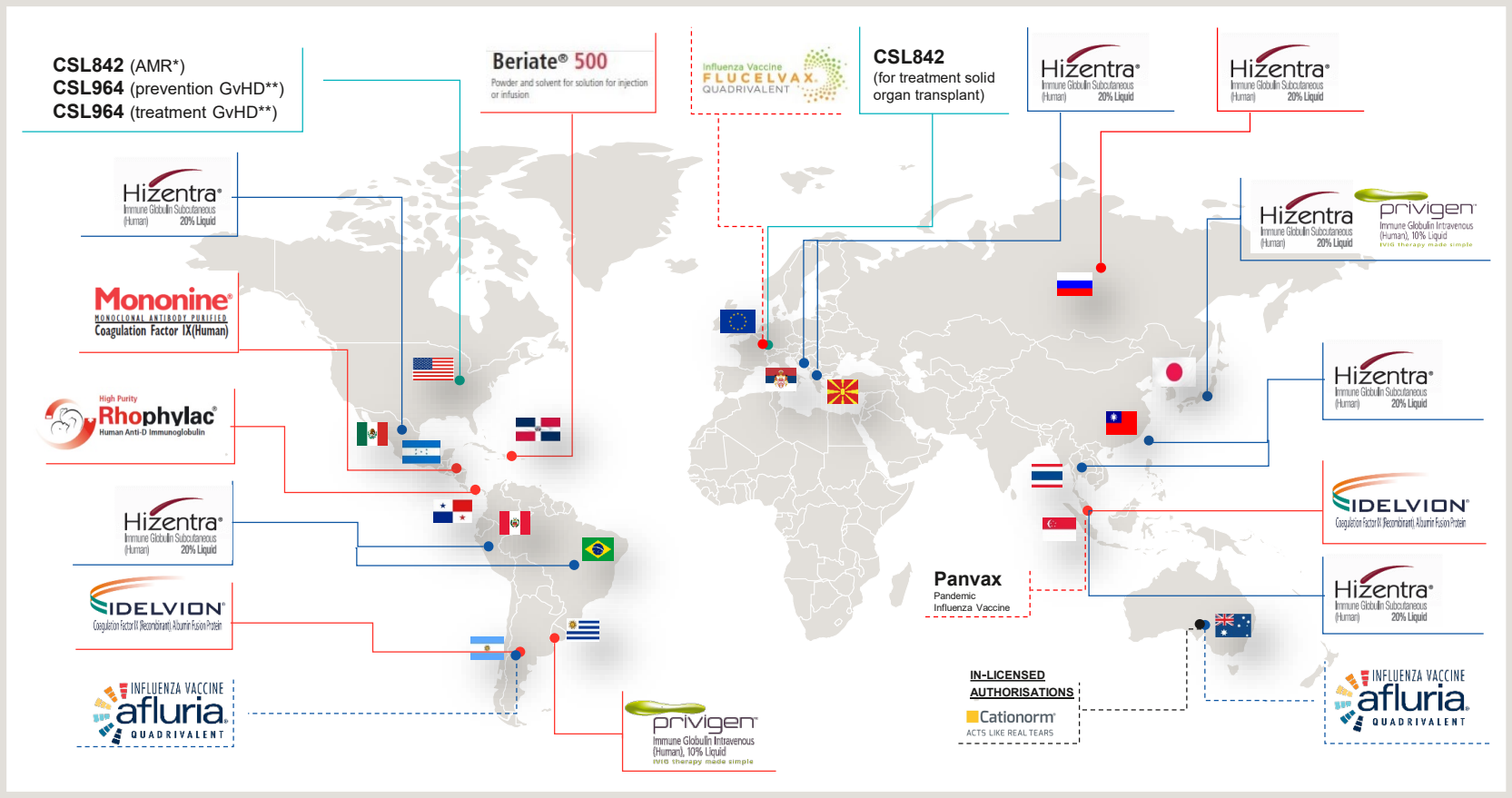
Immunology and Neurology | Haematology and Thrombosis | Respiratory | Cardiovascular and Metabolic | Transplant | Influenza Vaccines

# Key Past Launches from R&D Portfolio

	2013	2014	2015	2016	2017	2018	2019
Immun & Neuro	● PRIVIGEN® CIDP (EU)		Ig IsoLo® ●	PRIVIGEN® CIDP (US) ● HAEGARDA® (US) ●		● HIZENTRA® CIDP	● HIZENTRA® CIDP (Japan) ● PRIVIGEN® CIDP (Japan)
Haem & Throm	● VONCENTO® (EU) ● KCENTRA® (US)		IDELVION® ●	AFSTYLA® ●			
Respiratory		RESPREEZA® (EU) ●					
Influenza Vaccines			AFLURIA® QIV ● FLUCELVAX® ● FLUAD® (US) ●		FLUAD® (UK) ● FLUCELVAX® QIV (US) ●		FLUCELVAX® QIV 9yrs+ (EU) ● AFLURIA® QIV 6M+ (AUS) ●

# Notable Regional Regulatory Approvals

1 Dec 2018 – 20 Nov 2019



### Ongoing Activities

- CSL Behring**
  - Hizentra** (Human) 20% Liquid: Expanded Label for Enhanced Administration Parameters
  - IDELVION** (Recombinant) Human Factor Protein: Expanded Label for Dosing Every 21 days in Patients ≥12yrs of Age
- Seqirus**
  - FLUCELVAX** (Human) QUADRIVALENT: Geographic Expansion
  - afluria** (Human) QUADRIVALENT: Geographic Expansion
  - FLUAD** (Human) QUADRIVALENT: Special Population Label Expansion
  - aH5N1c**: New Registration in US

- CSL Behring
- Seqirus

- New Initial Marketing Authorization Approvals
- New Line Extensions/ Indications Approvals
- CSL Behring: CIDP Indication
- Seqirus: paediatrics
- Orphan Drug Designation

\*AMR - Antibody-Mediated Rejection  
 \*\*GvHD - Graft vs Host Disease



# Clinical Portfolio Progression in 2019

PRE-CLINICAL/PHASE I	PHASE II	PHASE III	REGISTRATION	POST-REGISTRATION
CSL200 (CAL-H) SCD	PRIVIGEN® SSc	HIZENTRA® DM	PRIVIGEN® PID Japan	PRIVIGEN® CIDP Japan
CSL312 Anti-FXIIa Thrombosis	HIZENTRA® SSc	CSL964 GvHD Treatment	AFLURIA® QIV 6M-4yrs AUS	HIZENTRA® CIDP Japan
CSL889 Hemopexin SCD			FLUCELVAX® QIV 9yrs+ EU, AUS	
CSL311 Anti-Beta Common			FLUAD® QIV 65yrs+ EU, AUS	
aQIVc (MF59 plus FLUCELVAX® antigen)			Pre-Pandemic aH5N1c	

Immunology and Neurology | Haematology and Thrombosis | Respiratory | Cardiovascular and Metabolic | Transplant | Influenza Vaccines

# Key Partnerships and Collaborations

PRE-CLINICAL	PHASE I	PHASE II	PHASE III
<p>P. gingivalis/POD</p> 	<p>CSL730 rFc Multimer</p> 	<p>Mavrilimumab GM-CSFR</p> 	<p>Clazakizumab Anti-IL-6</p> 
	<p>CSL334 / ASLAN004 IL-13R</p> 		<p>CSL964 GvHD Treatment</p> 

# R&D Portfolio – December 2019

RESEARCH	PRE-CLINICAL	PHASE I	PHASE II	PHASE III	REGISTRATION	POST-REGISTRATION
Discovery Projects	Improved Fibrinogen	CSL730 rFc Multimer	CSL312 Anti-FXIIa HAE	HIZENTRA® DM	PRIVIGEN® PID Japan	CSL830 C1-INH Subcut EU
Discovery Projects	CSL787 Nebulised Ig	CSL324 Anti-G-CSFR	HIZENTRA® SSc	CSL112 ApoA-I	FLUAD® QIV 65yrs+ US/EU/Canada	PRIVIGEN® CIDP US, Japan
Discovery Projects	aQIVc (MF59 plus FLUCELVAX® antigen)	CSL200 (CAL-H) SCD	PRIVIGEN® SSc	Clazakizumab AMR	Pre-Pandemic aH5N1c	HIZENTRA® CIDP US, Japan
Discovery Projects	P. gingivalis/POD	CSL889 Hemopexin SCD	HAEGARDA® Japan	CSL842 C1-INH rAMR		HAEGARDA® US
Discovery Projects		CSL312 Anti-FXIIa Thrombosis	CSL630 pdFVIII Ruide	CSL964 GvHD Prevention		IDELVION®
		CSL311 Anti-Beta Common	Mavrilimumab GM-CSFR	CSL964 GvHD Treatment		AFSTYLA®
		CSL346 Anti-VEGF-B		FLUCELVAX® 6M+		KCENTRA® Japan
		CSL334 / ASLAN004 IL-13R				ZEMAIRA® / RESPREEZA® AAT
						AFLURIA® QIV 6M+ US, AUS

▾ Partnered Projects

Immunology and Neurology | Haematology and Thrombosis | Respiratory | Cardiovascular and Metabolic | Transplant | Influenza Vaccines



# Research, Gene and Cell Therapy

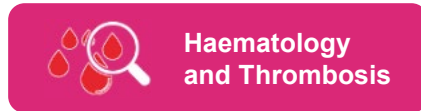
## Dr. Andrew Nash

Senior Vice President, Research  
CSL Behring



# CSL Research

- **Capabilities and facilities**



- **New product opportunities**

- **Plasma** – Haptoglobin for the treatment of Subarachnoid Haemorrhage (SAH)
  - Innosuisse grant awarded to the University Hospital Zürich and CSL Behring in 2017
- **Recombinant** – CSL311 for the treatment of inflammatory disease
- **Gene therapy** – Sickle Cell Disease (CSL200) and immune deficiencies

# CSL Research

## New Facilities



### Bio21 Institute, Melbourne

- ~ 4100m<sup>2</sup> of lab and office space
- Parkville precinct
- Melbourne University, MRI's
- 4 major teaching hospitals



### SITEM\*, Bern

- 2000m<sup>2</sup> of lab and office space
- Bern University and Hospital campus

\*SITEM – Swiss Institute for Translational and Entrepreneurial Medicine

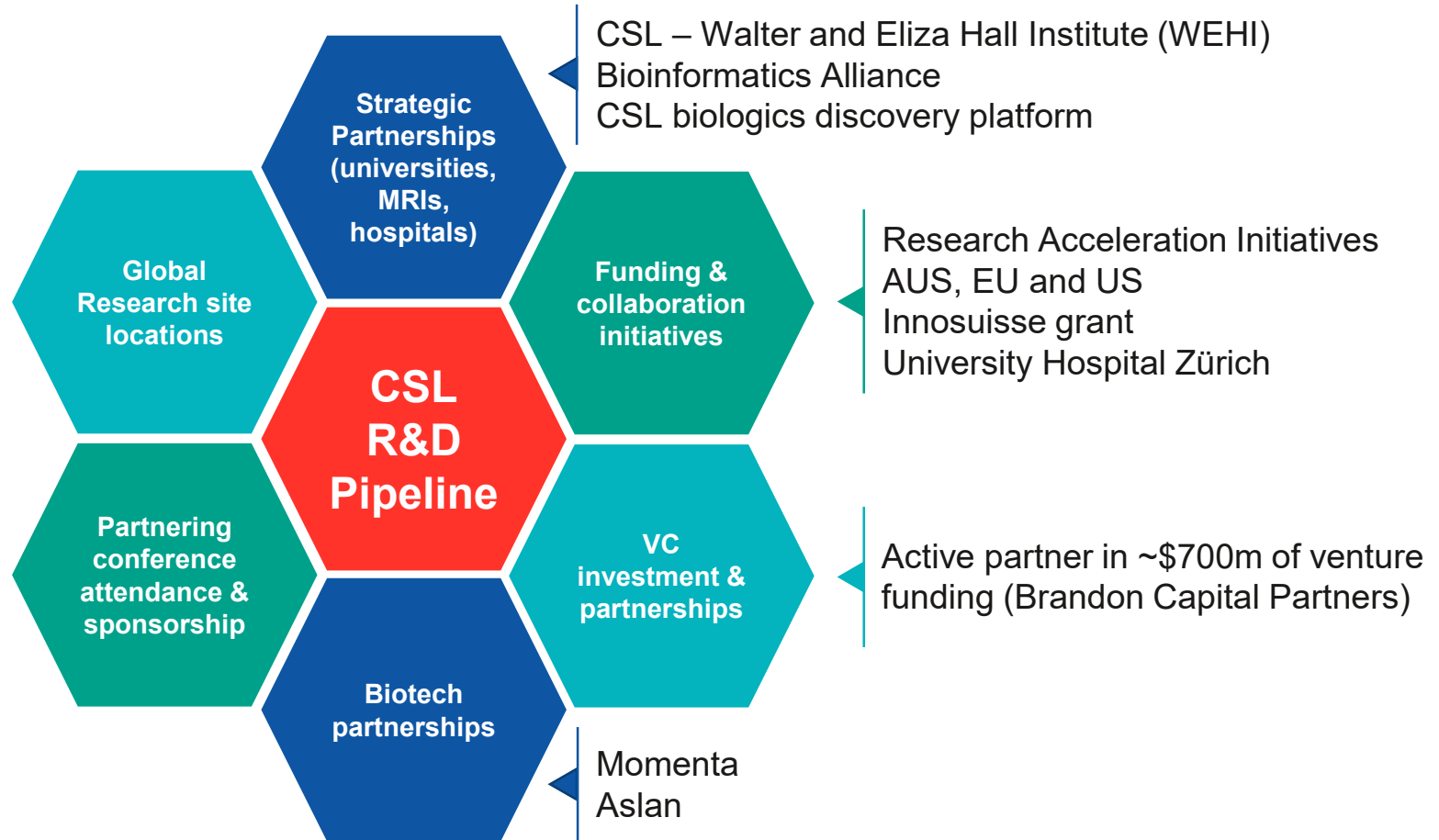


### Gene therapy, Pasadena

- Expanding gene therapy expertise
  - Research, QA, cell processing and manufacture
  - Wet-lab space (non-GMP) tripled from 132 to 480 m<sup>2</sup>
  - GMP space (330 m<sup>2</sup>) to engineering qualification level

# CSL Research

## External Innovation Strategy

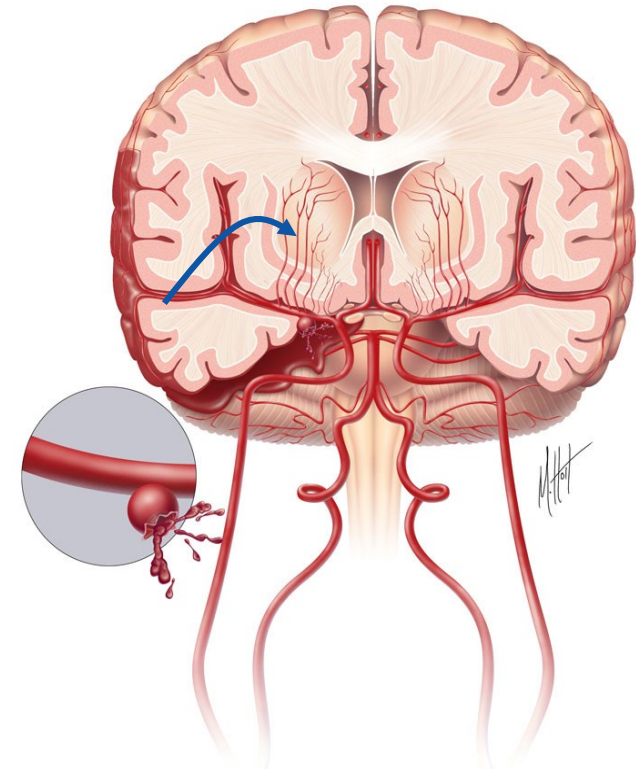


m = AU\$ millions

# Haptoglobin for the Treatment of Subarachnoid Haemorrhage (SAH)

## Pathophysiology of SAH

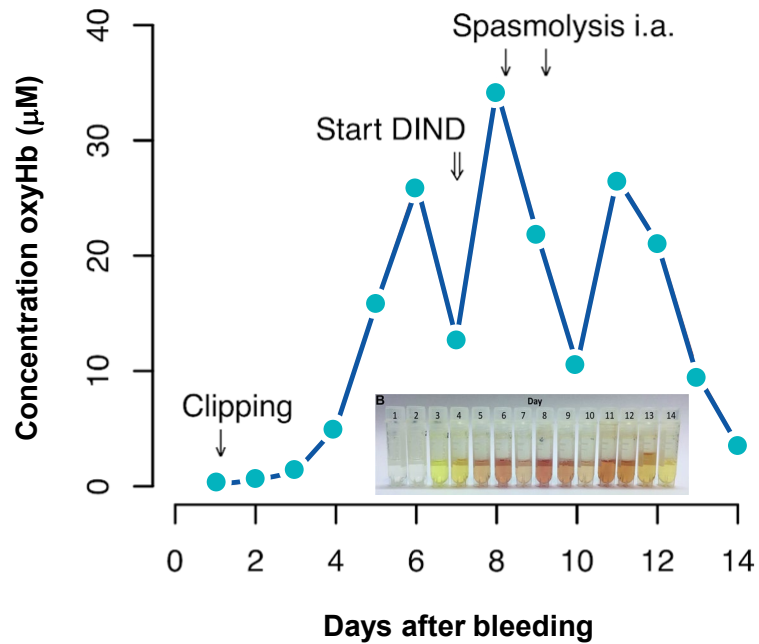
- Acute indication – rupture of an aneurysm in the brain, followed by bleeding and haemolysis within the subarachnoid space
- Survivors of initial bleeding are at risk for Delayed Ischemic Neurological Deficits (DIND)
- High mortality and morbidity
  - 5% of all strokes; high fatality rate
  - Very limited treatment options
- Haemoglobin (Hb) concentrations in cerebral spinal fluid (CSF) correlate with DIND in SAH patients



Source: [www.strokecenter.org](http://www.strokecenter.org)

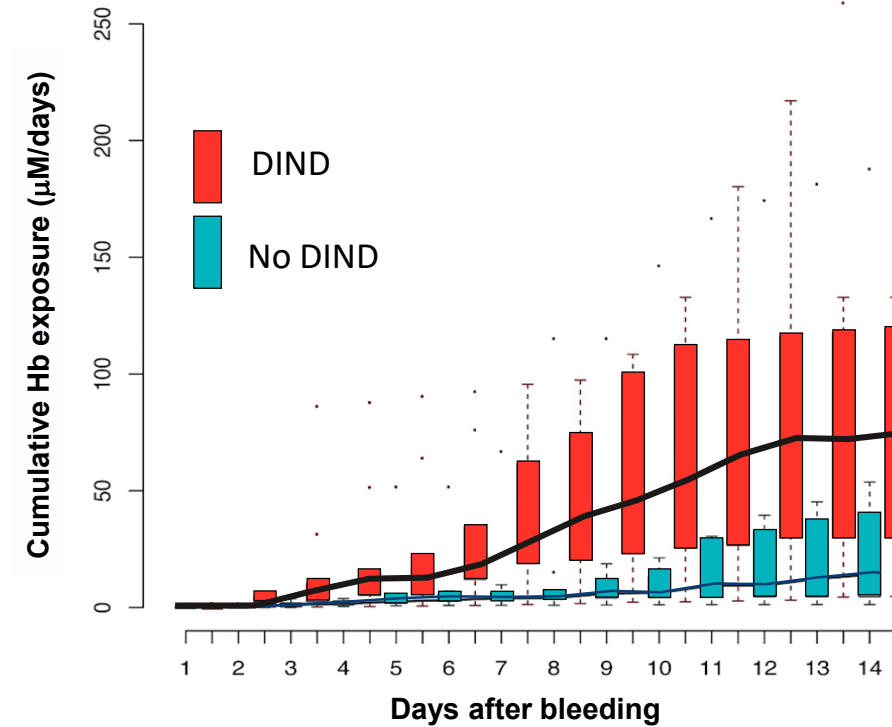
# Haptoglobin and SAH

## Link Between CSF Hb Levels and DIND



Hb levels in CSF correlate with DIND

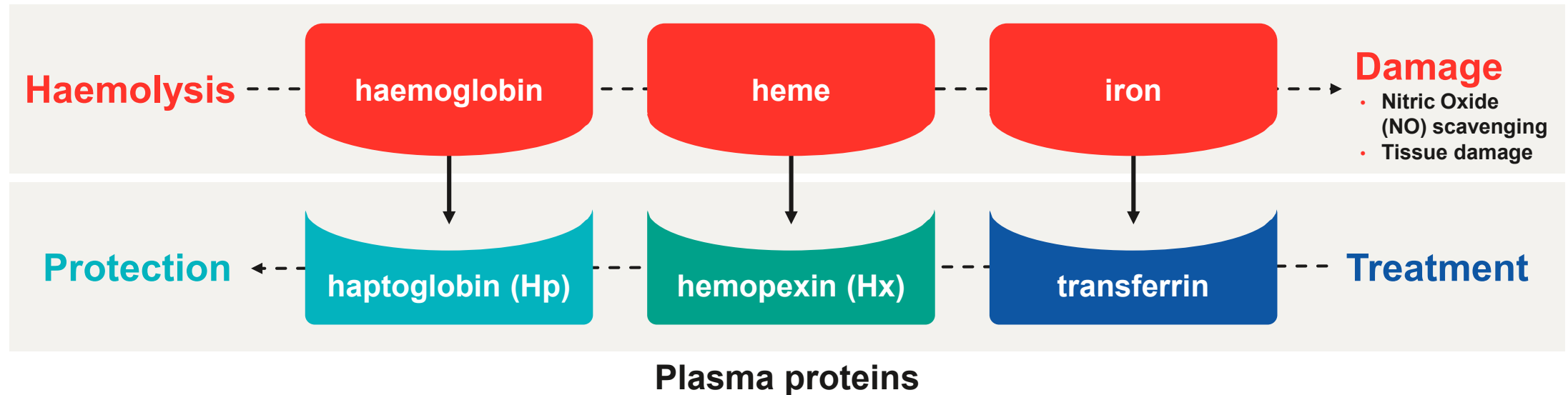
39 year old, right-handed female with thunderclap headache, vomiting and loss of consciousness



SAH patients (n=18) developing DIND have higher cumulative Hb exposure

Source: Hugelshofer et al. World Neurosurgery 2018

# How the Body Deals with Toxic Free Haemoglobin (Hb) and Heme



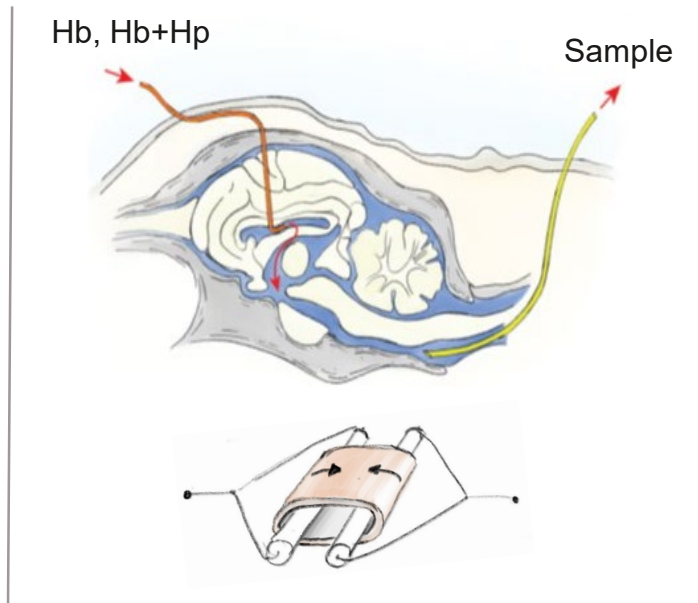
- Opportunities to treat chronic and acute haemolytic disease
- Replacement and/or augmentation therapy

# Haptoglobin for the Treatment of SAH

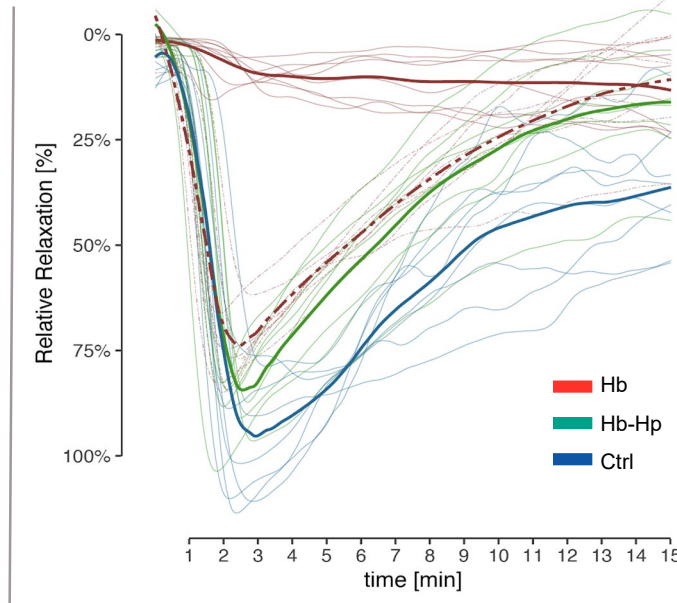
## Haptoglobin Prevents Vasospasms Induced by Haemorrhagic CSF – *ex vivo* Functional Assay



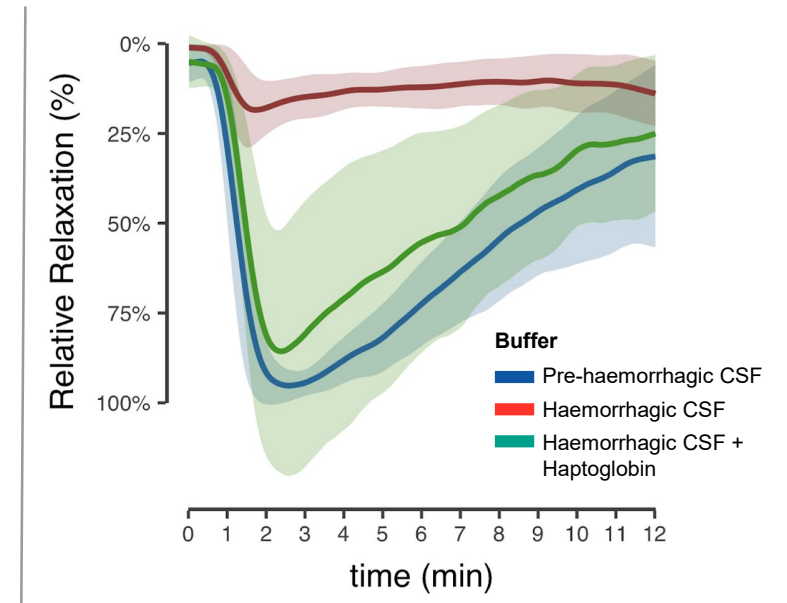
### Sheep Model of SAH



### CSF From Sheep SAH Model



### CSF Samples From SAH Patients

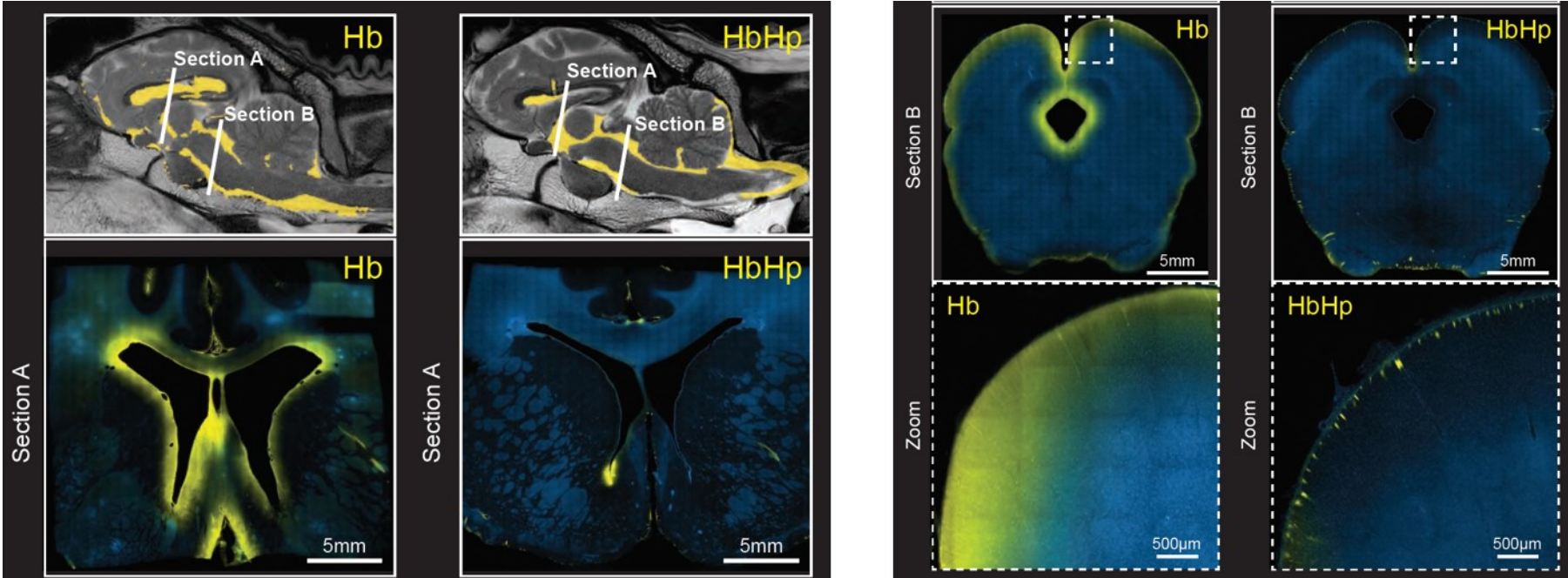


Source: J Clin Invest. 2019. <https://doi.org/10.1172/JCI130630>



# Haptoglobin for the Treatment of SAH

## Haptoglobin Prevents Penetration of Hb into Brain Tissue



Labeled Hb ± haptoglobin was injected into CSF 2 hours before analysis

Source: J Clin Invest. 2019. <https://doi.org/10.1172/JCI130630>

# Haptoglobin for the Treatment of SAH

## Summary

### Haemoglobin

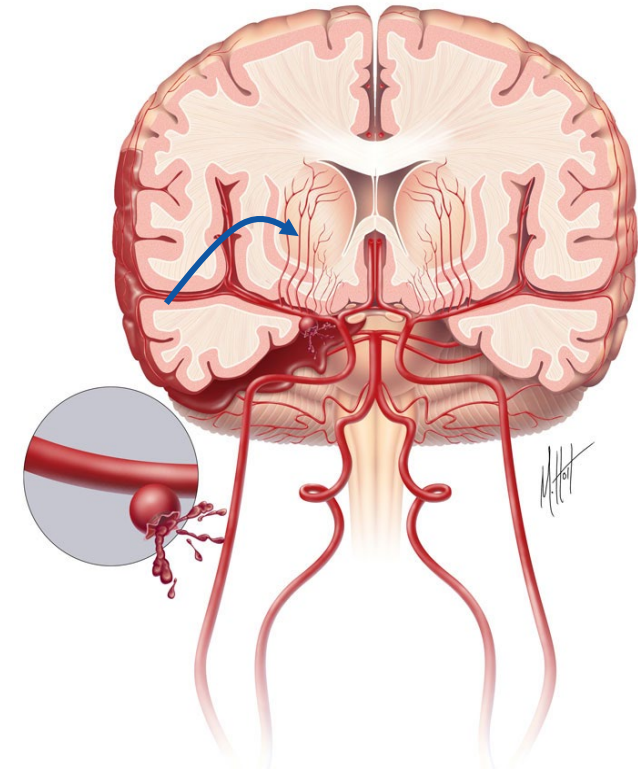
- Concentrations in CSF correlate with DIND in SAH patients
- Rapidly penetrates from CSF into the brain parenchyma
- Induces angiographic vasospasms in 100% of animals

### Haptoglobin

- Blocks tissue penetration of cell-free Hb
- Prevents Hb induced vasospasms in *ex vivo* assay
- Prevents Hb induced segmental vasospasm *in vivo*

**Current Status - enter development H2 2020**

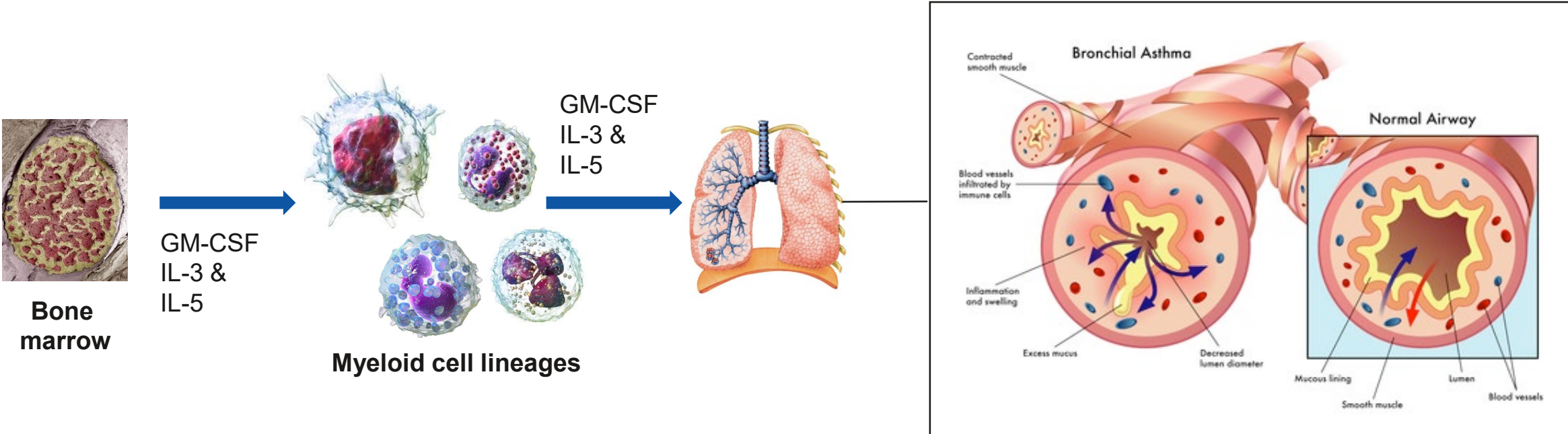
Source: [www.strokecenter.org](http://www.strokecenter.org)



# CSL311 for the Treatment of Airways Inflammation

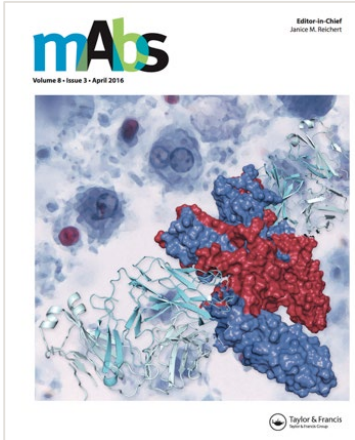
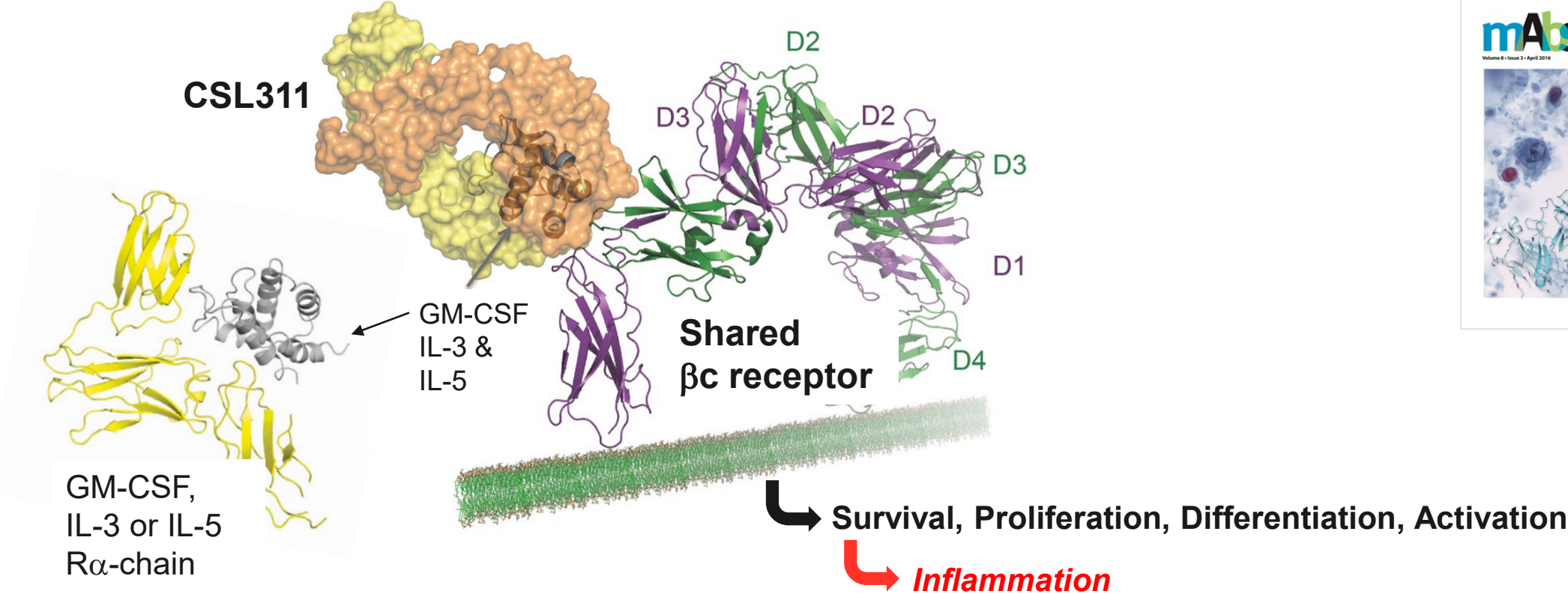
## Airways Inflammation

Targeting multiple inflammatory mediators with a single therapeutic



# CSL311 for the Treatment of Airways Inflammation

## CSL311 Targets Multiple Cytokines via a Shared Receptor

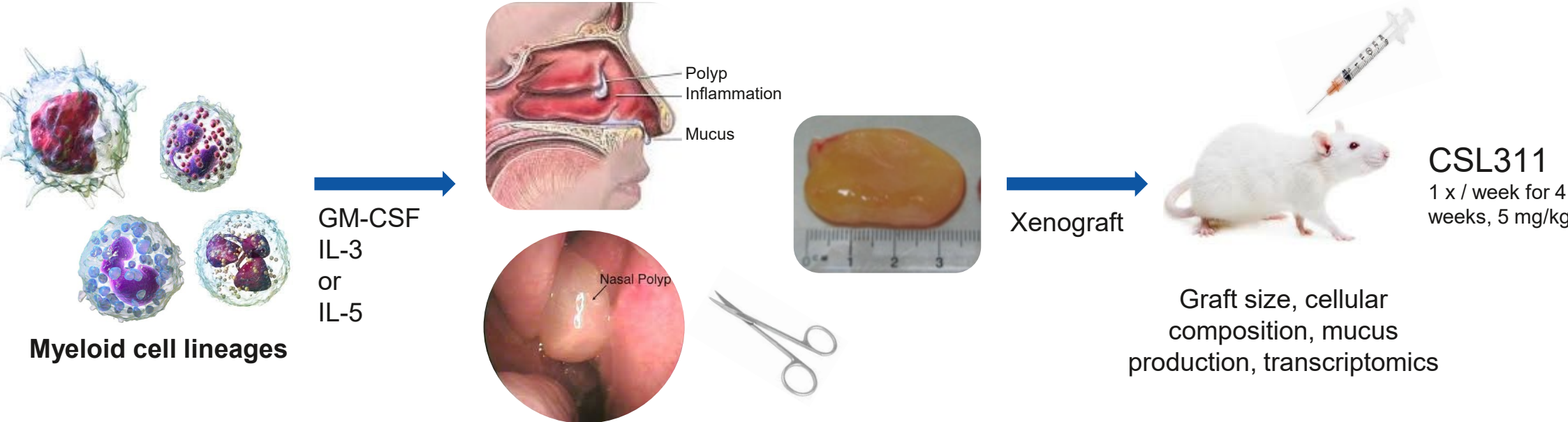


Source: Panousis et al., Mabs 8:436, 20126

# CSL311 for the Treatment of Airways Inflammation

## In Vivo Efficacy in a Mouse Model of Human Airways Inflammation

Xenografting human nasal polyps into immunodeficient mice

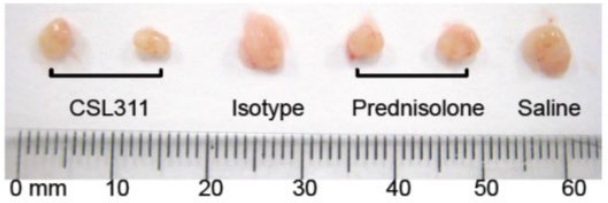
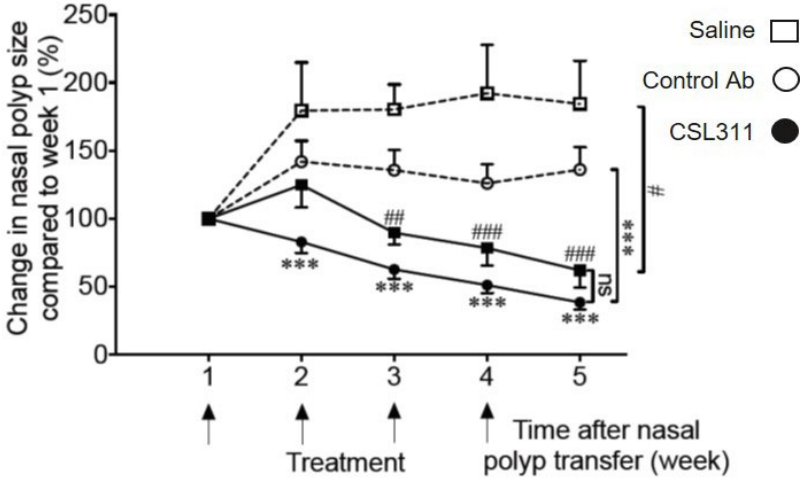


Source: Yip et al., Allergy 2019 Sep 10. doi: 10.1111/all.14041

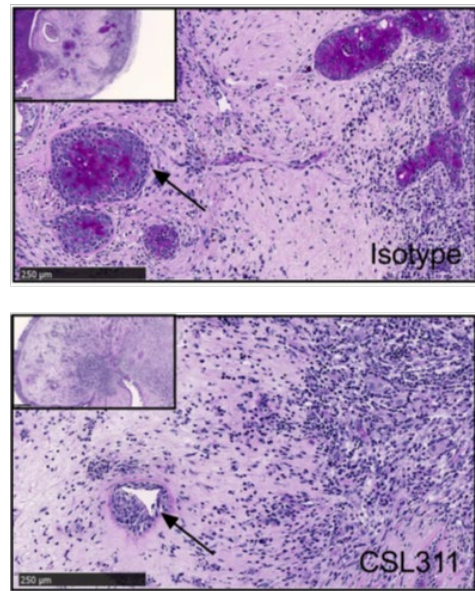
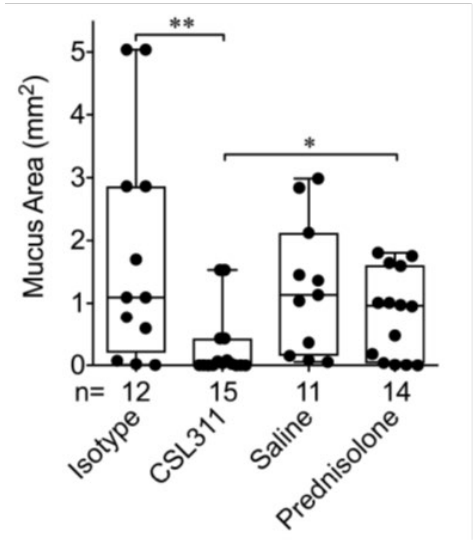
# CSL311 for the Treatment of Airways Inflammation

## In Vivo Efficacy – Mouse Model of Human Airways Inflammation

CSL311 restrains human nasal polyp xenograft progression *in vivo*



CSL311 treatment reduces mucous gland numbers and mucus production in nasal polyps *in vivo*

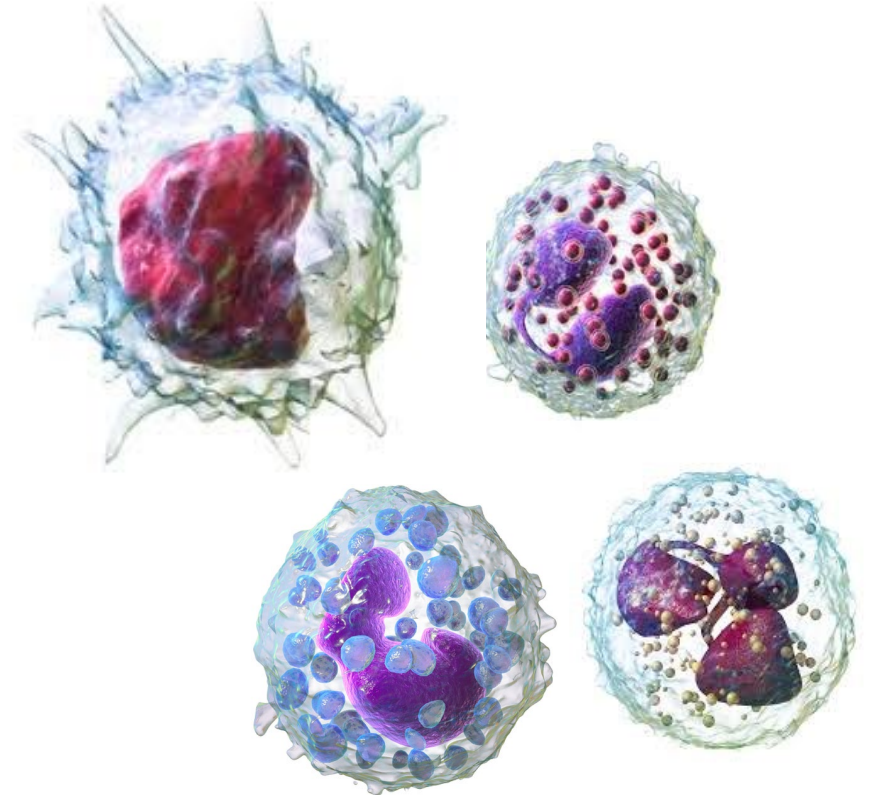


Source: Yip et al., Allergy 2019 Sep 10. doi: 10.1111/all.14041

# CSL311 for the Treatment of Airways Inflammation

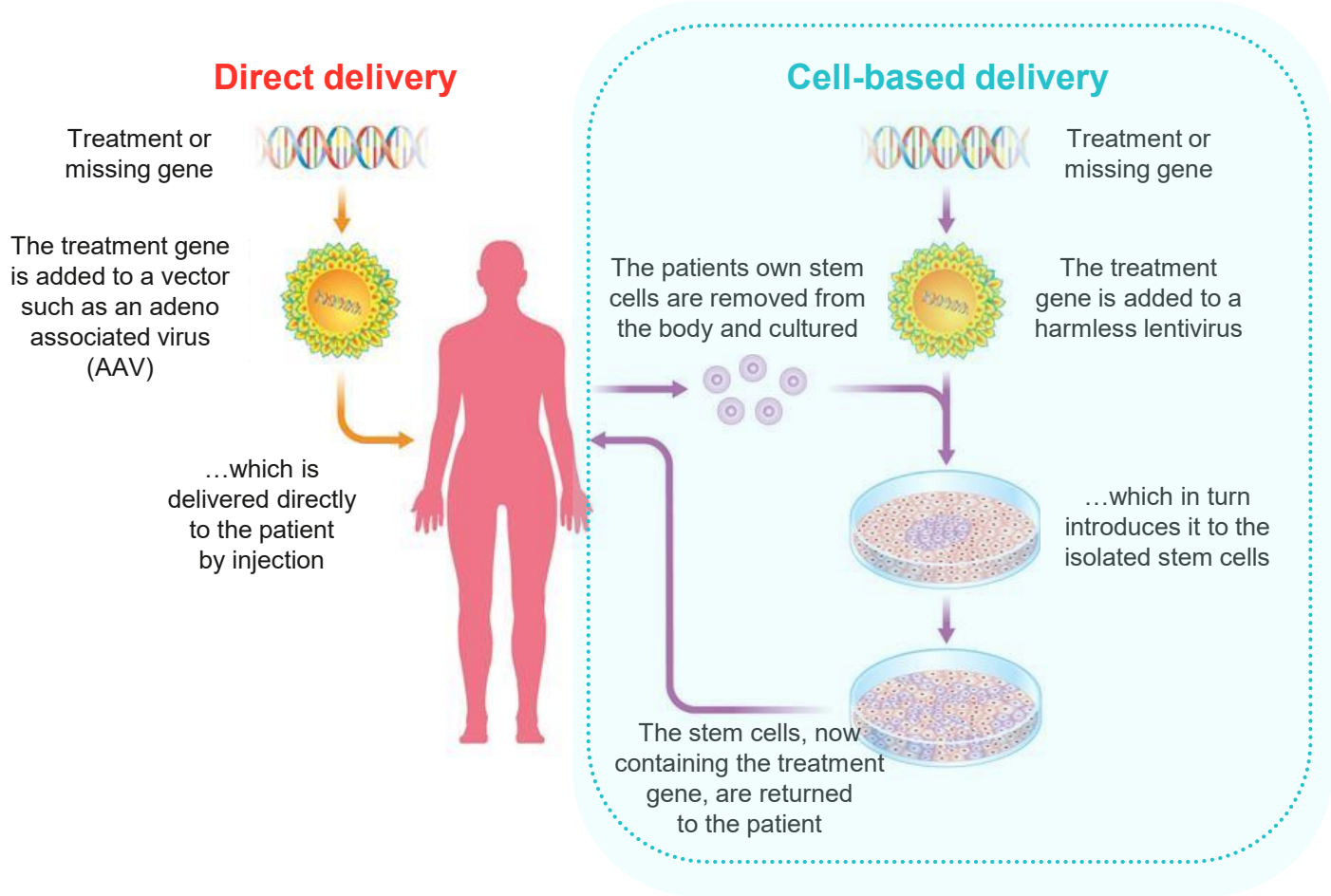
## Summary

- CSL311 is a potent antagonist of IL-3, IL-5 and GM-CSF *in vitro*
- CSL311 inhibits the activity of multiple cell types involved in inflammation
- CSL311 demonstrates efficacy in an *in vivo* translational model of airways inflammation
- GLP Toxicology program successfully completed



# CSL Gene Therapy

## In Vivo vs Ex Vivo Gene Therapy





# Cell and Gene Therapy Research and Product Development

- 2+ years post-acquisition of Calimmune
- Integration into CSL R&D complete
- First clinical program recruiting patients
- Pipeline of early stage gene therapy projects

## Expertise/Know-how Vector Design



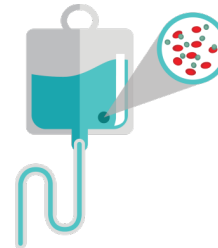
Ability to design and make extremely efficient therapeutic vectors

## *In Vivo* Selection Tool Select+™



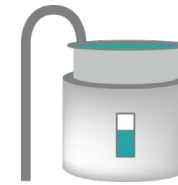
Genetic cassette to render stem cells protected against well-known drug to drive *in vivo* selection

## Cell Processing Proprietary Methods



Novel SOPs to achieve high cell yields and standardization of cell product

## Lenti Manufacturing Cytegrity™



Only large-scale, stable vector production system used clinically

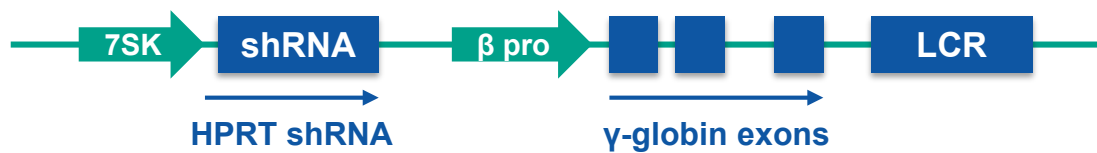
# CSL200 for the Treatment of Sickle Cell Disease (SCD)

## Sickle Cell Disease

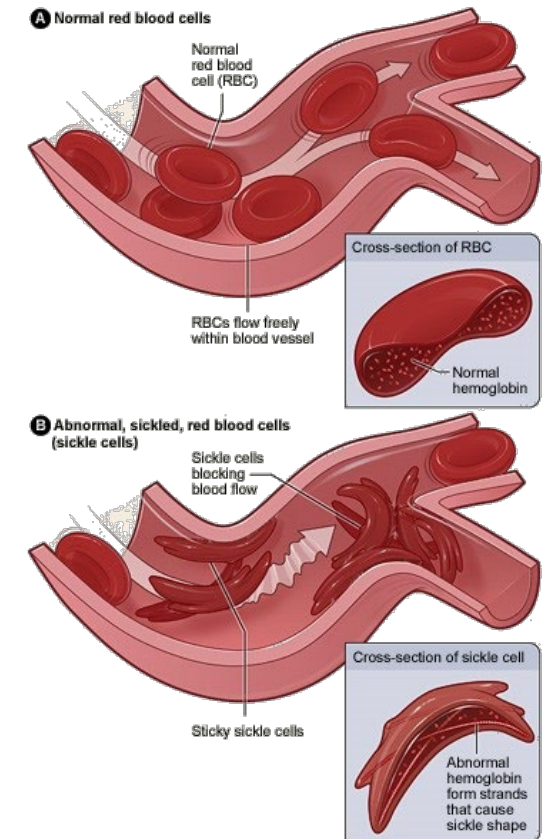
- Group of disorders caused by abnormal beta-globin gene resulting in sickled red cells
- High unmet need

## CSL200

Cytegrity™ lenti-backbone + Select+™ technology + SIN-LV  $\gamma$ -globin construct (sGbG<sup>M</sup>)



- CSL200 program aims to provide sufficient functional globin gene to prevent sickling

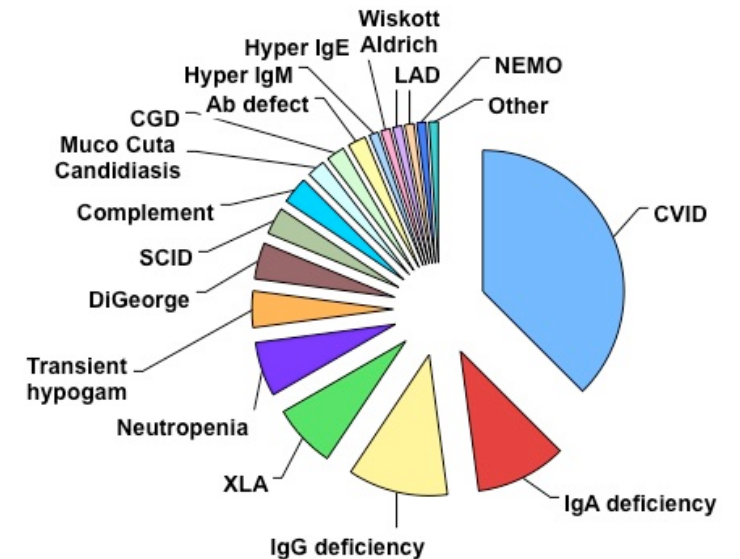


# Gene Therapy for Wiskott-Aldrich Syndrome (WAS)

- WAS is a rare X-linked PID (~ 1:100,000 live births)
  - Mutations in the gene that encodes the WAS protein (WASp)
- WAS is exclusively expressed in blood cells and plays a key role in organizing the actin cytoskeleton, signal transduction and terminal differentiation
- WAS is characterised by:
  - Recurrent infections, microthrombocytopenia and eczema
  - An increased risk of autoimmune disorders and malignancy
  - Currently treated with IVIG
- Allogeneic Hematopoietic Stem Cell transplantation (HSCT) is the only available curative treatment

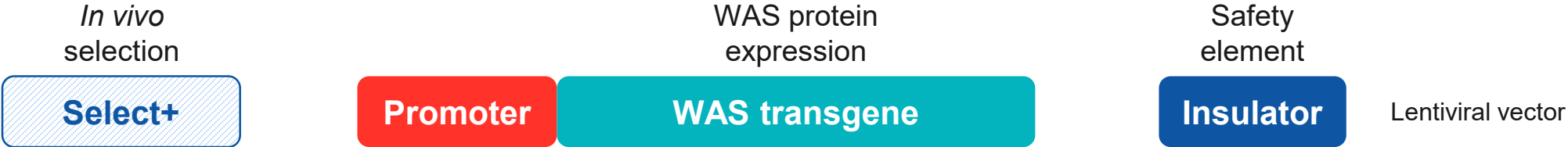
\* Source: Icahn School of Medicine at Mt Sinai

## Primary Immune Deficiencies\*





















# Gene Therapy for Wiskott-Aldrich Syndrome (WAS)




Design and generation of lentiviral candidates based on our Cytegrity stable producer cell line backbone is in progress



# Immunoglobulin Therapy

## Mechanism of Action Summary

	Pathogen Neutralisation	Reduction of Pathologic Ig	Complement Scavenging	FcγR Expression Modulation	Immune Cells Modulation	Cytokine Modulation
Ig Therapy						
IgG Fc Multimers						
FcRn Binding Agents						

 No Activity  
  Possible Activity  
  Activity

# CSL Research

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- Expanding capacity and capability across global research sites
- Continued investment in external innovation activities
- Leveraging our three strategic platforms across five therapeutic areas
- Continuing to innovate in areas of business strength
- Developing new opportunities in areas of unmet need
- Creating and progressing a sustainable portfolio of early stage opportunities
  - New gene therapy opportunities

# Clinical Development – Part 1

## Dr. Diana Lanchoney

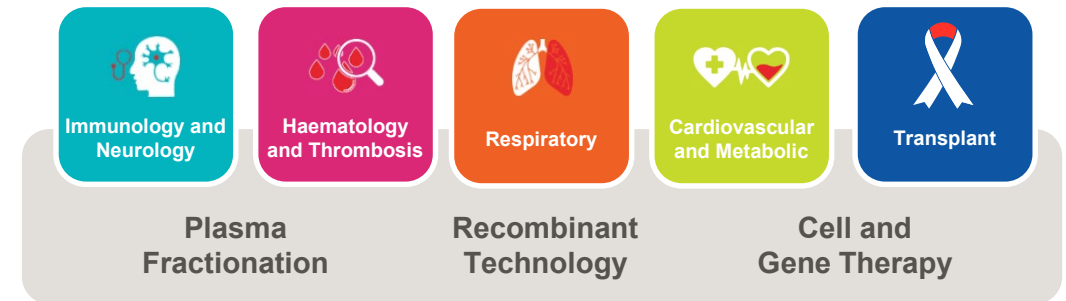
Vice President, Clinical Pharmacology and Translational  
Development  
CSL Behring



# CSL Pipeline Progressing into Multiple New Disease Areas Using All Three Product Development Platforms



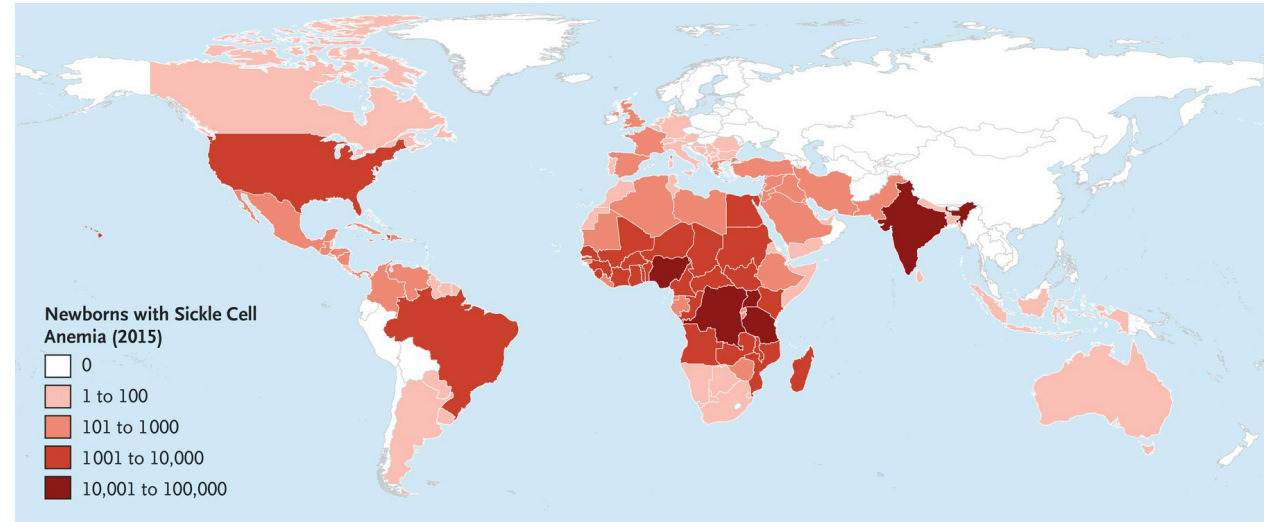
- **Sickle Cell Anemia** – CSL200 (lentiviral stem cell gene therapy), CSL889 (Hemopexin)
- **Contact Mediated Thrombosis** – Garadacimab (CSL312 Anti-Factor XIIa)
- **Respiratory Disease** – CSL311 (Anti-Beta Common)
- **Diabetic Nephropathy** – CSL346 (Anti-VEGF-B)
- **Neutrophilic Dermatoses** – CSL324 (Anti-GCSF)
- **Systemic Lupus Erythematosus** – CSL362 (Anti-IL-3Ra)
- **Scleroderma** – PRIVIGEN® and HIZENTRA®
- **Dermatomyositis** – HIZENTRA®
- **Hereditary Angioedema** – Garadacimab (Anti-Factor XIIa)





# Overview of Sickle Cell Disease (SCD)

- Missense mutation of the  $\beta$ -globin gene
- Worldwide incidence ~300,000/year (US ~155,000)
- Sickle red blood cells are fragile, prone to endothelial adhesion
- Many downstream consequences
  - Avg. life expectancy 40 - 60yrs
- Vaso-occlusive crisis (VOC): commonly leads to hospitalization

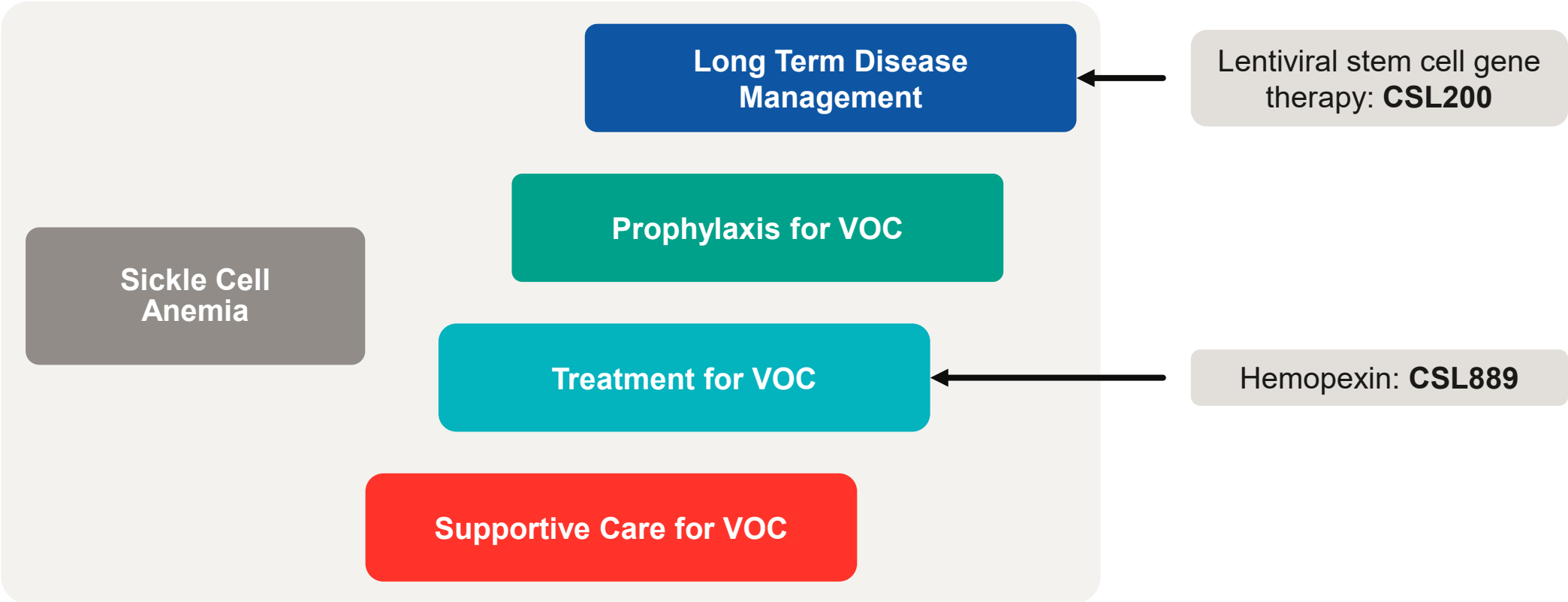


Global incidence of SSA in newborns, 2015

Source: <https://www.nejm.org/doi/full/10.1056/NEJMra1510865>

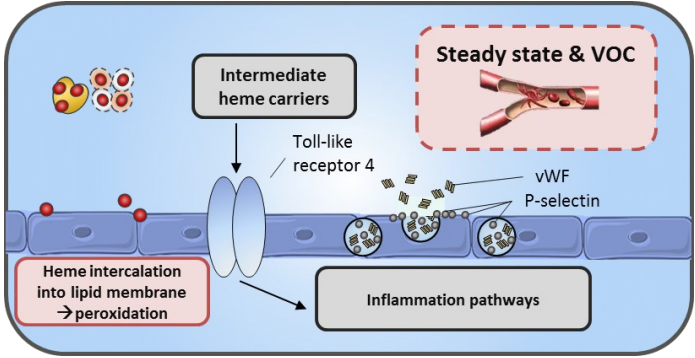
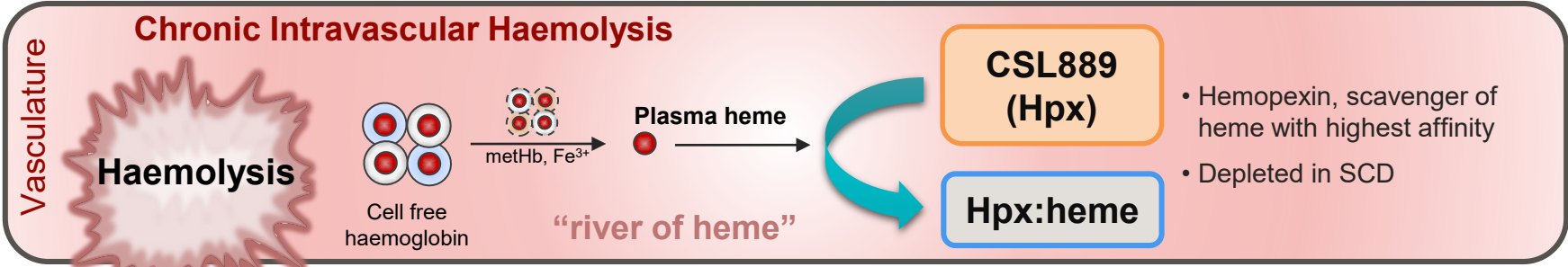
# Sickle Cell Anemia

## CSL Programs Poised to Evolve the Paradigm

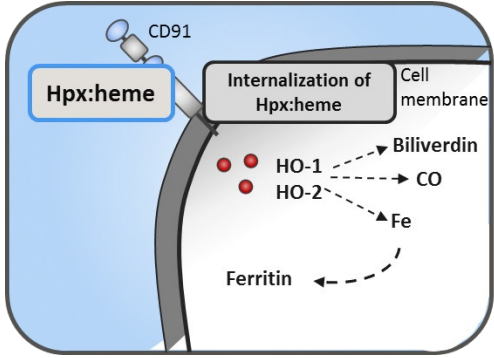


# CSL889 Hemopexin

## Addresses the Toxic Effects of Free Heme



**Endothelial Cells**

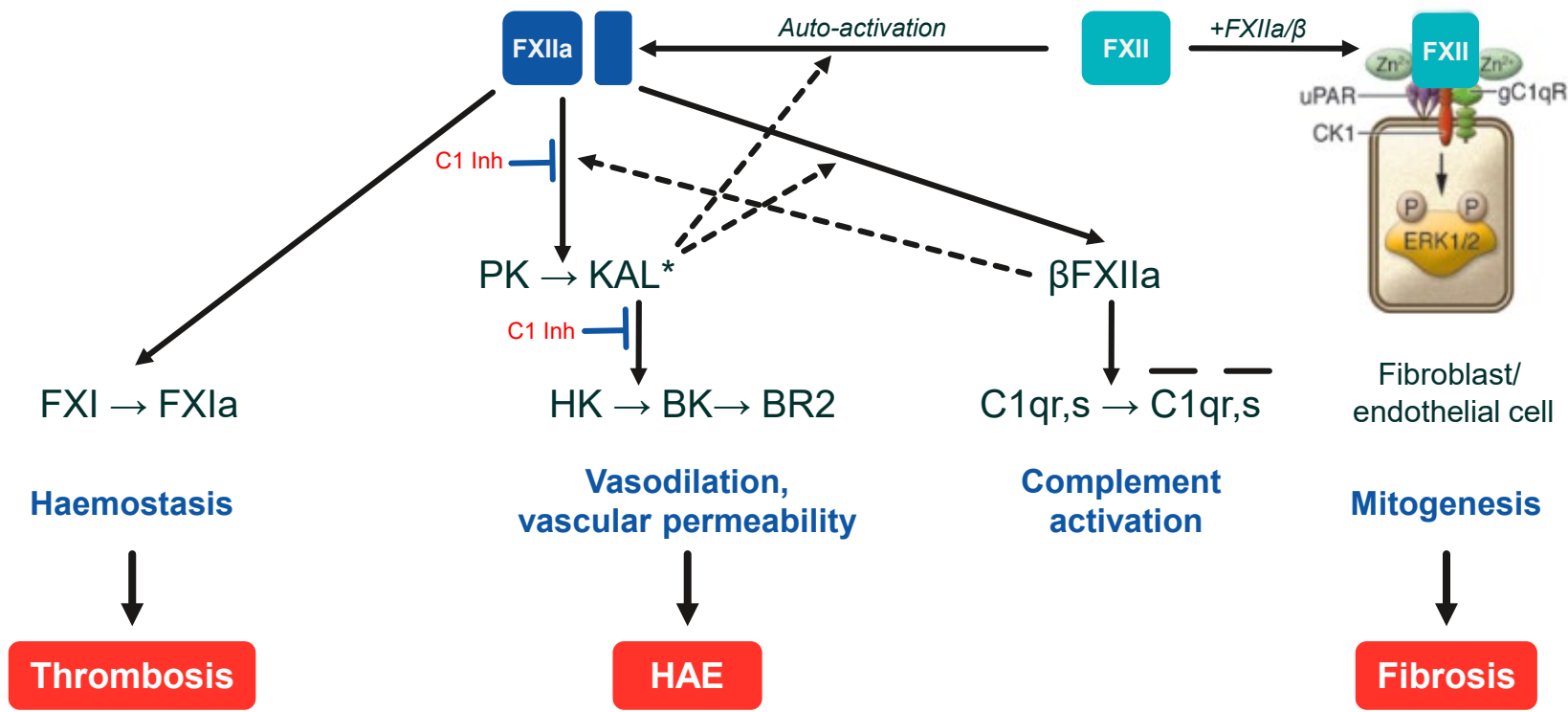


**Hepatocytes**

Clearance of free heme, and reduced inflammation

# Garadacimab (CSL312 Anti-Factor XIIa)

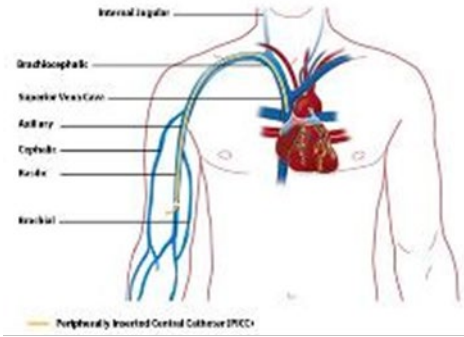
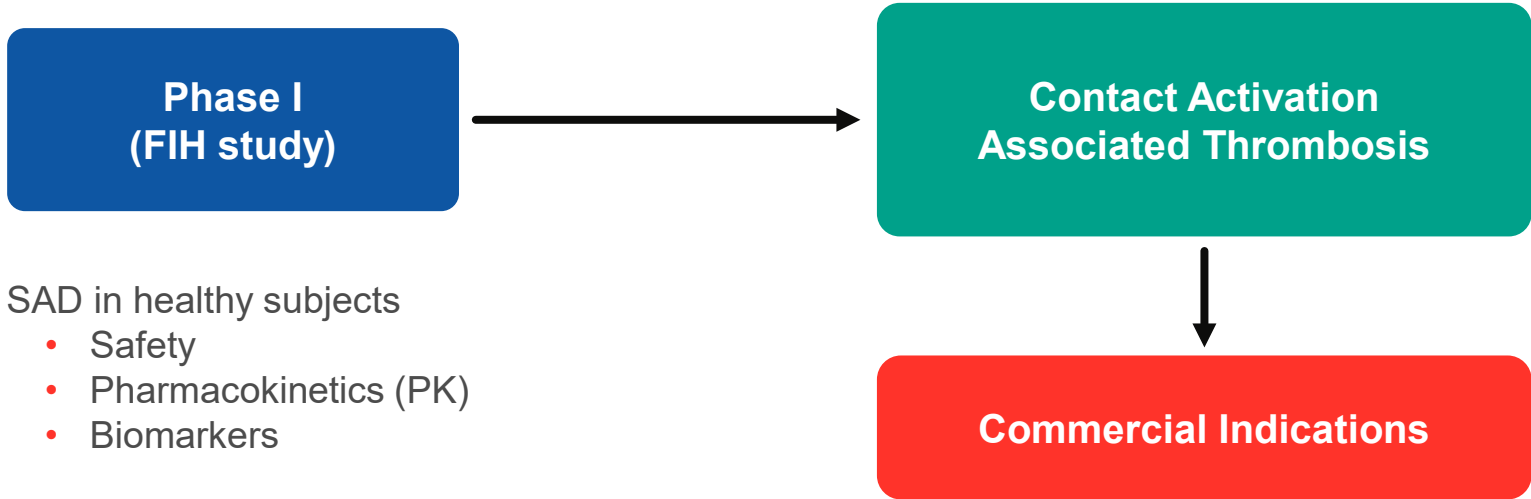
## Multiple Potential Indications



Adapted from: Schmaier, AH., J Clin Invest. 2008 Sep 2; 118(9): 3006–3009.

# Garadacimab (CSL312) Thrombosis Development Program Overview

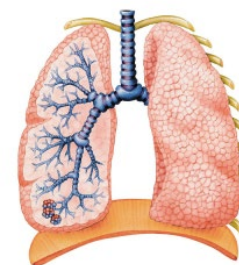
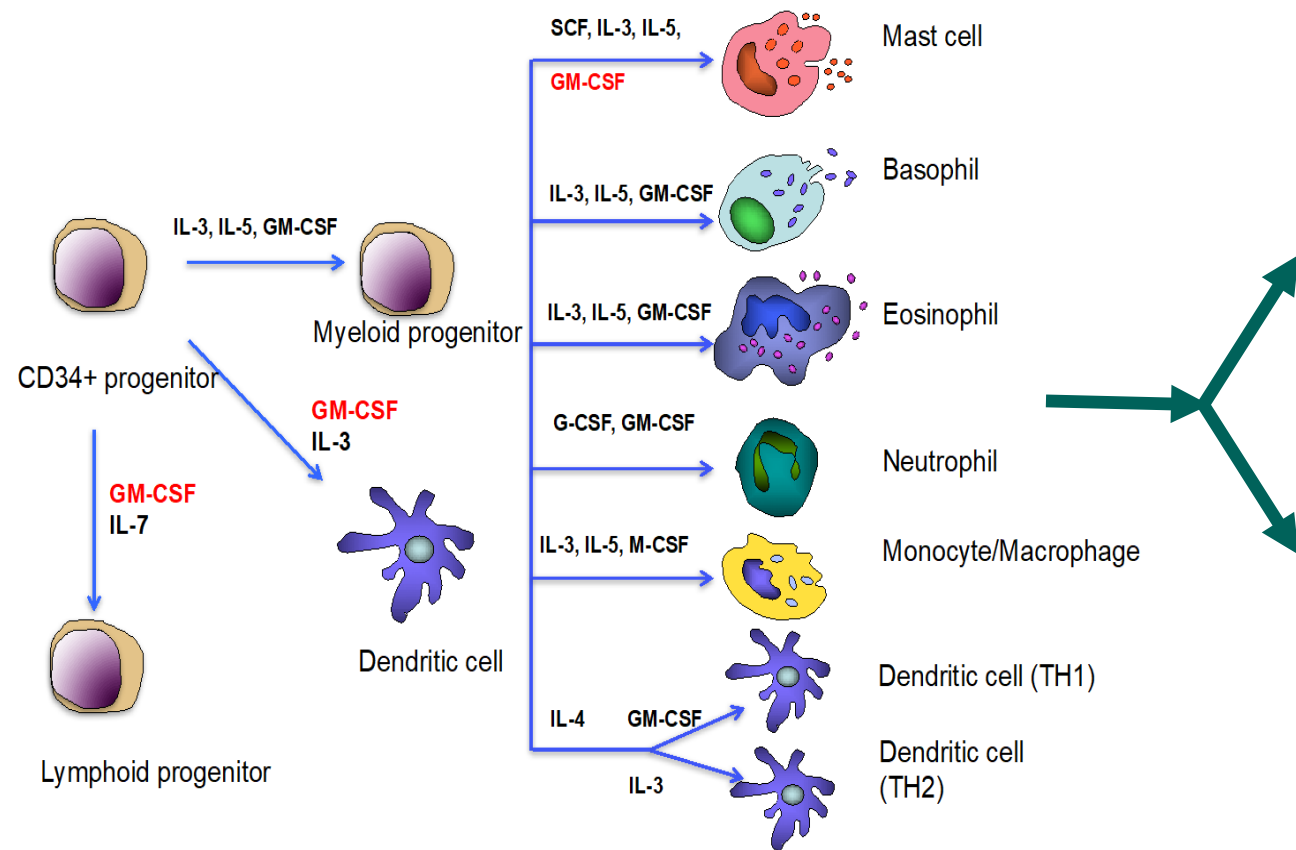
## Mechanism to Prevent Contact-Activated Thrombosis Without Bleeding Risk



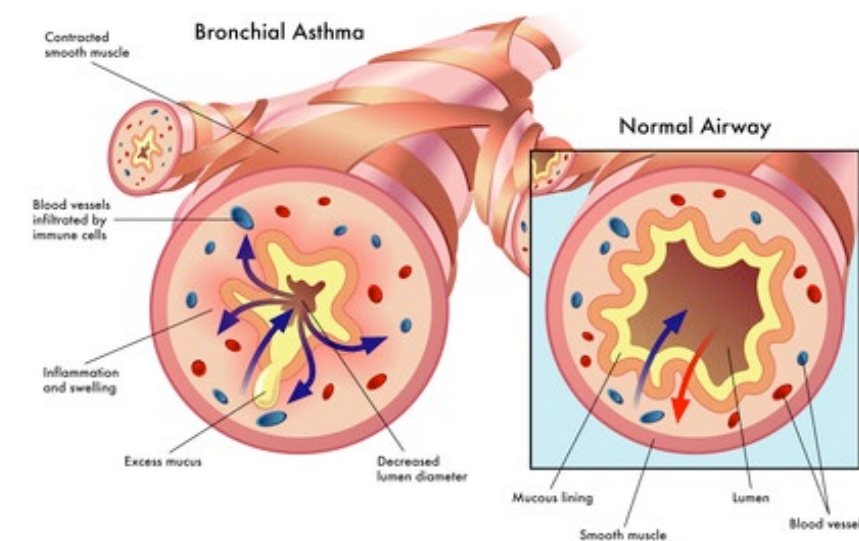
Peripherally Inserted Central Catheter (PICC) Thrombosis

# CSL311 Anti-Beta Common

## A Broad Mechanism of Action With Potential to Address the Entire Spectrum of Severe Asthma

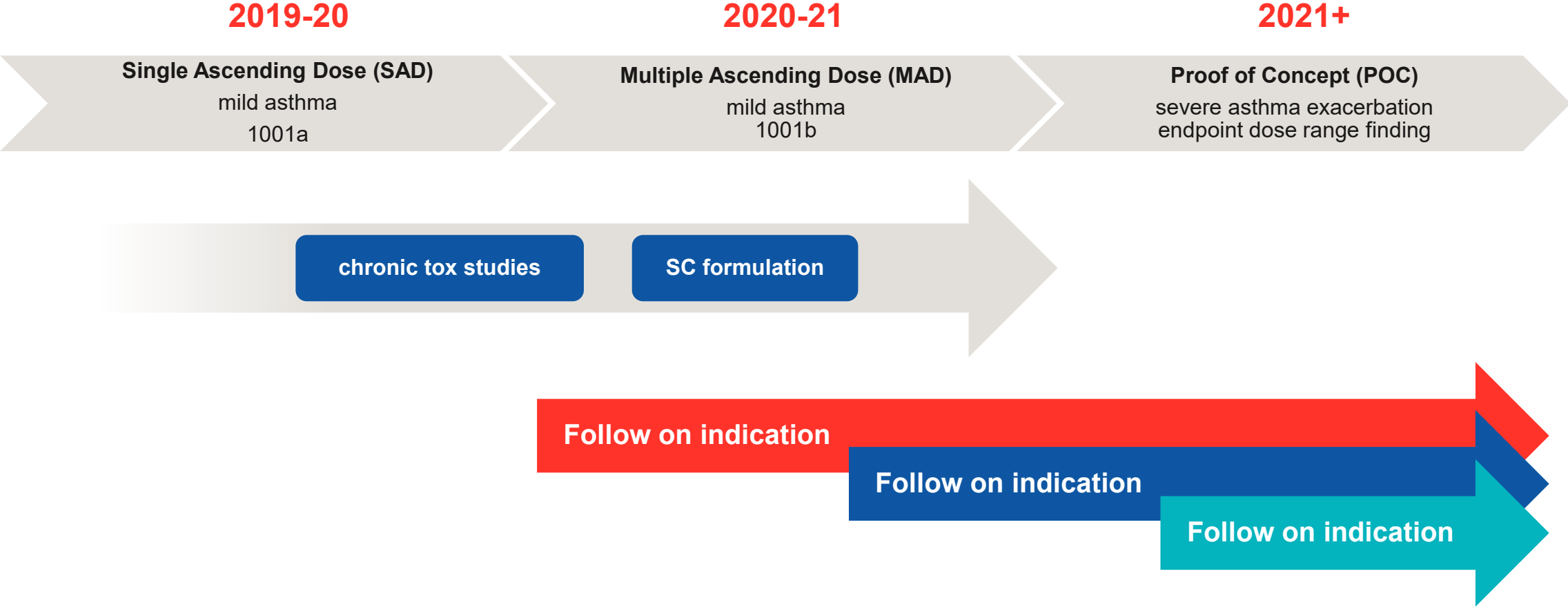


**Asthma: ~300 million globally**  
**Severe asthma: 2-10%**



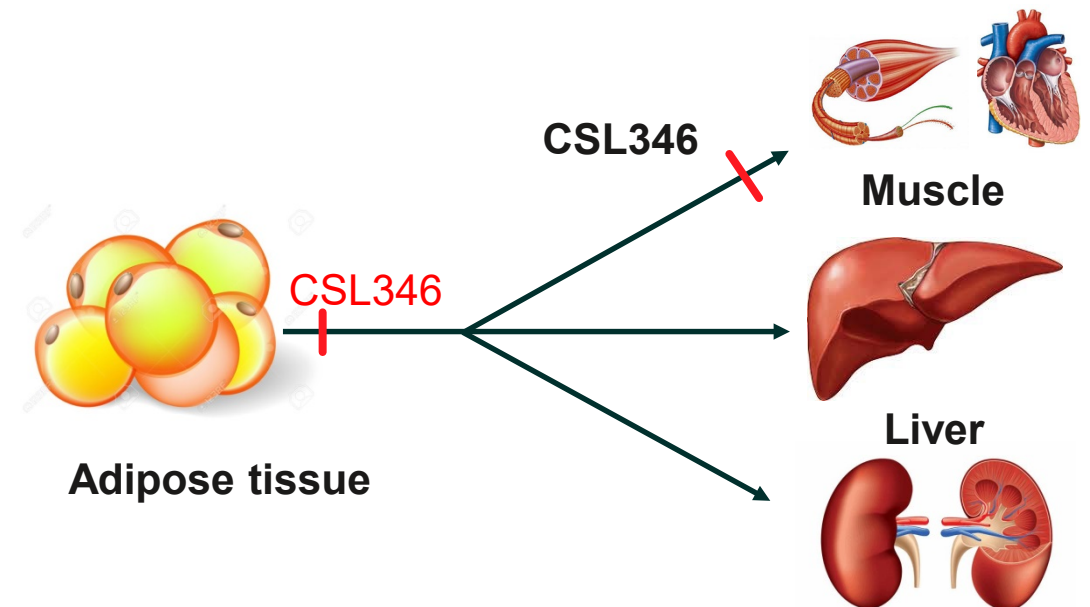
Source: <https://www.atsjournals.org/doi/pdf/10.1513/AnnalsATS.201508-514MG>

# CSL311 Phase I Clinical Strategy Informs Early POC Expansion



# CSL346 VEGF-B Antagonist

- CSL346 is a novel humanised monoclonal antibody (IgG4) that binds VEGF-B
- Strong renoprotective effects in diabetic kidney disease (DKD) animal models
- Phase II proof of concept study to start in early 2020

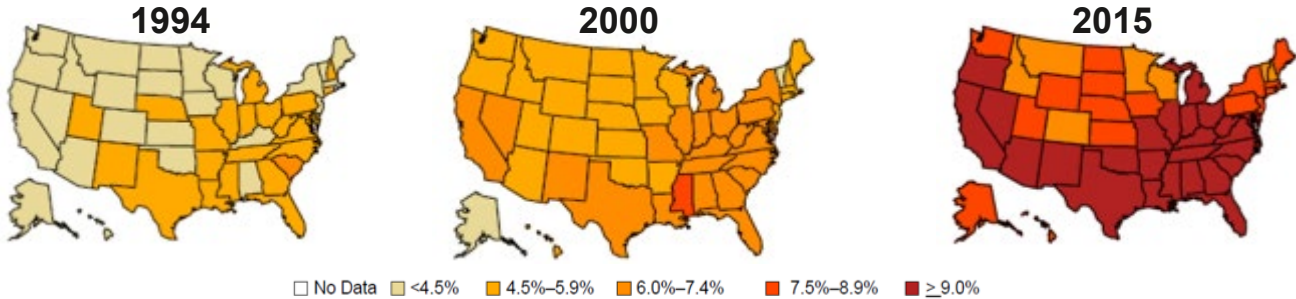


Source: <http://dx.doi.org/10.1016/j.cmet.2017.01.004>

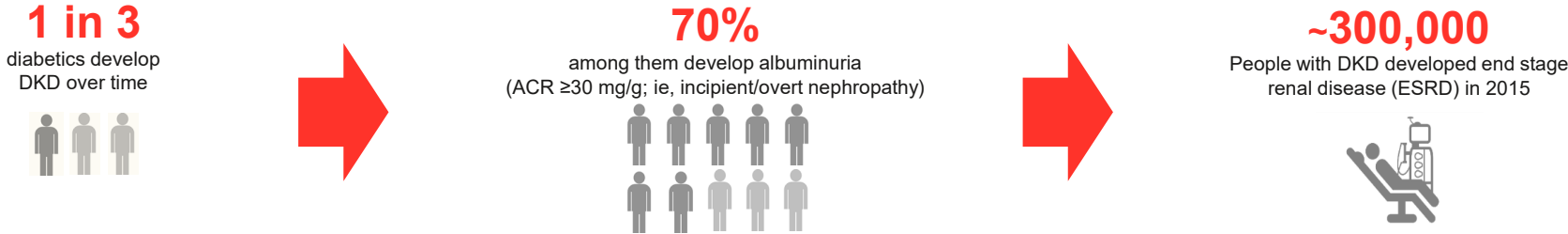


# Diabetes and Diabetic Kidney Disease

## Increasing Prevalence



## Diabetes accounts for 30-50% of all chronic kidney disease

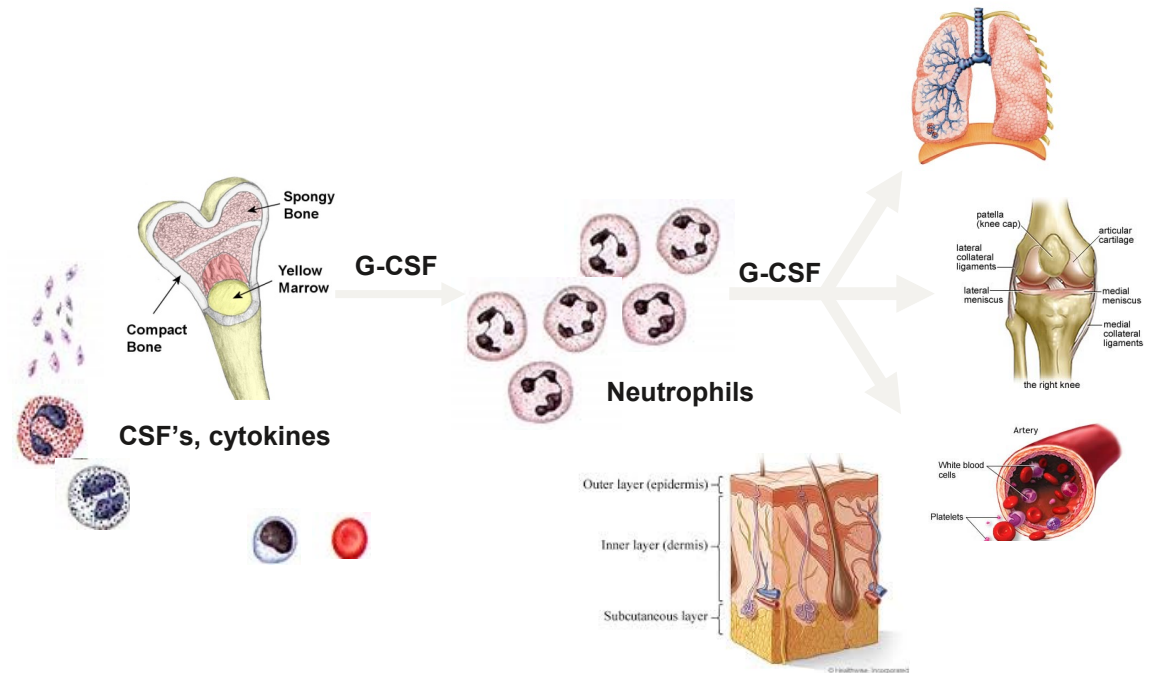


**Sources:** Map data: CDC Division of Diabetes Translation. US Diabetes Surveillance System ([www.cdc.gov/diabetes/data](http://www.cdc.gov/diabetes/data)) International Diabetes Federation 2015 Statistics; DN % - Calculated through consolidation of individual country sources. Top 7 markets: US, Japan, German, Italy, Spain, France, UK. Mayo Clinic; The National Institute of Diabetes and Digestive and Kidney Diseases. American Diabetes Association; Vecihi Batuman, Diabetic Nephropathy Workup, Medscape; International Diabetes Federation 2015 Statistics.

# CSL324 G-CSF Receptor Antagonist

## G-CSF, neutrophils and inflammatory disease

- Neutrophils are the most abundant white blood cells (WBC),  $\sim 10^9$  cells / kg body weight leave the bone marrow daily
- Excessive neutrophil production and persistence within tissues leads to chronic inflammation and tissue destruction
- G-CSF plays a key role in neutrophil production, migration, lifespan and activation
- No competitors known to pursue G-CSF inhibition: First-in-Class



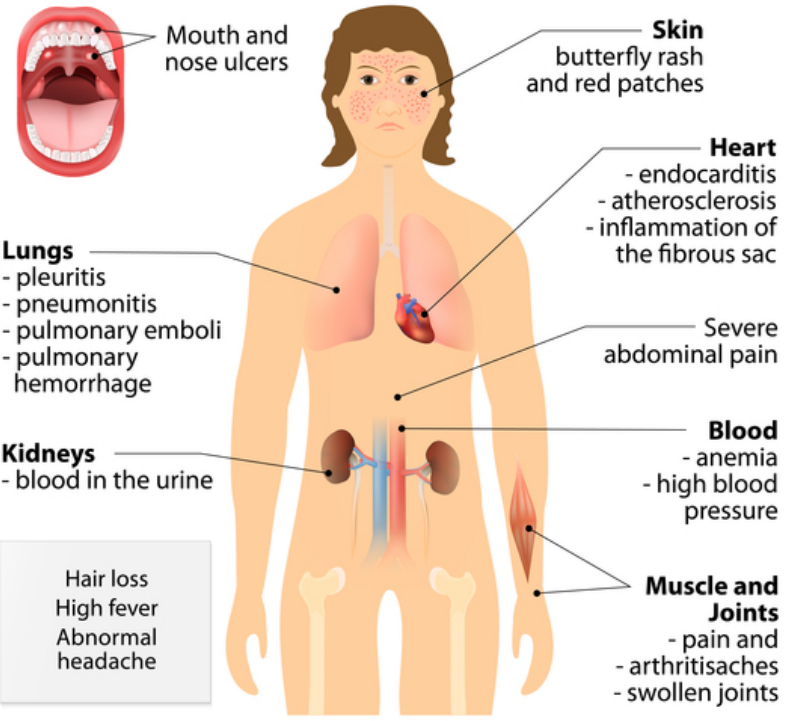
# CSL324 G-CSF Receptor Antagonist Begins Phase Ib Study in Neutrophilic Dermatoses

- Hidradenitis Suppurativa (HS) and Other Neutrophilic Dermatoses (ND)
  - Hidradenitis Suppurativa – 1% prevalence
    - A disease of hair follicles, immune dysregulation
    - Chronic inflammation, discharge, scarring
    - Growing in prevalence, limited treatments
    - High impact on quality of life
  - Phase I FIH trial complete
  - Initiation of Phase Ib in HS / ND patients
  - Safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and response



Source: <https://rd.springer.com/article/10.1007/s13671-013-0064-8>

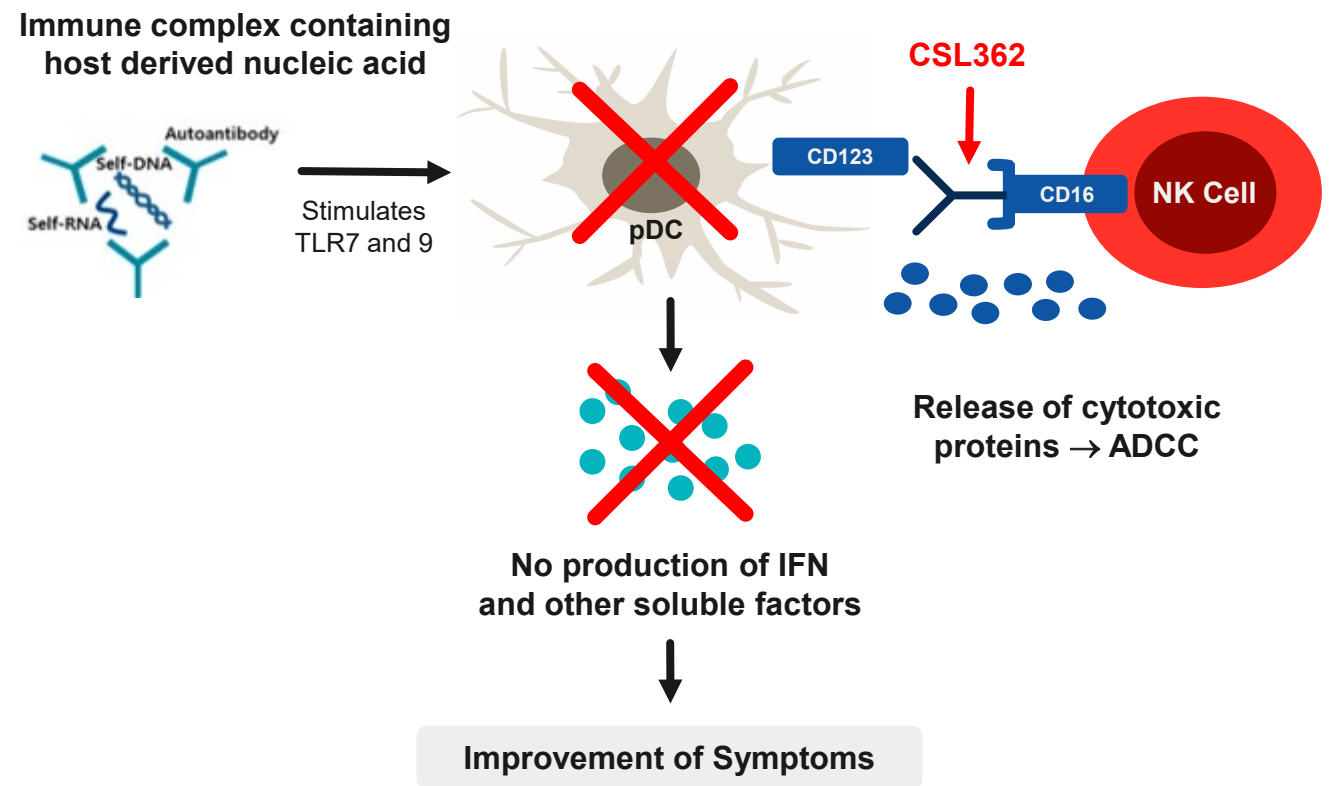
# Systemic Lupus Erythematosus (SLE)



<b>Disease Features</b>	<ul style="list-style-type: none"> <li>• Characterised by immunologic abnormalities, complex pathophysiology</li> <li>• Heterogeneous disease</li> </ul>
<b>Symptoms Diagnosis</b>	<ul style="list-style-type: none"> <li>• Nearly every organ system may be affected</li> <li>• Diagnosis based on clinical symptoms and laboratory testing</li> </ul>
<b>Risk Factors</b>	<ul style="list-style-type: none"> <li>• Women in childbearing years are most common</li> <li>• Prevalence is higher in non-Caucasian populations</li> </ul>
<b>Prognosis</b>	<ul style="list-style-type: none"> <li>• Survival rate is ~90% at 10 years, driven by organ damage</li> <li>• Quality of life may be significantly impacted</li> </ul>

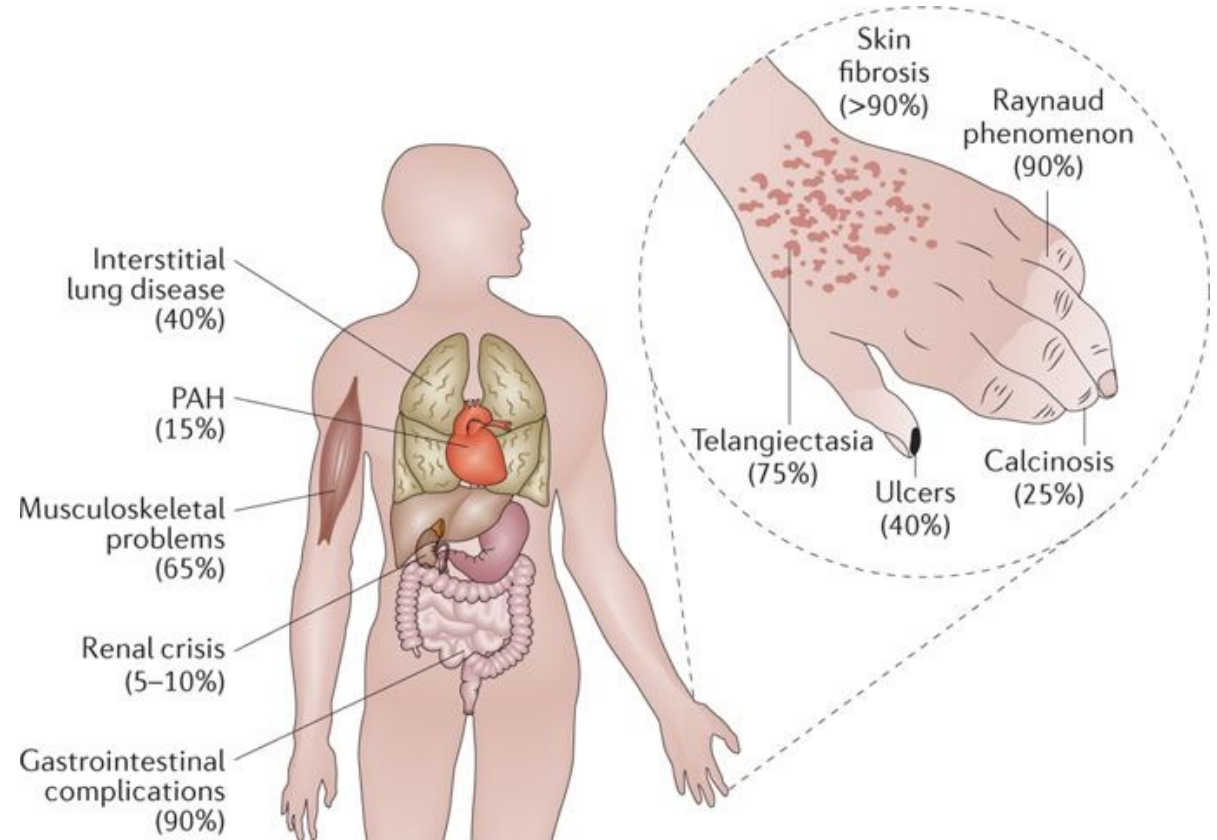
# Strong Rationale for CSL362 Anti-IL-3Ra (CD123) in SLE

- Type 1 IFNs known to play a pivotal role in pathogenesis of SLE
- pDCs are the major producer of Type 1 IFNs
- CSL362 *ex vivo*
  - pDC depletion
  - Reduced interferon (IFN) gene signature
  - Basophil depletion
- Phase Ib in healthy volunteers and SLE patients to start in 1H2020



# Systemic Sclerosis (SSc)

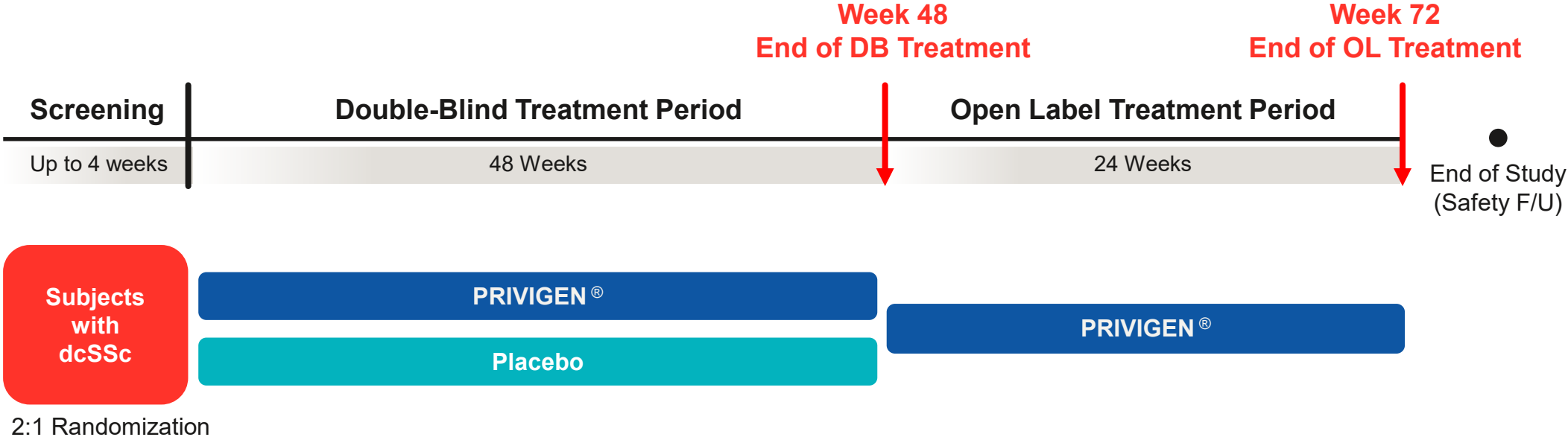
- Most life-threatening rheumatic disease: 10-year cumulative survival is 62.5%
- Limited approved disease modifying agents
- Most treatments aimed at improving symptoms and managing complications
- Prevalence 7 - 43/100,000 (US/EU)



Source: *Nature Reviews Disease Primers* volume 1, Article number: 15002 (2015) Clin Epidemiol. 2019; 11: 257-273

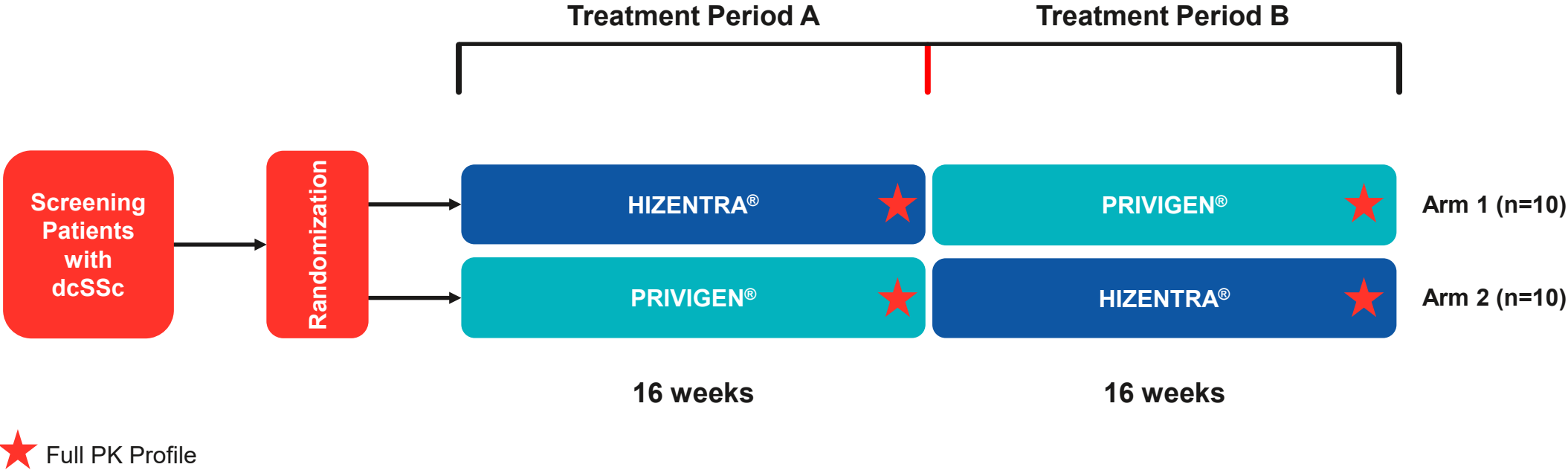
# IMPRESS

## PRIVIGEN® (IVIG) PhII, Efficacy and Safety Study



# SURPASS

## HIZENTRA® (SCIG) PhII, Safety and Bioavailability Study in Systemic Sclerosis





# Dermatomyositis (DM)

- Rare (2 - 9/100,000), serious, and life-threatening
  - 5-year mortality rate 10-30%
- Rash, muscle weakness, dysphagia, and systemic manifestations (heart, lung, gut, cancer) and specific autoantibodies
- Female predominant, typical onset in adults late 40's – 60's, in children 5 – 15yrs



Heliotrope Rash



Gottron's Papules

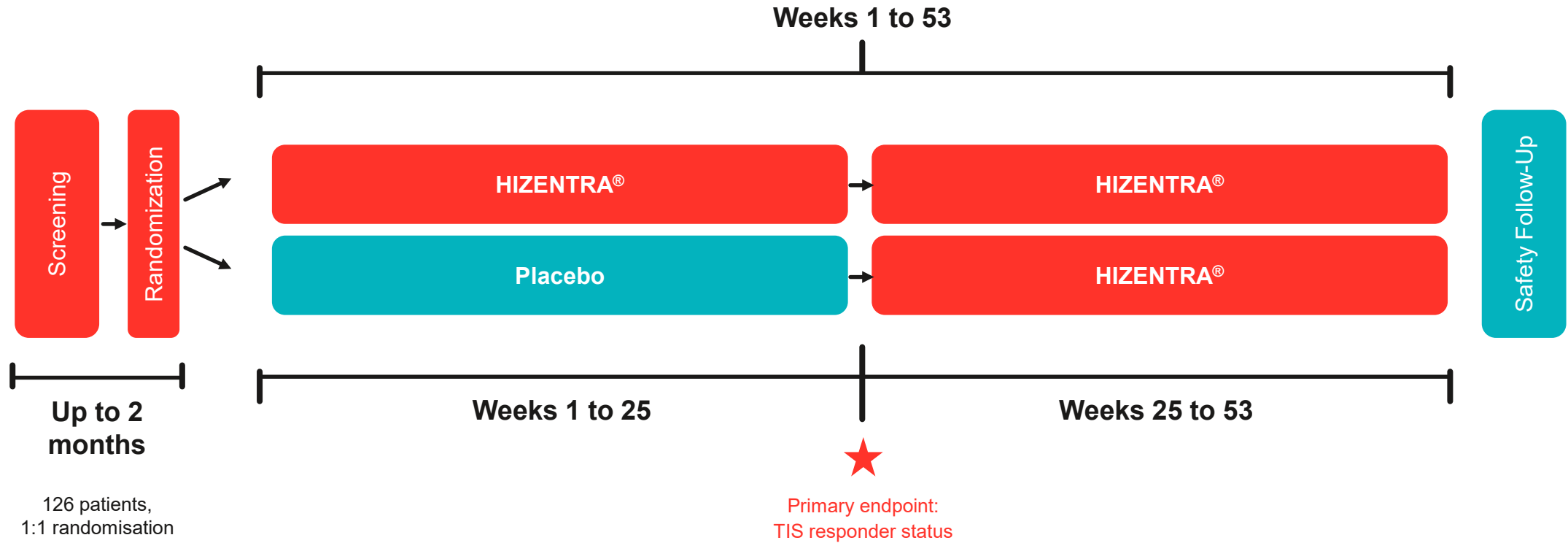


Skin Signs of DM

Sources: <https://www.ncbi.nlm.nih.gov/books/NBK532860/>; (2009) Epidemiology of Dermatomyositis. In: Dermatomyositis. Springer, Berlin, Heidelberg

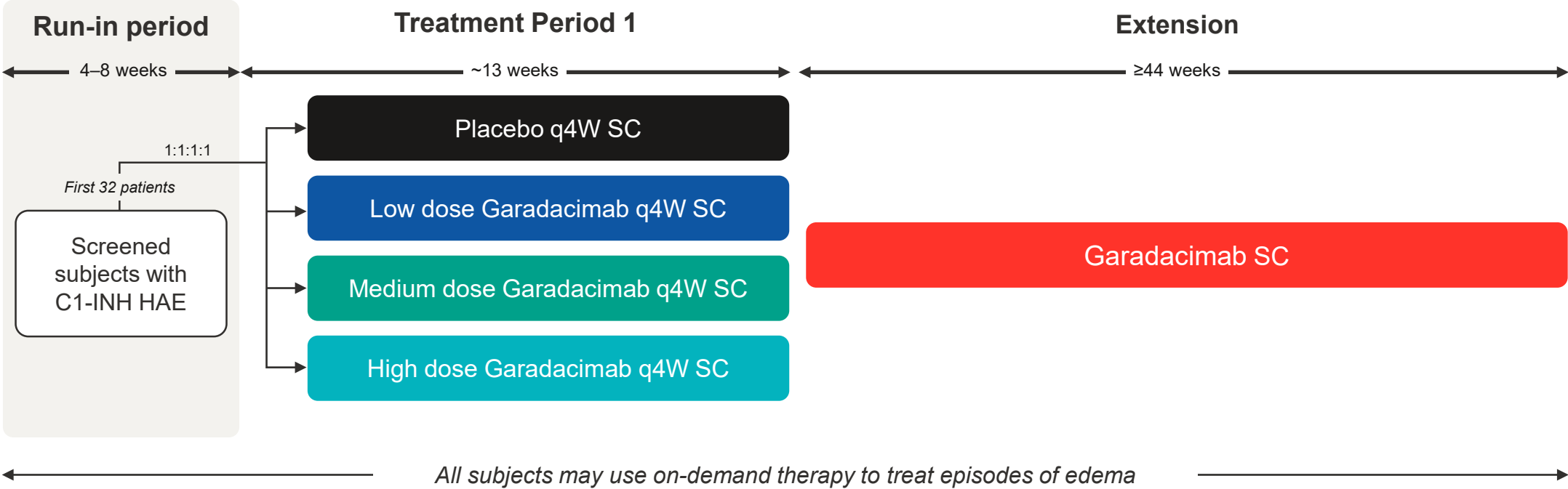
# RECLAIM

## HIZENTRA<sup>®</sup> DM Treatment Study Design



# Garadacimab Phase II Hereditary Angioedema (HAE) Study

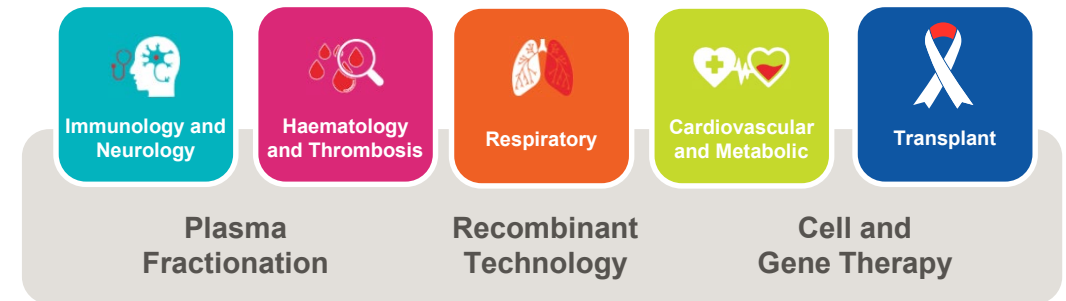
## Completed Double Blind Period



# CSL Pipeline Progressing into Multiple New Disease Areas Using All Three Product Development Platforms



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- **Dermatomyositis** – HIZENTRA®
- **Hereditary Angioedema** – CSL312 Garadacimab (Anti-Factor XIIIa)



# Commercial – Part 1

## Mr. Bill Campbell

Executive Vice President and Chief Commercial Officer  
CSL Behring



# Global Commercial Operations at a Glance



~1,800

Commercial employees



35 Affiliate  
Offices

Conducting business in **100+ Countries**



US\$7.2

Billion in annual revenue



4 Commercial **Regions**



5 Therapeutic **Areas**

# FY'19 Highlights



Strong Business Performance



Balanced Regional Growth:  
9% – 17%



Executing to Plan on New Launches



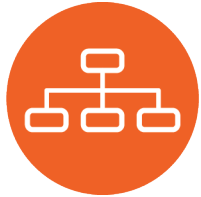
Ig Growth well Above Market



Expanding Market Presence through New Affiliates










China GSP License Establishment



Implemented TA Structure / Model

# Strong Demand Across the Portfolio

 <p><b>privigen</b><sup>®</sup> Immune Globulin Intravenous (Human), 10% Liquid</p>	 <p><b>Hizentra</b><sup>®</sup> Immune Globulin Subcutaneous (Human) 20% Liquid</p>	<p><b>Ig</b></p>	<ul style="list-style-type: none"> <li>• Strong underlying market growth</li> <li>• Disciplined approach to market expansion</li> <li>• Growth driven by volume and mix improvements</li> </ul>
 <p><b>IDELVION</b><sup>®</sup> Coagulation Factor IX (Recombinant), Albumin Fusion Protein</p>	 <p><b>AFSTYLA</b><sup>®</sup> Antihemophilic Factor (Recombinant), Single Chain</p>	<p><b>Coagulation</b></p>	<ul style="list-style-type: none"> <li>• Market leadership with IDELVION<sup>®</sup> in key markets</li> <li>• Additional launch opportunities for AFSTYLA<sup>®</sup> / IDELVION<sup>®</sup></li> <li>• Life-cycle expansion (21-day dosing)</li> </ul>
 <p><b>HAEGARDA</b><sup>®</sup> C1 Esterase Inhibitor Subcutaneous (Human)</p>	 <p><b>Kcentra</b><sup>®</sup> Prothrombin Complex Concentrate (Human)</p>	<p><b>Specialty</b></p>	<ul style="list-style-type: none"> <li>• New launches with HAEGARDA<sup>®</sup></li> <li>• Continued growth of KCENTRA<sup>®</sup> in the US</li> </ul>
<p><b>AlbuRx</b><sup>®</sup></p>	 <p><b>Albuminar</b><sup>®</sup> Albumin (Human) USP, 5%/25%</p>	<p><b>Albumin</b></p>	<ul style="list-style-type: none"> <li>• Disciplined approach in China</li> <li>• Volume growth in all regions</li> </ul>



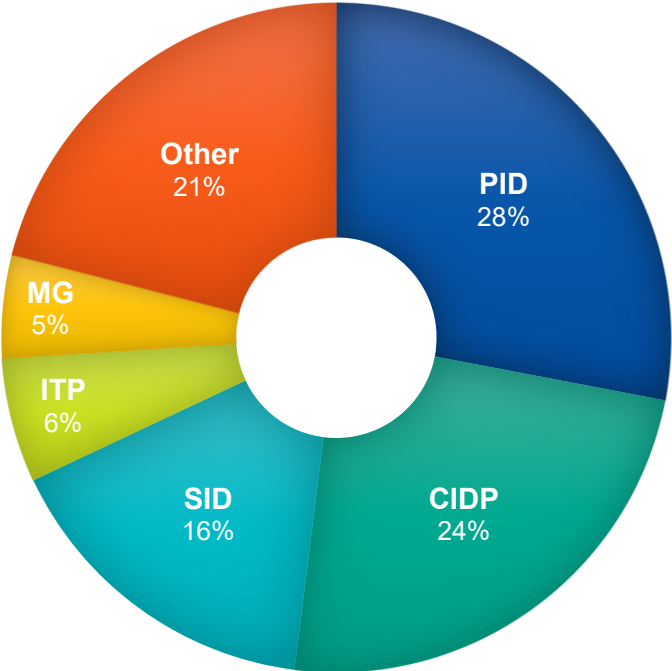
# Immunoglobulin Market

## Market Dynamics

- Increasing awareness and diagnosis
- Growth in PID and CIDP
- Expanding usage for SID
- Potential new indications
- Continued market supply tightness

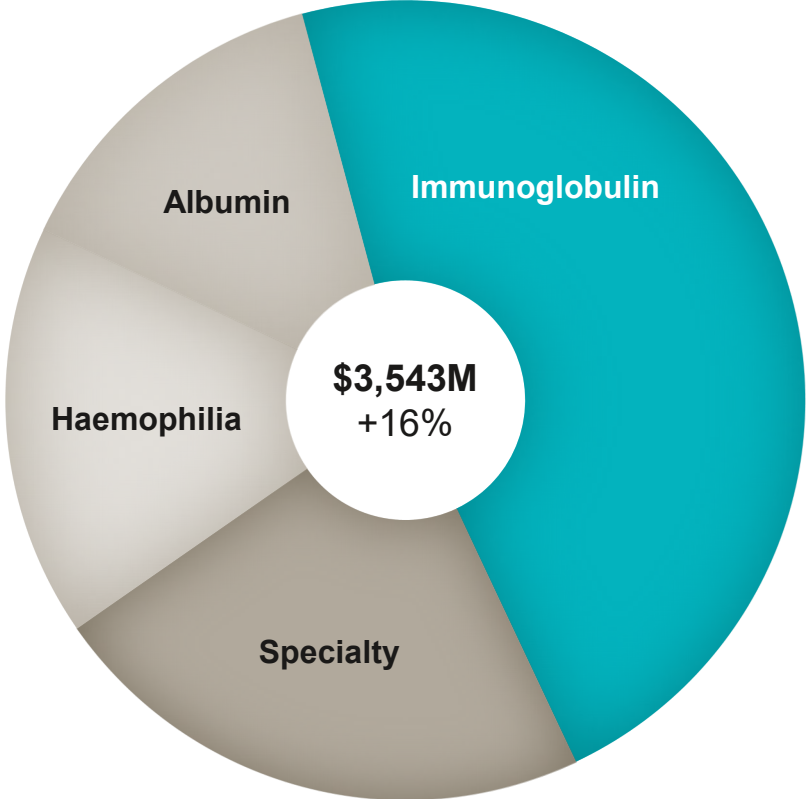
Source: Data on file

## Global IG Volume by Indication 8% Growth



## Positioned for Continued Growth

- Market Leading Products
- Substantial volume and share growth
- Balanced growth across all regions
- IV and SC for CIDP
- History of Innovation



Source: Data on file  
M = US\$ millions

### #1 Prescribed IVIG Worldwide

Proven effective and well tolerated in **12+ years**

Used in **>100,000 patients** with chronic disease in the last year

Approved for use in multiple indications

**Indications:**

**EU:** PID, SID, ITP, GBS, KD, CIDP, MMN

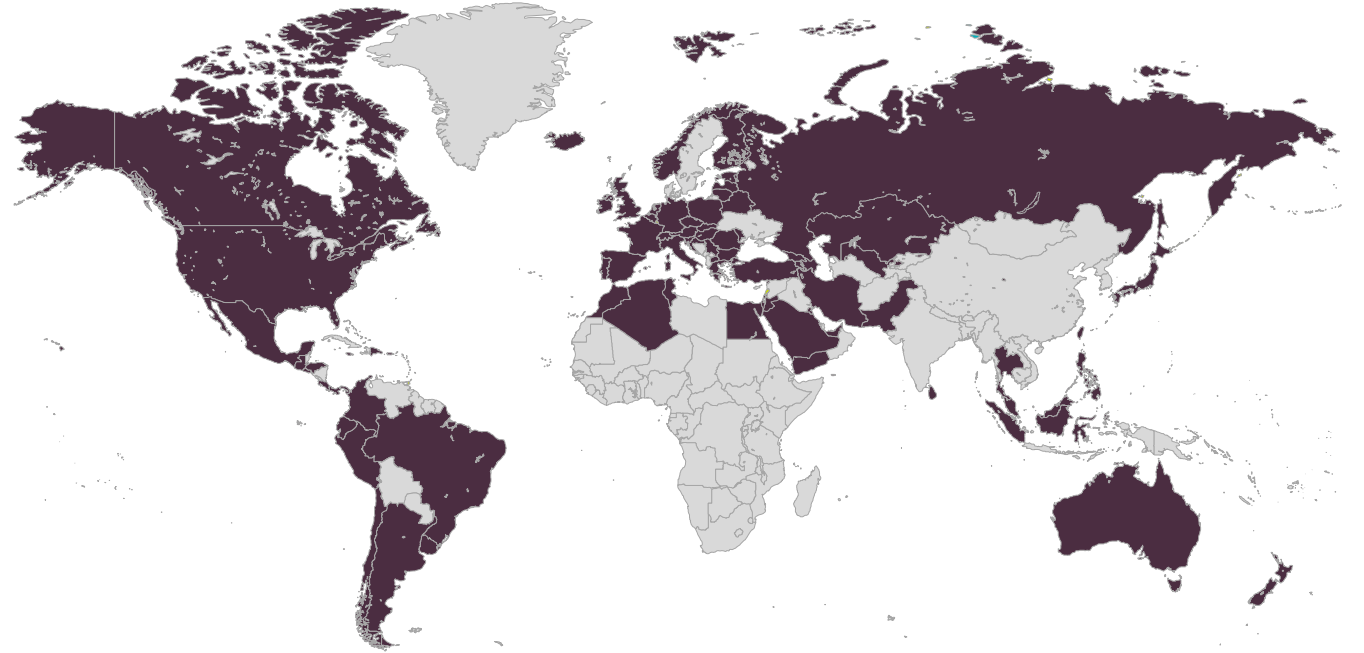
**US:** PID, ITP, CIDP

**CA:** PID, SID, ITP, CIDP

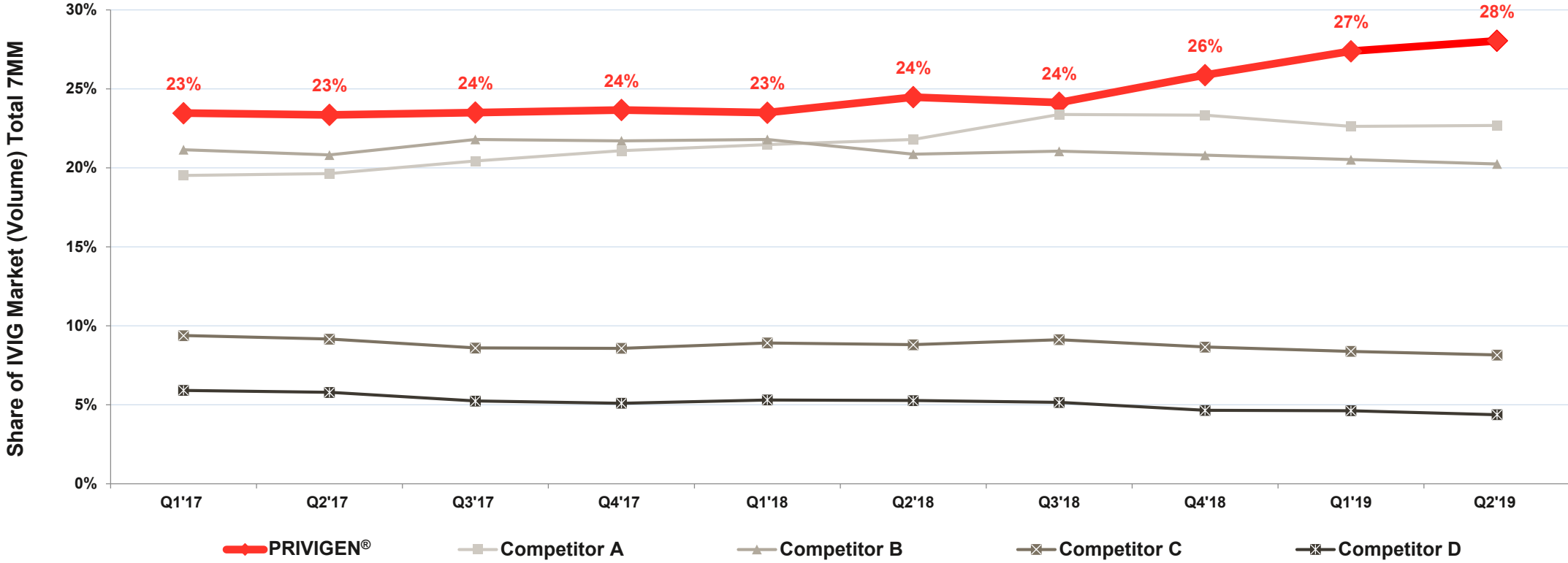
**JP:** CIDP

**AUS:** PID, SID, ITP, GBS, CDP, MMN, MG, Lambert-Eaton Myasthenic Syndrome (LEMS), Stiff Person Syndrome (SPS)

Source: Data on file



# PRIVIGEN® Performance Through Q2'19



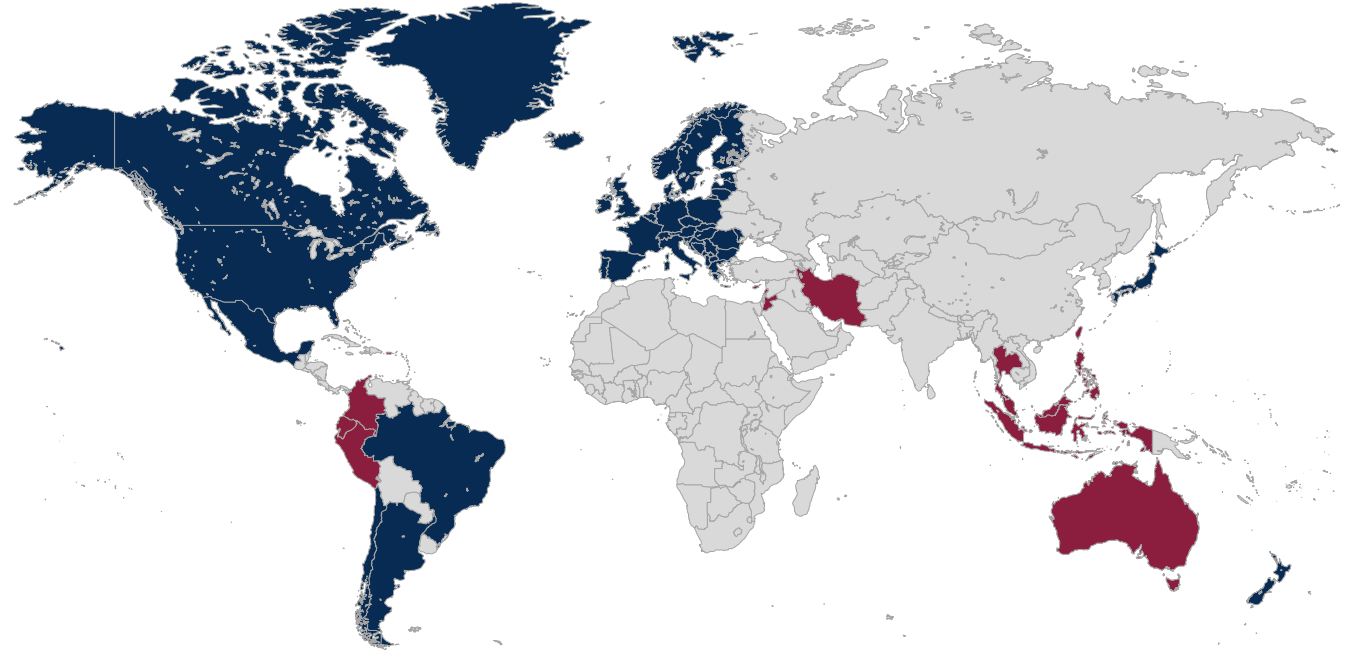
Source: Data on file

### Innovator, Market Leader, Most Prescribed SCIG Worldwide

Proven efficacy and tolerability since **2010**

**100,000** patient-years of experience

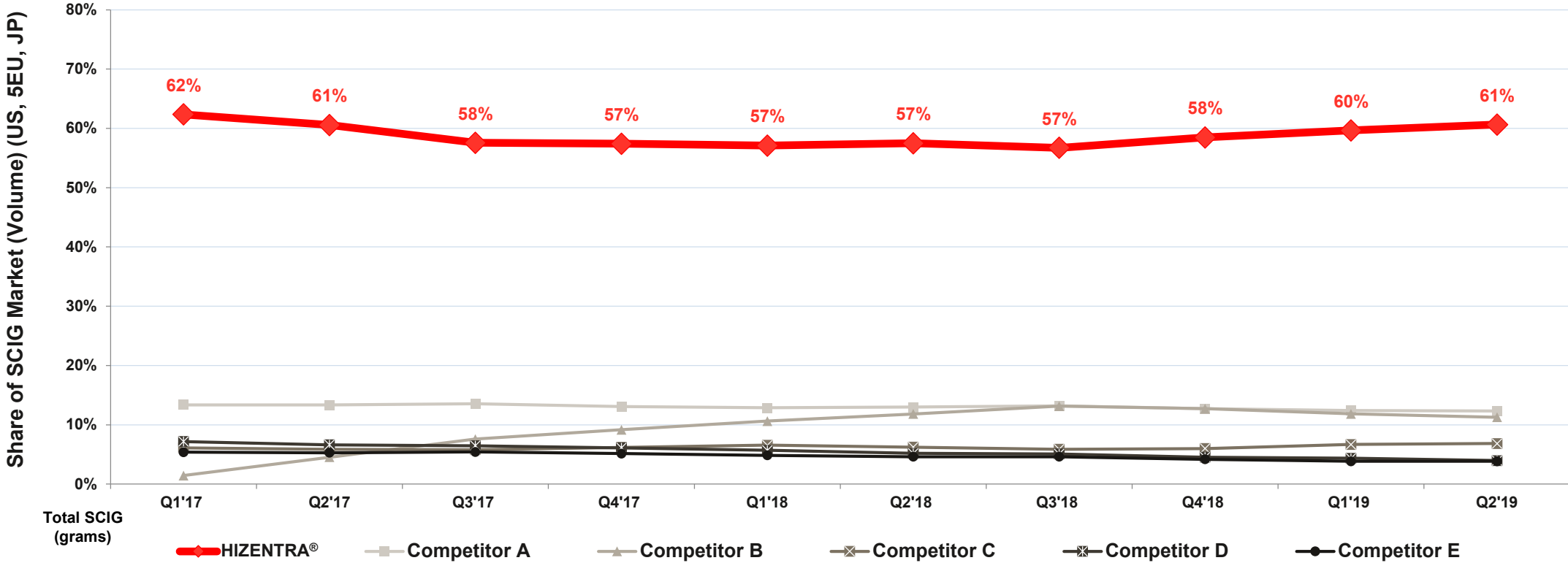
More than **6,000,000** exposures worldwide\*



Source: Data on file

\*Hizentra® also has SID indication in most countries outside of the US.

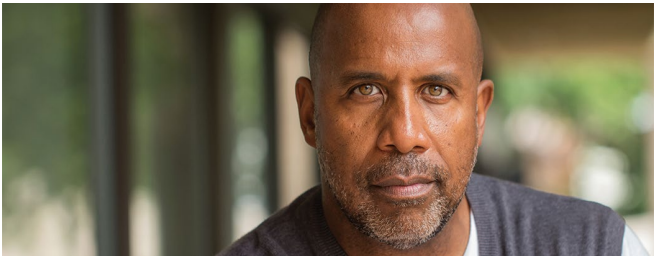
# HIZENTRA® Undisputed Market Leader in SCIG



Source: Data on file



# HIZENTRA® Addresses Unmet Needs in CIDP



Experience IV-related systemic adverse reactions

5x as many patients said they felt fewer side effects with HIZENTRA®



Seek the flexibility, freedom, and control of self-infusing

8x as many patients said HIZENTRA® offers more freedom than IVIG

Approved March '18 US & EU  
Approved March '19 Japan

Interest & Awareness Remains High

Market Share Growth With Both Privigen & Hizentra

Orphan Exclusivity Granted for Hizentra CIDP



Have venous access issues

HIZENTRA® does not require venous access

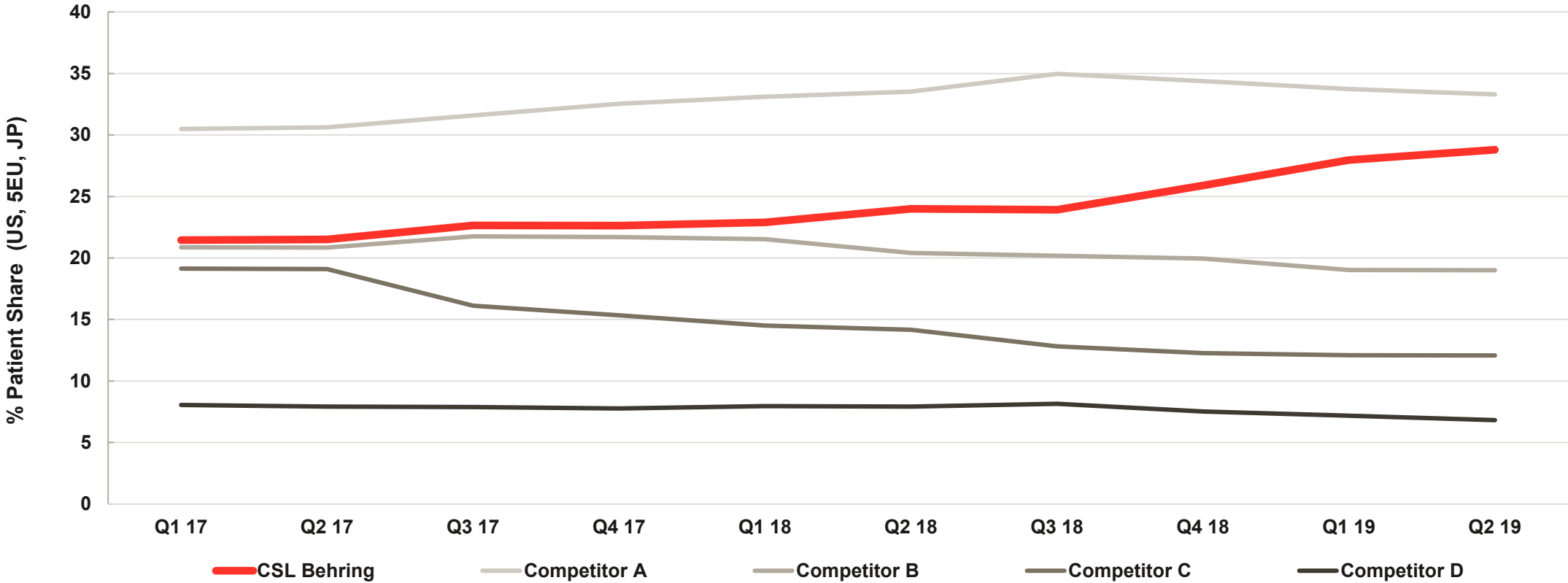


Require more frequent infusions to manage their disease

HIZENTRA® provides steady state Ig levels for continuous control

Source: Data represents patients reporting a preference between IVIG in the pre-randomised phase and HIZENTRA® in the randomised phase of the phase III study of subcutaneous immunoglobulin for the treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) – the PATH study.

# CSL Behring on Track to Become Market Leader in CIDP



Source: Data on file





# Market Leadership in Ig Therapy

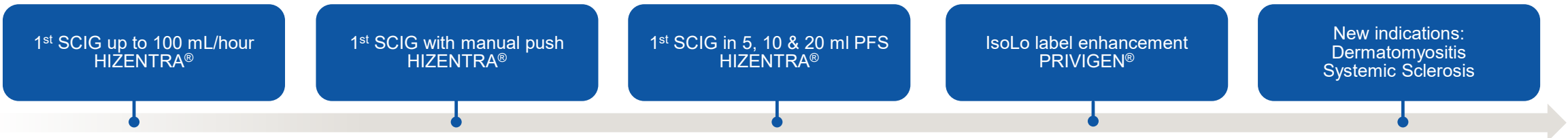
## Past



## Present



## Future



# Panel Q&A Session



# Break – 15 minutes



# Commercial – Part 2

## Mr. Bill Campbell

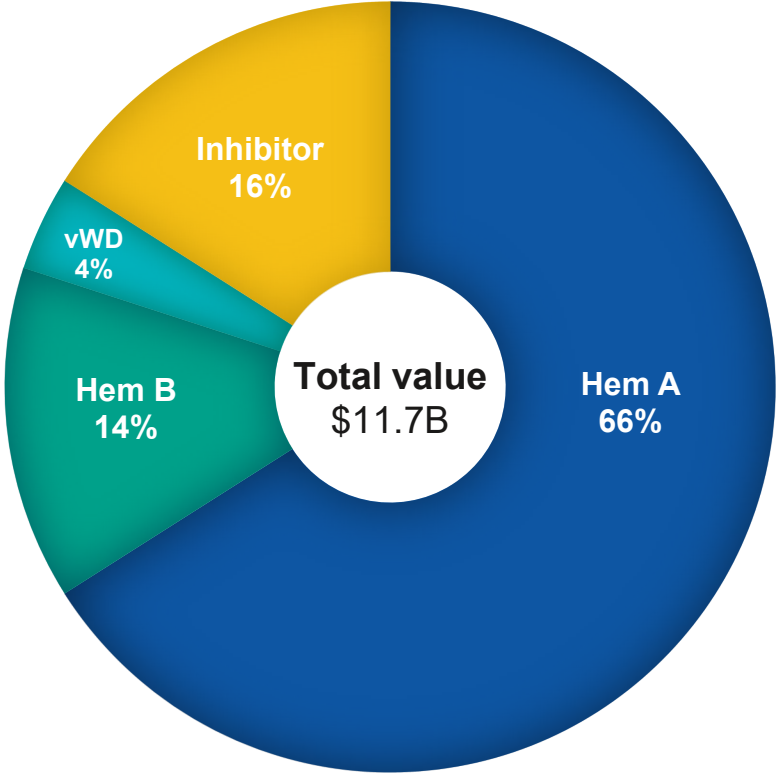
Executive Vice President and Chief Commercial Officer  
CSL Behring



# Haemophilia Market

## Market Dynamics

- New therapies continue to increase competitiveness in Hem A segment
- Patient education about Prophylaxis in Hem B driving utilization of long acting products
- VWD is underserved due to lack of awareness/understanding of the disease



Source: Data on file  
B = US\$ billions

# Haemophilia Portfolio



- 40% growth\*
- Continued patient switching
- Additional countries to launch
- 21 day dosing
- Transformational product



- 85% growth\*
  - Long lasting and reliable bleed protection
  - Successful product transition
- HELIXATE® phased out*



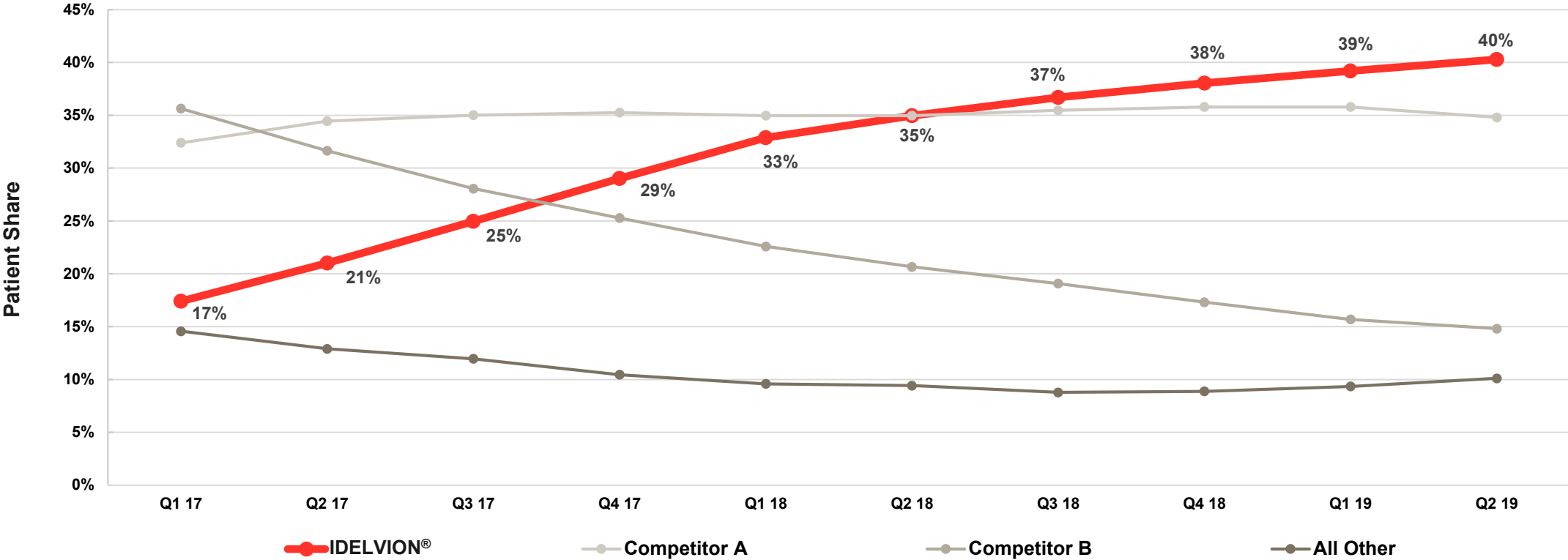
- Leadership position in VWD: 59%^ market share globally

**Recombinant Coags +7%\***

**vWD +7.5%\***

\* Growth percentages shown at constant currency to remove the impact of exchange rate movements, facilitating comparability of operational performance.  
^Source: Data on File

# IDELVION® Prophylaxis Market Leadership



Based on 5 major markets (US, Japan, Germany, Italy and UK) where IDELVION® is reimbursed and commercially available.  
 Source: Data on File

# Positioning AFSTYLA® in a Competitive Market



## Higher binding affinity to vWF

- Unique single-chain molecular structure provides increased binding
- Enhanced binding affinity protects AFSTYLA® from degradation, extending time in circulation

## 2x weekly dosing

- FDA-approved for 2x or 3x weekly dosing
- Factor trough levels above 1.9% with 2x weekly dosing

## Excellent bleed protection

- ZERO bleeds (median AsBR\*) in all patients, regardless of age and dosing frequency

## Low annual consumption

- AFSTYLA® delivers the benefits of an EHL† with the lowest annual consumption

\* AsBR: Annualised spontaneous bleeding rate

† EHL: Extended half life



# CSL Portfolio: Specialty Products

**BERINERT**  
C1 Esterase Inhibitor, Human  
*On-Demand Treatment*

**HAEGARDA**  
C1 Esterase Inhibitor  
Subcutaneous (Human)

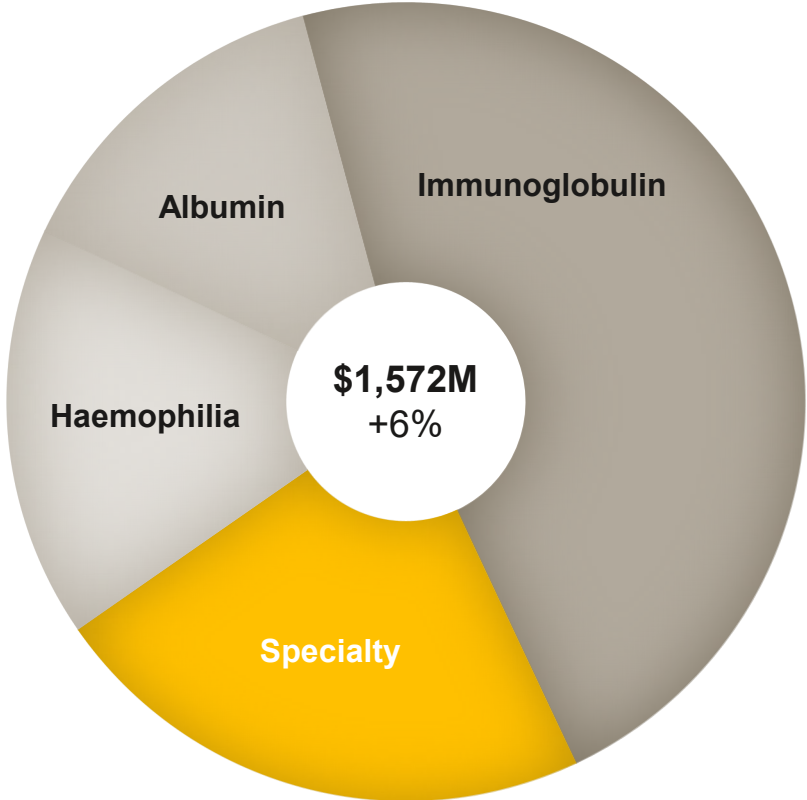
**Kcentra**  
Prothrombin Complex  
Concentrate (Human)

**Zemaira**  
alpha<sub>1</sub>-proteinase inhibitor (Human)

**Respreeza**  
alpha<sub>1</sub>-proteinase inhibitor (Human)

**RiaSTAP**  
Fibrinogen Concentrate (Human)  
*Strengthens clots. Supports hemostasis.*

**HAEMOCOMPLETTAN P**



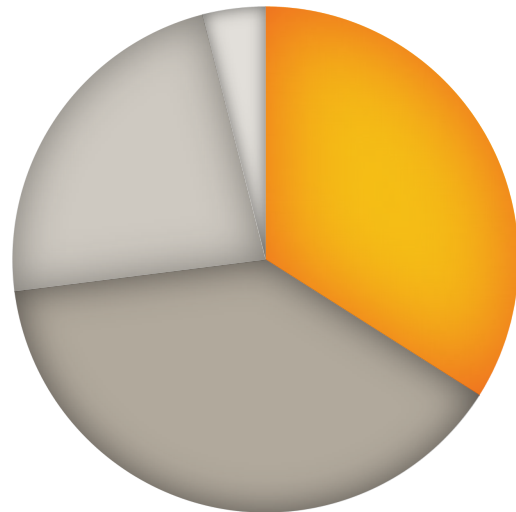
M = US\$ millions

# Continued Growth Opportunity for KCENTRA®

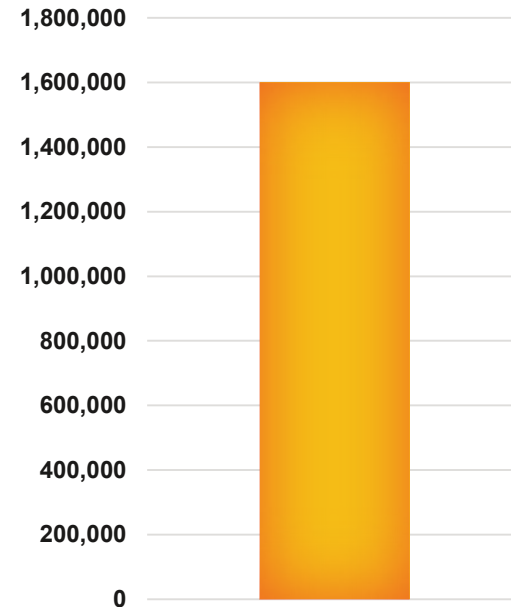
US clinical practice guidelines recommend KCENTRA® over FFP to reverse the effects of Warfarin\*

Anticoagulation Market US<sup>1</sup>

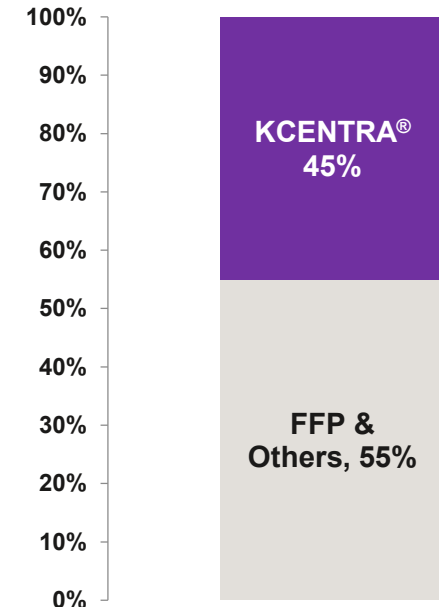
Warfarin Product A Product B Other



Warfarin Market US (Patients)<sup>1</sup>



Warfarin Reversal Market US<sup>2</sup>



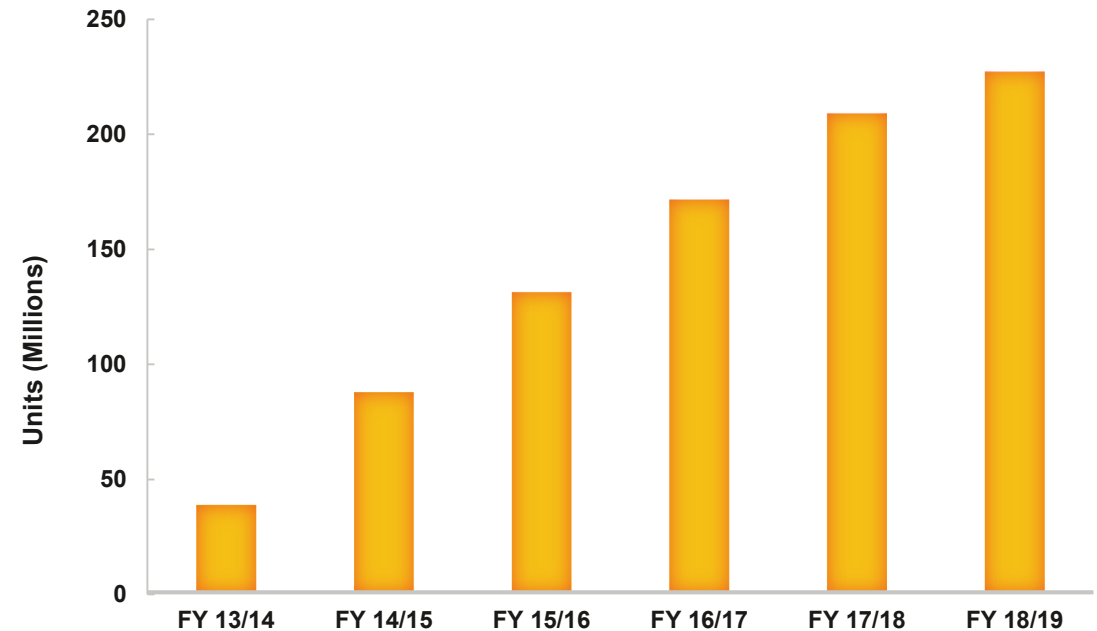
\*Neurocritical Care Society, Society of Critical Care Medicine, American College of Cardiology, American College of Chest Physicians, American Society of Gastrointestinal Endoscopy, American College of Surgeons  
Sources: 1. Data on File. 2. (RWD) Charge Master Data & Medical History Data.

# KCENTRA® Growth in US Since Launch

## KCENTRA®

- KCENTRA® remains the first and only FDA approved 4F-PCC for reversing patients on warfarin
- KCENTRA® is supported by multiple clinical guidelines as the preferred reversal agent
- KCENTRA® growth driven by:
  - Penetration within existing large hospital systems
  - Expansion into new regional accounts

Source: Data on file



## #1 prescribed therapy in the US for the prevention of HAE attacks

Address C1-INH deficiency with HAEGARDA®

---

C1-INH has been used in HAE > 35 years

---

HAEGARDA® reduced HAE attacks by 95%\*

---

Rescue medication use was reduced by >99%†‡1

\*Median reduction in number of attacks in patients receiving 60 IU/kg of HAEGARDA® vs placebo.

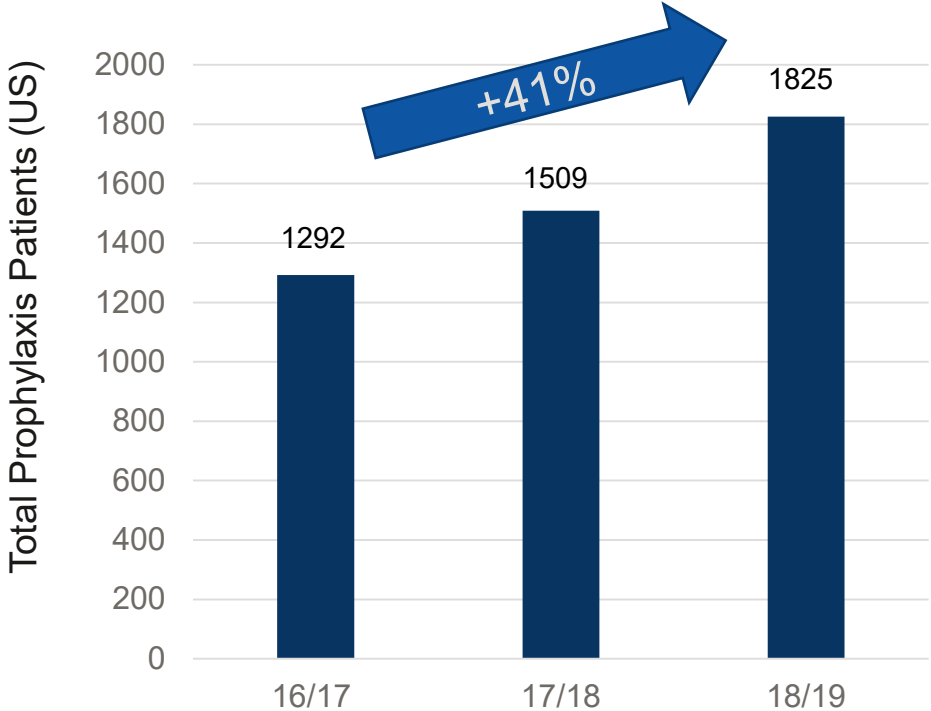
†Median reduction in rescue medication use in patients receiving 60 IU/kg of HAEGARDA® vs placebo.

‡The World Allergy Organization (WAO) guidelines for the management of HAE state that patients should have HAE rescue medication available at all times.

References: 1. Data on file



# HAE Prophylaxis Market



Source: Data on file

- HAEGARDA<sup>®</sup> is the market leader in HAE prophylaxis in the US
- Rapid uptake at launch
- Significant brand loyalty
- Additional capacity to support new launches

# Why HAEGARDA® ?

## HAEGARDA® Patients Rely On C1-INH For Efficacy And Safety



*“I’ve been on HAEGARDA for one year, and I haven’t had an attack. It allows me to be more independent, confident, and free because I can take it with me wherever I go and don’t have to depend on anyone.” – Zahra*



*“Having a therapy that addresses the root cause of HAE is important to me. It’s like filling in the missing puzzle piece of C1-INH my body doesn’t make, versus putting a mystery compound in my body.” –Cheryl*



*“For me, I find it’s easier to give myself injections at night so it’s just part of my routine. And knowing how HAEGARDA works motivates me to take it on schedule.”  
–Cheryl B-J.*

## Physicians Highly Satisfied with HAEGARDA®, Delivering On Its Promise of Efficacy With a Known MOA



*“People ask about Takhzyro but they’re so well controlled on HAEGARDA® that they don’t want to take a chance on it”*

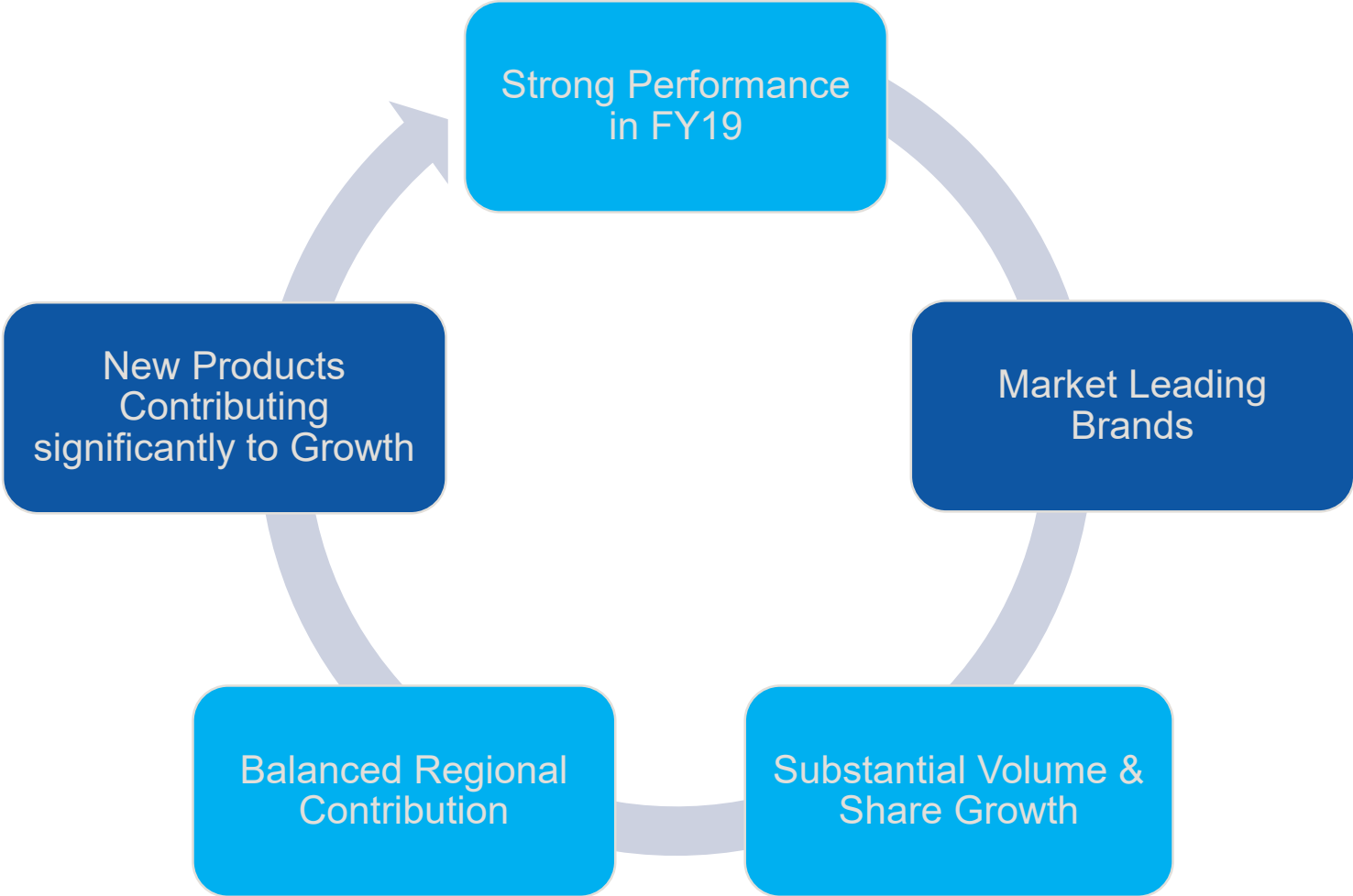
– February 2019 KOL Advisory Board Participant



*“HAEGARDA® represents a “natural approach, which some of my female patients prefer”*

– February 2019 KOL Advisory Board Participant

# Commercial Summary



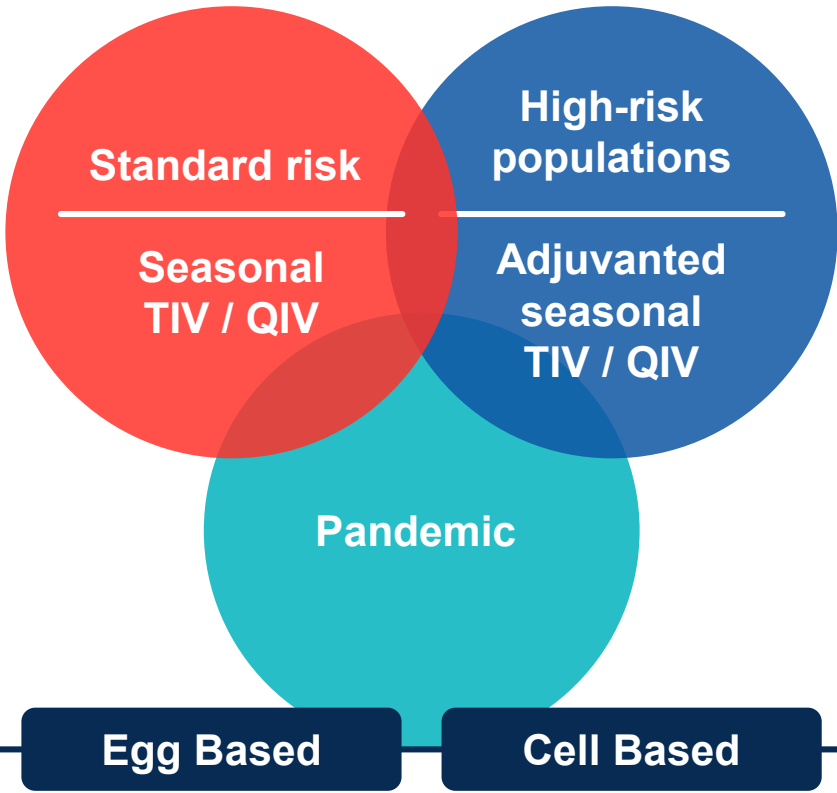
## **Dr. Russell Basser**

Senior Vice President, Research and Development  
Seqirus





# Seqirus Influenza Vaccines



**Influenza Science**

# Milestones in 2019

## AFLURIA® QUADRIVALENT

- AUS approval for 6M – 4yrs

## FLUCELVAX® QUADRIVALENT

- European approval for 9yrs and older
- Paediatric efficacy study (2 - 17yrs) – met all clinical endpoints
- Canadian approval for 9yrs and older

## FLUAD® TRIVALENT

- Strong effectiveness data in UK – again recommended by JCVI for people 65yrs and older

## FLUAD® QUADRIVALENT

- AUS approval for 65yrs and older, with positive PBAC recommendation
- Submission of dossier EU

## Pre-Pandemic vaccine (MF59-adjuvanted H5N1 cell = aH5N1c)

- US submission

## aQIVc (MF59 plus FLUCELVAX® antigen) product development commenced

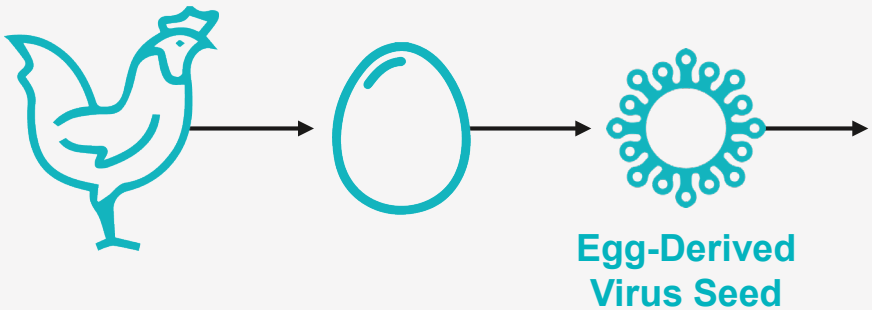
JCVI - Joint Committee on Vaccination and Immunisation



# Influenza Vaccine Innovation Through Cell-based Manufacturing

## Eggs

- Most influenza vaccines
- Egg supply – long lead times
- Low flexibility

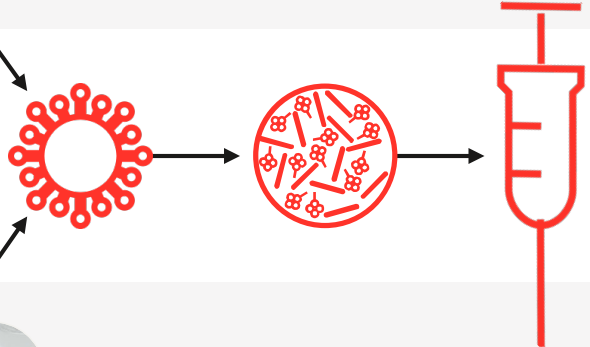


Circulating Virus



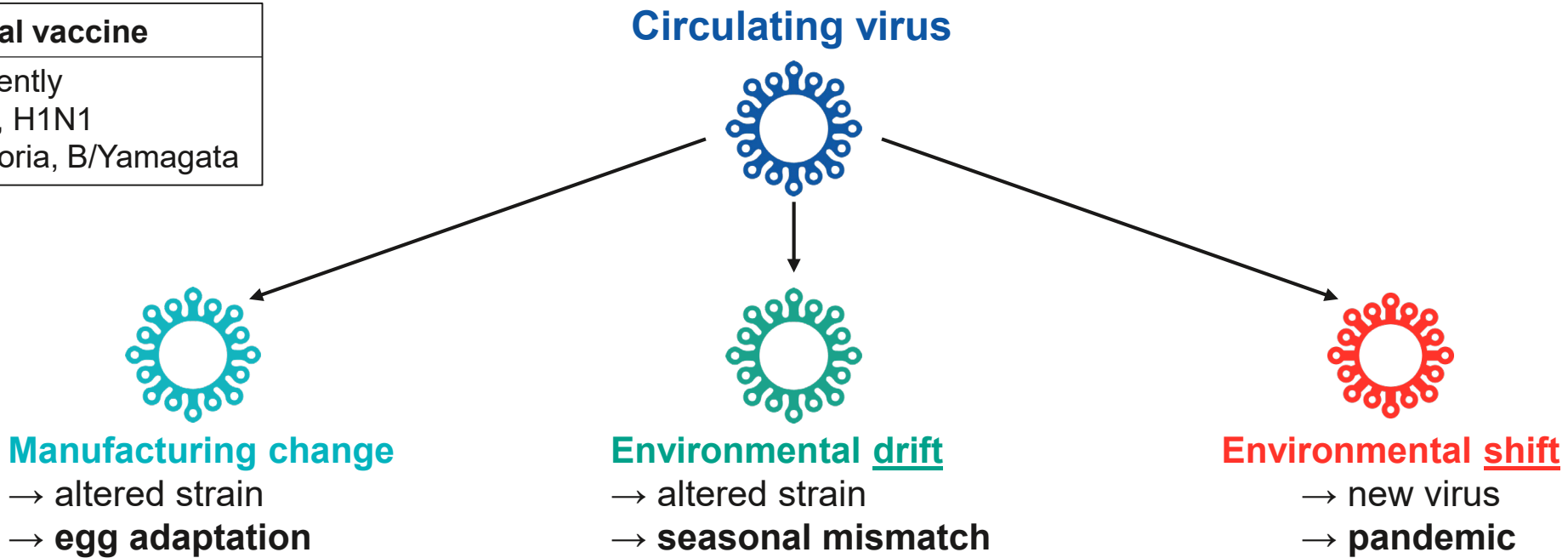
## Cell Culture

- Closed reactor
- High yield and volume
- Potential for rapid pandemic response



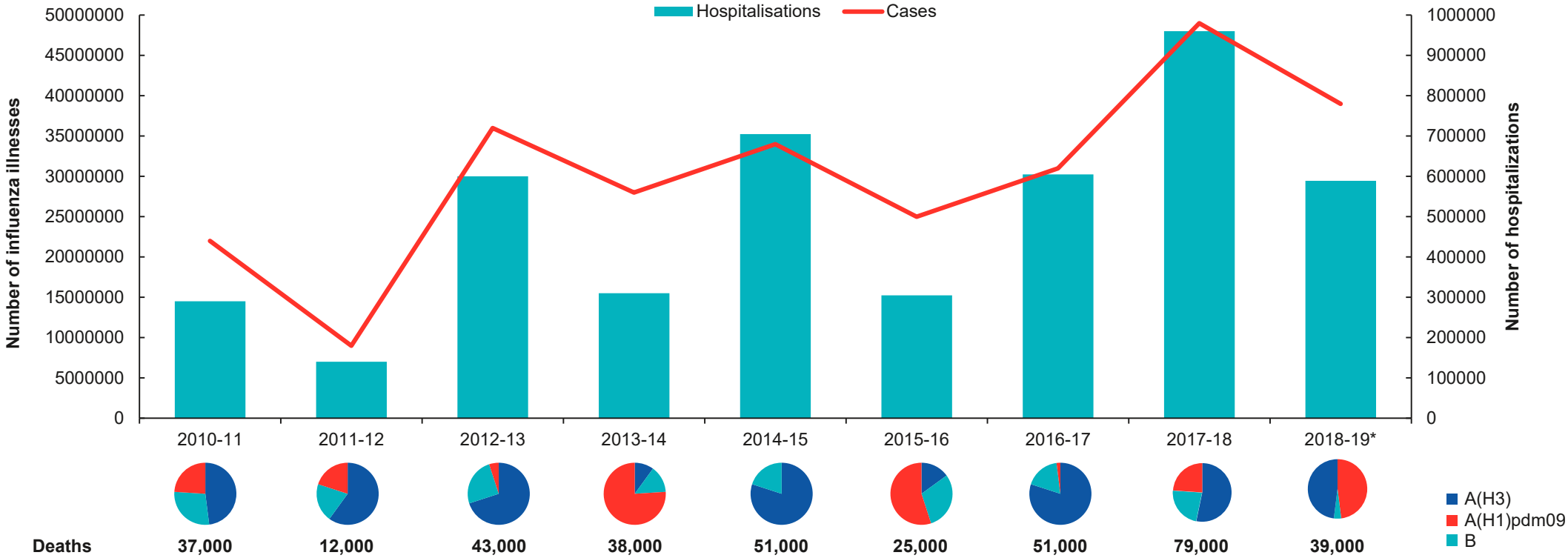
# Science of Influenza Virus Mutation and the Rationale for Non-egg Vaccines

<b>Yearly seasonal vaccine</b>
4 strains – currently
2 x “A” – H3N2, H1N1
2 x “B” – B/Victoria, B/Yamagata



# 2018-19 was a Moderate Influenza Season in US (and elsewhere)

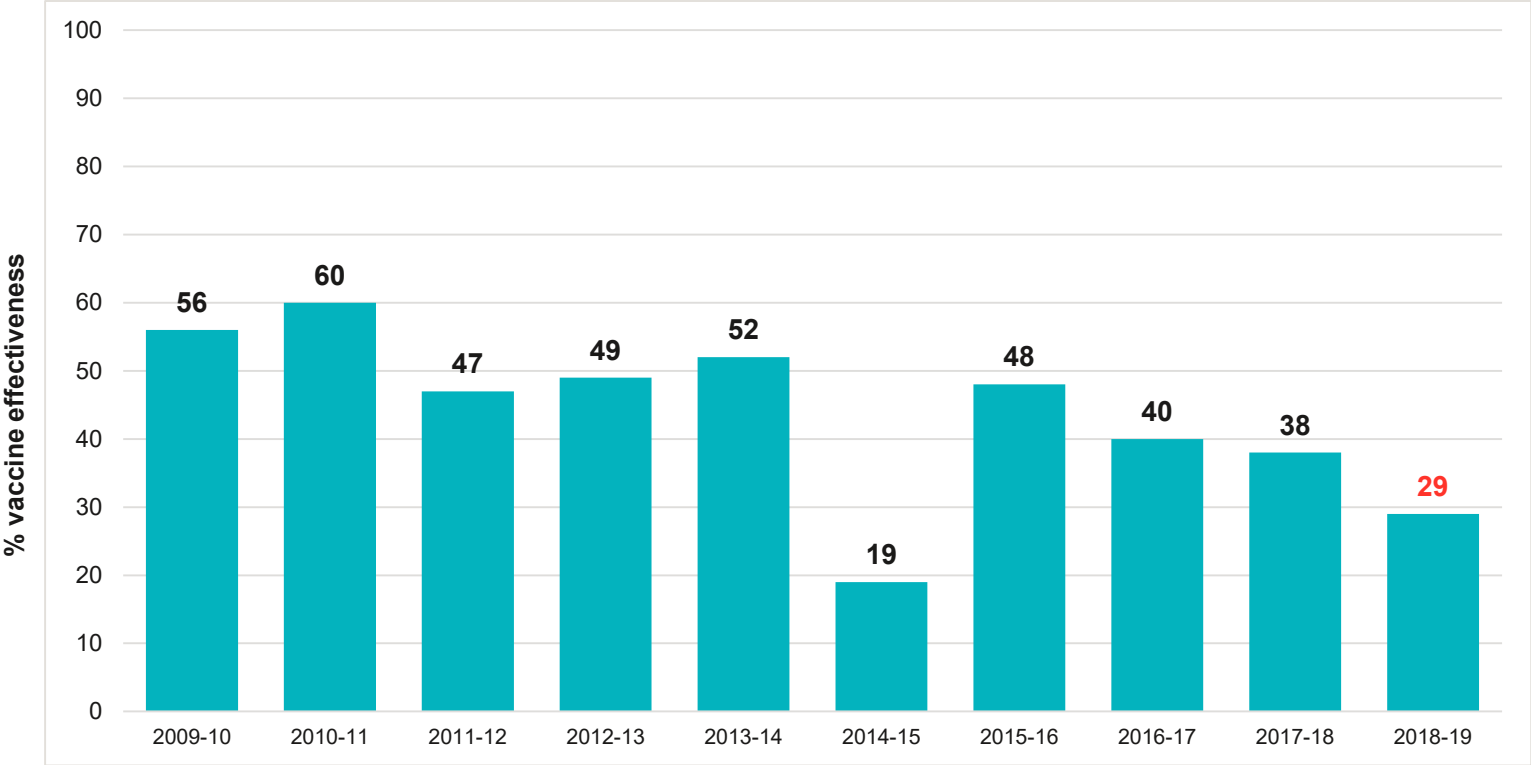
Estimated Cases of Influenza and Related Hospitalizations, U.S 2010-19 Seasons



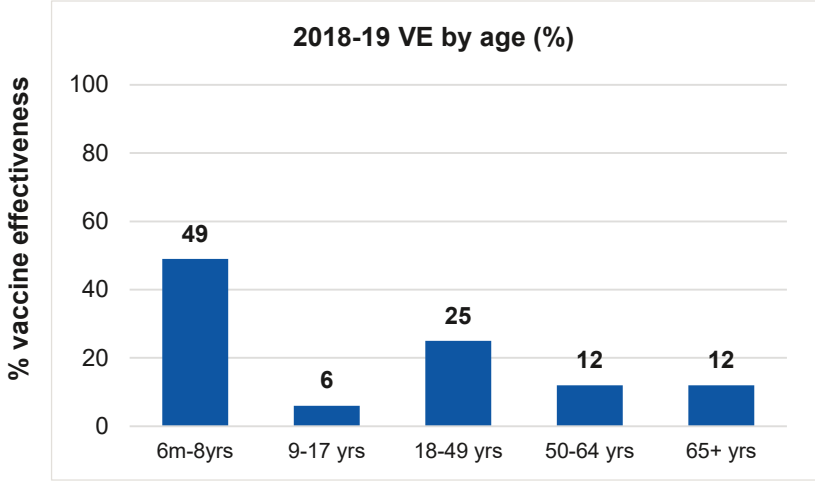
Source: US data from CDC. <https://www.cdc.gov/flu/about/burden/2017-2018.htm>.  
 \*2018-19 data are current estimates, <https://www.cdc.gov/flu/about/burden/preliminary-in-season-estimates.htm>

# Influenza Vaccine Effectiveness Varies by Year and Age

2018-19 affected by strain mismatch due to “drift” in US



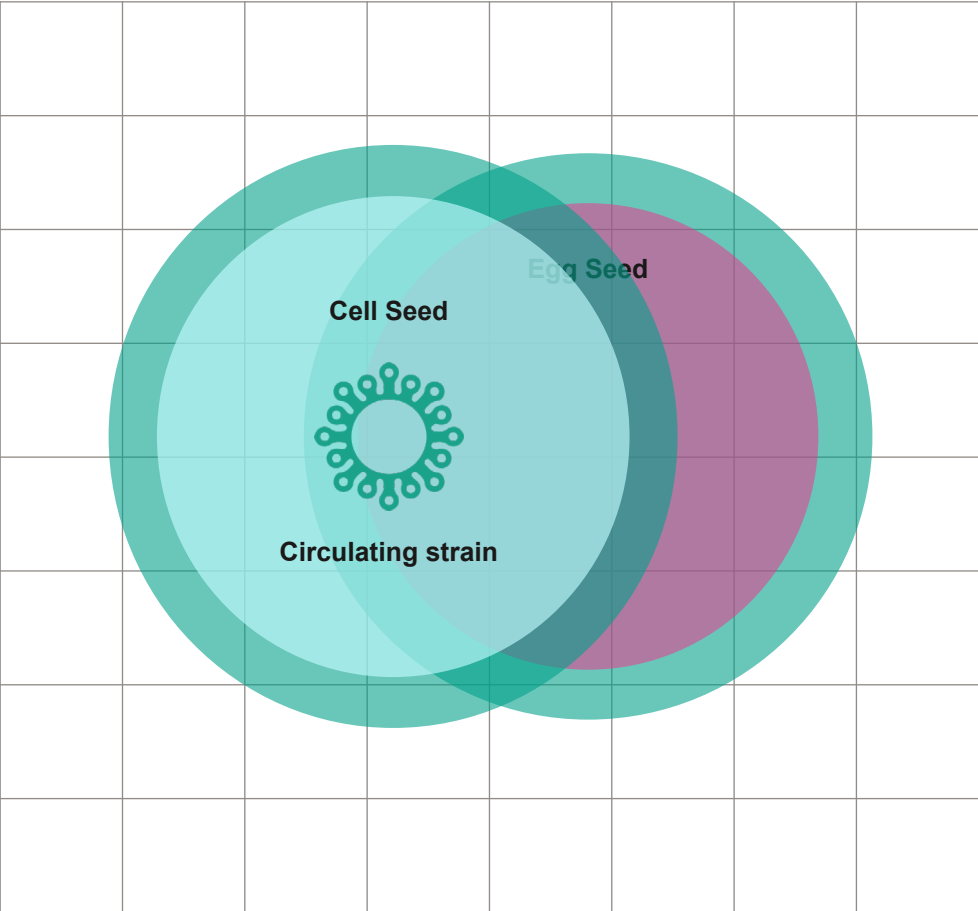
Vaccines least effective in older adults



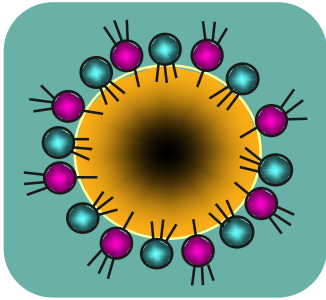
Source: US VE Network estimates of seasonal influenza vaccine effectiveness. <https://www.cdc.gov/flu/vaccines-work/effectiveness-studies.htm>



# Bringing the Benefits of MF59 Adjuvant and Cell-based Vaccine Together - aQIVc



Antigenic distance



**MF59 adjuvant**

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Increases “breadth” of immunity

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Increases antibody response

# Potential Benefits\* of Cell-based Vaccine

- Evidence of egg adaptation strongly supported by non-clinical data<sup>#</sup>
- Studies of *Real World Evidence* from 2017-18 season show benefit of cell-based vs egg-based vaccine in a season dominated by H3N2 strain (~2 of every 4 years)
  - **36% reduction in outpatient Influenza-like Illness** (electronic health record<sup>+</sup>)
  - **11% reduction in influenza-related hospital encounters** (CMS/claims data<sup>\*\*</sup>)
  - 43% reduction in H3N2-related influenza positive hospitalisation in people less than 65yrs old (Kaiser Permanente Southern California<sup>^</sup>)
- **Executive Order** from White House September 2019 called for modernisation of influenza vaccines and overhaul of seasonal flu vaccine production

\* Superior efficacy has not been demonstrated in RCT

<sup>#</sup> Kishida et al. Clin Vaccine Immunol 2012. PMID 22492743; Raymond, et al. Nat Med 2016. PMID 27820604; Parker et al. J Gen Virol 2016. PMID 26974849; Wu et al. PLoS Pathog 2017. PMID 29059230; Zost, et al. Proc Natl Acad Sci U S A 2017. PMID 29109276; Garretson, et al. Vaccine 2018. PMID 29861178.

<sup>+</sup> Boikos et al, US National Foundation for Infectious Disease 2018 Clinical Vaccinology Course, November 2018, (Poster), Bethesda MD.

<sup>\*\*</sup> Izurieta, et al. J Infect Dis 2019 220(8): 1255-1264.

<sup>^</sup> Bruxvoort KJ et al. Vaccine. 2019 37(39):5807-5811.



# Real World Evidence and the Important Impact of FLUAD<sup>®</sup>

- Recent data comparing **FLUAD<sup>®</sup>** to non-adjuvanted egg-based vaccines in people 65 years and above
  - US nursing home observational study\* in 52,000 residents in 2016-17
    - **6% reduction in all-cause hospitalisation**
  - Public Health England# analysis of first season of FLUAD<sup>®</sup> (2018-19) for older population
    - **30% reduction in influenza-related hospitalisation**
  - 15 year experience in Italy^ in 43,000 people from 2002 - 2016
    - **39% reduction in hospitalisation due to pneumonia and cardiovascular events**

- **Ongoing recommendation for FLUAD<sup>®</sup> (TIV) by National Immunisation Advisory Groups in US, UK and Australia for people 65 years and older**
- **Rapid approval and reimbursement support for FLUAD<sup>®</sup> QIV in Australia – launch 2020**

\* Presented at National Foundation for Infectious Diseases, November 2019.

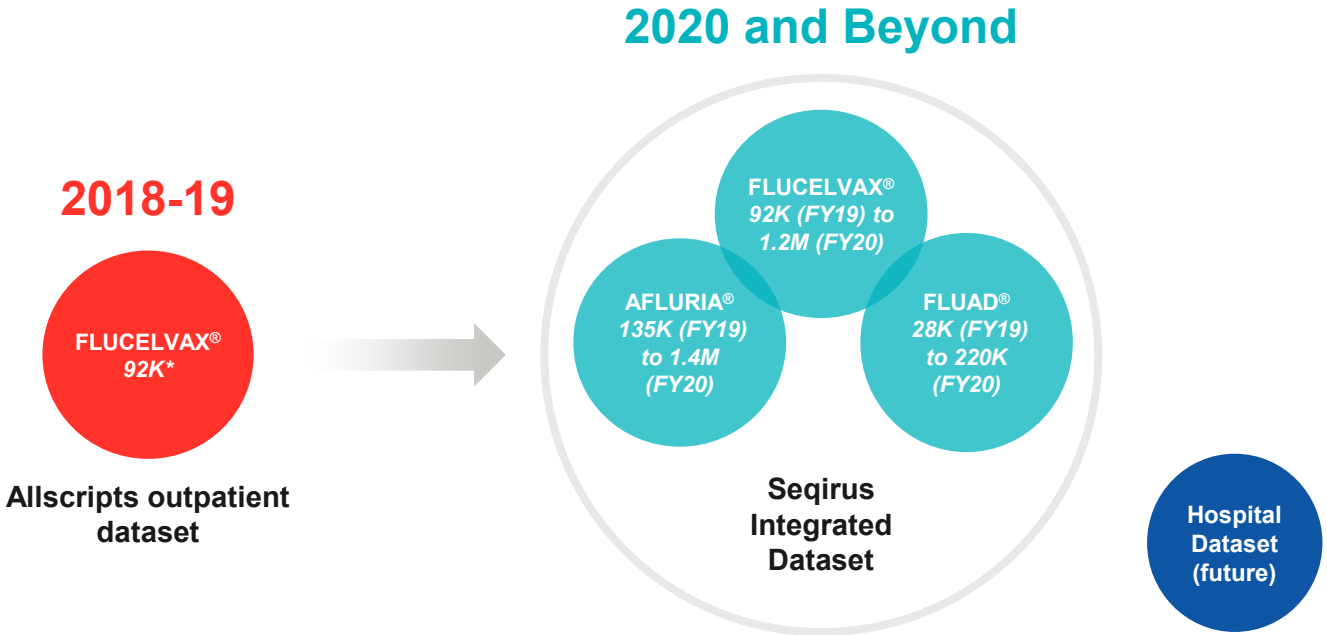
# Pebody et al. Vaccine 2019 Oct 22. pii: S0264-410X(19)31405-7. doi: 10.1016/j.vaccine.2019.10.032. [Epub ahead of print]

^ Lapi, F., et al. Expert Rev Vaccines 2019 18(6): 663-670.

# Strengthening the Power of RWE at Seqirus

## From Electronic Medical Record to Integrated Understanding

- **Real world evidence (RWE)** is data regarding potential benefits or risks of a vaccine from sources other than traditional randomised clinical trials
- Influences decisions of policy makers, healthcare professionals, Regulatory Agencies (FDA *Framework for RWE Program*, December 2018)

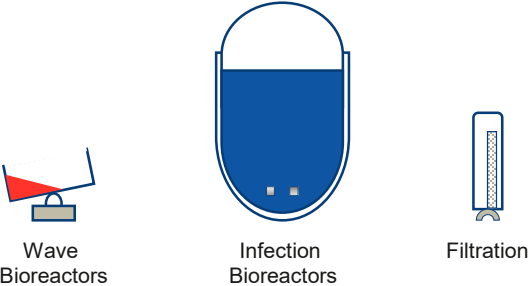


\*Refers to number of vaccinated people included in database for which healthcare outcomes can be assessed

# Focus on Influenza – Ongoing Process and Seed Innovation

## Process Improvement

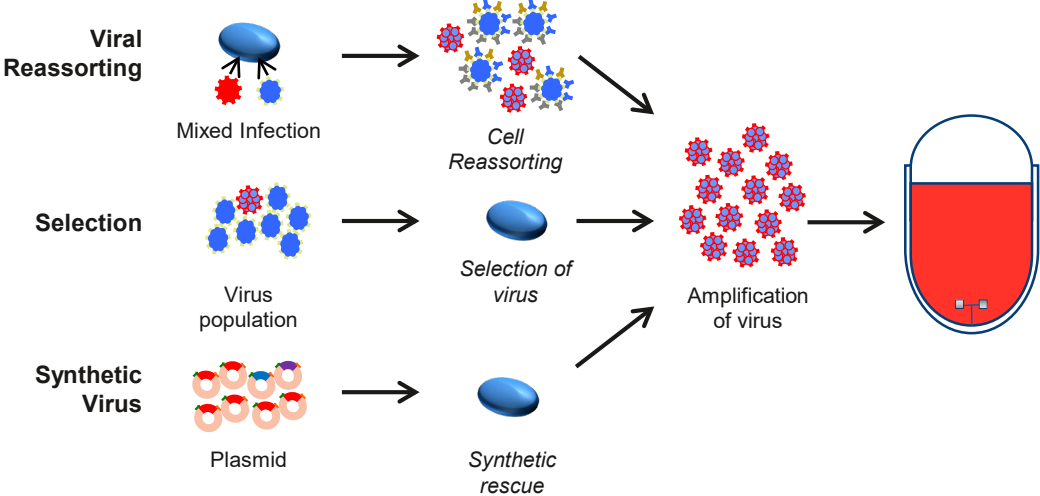
“Upstream” growth and isolation of virus



“Downstream” viral inactivation and purification of vaccine components



## Seed Innovation



# Shift to Differentiated Products is Expected to Drive Future Value Growth

- Global influenza vaccine market volumes between 500-600 million doses
  - 150 million doses distributed in US\* in 2018-2019 season
  - Slow future growth, largely due to ageing population
- Seasonal global market value ~US\$4B
- Differentiation a key driver of growth, especially in US – doses shifting to
  - Cell-based vaccines
  - Enhanced vaccines in 65 years and older segment (currently US, UK, AUS, Sth EU)
    - Potential for benefit in infants (6 months - 6 years)
  - Variable pace in geographical uptake

\* Source: <https://www.cdc.gov/flu/prevent/vaccine-supply-historical.htm>

# Anticipated Milestones in 2020

## FLUCELVAX® QUADRIVALENT

- AUS approval  
9yrs+
- Clinical study  
data  
for 6M - 4yrs

## FLUAD® QUADRIVALENT

- US approval for  
65yrs+
- EU approval for  
65yrs+

## Pre-Pandemic aH5N1c

- US approval

## aQIVc

- Commence  
clinical program

# Clinical Development – Part 2

## **William Mezzanotte, M.D.**

Executive Vice President, Head of Research and Development  
CSL Behring

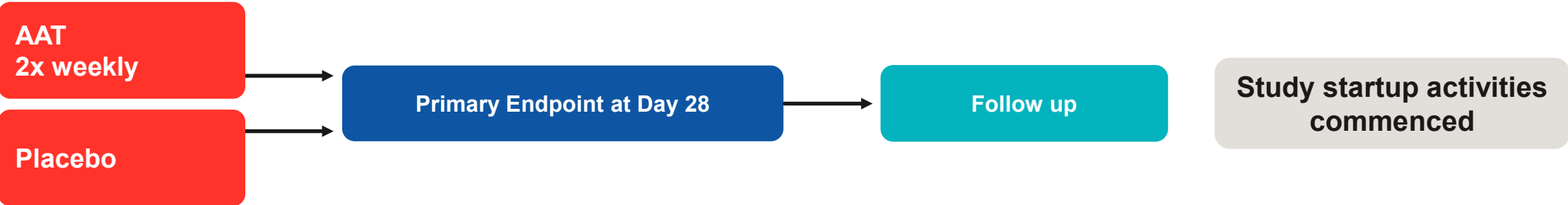


# Investigating the Benefit of Alpha-1 Antitrypsin in Graft vs Host Disease (GvHD)

## Alpha-1 Antitrypsin (CSL964) for GvHD Prevention

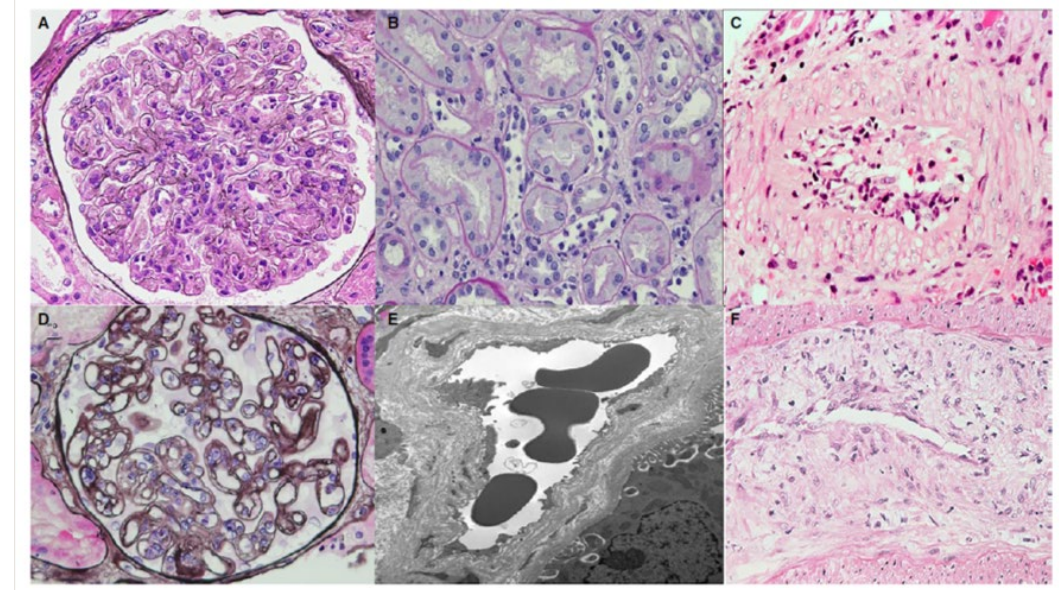


## Bone Marrow Transplant Clinical Trial Network Collaborative Study CSL964 for GvHD Treatment



# Antibody-Mediated Rejection (AMR) in Renal Allografts

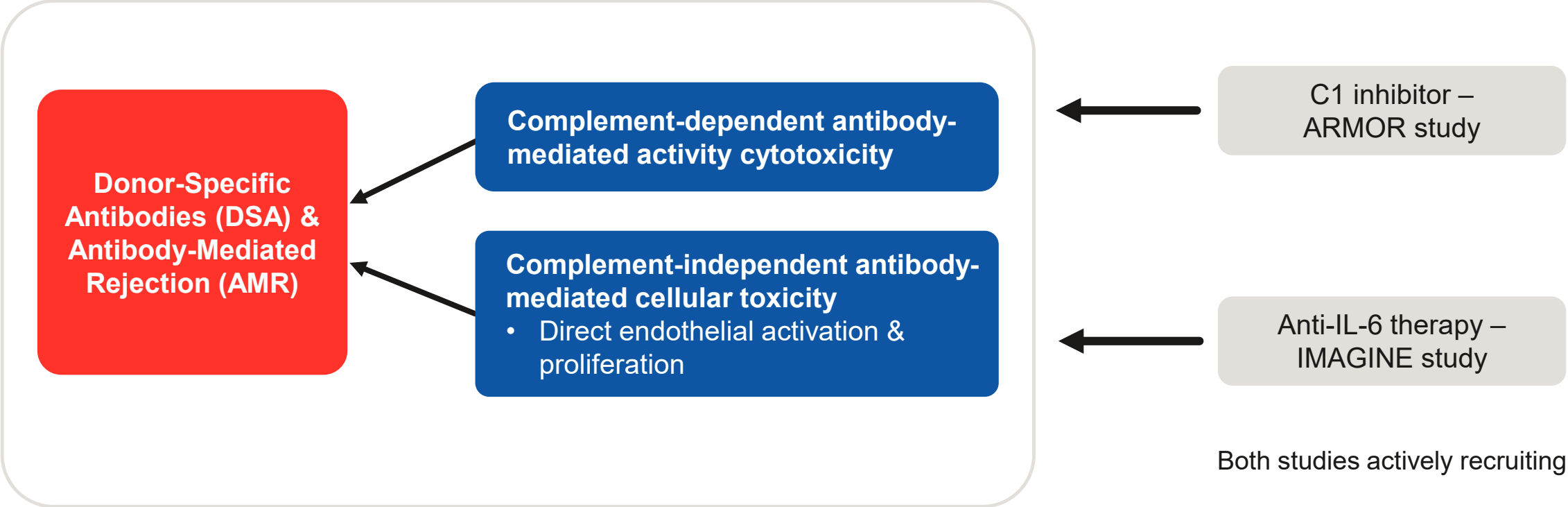
- Development of Donor Specific Antibodies (DSAs)
- Late in the post-transplant period
- Progressive decline in kidney function
- Loss of graft
- No approved therapies
  - Pilot data for C1 inhibitor and anti-IL-6



Source: Am J Transplant. 2018; 18:2849-2856

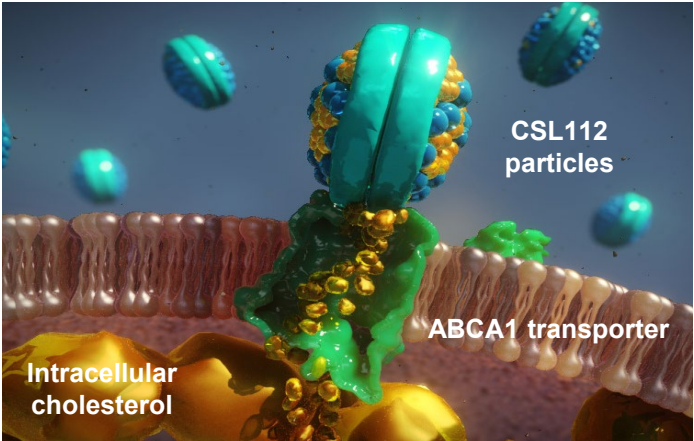


# AMR: Complement Dependent and Independent Pathways

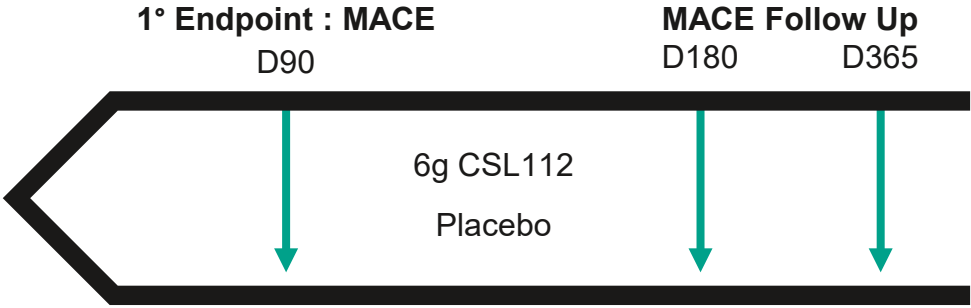
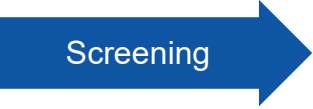


# CSL112 ApoA-1

- Study enrolment is active in >45 countries and progressing well
  - PMDA approval for Japan to join trial
- Independent Data Monitoring Committee – no safety concerns
- First futility analysis in 2020



>17,000 AMI subjects  
≥18yrs of age with Acute  
Coronary Syndrome



# Summary

## **William Mezzanotte, M.D.**

Executive Vice President, Head of Research and Development  
CSL Behring



# R&D Portfolio – December 2019

RESEARCH	PRE-CLINICAL	PHASE I	PHASE II	PHASE III	REGISTRATION	POST-REGISTRATION
Discovery Projects	Improved Fibrinogen	CSL730 rFc Multimer	CSL312 Anti-FXIIa HAE	HIZENTRA® DM	PRIVIGEN® PID Japan	CSL830 C1-INH Subcut EU
Discovery Projects	CSL787 Nebulised Ig	CSL324 Anti-G-CSFR	HIZENTRA® SSc	CSL112 ApoA-I	FLUAD® QIV 65yrs+ US/EU/Canada	PRIVIGEN® CIDP US, Japan
Discovery Projects	aQIVc (MF59 plus FLUCELVAX® antigen)	CSL200 (CAL-H) SCD	PRIVIGEN® SSc	Clazakizumab AMR	Pre-Pandemic aH5N1c	HIZENTRA® CIDP US, Japan
Discovery Projects	P. gingivalis/POD	CSL889 Hemopexin SCD	HAEGARDA® Japan	CSL842 C1-INH rAMR		HAEGARDA® US
Discovery Projects		CSL312 Anti-FXIIa Thrombosis	CSL630 pdFVIII Ruide	CSL964 GvHD Prevention		IDELVION®
		CSL311 Anti-Beta Common	Mavrilimumab GM-CSFR	CSL964 GvHD Treatment		AFSTYLA®
		CSL346 Anti-VEGF-B		FLUCELVAX® 6M+		KCENTRA® Japan
		CSL334 / ASLAN004 IL-13R				ZEMAIRA® / RESPREEZA® AAT
						AFLURIA® QIV 6M+ US, AUS

▾ Partnered Projects

Immunology and Neurology | Haematology and Thrombosis | Respiratory | Cardiovascular and Metabolic | Transplant | Influenza Vaccines

# Expected Progress in Next 12 Months

PRE-CLINICAL	PHASE I	PHASE II	PHASE III	POST-REGISTRATION
recC1-INH	CSL362 Anti-IL-3Ra	CSL346 Anti-VEGF-B	HAEGARDA® Japan	PRIVIGEN® PID Japan
Novel Complement Inhibitor	CSL787 Nebulised Ig	aQIVc (MF59 plus FLUCELVAX® antigen)	Garadacimab (Anti-FXIIa) HAE	IDELVION® 21 Day Dosing
Haptoglobin SAH				FLUCELVAX® QIV 9yrs+ AUS
				FLUAD® QIV 65yrs+ US, EU, Canada
				Pre-Pandemic aH5N1c

Immunology and Neurology | Haematology and Thrombosis | Respiratory | Cardiovascular and Metabolic | Transplant | Influenza Vaccines







# Significant Target Launch Dates

2019	2020	2021-2025	
HIZENTRA® CIDP Japan	PRIVIGEN® PID Japan	Garadacimab (Anti-FXIIa) HAE	Clazakizumab AMR
PRIVIGEN® CIDP Japan	IDELVION® 21 Day Dosing	HIZENTRA® DM	IVIG Kidney AMR
AFLURIA® QIV 6m+ (AUS)	FLUAD® QIV 65yrs+ US, EU	HAEGARDA® Japan	CSL842 C1-INH rAMR
FLUCELVAX® QIV 9yrs+ EU		Improved Fibrinogen	CSL964 GvHD
		FLUCELVAX® 6m+ US, EU, AUS	CSL112 ApoA-I
		aQIVc 50yrs+	

▼ Partnered Projects

Immunology and Neurology | Haematology and Thrombosis | Respiratory | Cardiovascular & Metabolic | Transplant | Influenza Vaccines

# 2019 Highlights

 <b>Immunology and Neurology</b>	<ul style="list-style-type: none"><li>• HIZENTRA® and PRIVIGEN® approved for treatment of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) in Japan</li><li>• HIZENTRA® granted Orphan Drug Exclusivity for CIDP</li><li>• HIZENTRA® Dermatomyositis (DM) Phase III Study initiated</li><li>• Garadacimab (Anti-FXIIa) in Hereditary Angioedema (HAE) Phase II double blind period complete</li></ul>
 <b>Haematology and Thrombosis</b>	<ul style="list-style-type: none"><li>• CSL200 (CAL-H) in Sickle Cell Disease (SCD) Phase I Study initiated</li><li>• CSL889 Hemopexin in SCD Phase I Study initiated</li></ul>
 <b>Respiratory</b>	<ul style="list-style-type: none"><li>• CSL311 (Anti-Beta Common) Phase I study commenced</li><li>• Approval of convenient single-vial dosing for ZEMAIRA® (Alpha1-Proteinase Inhibitor) in the US</li></ul>
 <b>Cardiovascular and Metabolic</b>	<ul style="list-style-type: none"><li>• CSL112 (ApoA-1) Phase III study (AEGIS-II) progressing well with &gt;7000 patients recruited</li><li>• CSL346 (Anti-VEGF-B) Phase II Diabetic Nephropathy study initiation planned for 1H20</li></ul>
 <b>Transplant</b>	<ul style="list-style-type: none"><li>• CSL964 Alpha-1 Antitrypsin (AAT) for prevention of Graft versus Host Disease (GvHD) after Transplantation of Allogenic Hematopoietic Cell Transplantation (HCT) Phase III study actively recruiting and on track</li></ul>
 <b>Influenza Vaccines</b>	<ul style="list-style-type: none"><li>• First cell-based quadrivalent seasonal influenza vaccine, FLUCELVAX® TETRA, approved in Europe</li><li>• AFLURIA® QUAD (quadrivalent influenza vaccine) granted expanded indication for use in children 6M+ in Australia</li><li>• aQIVc (MF59 plus FLUCELVAX® antigen) new product development commenced</li></ul>

# Panel Q&A Session





## CSL Continues to Advance R&D Capabilities

*Unique portfolio mix of plasma, cell and gene therapy, recombinant proteins and antibody assets highlighted at Research & Development Briefing*

**Sydney, Australia, 4 December 2019** – CSL Limited (ASX:CSL; USOTC:CSLLY) is steadily advancing its Research & Development (R&D) pipeline and capabilities to deliver a highly differentiated product portfolio mix, addressing a broader range of patients' unmet needs," said Head of Research & Development Dr. William Mezzanotte today.

At CSL's annual R&D briefing to investors, Dr. Mezzanotte noted the company is building on its leadership in plasma therapies through the identification of emerging new medicines from both within its existing portfolio of plasma-derived products, and through newer platforms such as gene and cell therapies and recombinant proteins.

To support this approach, CSL has forged targeted innovation partnerships in close proximity to its R&D locations, including at the Bio21 Institute in Melbourne, Australia, the Swiss Center for Translational Medicine in Bern, Switzerland and the University Science Center in Philadelphia, US.

"Our Phase 3 clinical program targeting the reduction of early recurrent cardiovascular events in heart attack survivors, CSL112, continues to track well.

"We continue our focus on developing new medical indications for immunoglobulins while improving manufacturing efficiencies across our plasma product portfolio," Dr Mezzanotte said.

In FY19, CSL invested US\$832 million into its R&D portfolio, representing 9.7% of total revenues.

### R&D Pipeline Highlights

A novel treatment for asthma which has this month advanced to Phase 1, first-in-human trials for patients with mild to moderate asthma. Asthma is a common chronic respiratory disease that is estimated to affect as many as 235 million<sup>1</sup> people worldwide and is the most common chronic disease among children. Despite advances in the treatment of asthma, it is estimated that every year, more than 1,000<sup>2</sup> people around the world die each day from this disease.

CSL's trial will test for the safety of a therapy delivered by subcutaneous injection that asthma sufferers could self-administer at home once every two to four weeks, acting prophylactically to prevent asthma attacks.

<sup>1</sup> World Health Organisation: <https://who.int/respiratory/asthma/en/>

<sup>2</sup> The Global Asthma Report 2018: <http://globalasthmareport.org/burden/mortality.php>

For more information about CSL Limited, visit [www.csl.com.au](http://www.csl.com.au)

The potential therapy, which currently holds the working title “CSL311,” is a monoclonal antibody that targets multiple inflammatory agents involved in various diseases.

CSL311 is the first monoclonal antibody to simultaneously target three cell-signaling cytokines, or molecules, that are responsible for the immune response that causes asthma and in doing so, suppresses inflammation of airways.

Commenting on the potential of the research, University of Melbourne Professor Jo Douglass, Head of the Immunology and Allergy Department at the Royal Melbourne Hospital and a research collaborator on the project, said, “Asthma is a serious disease that in extreme cases can be fatal. Currently, our treatment options for severe asthma are limited. We are excited by the potential of CSL311 to address a problem that affects the lives of so many.”

## Addressing Severe Muscle Disease

Another pipeline project featured today is a Phase 3 clinical trial for novel use of CSL Behring’s existing subcutaneous Immunoglobulin (Ig) product in patients with a severe condition called Dermatomyositis. The Ig product is currently indicated for use in a rare neurological disorder, Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) as well as primary and secondary immunodeficiencies.

Dermatomyositis is one of a group of acquired muscle diseases called inflammatory myopathies which are characterized by chronic muscle inflammation accompanied by muscle weakness. If the disease goes untreated it can lead to difficulty in walking or the need for a wheelchair or even becoming bedridden.

“Our pipeline is as robust and promising as ever,” Dr. Mezzanotte said. “Our R&D portfolio holds the potential to unlock a broad range of new therapies for people with challenging medical conditions. That promise is what drives our 1,700-plus scientists to work every day as if someone’s life depends on it – because it really does.”

**About CSL:** CSL (ASX:CSL) is a leading global biotechnology company with a dynamic portfolio of life-saving medicines, including those that treat haemophilia and immune deficiencies, as well as vaccines to prevent influenza. Since our start in 1916, we have been driven by our promise to save lives using the latest technologies. Today, CSL — including our two businesses, CSL Behring and Seqirus - provides life-saving products to more than 70 countries and employs more than 25,000 people. Our unique combination of commercial strength, R&D focus and operational excellence enables us to identify, develop and deliver innovations so our patients can live life to the fullest.

For more information about CSL Limited, visit [www.csl.com](http://www.csl.com)

## Media Contact

Christina Hickie  
Senior Manager Communications  
CSL Limited  
Phone: +61 429 609 762