

## Legal Notice

#### Important Notice and Disclaimer

This presentation contains summary information about CSL Limited (ACN 004 089 936) and its related bodies corporate (together, CSL) and CSL's activities as at the date of this presentation. It is information given in summary form only and does not purport to be complete. It should be read in conjunction with CSL's other periodic corporate reports and continuous disclosure announcements filed with the Australian Securities Exchange (ASX), available at <a href="https://www.asx.com.au">www.asx.com.au</a> This presentation is for information purposes only and is not a prospectus or product disclosure statement, financial product or investment advice or a recommendation to acquire CSL shares or other securities. No representation or warranty, express or implied, is made as to the fairness, accuracy, completeness or correctness of the information, opinions and conclusions contained in this presentation. To the maximum extent permitted by law, none of CSL or its directors, employees or agents, nor any other person, accepts liability for any loss arising from the use of this presentation or its contents or otherwise arising in connection with it, including, without limitation, any liability from fault or negligence on the part of CSL or its directors, employees, contractors or agents.

This presentation contains forward-looking statements in relation to CSL, including statements regarding CSL's intent, belief, goals, objectives, initiatives, commitments or current expectations with respect to CSL's business and operations, market conditions, results of operations and financial conditions, products in research and risk management practices. Forward-looking statements can generally be identified by the use of words such as "forecast", "estimate", "plan", "will", "anticipate", "may", "believe", "should", "expect", "project," "intend", "outlook", "target", "assume" and "guidance" and other similar expressions.

The forward-looking statements are based on CSL's good faith assumptions as to the financial, market, risk, regulatory and other relevant environments that will exist and affect CSL's business and operations in the future. CSL does not give any assurance that the assumptions will prove to be correct. The forward-looking statements involve known and unknown risks, uncertainties and assumptions and other important factors, many of which are beyond the control of CSL, that could cause the actual results, performances or achievements of CSL to be materially different to future results, performances or achievements expressed or implied by the statements. Factors that could cause actual results to differ materially include: the success of research and development activities, decisions by regulatory authorities regarding approval of our products as well as their decisions regarding label claims; competitive developments affecting our products; the ability to successfully market new and existing products; difficulties or delays in manufacturing; trade buying patterns and fluctuations in interest and currency exchange rates; legislation or regulations that affect product production, distribution, pricing, reimbursement, access or tax; acquisitions or divestitures; research collaborations; litigation or government investigations, and CSL's ability to protect its patents and other intellectual property.

Readers are cautioned not to place undue reliance on forward-looking statements, which speak only as at the date of the presentation. Except as required by applicable laws or regulations, CSL does not undertake any obligation to publicly update or revise any of the forward-looking statements or to advise of any change in assumptions on which any such statement is based.

#### Trademarks

Except where otherwise noted, brand names designated by a  $^{\text{TM}}$  or  $^{\text{B}}$  throughout this presentation are trademarks either owned by and/or licensed to CSL.



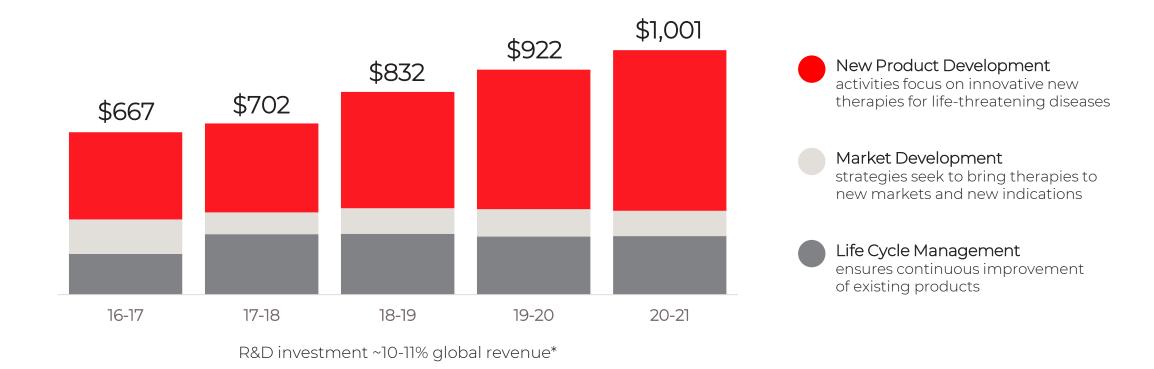


# Agenda

<u>01</u>	<u>02</u>	03	04
Welcome	Introduction – FY21 Retrospective & Highlights	Research	Development
Mark Dehring	Bill Mezzanotte	Andrew Nash	Deirdre BeVard
05	06	<b>07</b>	08
Commercial	Seqirus	Looking toward FY22 & Summary	Q&A
Bill Campbell	Russell Basser & Ethan Settembre	Bill Mezzanotte	Panel



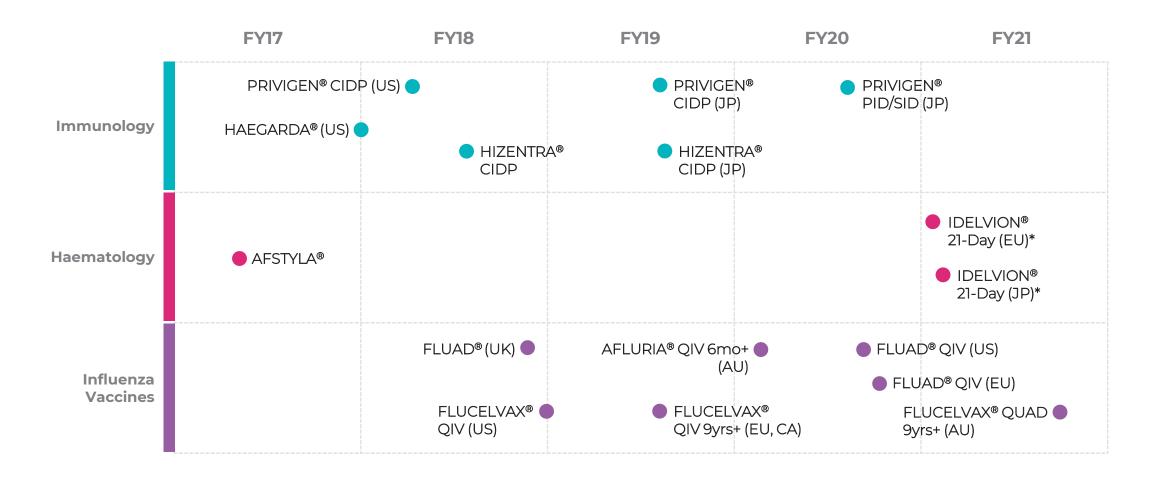
### Commitment to Research and Development





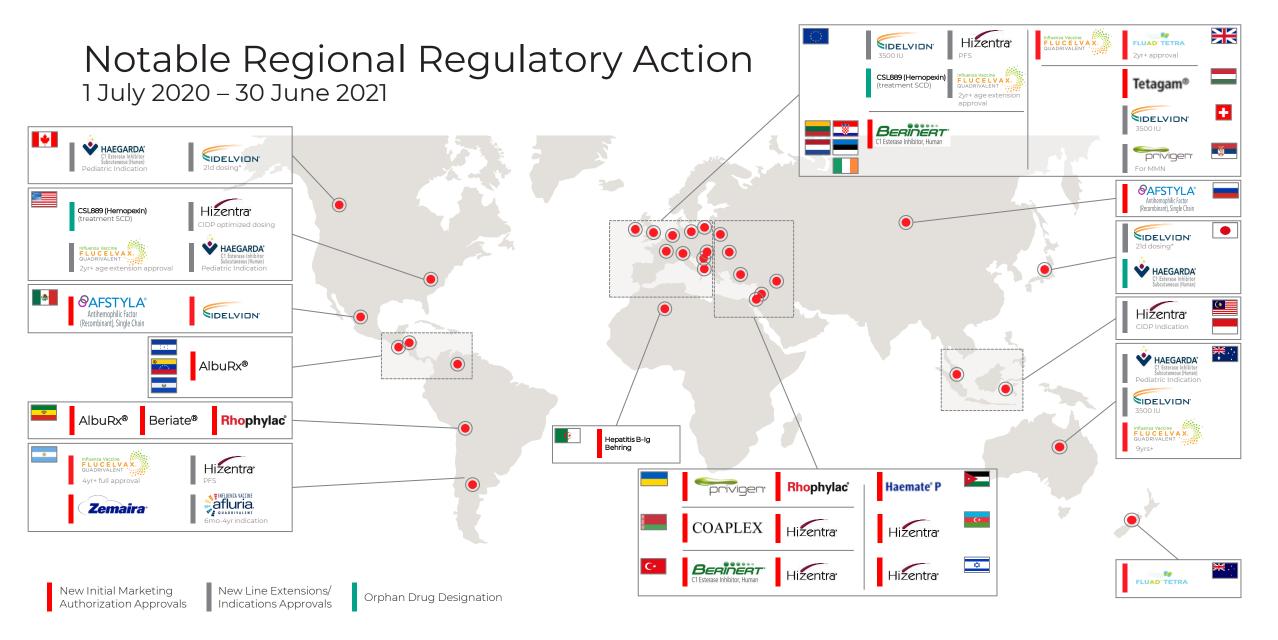
<sup>\*</sup> Investment reported in US\$ millions; Includes R&D for CSL Behring and Seqirus

### Key Past Launches from R&D Portfolio



<sup>\*</sup> Expanded label for dosing every 21 days for patients ≥12 years in age, depending on individual patient and efficacy (and jurisdiction)





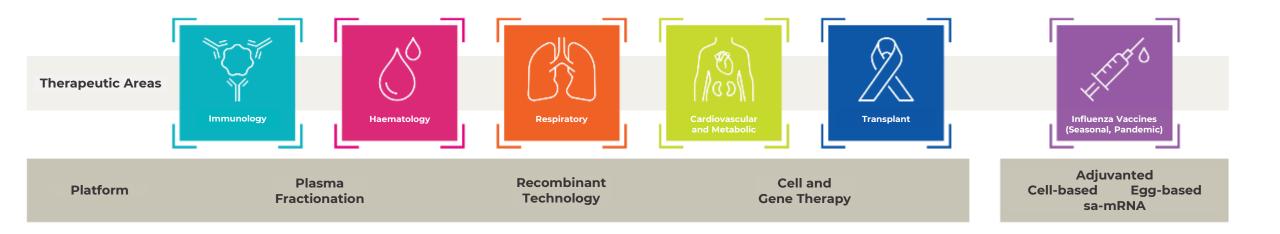
<sup>\*</sup> Every 21 days in patients ≥12 years of age, depending on individual patient and efficacy (and jurisdiction)

Abbreviations: SCD - Sickle Cell Disease; PFS - Pre-filled Syringe; MMN - Multifocal Motor Neuropathy;

CIDP - Chronic Inflammatory Demyelinating Polyneuropathy



### Focus Through Our Therapeutic Areas and Platforms





### R&D Highlights – FY21



- HIZENTRA® 5-, 10- & 20-mL pre-filled syringes launched in US
- PRIVIGEN® for CIDP launched in Japan
- HAEGARDA® approval for paediatric patients (US, AU & CA)
- HAEGARDA® ODD approved in Japan
- First patients enrolled in Garadacimab
   Phase III studies



# Cardiovascular & Metabolic

- CSL112 (ApoA-1) Phase III study (AEGIS-II)
   >13,000 patients enrolled, successful completion of 1st & 2nd futility analyses
- First patient enrolled in CSL346 Anti-VEG-B DKD Phase II study



### Haematology

- uniQure announced positive data from Phase III trial of EtranaDez
- Anti-trust clearance received; licence agreement with uniQure completed for EtranaDez
- CSL889 Hemopexin ODD approved in EU & US
- CSL889 Hemopexin fast track designation for SCD approved by US FDA; first patient enrolled in Phase I study
- IDELVION® 21 day extended dosing option approved in Japan
- Recombinant FIX approved in Mexico as IDELVIAN
- AFSTLYA® approved in Great Britain, Russia & Mexico



 First patient enrolled in CSL787 Nebulised Ig Phase I study



### **Transplant**

 Last patient dosed in Part 1 of CSL964 for prevention of GVHD study



- Commencement of aQIVc Phase II study
- Pre-clinical assessment of self-amplifying mRNA vaccine for seasonal & pandemic influenza

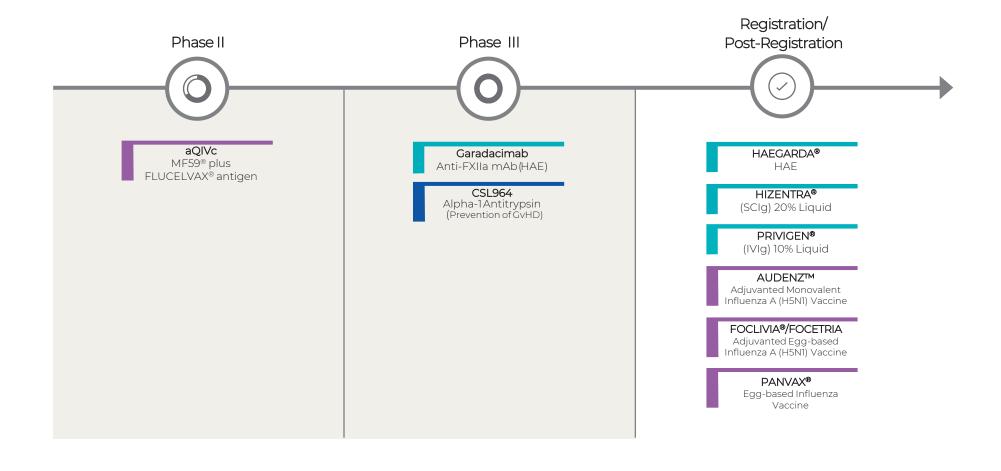


### R&D Portfolio – October 2020

Research	Pre-Clinical	Phase I	Phase II	Phase III	Registration/ Post-Registration
Gene Therapy Treatments PID  Discovery Projects  Discovery Projects	CSL888 Haptoglobin (SAH)  CSL510 Modified Fibrinogen  CSL040 Novel Complement	CSL324 Anti-G-CSFR mAb (HS)  CSL730 rFc Multimer  CSL889 Hemopexin (SCD)	HIZENTRA® (SSc)  CSL630 pdFVIII Ruide  CSL346 Anti-VEGF-B mAb	HIZENTRA® (DM)  HAEGARDA® Japan  Garadacimab Anti-FXIIa mAb(HAE)	PRIVIGEN® (PID) JP  IDELVION® rFIX-FP (Haem B)  AFSTYLA® rFVIII (Haem A)
Discovery Projects  Discovery Projects	Inhibitor  sa-mRNA Influenza Vaccine  LASN01 Anti-IL-11R	CSL200 CAL-H (SCD) CSL787 Nebulised Ig	(DKD)  Garadacimab  Anti-FXIIa mAb (ILD/IPF)  Garadacimab  Anti-FXIIa mAb (ARDS)	EtranaDez* Etranacogene dezaparvovec  KCENTRA®  4F-PCC (Trauma)	ZEMAIRA®/RESPREEZA® Alpha1-Proteinase Inhibitor  AFLURIA® QUAD Egg-based Influenza
Discovery Projects	P. Gingivalis (Periodontal Disease)	CSL311 Anti-Beta Common mAb  UQ/CSLV451 (aCoV2)  CSL334/ASLAN004 Anti-IL-13R mAb (AD)	Adjuvanted Cell Culture Influenza Vaccine (aQIVc)  Mavrilimumab Anti-GM-CSFR mAb	CSL112 ApoA-1 (ACS)  Clazakizumab Anti-IL-6 mAb (AMR)  CSL964 Alpha-1 Antitrypsin (Treatment of GVHD)  CSL964 Alpha-1 Antitrypsin (Prevention of GVHD)	Vaccine  FLUCELVAX® Quadrivalent Cell-based Influenza Vaccine  FLUAD® Quadrivalent Adjuvanted Influenza Vaccine  AUDENZ™ Adjuvanted Monovalent Influenza A (H5N1) Vaccine
clearances before closing	subject to customary regulatory ematology Respiratory OVID Outlicense	y Cardiovascular		COVID-19 Hyperimmune Therapy	



# R&D Product Progression in FY21





Transplant

Influenza Vaccines

Immunology

### Kcentra® in Trauma



### Trauma is the leading cause of morbidity and mortality in the US\*

Haemorrhage is the most common, preventable cause of early death following Trauma

### ~880k

patients suffer traumatic injury annually in US



~85%

of haemorrhagic deaths occur within 6 hours

**35-40%** 

of Trauma patients experience life threatening Acute Major Bleeding (AMB)



Through early administration in the Emergency Department, Kcentra® is intended to restore effective hemostasis, stop bleeding quickly, and improve survival of Trauma patients with AMB



Data from preclinical and clinical studies<sup>1-3</sup> support use of Kcentra® in trauma resuscitation

#### Trauma and 4-F PCC Phase III Study

- Kcentra® + Standard of Care vs. Standard of Care
- Primary endpoint: 6-hr all-cause mortality
- Up to 8,000 patients





<sup>\*</sup> Among children, adolescents and young adults 1-44 years old Abbreviations: 4-F PCC- Four-Factor Prothrombin Complex Concentrate

<sup>&</sup>lt;sup>1</sup> Ghosh, S. et al., (2021) https://doi.org/10.1371/journal.pone.0258192

<sup>&</sup>lt;sup>2</sup> Zeeshan, M. et al., (2019) J Trauma Acute Care Surg 87(2):274-281

<sup>&</sup>lt;sup>3</sup> Joseph, B. et al., (2014) World J Surg 38(8):1875-81

# Hizentra® Secondary Immune Deficiency (SID)



Infections Remain Leading Cause of Death in Chronic Lymphocytic Leukemia (CLL) – Effective Infection Prevention is an Unmet Need

Phase III Efficacy, Safety and Pharmacokinetic Study of Hizentra® for Prevention of Infection in Adults with CLL and Hypogammaglobulinemia



• Study Objective: Demonstrate benefit of treatment with subcutaneous immunoglobulin in prevention of infections in patients with CLL and hypogammaglobulinemia





# CSL Behring Research



**CSLB Global Research** 

Research / Candidate Discovery & Optimisation Toxicology
- Enabling-toxicology

Research & Clinical Bioanalytics
- GLP & GCLP assays

Research External Innovation (REI)

TA Leaders & Teams

- Research Strategy
- Project Portfolio











Functions / Capabilities

- Discovery Platforms
- Molecular Biology & Protein Engineering
- Cell Biology & Physiology
- In vivo Biology
- Translational Science
- Bioinformatics & Data Science
- etc.



# CSL Behring Research – Strategy & Focus

#### **TA Research Strategy**

Therapeutic discovery (internal & external)

Extend existing Research assets

MoA and LCM for clinical/ on market assets

Develop and expand core platforms

Identify & validate external clinical stage assets

Plasma

Recombinant Proteins

Cell & Gene Therapy

- Lead strategically aligned discovery research through:
  - Internal & external innovation
  - External asset procurement
- Translate forward and reverse to better understand opportunities and reduce risk
- Accelerate discovery outcomes through to FIH
- Extend current Research assets for TA-aligned indications
- Develop and expand core platforms
- Drive clinical stage asset development including through MoA and LCM studies



Individual Therapeutic Area (TA)
Research Strategies









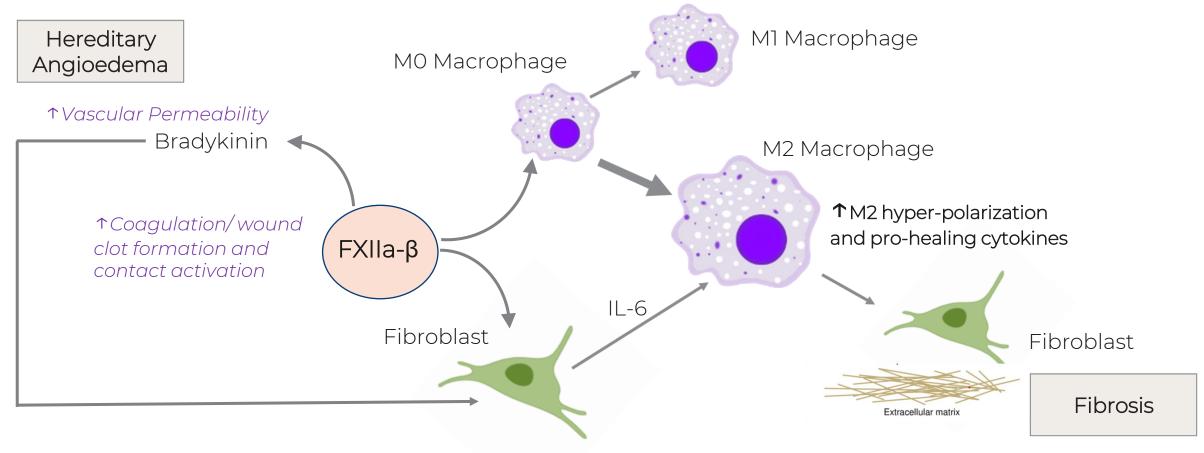


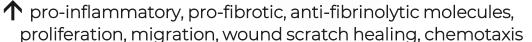




# Development of Garadacimab for Progressive Fibrosing Interstitial Lung Disease (PF-ILD)/ Idiopathic Pulmonary Fibrosis (IPF)

Role of FXII in Fibrogenesis







# Development of Garadacimab for PF-ILD/IPF

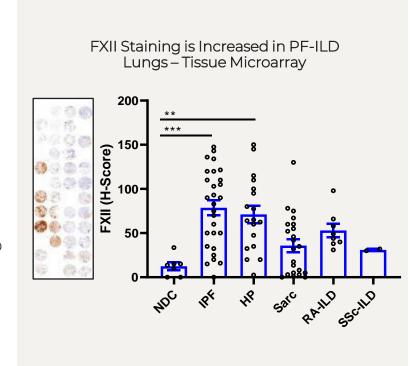
### Summary of Key Supportive Research Data

#### Clinical Data

• FXII increased in IPF lung tissues and in blood from patients with progressive IPF

#### **Experimental Data**

- Garadacimab inhibits FXIIa- $\beta$ -induced fibrotic function of primary human lung fibroblasts
- FXIIa-β promotes fibrotic M2-type macrophages, reinforced by IL-6 → feedback loop
- Blocking FXIIa- $\beta$  with 3F7\* inhibits fibrosis in experimental mouse models:
  - Lung, liver and renal fibrosis models





Phase II – expected to commence H2 FY22



<sup>\*</sup> Parental Monoclonal Antibody (mAb) of Garadacimab

# Research External Innovation & Collaboration Strategy



Parkville

The Competition for Innovation



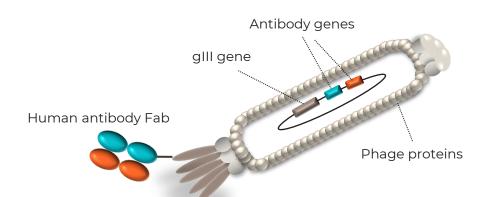




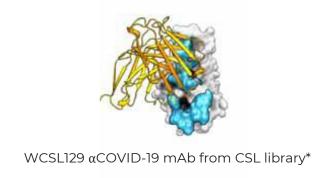
### Research External Innovation & Collaboration Strategy

### Centre for Biologic Therapies





- New jointly funded strategic initiative based in Parkville precinct
- · Novel biological therapies for treatment of serious unmet medical need
- Translational / commercialisation opportunities for WEHI
- Potential new pipeline opportunities for CSL
- Address gap in biologics drug discovery in Australian medical research
- Develop Australian workforce expertise and career opportunities





<sup>\*</sup>Source: Wheatley, A.K. et al., (2021) Cell Reports 37, 109822; 1-26

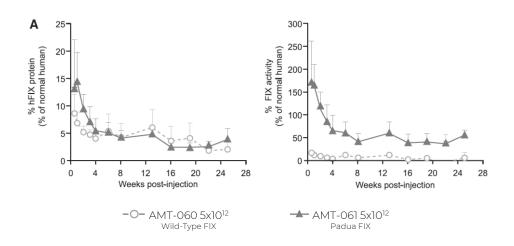
# Gene Therapy Technologies



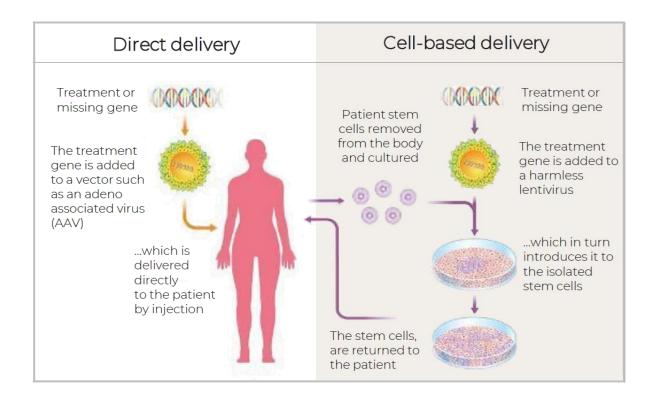
Research Institute

#### EtranaDez (Etranacogene dezaparvovec)

Enhanced Factor IX Activity following Administration of AAV5-R338L "Padua" Factor IX in NHPs



#### Gene Therapies for Immune Deficiencies





# Gene Therapy for Immune Deficiencies



Research Institute

- Agreement with Seattle Children's Research Institute (SCRI) signed March 2020 (extended in April 2021 for Gene Editing)
- Preclinical expertise in lentiviral and gene-editing-based PID gene therapy (GT)
- Extensive clinical experience in ex vivo GT (>400 patients treated with CAR-T)
- Access to PID patients and patient samples

#### Platform

Ex Vivo HSC Gene Therapy Platform

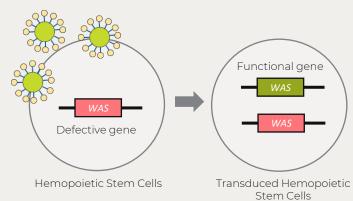
#### **Technologies**

Lentiviral Gene Therapy Other Gene Editing Approaches

#### **PIDs**

Wiskott-Aldrich Syndrome (WAS) X-linked Agammaglobulinemia (XLA) X-linked hyper IgM Syndrome (XHIM)

#### Lentiviral-Based Gene Therapy





# Gene Therapy for Immune Deficiencies



Research Institute

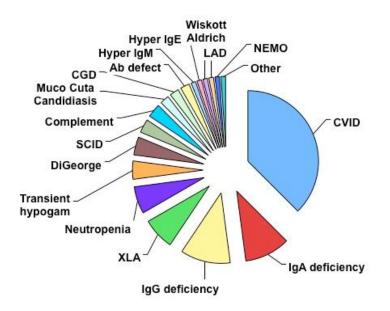
### WAS Gene Therapy Program

- Mutation in gene that produces WAS protein (WASp)
- Incidence one in 100,000 male births per year (100-300pts/yr)
- Bleeding, eczema, and recurrent infections



# Phase I/II – expected to commence H1 FY23

#### Primary Immune Deficiencies\*





Biotech Out-Licensing & Partnering



### ASLAN Pharmaceuticals - Atopic Dermatitis



- In May 2019, CSL granted ASLAN full global rights to develop, manufacture and commercialise ASLAN004 (formerly CSL334) in all indications. CSL receives milestones and royalties
- ASLAN004 is a novel, first-in-class monoclonal antibody that targets the IL-13 receptor  $\alpha$ 1 subunit (IL-13R $\alpha$ 1), one of the components of Type 2 IL-4 / IL-13 receptor
- By blocking Type 2 receptors, ASLAN004 prevents signalling of both IL-4 and IL-13, key drivers of inflammation and central to triggering symptoms of allergy in atopic dermatitis
- Dupilumab / Dupixent targets Type I and Type II receptors to block both IL-4 and IL-13 activity
   rate of dupilumab-associated ocular surface disease was 32%<sup>1</sup>

Program & Target	Discovery	Preclinical	Phase I	Phase II	Anticipated Milestones
ASLAN004	Atopic Derma	titis (AD)			11: iti-ta Dhana III. (0.2021
Anti-IL-13Rα1	Asthma*				Initiate Phase IIb - 4Q 2021

\*second indication to be confirmed



<sup>&</sup>lt;sup>1</sup> Popiela, M.Z. et al., (2021) Eye; https://doi.org/10.1038/s41433-020-01379-9

### ASLAN Pharmaceuticals - Atopic Dermatitis



#### Phase I MAD Study (ASLAN004)

- Moderate-to-severe atopic dermatitis patients (n=50)
- 200mg, 400mg and 600mg weekly
- ASLAN004 n=6, placebo n=2 per cohort
- Expansion cohort 600mg weekly, ASLAN004 n>18, placebo n>9
- Primary endpoint safety and tolerability
- Secondary end point clinical efficacy as measured by % change in Eczema Area Severity Index (EASI)

	RITT (n=29)			
Endpoint (8 weeks)	600mg (n=16)	Placebo (n=13)	p-value <sup>1</sup>	
Mean % change from baseline in EASI	-64.9	-27.2	0.021	
EASI-50 (%)	81.3	30.8	0.008	
EASI-75 (%)	68.8	15.4	0.005	
EASI-90 (%)	37.5	15.4	0.183	
IGA 0/1 (%)	43.8	15.4	0.107	
Mean % change from baseline in peak pruritus Numerical Rating Scale	-38.6	-15.3	0.051	
Mean change from baseline in POEM	-9.8	-2.5	0.007	

- Proportion of patients with adverse events and treatment-related adverse events were similar across treatment and placebo arms
- No incidences of conjunctivitis in expansion cohort



Phase II - initiating 40 2021



### Kiniksa - Giant Cell Arteritis (GCA) and COVID



- In Dec 2017, AstraZeneca / CSL granted Kiniksa full global rights to develop, manufacture and commercialise Mavrilimumab in all indications. CSL receives milestones and royalties
- Mavrilimumab targets GM-CSF receptor and inhibits action of GM-CSF, a key mediator in inflammation and autoimmune disease
- Positive data reported from Phase II trial of Mavrilimumab in GCA, a chronic inflammatory disease of medium-large arteries (75,000-150,000 cases estimated in US)
- Reduced need for mechanical ventilation and improved survival reported for Mavrilimumab (compared to placebo) in Phase II portion of Phase II/III clinical trial in patients with COVID-19-related ARDS; enrolment ongoing 1

Program & Target	Preclinical	Phase I	Phase II	Phase III
Mavrilimumab Anti-GM-CSFRα	COVID-19 Pneumonia	& Hyperinflammation		
	Giant Cell Arteritis			



<sup>&</sup>lt;sup>1</sup> Pupim, L. et al., (2021) Ann. Rheum Dis 80(1): 198-199. Abbreviations: ARDS - Acute Respiratory Disease Syndrome

## Kiniksa - Giant Cell Arteritis (GCA) and COVID



#### Phase II Study - GCA

- Active biopsy- or imaging-proven new onset or relapsed refractory GCA
- n=70; 35 NO and 35 R/R
- 150mg g2wk for 26 wks, Mavri:placebo 3:2
- 26 week steroid taper
- Primary endpoint time to first adjudicated flare
- Secondary endpoint sustained remission through week 26



**Time from Randomization (Weeks)** 

Mavrilimumab reduces risk of flare and increases



sustained remission in patients with GCA<sup>1</sup> Probability of Sustained Remission (%) Mavrilimumah Placebo Mavrilimumab Placebo (n=42)(n=28)20-Patients with Flare 8 (19) 13 (46.4) by Week 26, n (%)

<sup>&</sup>lt;sup>1</sup> Cid, M.C. et al., (2021) Ann. Rheum Dis 80(1); 31-32 Abbreviations: NO - New Onset; R/R - Relapsing/Refractory; q2wk - every 2 weeks

### CSL Behring Research

Creating and progressing a sustainable portfolio of early stage opportunities

- Continuing to innovate in areas of business strength
- Developing new opportunities in areas of unmet need

Three drug discovery platforms applied across five TAs

Leveraging in-house technologies to support external innovation

Expanding capacity and capability across global Research sites

Continued investment in external innovation

 From venture capital investment to long term strategic collaborations



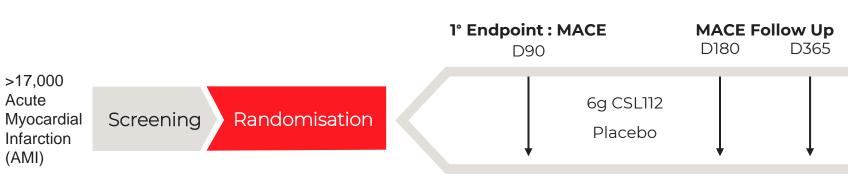


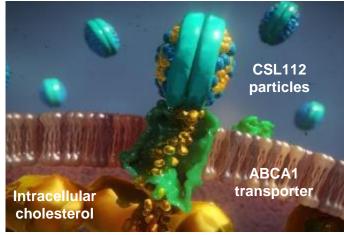


# CSL112 Apolipoprotein A-I (human) - AEGIS-II



- Managing recruitment through COVID-19 impact on sites and patients
- 2<sup>nd</sup> futility analysis in 2021 passed
- 3<sup>rd</sup> interim analysis end FY22









### EtranaDez



### Gene Therapy (AAV5-Padua FIX) for Treatment of Haemophilia B

- CSL acquired exclusive global rights to commercialise EtranaDez from uniQure in May 2021
- Clinical program includes:
  - Phase IIb study: Open-label, single-dose, single-arm trial, using Padua FIX, in adult males with severe or moderately severe Haemophilia B (HB)
  - Phase III HOPE-B study: Open-label, single-dose, single-arm, trial in adult males with severe or moderately severe HB (FIX ≤ 2%) on routine FIX prophylaxis and with/without pre-existing neutralizing antibodies (nAbs) to AAV5
- BLA/MAA submissions H2 FY22

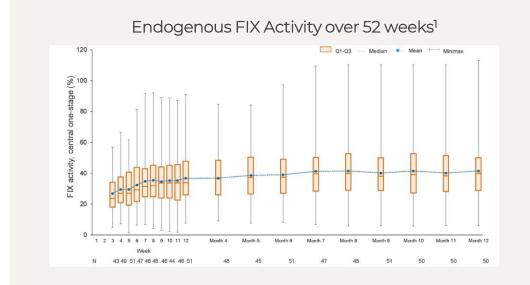


### EtranaDez – HOPE-B Study 12 Month Data



Haematology

- FIX activity increased rapidly to mid- to normal range with mean of 41.5 IU/dL (±21.7; 5.9, 113.0) at Wk 521
- FIX activity similar (~44%) in participants with and without pre-existing nAbs to AAV5<sup>1</sup>
- 96% of patients discontinued prophylaxis<sup>1</sup>
- Mean FIX activity Ph IIb patients stable and durable at 2.5 years<sup>2</sup>
- Phase III preliminary data translates into meaningful clinical response with reduction in Annualised Bleeding Rates (ABR)
- Majority of patients did not report any bleeding during 52 weeks after dosing<sup>1</sup>



Adjusted Annualized Bleeding Rates (ABR) in the First 12 months Post-treatment<sup>1</sup>

All subjects (N=54)	Lead-in ABR	Year 0-1 ABR	Ratio (% Reduction)	P-value
All bleeds <sup>a</sup>	3.98	1.33	0.34 (66.6)	p<0.0001
All bleeds treated with FIX	3.39	0.68	0.20 (80.0)	p<0.0001
Spontaneous bleeds treated with FIX	1.16	0.18	0.15 (84.5)	p<0.0001
Traumatic bleeds treated with FIX	1.75	0.30	0.17 (82.9)	p<0.0001
Joint bleeds treated with FIX	1.92	0.30	0.16 (84.4)	p<0.0001



<sup>&</sup>lt;sup>1</sup> Pipe. S.W. et al., (2021) ISTH, PB0653

<sup>&</sup>lt;sup>2</sup> Gomez, E. et al., (2021) ISTH, LPB0020 Abbreviations: AAV5 - Adeno-Associated Virus serotype 5

### Ongoing New Investigations with Hizentra®



### Systemic Sclerosis (SSc)

A rare, heterogeneous, multi-systemic, progressive autoimmune disease with significant morbidity

- Incidence: 0.8 5.6 per 100,000<sup>1</sup>
- Prevalence rate: 3.8 34.1 per 100,000<sup>1</sup>
- 3-4 times more common in females than males<sup>2</sup>

Presents with hardening of skin, inflammation and scarring of internal organs, endothelial injury leading to microangiopathy and dysregulation of autoimmunity

Highest mortality among systemic autoimmune diseases No treatment currently addresses all of the multi-system impact

### Dermatomyositis (DM)

A severe inflammatory autoimmune disease that leads to muscle weakness and skin changes with high comorbidity

- Incidence 11 per 1,000,000
- Prevalence rate 14 per 100,000
- Increases with age (peak ages 70-79)<sup>3</sup>

The disease can also affect other organs such as lungs, heart and the esophagus and in general is associated with a higher rate of malignancy (cancer)

Mortality rate: 10-30% (5y), high comorbidity

High unmet need for long-term treatments without systemic side effects



<sup>&</sup>lt;sup>1</sup> Varga, J. (2020) In J.S. Axford (Ed.), UptoDate, Accessed June 1, 2021.

<sup>&</sup>lt;sup>2</sup> National Organization for Rare Diseases. Scleroderma. Accessed June 4, 2021.

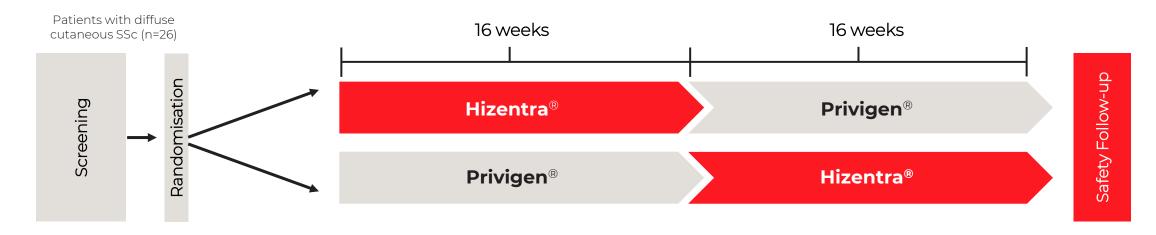
<sup>&</sup>lt;sup>3</sup> Svensson J. (2017) Clin Exp Rheumatol. 35(3):512-515

### Hizentra® SSc - SURPASS



Phase II Safety and Bioavailability Study of Hizentra® in Adults with Systemic Sclerosis (SSc)

- Study fully enrolled ahead of schedule
- Anticipated study completion 2022



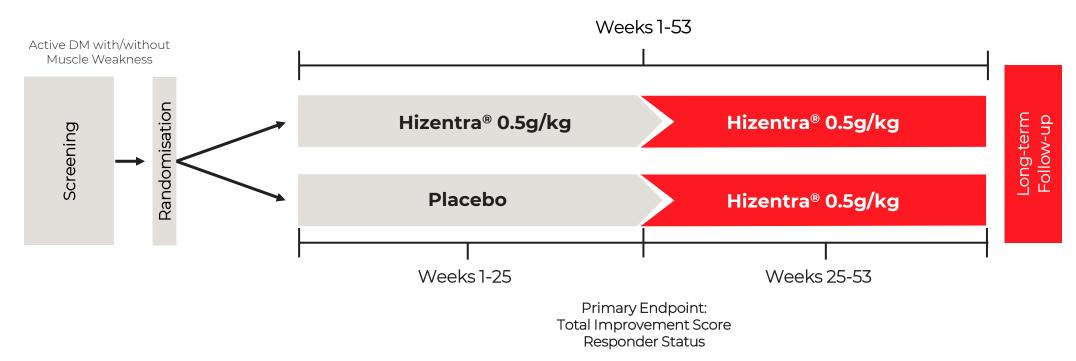


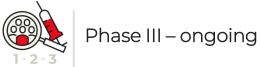


### Hizentra® DM - RECLAIIM

**Immunology** 

Phase III Study of Hizentra® in Adults with Dermatomyositis







# Hereditary Angioedema (HAE)



Autosomal dominant genetic condition 1 in 10,000 – 50,000 people

Unregulated protein cascade

- → elevated levels of bradykinin
- → fluid release into tissues
- → swelling in specific parts of body

Unpredictable onset, severity and attack location, lasts for 2-5 days



Normal appearance



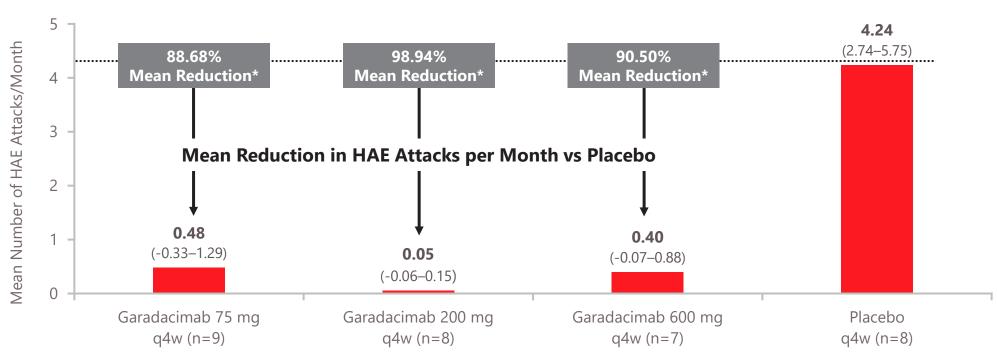
During cutaneous attack



## Garadacimab – A First-in-Class, Fully Human mAb that Inhibits FXIIa to Treat HAE







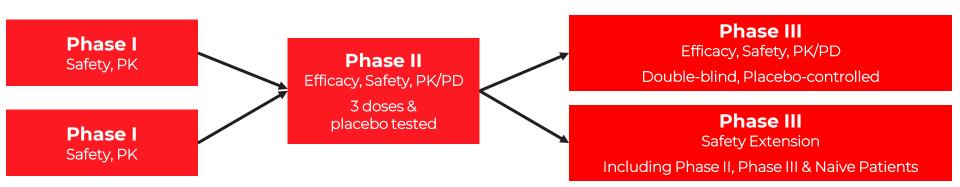




### Garadacimab - CSL's First mAb in Phase III







Completed Healthy

Broad dose range IV & SC

Completed ~40 HAE patients

POC Dose selection. Safety, PK/PD

Ongoing ~60 HAE patients

Pivotal, Confirmatory Efficacy, Safety, PK/PD, QoL

Ongoing ~150 HAE patients

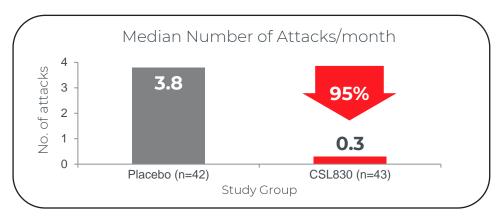
Long term safety Efficacy, PK/PD, QoL

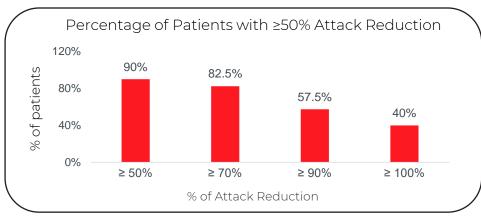


# Comparable Efficacy of HAEGARDA® for HAE in Japanese Patients

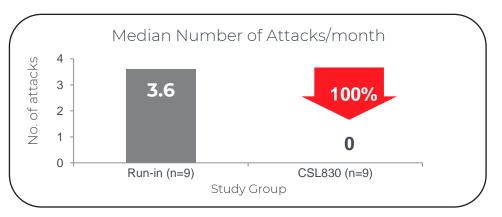


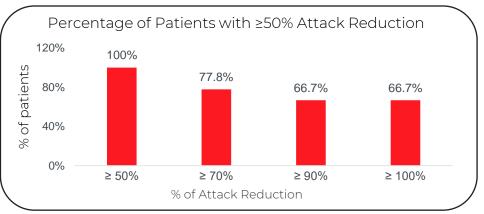
### Global Phase III Pivotal Study





### Japan Phase III Study

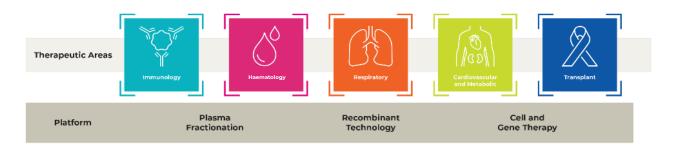






### Progress Across All of our TAs and Scientific Platforms

- Our scientists continue to grow our pipeline through internal discovery and external collaborations
- Our focus drives continued progress in the Phase II and Phase III portfolio
- Our innovation in other novel mAbs CSL324, CSL311, CSL346 and Clazakizumab and other novel plasma proteins – CSL889 (Hemopexin) and CSL787 (Nebulised Ig) continues to progress well
- Our patient focus leads to optimisation and expansion of Established Products with new indications and markets





# CSL R&D - Together We Deliver on our Promise to Patients





## CSL Behring FY21 Commercial Highlights



- Ig
- Albumin
- Haemophilia

\$1,770

\$1,107

Revenue

US \$8,574M

\$1,071

6%1

- Specialty
- Other<sup>2</sup>



#### Performance

■ Global revenue of \$8,574M/+6%<sup>1</sup>



\$4,238

### Immunology

- Underlying Ig demand remained strong through pandemic
- 15% Hizentra® revenue growth; continued success in CIDP



#### Albumin

- Sales normalized in China under new GSP
- Significant contribution to FY21 YoY growth



### Haemophilia

Maintained IDELVION® leadership in key markets³

#### Source:

- Orowth percentages shown at constant currency to remove the impact of exchange rate movements, facilitating comparability of operational performance.
- <sup>2</sup> Includes HPV royalties & Ig Hyperimmunes
- <sup>3</sup> Data on file

Abbreviations: CIDP - Chronic inflammatory demyelinating polyneuropathy; FFP - Fresh Frozen Plasma; GSP – Good Supply Practices; YoY – Year on Year

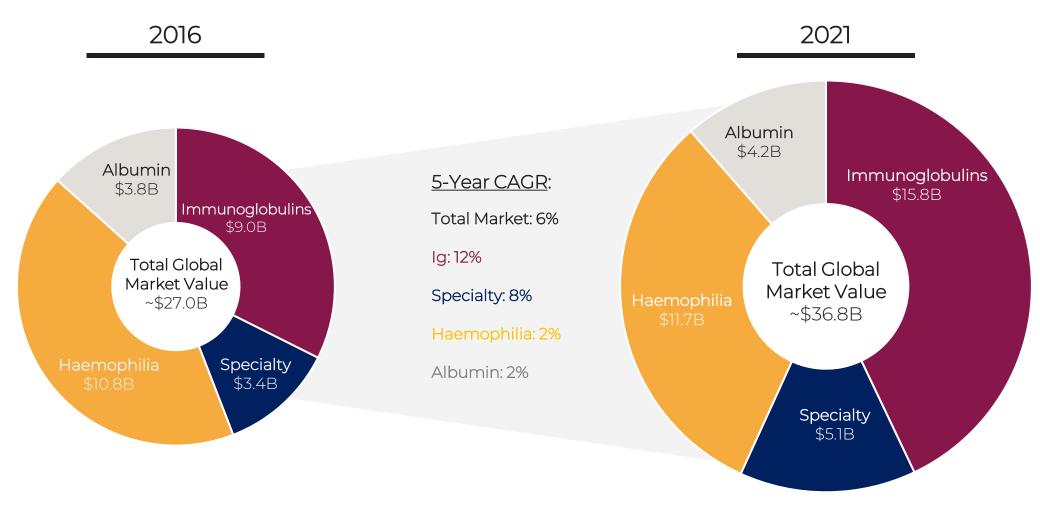


### Specialty

- Strong growth from HAEGARDA® and KCENTRA®
- HAEGARDA® most patients since launch; 14% revenue growth
- KCENTRA® continued penetration vs FFP



## Targeted Protein Therapeutic Market Continues to Grow



Source: Company 3Q 2016 reports/financial schedule; MRB global Coagulation Factors Concentrate Market 2015 & 201; MRB WW Plasma Fractionation Market 2015 interim report; CSL Actuals FY16

Source: Analyst Reports; Company Annual Reports; Data on file; CSL Actuals FY21; Immunoglobulins market include Hyperimmunes; Haemophilia market include Factor XIII and non-factor; Specialty includes AAT, HAE, Fibrinogen, PCC, ATT markets

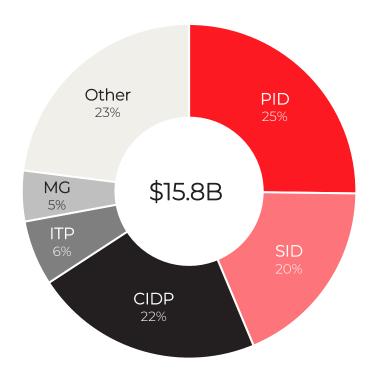


## Immunoglobulin Market

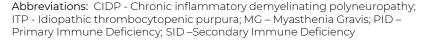
### Market Dynamics

- COVID-19: Industry-wide impact on plasma collection
- Underlying demand remains strong
  - Significant patient needs in PID & CIDP
  - Expanding usage for SID
- Shifting preference to SCIg and home administration

### Global Ig Volume by Indication



Source: Data on file for 2020







### Immunoglobulins

FY21 Sales: \$4,238M<sup>1</sup>

Up 3%<sup>2</sup>

Christal: living with chronic inflammatory demyelinating polyneuropathy (CIDP)

- <sup>1</sup> Excludes Ig hyperimmunes
- <sup>2</sup> Growth percentages shown at constant currency to remove the impact of exchange rate movements, facilitating comparability of operational performance.
- <sup>3</sup> CSL Internal Data

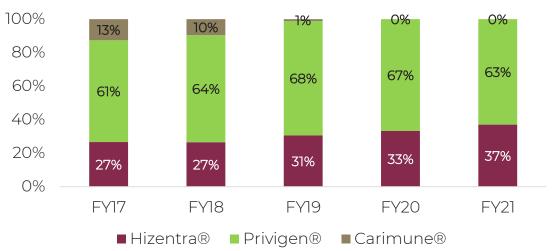


- Hizentra® +15% revenue growth²; remains the clear SCIq market leader
- Increased preference for at-home treatment
- Continued uptake in CIDP
- Recent Medicare Part B reimbursement approval



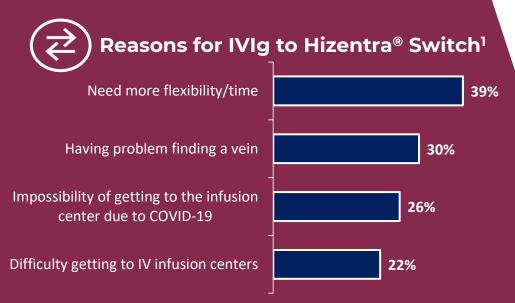
- Supply tightness intensified by COVID-19
- Privigen® volume impacted by shift to Hizentra®
- Global demand remains strong in core indications











Covid has impacted thinking - "At this point, after seeing what has happened ..., we really need to try to transition these patients to something that's going to be more manageable if there's ever something like this again."

- Lisa, Neurologist



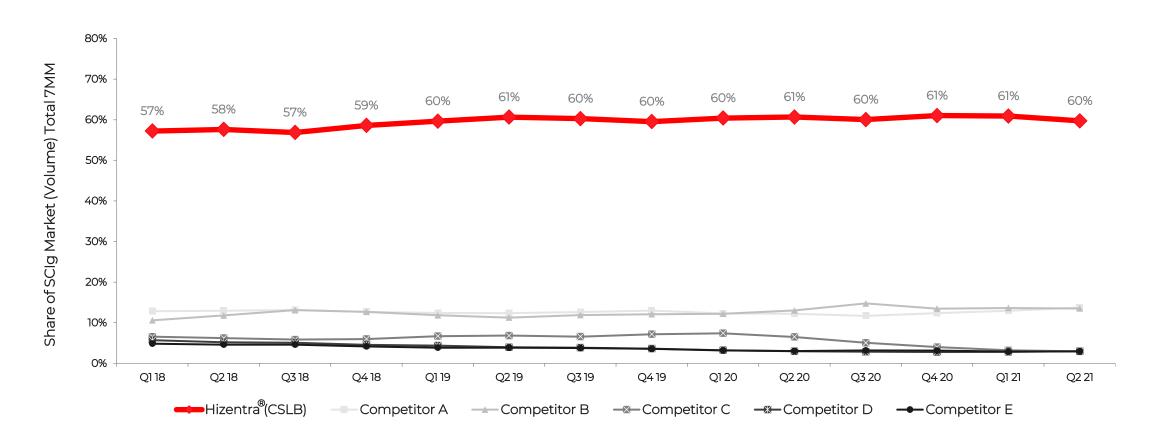
- #1 Ig used worldwide for PID<sup>1</sup> and the only SCIg approved for use in CIDP
- Proven long-term protection with over 3.5 years of clinical evidence and 10+ years of real-world experience
- Continue to lead within SCIg as we bring more innovative and personalized treatment options to patients





# Hizentra® - Continued Strong Performance

Robust SCIg Market Growth of 13.1% During Same Period





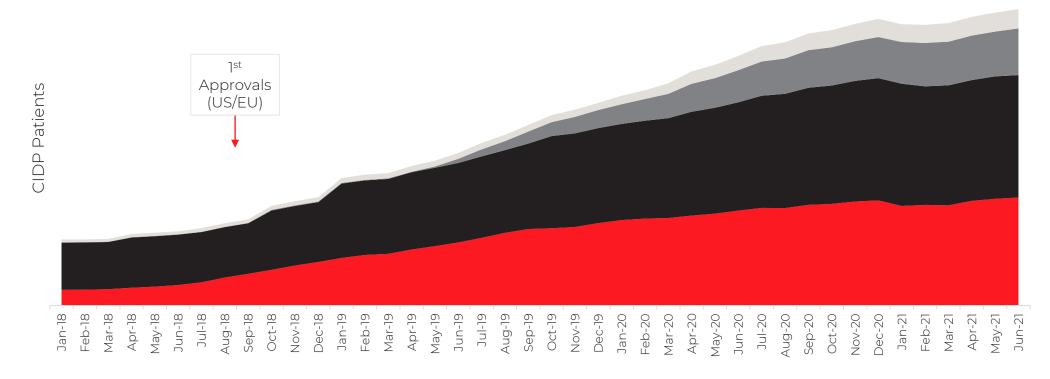


### Hizentra® Immune Globulin Subcutaneous (Human) 20% Liquid

# CIDP Patients Benefitting From Hizentra® Across the Globe

Total Hizentra® CIDP Patients by Region<sup>1,2</sup>





<sup>&</sup>lt;sup>1</sup> Countries Included – JP, AT, IT, NL, SK, UK, IS, CH, US, GER, GR, DE.



<sup>&</sup>lt;sup>2</sup> Data on file



# Coagulation Factor IX (Recombinant), Albumin Fusion Protein

### Antihemophilic Factor (Recombinant), Single Chain





### Haemophilia

FY21 Sales: \$1,107M Down 4%<sup>1</sup>

Logan: living with Haemophilia B.

#### **IDELVION®**

Standard of care for Haemophilia B

Maintained leadership<sup>2</sup> in several key markets, including US,
Germany, Italy, Switzerland & Japan

Recent strong launches in France,
 Spain and Taiwan

#### **AFSTYLA®**

 Impacted by competitive market & reduced doctor visits during COVID-19

#### pdFVIII

 Maintained market leadership globally in vWD with 56% patient share<sup>2,3</sup>

#### **HUMATF®**

 Strong revenue growth of 13%<sup>1</sup> in the US



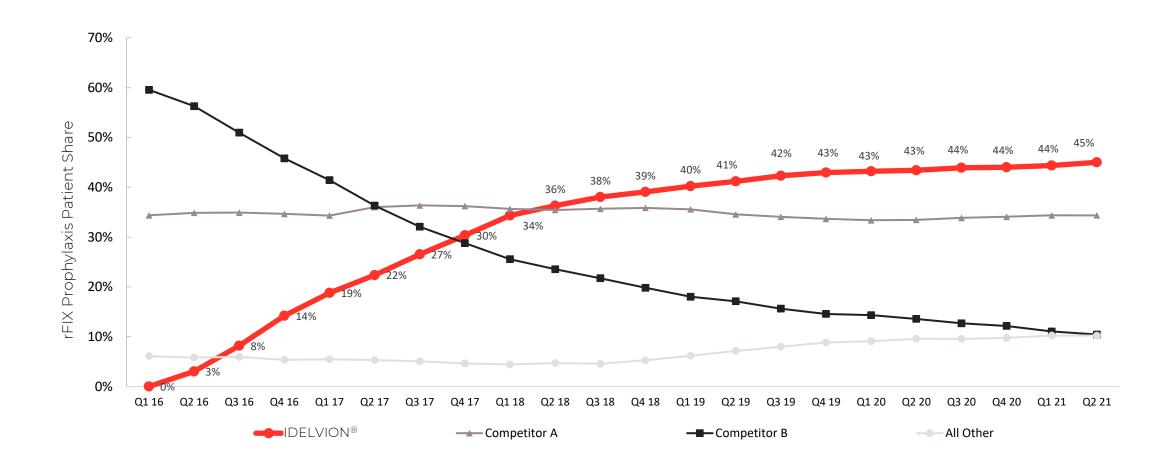
<sup>&</sup>lt;sup>1</sup> Growth percentages shown at constant currency to remove the impact of exchange rate movements, facilitating comparability of operational performance.

<sup>&</sup>lt;sup>2</sup> Data on file

<sup>&</sup>lt;sup>3</sup> Includes HUMATE®/HAEMATE® and VONCENTO® Abbreviations: vWD – von Willebrand Disease

# IDELVION® - Maintaining Market Leadership





Based on data from US, JP, DE, IT, ES, CH and UK where IDELVION® is reimbursed and commercially available. Source: Data on file

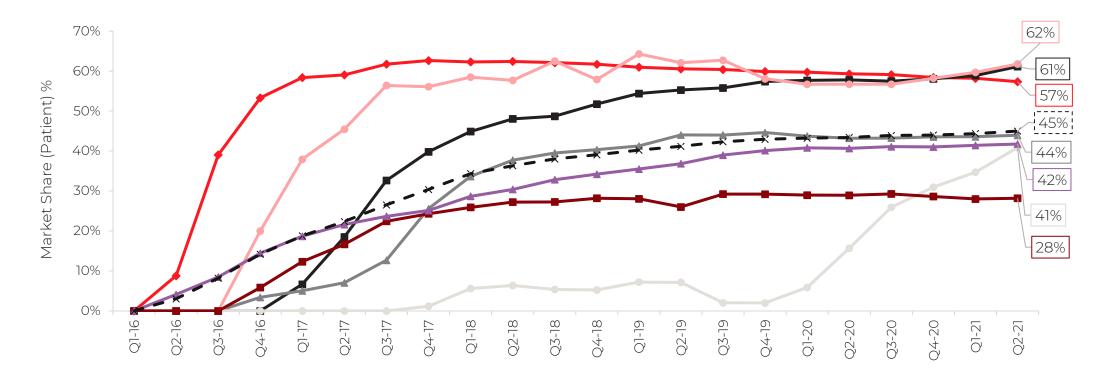


# IDELVION® - Market Shares Within Key Markets



#### IDELVION® rFIX Prophylaxis Patient Share by Country



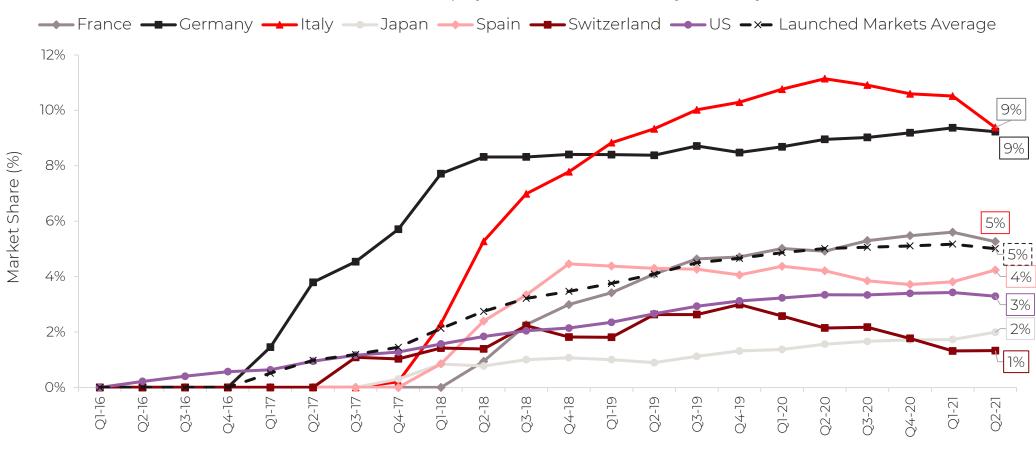






# AFSTYLA® - Market Shares Within Key Markets

### AFSTYLA® rFVIII Prophylaxis Patient Share by Country















### **Specialty Products**

FY21 Sales: \$1,770M Up 2%<sup>1</sup>

#### Cheryl: living with Hereditary Angioedema (HAE).

#### **KCENTRA®**

Remains the gold standard for warfarin reversal in the US

Substantial growth opportunities, with FFP still used in ~40% of patients<sup>2</sup> in the US

Demand rebounded to pre-COVID levels in the US

#### HAEGARDA®/Berinert SC®

- Offers best in class efficacy<sup>3</sup>
- US: Most patients since launch
- Treatment paradigm further shifts from on-demand to longterm prophylaxis

#### Respreeza®/Zemaira®

 Investing to enhance supply chain & ensure future supply



<sup>&</sup>lt;sup>1</sup> Growth percentages shown at constant currency to remove the impact of exchange rate movements, facilitating comparability of operational performance.

<sup>&</sup>lt;sup>2</sup> Data on file

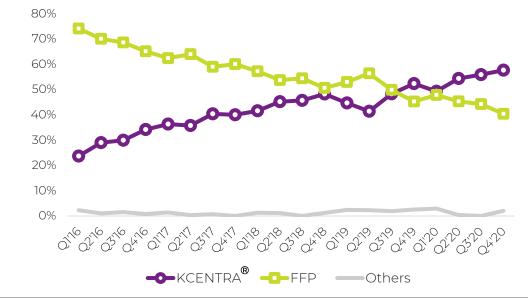
<sup>&</sup>lt;sup>3</sup> In the clinical trial, 95% median reduction in number of attacks in patients receiving 60 IU/kg of HAEGARDA® vs placebo, and a >99% median reduction in rescue medication use in patients receiving 60 IU/kg of HAEGARDA® vs placebo.

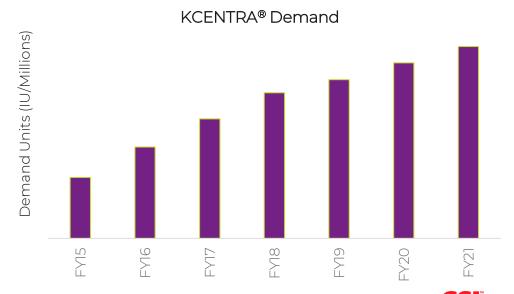


### KCENTRA® Growth in US

- KCENTRA® remains first and only FDA approved 4F-PCC for reversing patients on warfarin
- KCENTRA® is supported by multiple clinical guidelines as the preferred reversal agent<sup>1</sup>
- ~1.7M patients on warfarin, with ~25k new patient starts per month<sup>2</sup>
- KCENTRA® growth driven by:
  - Superior efficacy data versus fresh frozen plasma
  - Penetration within existing large hospital systems
  - Innovative digital promotion and education programs

#### Warfarin Urgent/Major Bleed Reversal Shares







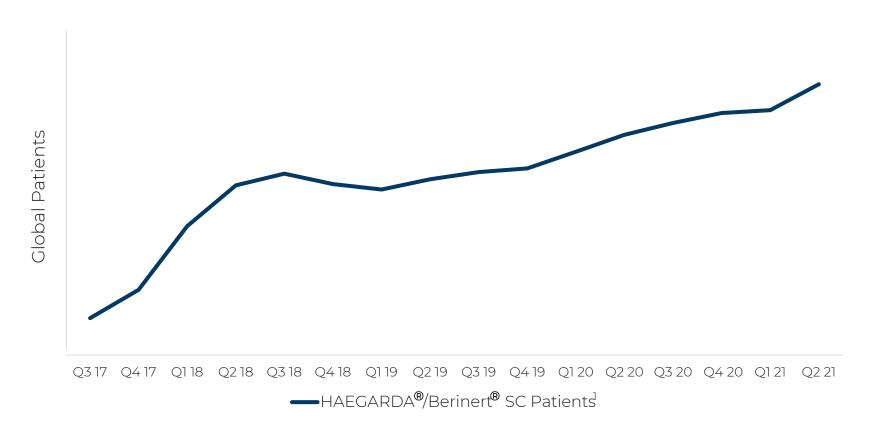
Neurocritical Care Society; Society of Critical Care Medicine; American College of Cardiology; American College of Chest Physicians; American Society of Gastrointestinal Endoscopy; American College of Surgeons
 Data on file – represents US market only

# HAEGARDA® /Berinert® SC

### Growth in the Face of Competition







### Regional Progress

- US: Most patients since launch
- EU/AU: New launches exceeding expectations
- Spain achieved 55% patient share<sup>1,2</sup> within a year of launch
- Five additional launches planned by end of 2022



<sup>&</sup>lt;sup>1</sup> Data on file

<sup>&</sup>lt;sup>2</sup> Patient share in the non-steroidal prophylaxis segment

### HAEGARDA® /Berinert® SC Growth Potential









 Prophylaxis segment continues to grow but ~60% of patients still on acute therapy

 HAEGARDA® /Berinert® SC has proven record of high efficacy and safety²

 Continue to see patients switch back from competing products to the benefits of HAEGARDA® /Berinert® SC¹

**Efficacy ultimately drives patient preference**. Patients define convenience as being free from attacks, not just frequency and ease of administration<sup>3</sup>. Prophylaxis treatment with **HAEGARDA® /Berinert® SC** addresses this need.

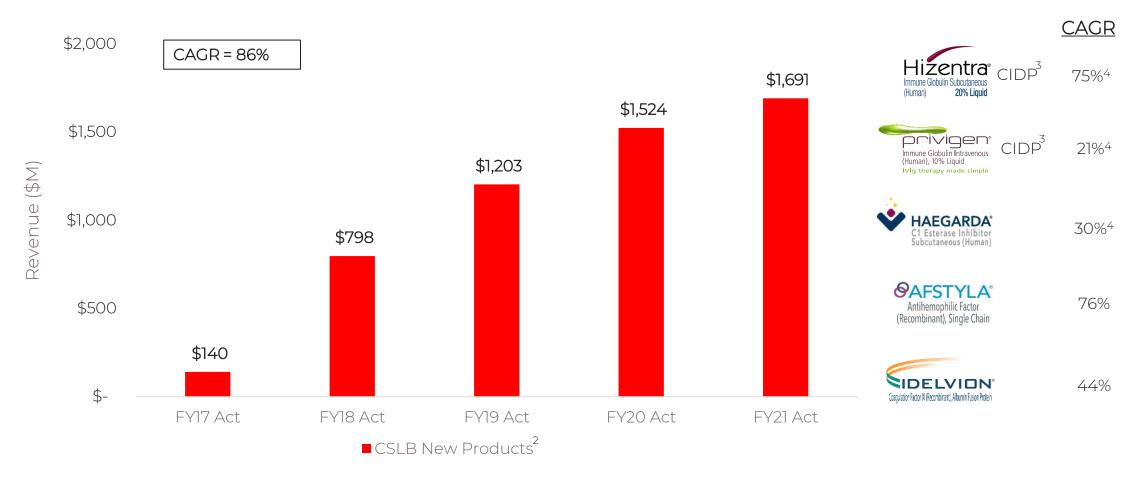


<sup>&</sup>lt;sup>1</sup> Data on file – Represents US, DE & ES. Includes all HAE markets, split on long term prophylaxis vs. on-demand

<sup>&</sup>lt;sup>2</sup> In the clinical trial, 95% median reduction in number of attacks in patients receiving 60 IU/kg of HAEGARDA® vs placebo, and a >99% median reduction in rescue medication use in patients receiving 60 IU/kg of HAEGARDA® vs placebo.

<sup>&</sup>lt;sup>3</sup> Per 2020 Harris Poll

# New Products Contributing Significantly to Growth<sup>1</sup>



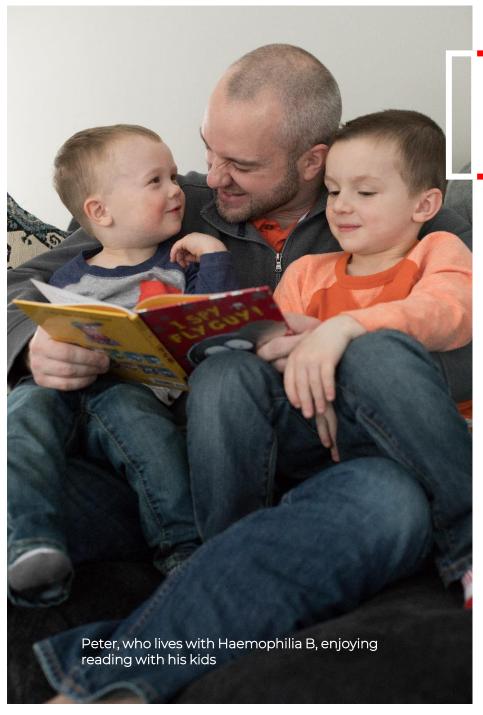
<sup>1</sup> Revenues shown at constant currency to remove the impact of exchange rate movements, facilitating comparability of operational performance.



<sup>&</sup>lt;sup>2</sup> CSLB New Products include Hizentra® CIDP, Privigen® CIDP, HAEGARDA®/Berinert® SC, AFSTYLA® & IDELVION®

<sup>&</sup>lt;sup>3</sup> CIDP revenue represents markets where the indication was recently acquired

<sup>&</sup>lt;sup>4</sup> CAGR calculated off base of FY18 when launch occurred



# Commercial Summary



Executing on strategies



Strong underlying demand across the portfolio



COVID restrained commercial activity



Balanced regional & key market growth



New products contributing significantly to growth

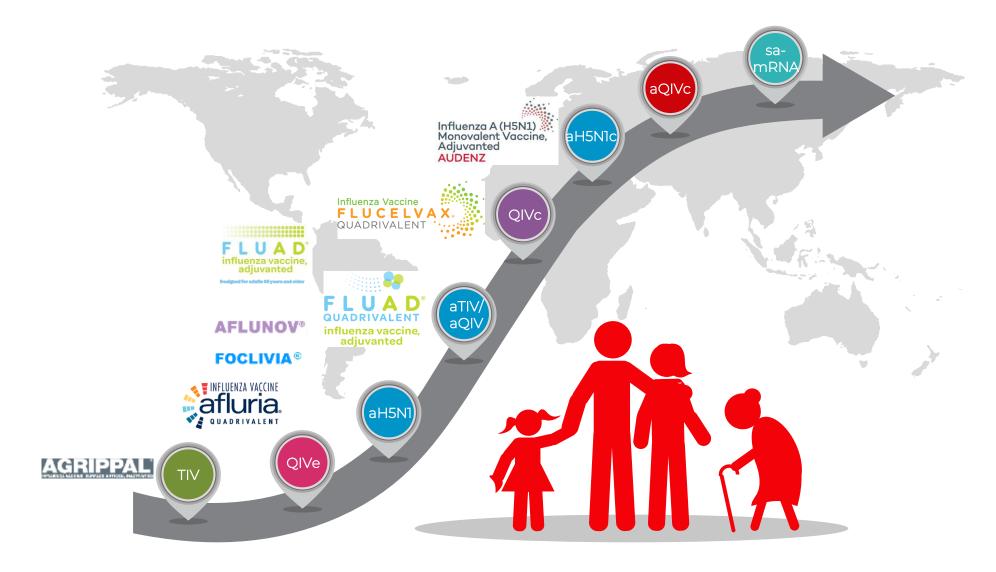


Robust new product pipeline to fuel growth





# Population Protection Through Innovation





# Segirus Milestones in FY21 & FY22 (to date)

#### FLUCELVAX® QUAD

- Paediatric efficacy study (2-17yrs) published in New England Journal of Medicine - 14 Oct 2021
- US 6mo+ age extension approval
- Regulatory approvals 2yr+ in US/EU/UK/CA, 9yr+ in AU (5 further regulatory approval submissions)
- Paediatric immunogenicity (6mo-4yr) met all endpoints

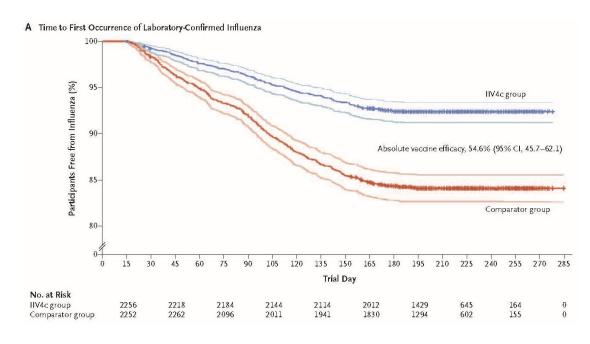
#### FLUAD® QUAD

• UK, NZ approval for 65yrs+ (2 further regulatory approval submissions)

#### aQIVc

- Phase II clinical trial standard dose completed
- Phase II clinical trial dose ranging study completed recruitment







# New Cell Culture Facility in Australia

### Tullamarine, Victoria

- Under construction open in 2026
- A\$800m capital investment from Seqirus
- Commercial export manufacturing facility
- Next-generation, cell-based seasonal influenza vaccines
- A\$800m/10 year supply agreement with Commonwealth for antivenoms, Q-fever vaccines, pandemic influenza vaccines





### Collaboration with BARDA

### Biomedical Advanced Research and Development Authority



Agreement to develop and evaluate 2 influenza A virus (H2Nx) vaccine candidates to support pandemic preparedness

- 1. Adjuvanted (MF59®) and cell-based based technologies
- 2. Self-amplifying mRNA (sa-mRNA) platform

US\$35M multi-year contract extends to clinical proof of concept early trials

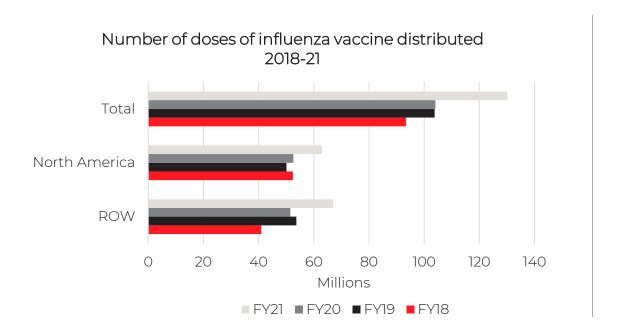


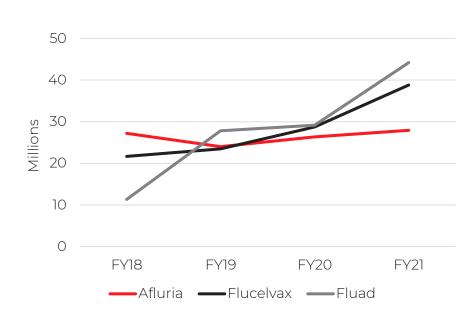
## Impact of COVID-19 on Influenza and Vaccination

Suppression of circulating influenza virus so far but ongoing concerns on potential of "twindemic"

- low level circulation
- bird and animal reservoirs remain

Strong demand for influenza vaccine – increased doses and differentiated products

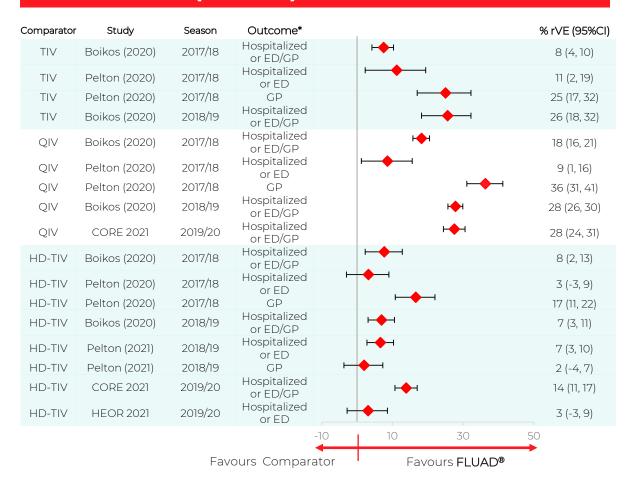






# Real World Evidence – Consistent Benefit of MF59® Adjuvant and Cell Technology over Multiple Seasons

### Fluad® (3 strain) – Benefit of MF59®



#### Flucelvax® - Benefit of Cell Culture

Comparator	Study	Season	Age Group	Outcome*			% rVE (95%CI)	
QIV	Boikos (2020)	2017/18	≥4	GP		<b>—</b>	<b>4</b> 36 (26, 45)	
QIV	Divino (2020)	2017/18	4-64	Hospitalization	<b>⊢</b>		14 (9, 20)	
QIV	Boikos (2021)	2018/19	≥4	Hospitalized or ED/GP	•		8 (7, 9)	
QIV	Krishnarajah (2021)	2018/19	4-64	Hospitalization	<b>—</b>		7 (0.1, 13)	
QIV	CORE (2021)	2019/20	≥4	Hospitalized or ED/GP	•		17 (16, 19)	
QIV	HEOR (2021)	2019/20	4-64	Hospitalization	<b>—</b>		5 (1, 10)	
				-10	10	30	50	
	Favours Comparator					Favours <b>FLUCELVAX®</b>		

\*Outcomes due to influenza or pneumonia

2017/18 was the first season a cell-based seed (H3N2) was included in FLUCELVAX®

Boikos, C. et al., (2020) CID 73:816-823 Pelton, S.I. et al., (2020) Vaccines 8:446 Pelton, S.I. et al., (2021) Vaccine 39:2396-2407

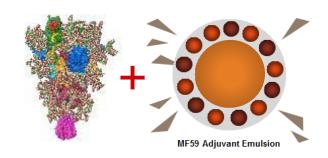
CORE (2021): Presented at ECCMID 2021, manuscript pending

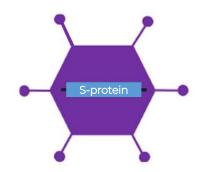
HEOR (2021): Manuscript pending

Abbreviations: CI - Confidence Interval; ED - Emergency Department; GP - General Practitioner; (r)VE - (relative) Vaccine Effectiveness; TIV /QIV - standard dose Trivalent/ Quadrivalent Vaccine; HD - High Dose



### CSL Strengths Applied to COVID-19





## University of Queensland

(V451)

Recombinant S-clamp protein MF59® adjuvant

Collaboration between UQ, CSL & AU Government Abandoned due to false positive HIV tests

### AstraZeneca

(AZD1222)

Recombinant replication competent vector that expresses S-protein

Manufacturing under contract to supply to AZ for AU

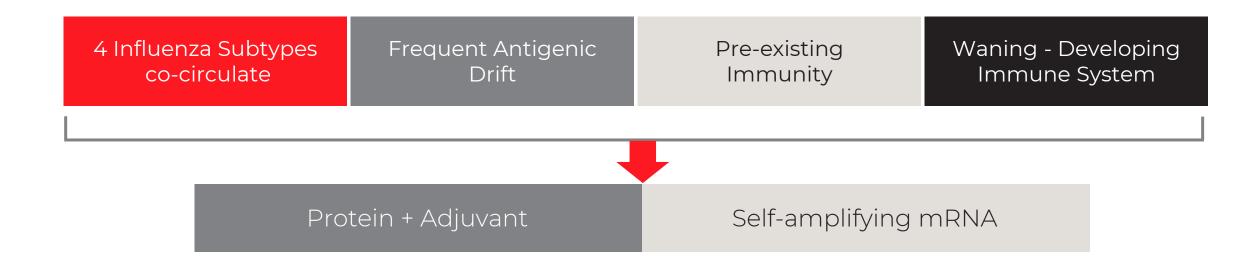


## What to Expect from Next-Generation Influenza Vaccines

aQIVc Self-amplifying mRNA

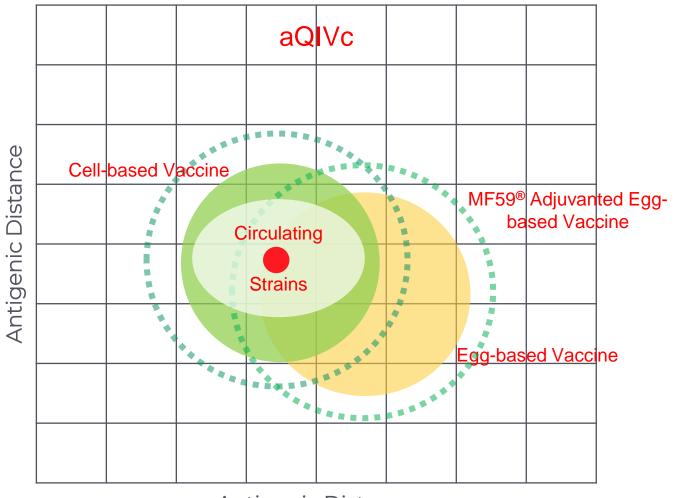


# Seqirus is Experienced in Protecting People from Seasonal Influenza Despite its Complicated Nature

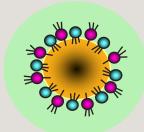




# Improving Influenza Vaccines by Combining Two Advanced Technologies







### MF59® Adjuvant

Increases "breadth" Increases antibody response Dose-sparing potential (pandemic)



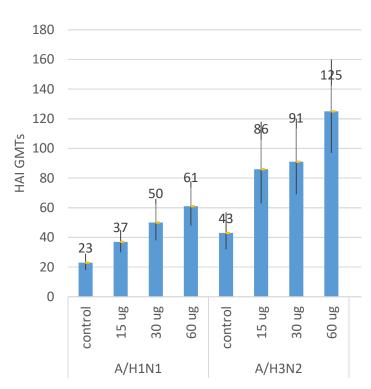
### Cell Culture

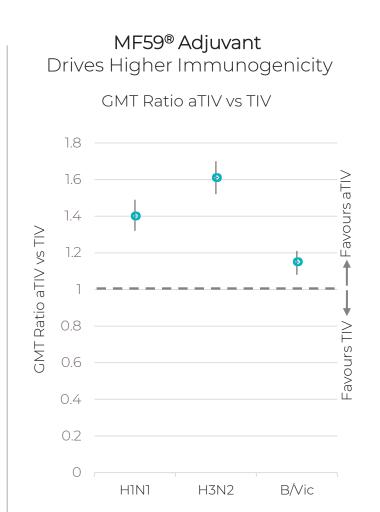
Closer match to circulating strain More efficient manufacture than egg Greater flexibility – faster in pandemic



### Pulling Key Levers to Further Improve Protein-based Influenza Vaccines

#### Higher Antigen Dose Drives Higher Immunogenicity Hemagglutination Inhibition Titers





- Higher antigen dose drives T immune response
- MF59® drives 1 immune response
- aQIVc combines benefits of adjuvant, dose and cell-derived antigen to increased influenza protection

Unpublished data, Segirus

### RNA-based Vaccines Have Shown Value in SARS-CoV-2 Pandemic



#### The mRNA vaccine revolution is the dividend from decades of basic science research

The Journal of Clinical Investigation 2021;131(19):e153721. https://doi.org/10.1172/JCl153721.

#### Now proven against coronavirus, mRNA can do so much more

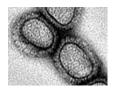


Vaccine research and development might never be the same again. By Elie Dolgin

Nature | Vol 589 | 14 January 2021 |



### Segirus Has a Long Research History in Self-amplifying mRNA





Research on viral targets (RSV, CMV, Flu, HIV) with multiple partners





H7N9 sa-mRNA vaccine made in 8 days from on-line sequence



H5N1 vaccine candidate generated



COVID vaccine candidate generated



2008 Initiation of sa-mRNA research

NOVARTIS

Flu vaccine development

2019 seasonal Flu into Development



2012 DARPA funds 2015 SEQ continues platform development



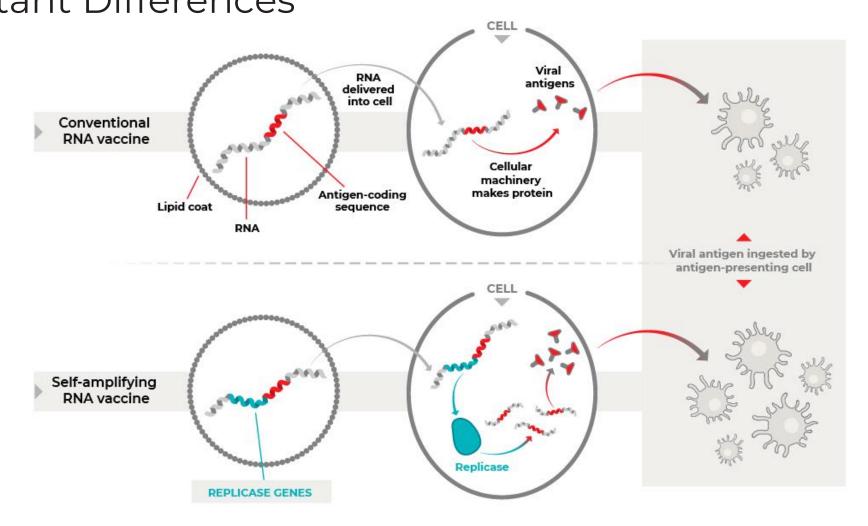








mRNA Technology – Two Main Approaches Have Important Differences





### Seasonal Influenza Challenges Differ from SARS-CoV-2



Flu is more complicated; may expect efficacy lower than for SARS-CoV-2



### sa-mRNA – Two Key Elements Drive Immune Responses

#### Self-amplifying mRNA payload

Monocistronic = 1 gene of interest encoded by mRNA

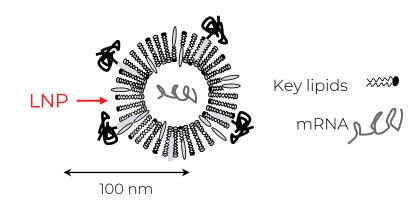
**Replicon Genes Gene of Interest** 

Bicistronic = 2 genes of interest encoded by mRNA

**Replicon Genes Gene of Interest 1 Gene of Interest 2** 

- Ability to include multiple antigens means vaccine can have greater control of gene expression with increased safety
- With lower dose it is easier to include additional antigens on the same sa-mRNA

#### Lipid Nanoparticle (LNP)

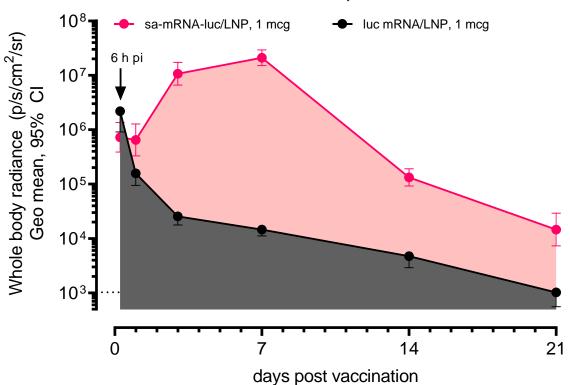


- Cationic Lipid is main component of LNP that mediates entry
- Cationic Lipid drives some reactogenicity, different companies have different lipids



### sa-mRNA Platform Expresses More Protein than First Generation mRNA

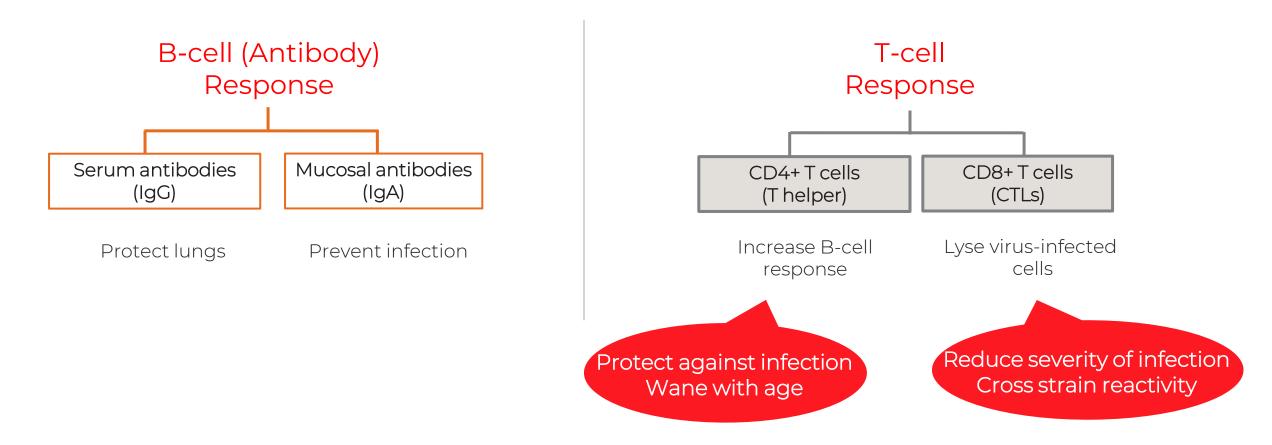
#### In vivo Protein Expression



- sa-mRNA expresses 100+ fold more protein than mRNA
- sa-mRNA expression prolonged compared to mRNA
- Lower potential dose is benefit for influenza vaccines that require multiple strains



### More Engaged Immune System = More Protective Response

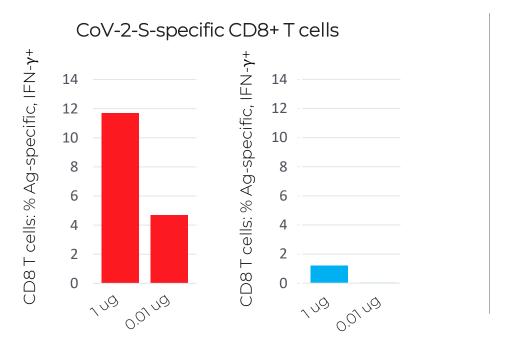


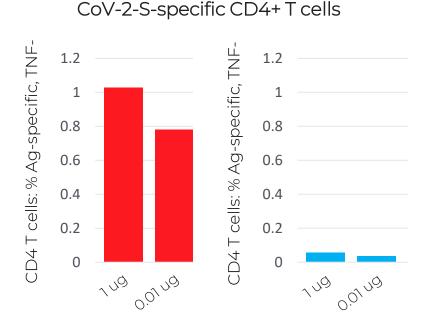
CD8+ T-Cell responses to conserved epitopes add a new protective layer



# sa-mRNA Platform Raises More Robust T-cell Responses (CD8+/CD4+) than mRNA

#### COVID sa-mRNA Vaccination Cellular Responses





- sa-mRNA > Moderna mRNA (~5x-8x) published cellular responses
- SI peptide mix used in similar experiments published by Moderna

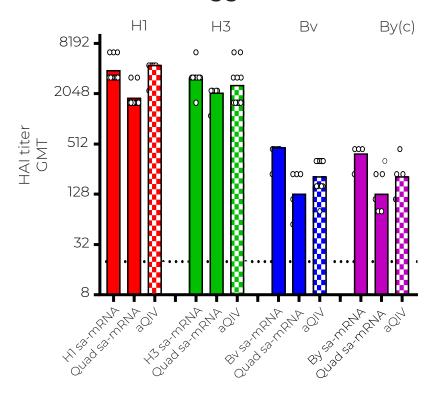


CoV-2-S sa-mRNA (Seqirus)CoV-2-S mRNA (Moderna\*)

<sup>\*</sup>Moderna data; Corbett, K.S. *et al.*, (2020) BioRxiv. Unpublished data, Segirus

### sa-mRNA Influenza Vaccine Induces Antibody Response Equal to MF59® Vaccine AND Superior CD8+ T-Cell Responses

#### Influenza Hemagglutination Inhibition

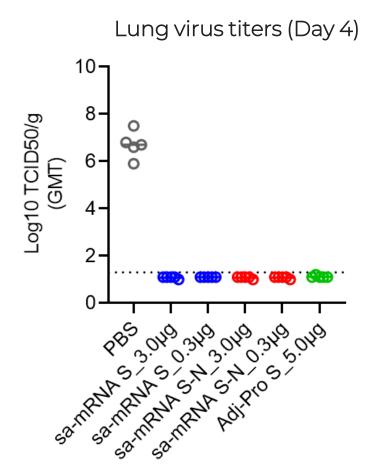


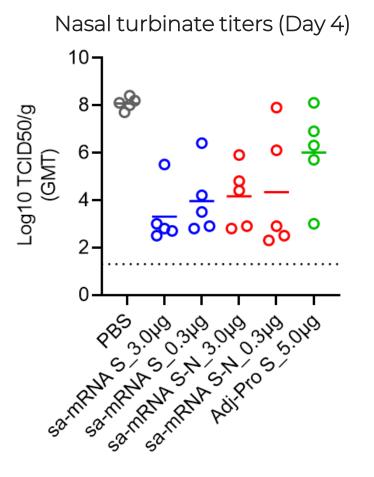
sa-mRNA Monovalent vaccine at 1 ug dose per target strain; sa-mRNA Quadrivalent vaccine at 1 ug dose per strain

- sa-mRNA quadrivalent vaccines raise robust Hemagglutination Inhibition (HAI) titers
- Hemagglutinin, Neuraminidase (NA), Matrix, and Nucleoprotein all raise strong CD8+ and CD4+ responses
- Neuraminidase raises strong neutralization and NA-blocking antibody responses



### sa-mRNA SARS-CoV-2 Vaccines Protect Hamsters Against Viral Challenge







Seqirus and Future Influenza Vaccine Portfolio



### FY22 Segirus Milestones

#### FLUCELVAX® QUAD

- Australia 2yr+ age extension approval
- Argentina 6mo+ age extension approval

#### FLUAD® QUAD

Adult 50-64yr immunogenicity study start

#### aQIVc

Phase II Older Adult study results

#### Self-amplifying mRNA

Completion of GLP Tox study



### The Promise and Challenges of New Influenza Vaccines

aQIVc has the potential to be the most effective differentiated influenza vaccine with currently approved technology

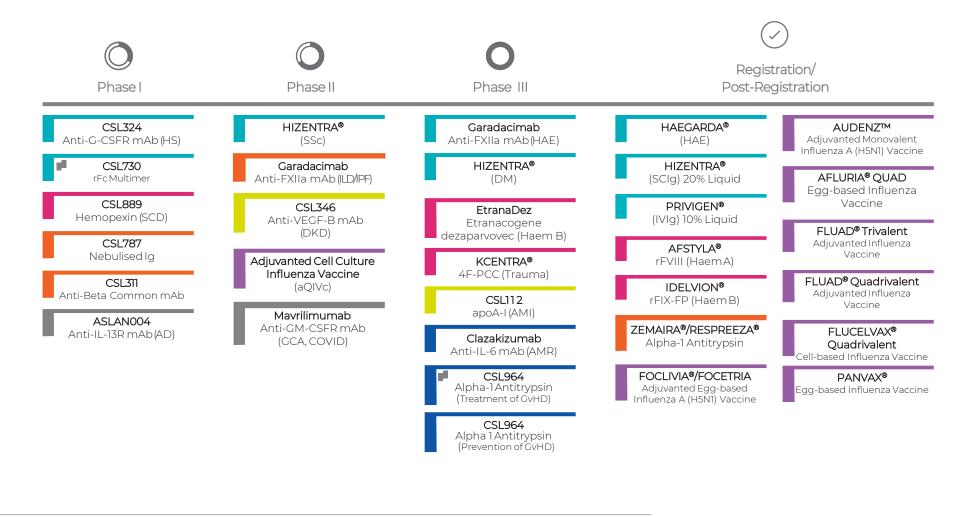
sa-mRNA provides great promise for influenza and is a high priority project for CSL/Seqirus

- Potential efficacy benefit, enhanced readiness (speed), simplification of manufacturing, antigen-agnostic technology readiness
- Challenges in influenza include efficacy (*influenza is not SARS-CoV-2*), side-effects, stability, presentation





#### R&D Portfolio – FY22



Cardiovascular & Metabolic

Transplant



Haematology

Outlicensed Programs

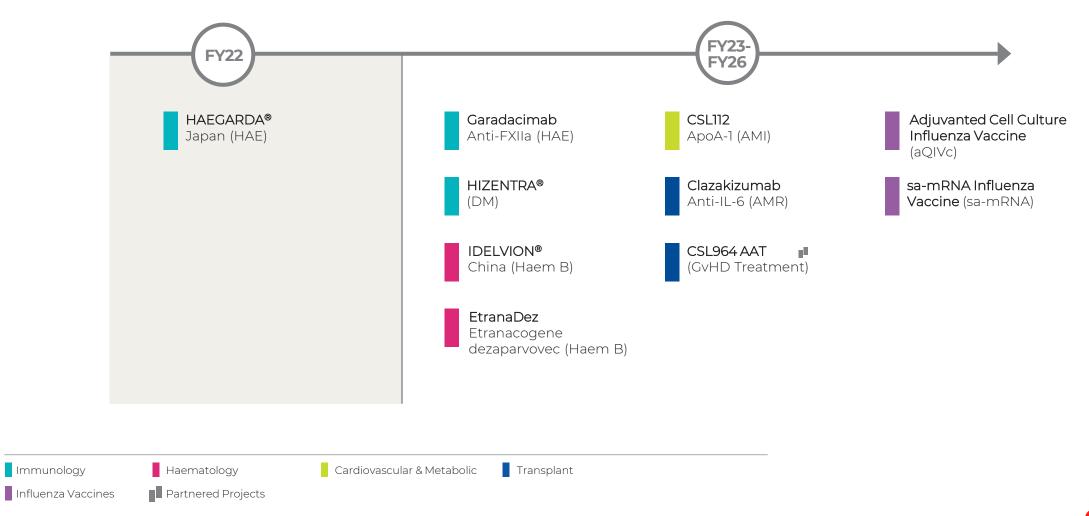
Respiratory

■ Partnered Projects

Immunology

Influenza Vaccines

### Significant Target Launch Dates





### R&D Portfolio Highlights – FY22



- Garadacimab (Anti-FXIIa) complete Phase III HAE study enrolment
- CSL324 (Anti-G-CSFR) complete PK/Ethnicity study for SC formulation and inclusion of Japan
- HAEGARDA® submission to PMDA for treatment of HAE
- HIZENTRA® SID CLL initiate Phase III study



- CSL311 (Anti-Beta Common) initiate POM study in mild asthmatic patients
- Garadacimab (Anti-FXIIa) initiate Phase II IPF study
- CSL787 (Neblg) complete Phase I study



#### Haematology

- KCENTRA® initiate Phase III study for treatment of massive haemorrhage associated with severe traumatic injury
- EtranaDez (Haem B gene therapy) BLA/MAA submission (US/EU)
- IDELVION® rFIX-FP (Haem B) China CTA filing
- AFSTYLA® rFVIII (Haem A) China IND submission



## Cardiovascular and

- CSL112 (apo A-I) complete 3<sup>rd</sup> interim analysis
- CSL346 (Anti-VEGF-B) complete enrolment Phase II POC study for DKD



CSL964 (AAT) for prevention of GvHD initiate Phase III study



- aQIVc (cell antigen + MF59®) complete Phase II safety & immunogenicity study
- FLUCELVAX® Quadrivalent US approval 6mo+ indication
- FLUCELVAX® QUAD Australia 2yr+ extension approval
- FLUAD® Quadrivalent Adults 50-64yr initiate Phase III study



