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ASX Announcement

For immediate release 22 October 2024

Research & Development Investor Briefing

CSL Limited (ASX:CSL; USOTC:CSLLY) is holding its 2024 Research & Development Investor Briefing today commencing at 9.00am Australian Eastern Daylight Time.

This briefing will be webcast on the Company website at www.csl.com in the 'Investors' section. An archived copy of the webcast will be uploaded to the site later today.

The presentation materials are attached for the information of investors and can also be accessed in the 'Investors' section of the Company website at www.csl.com.

Authorised by
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Zahra, Living with
Hereditary Angioedema

R&D Investor Briefing

October 22, 2024

Legal Notice

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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.

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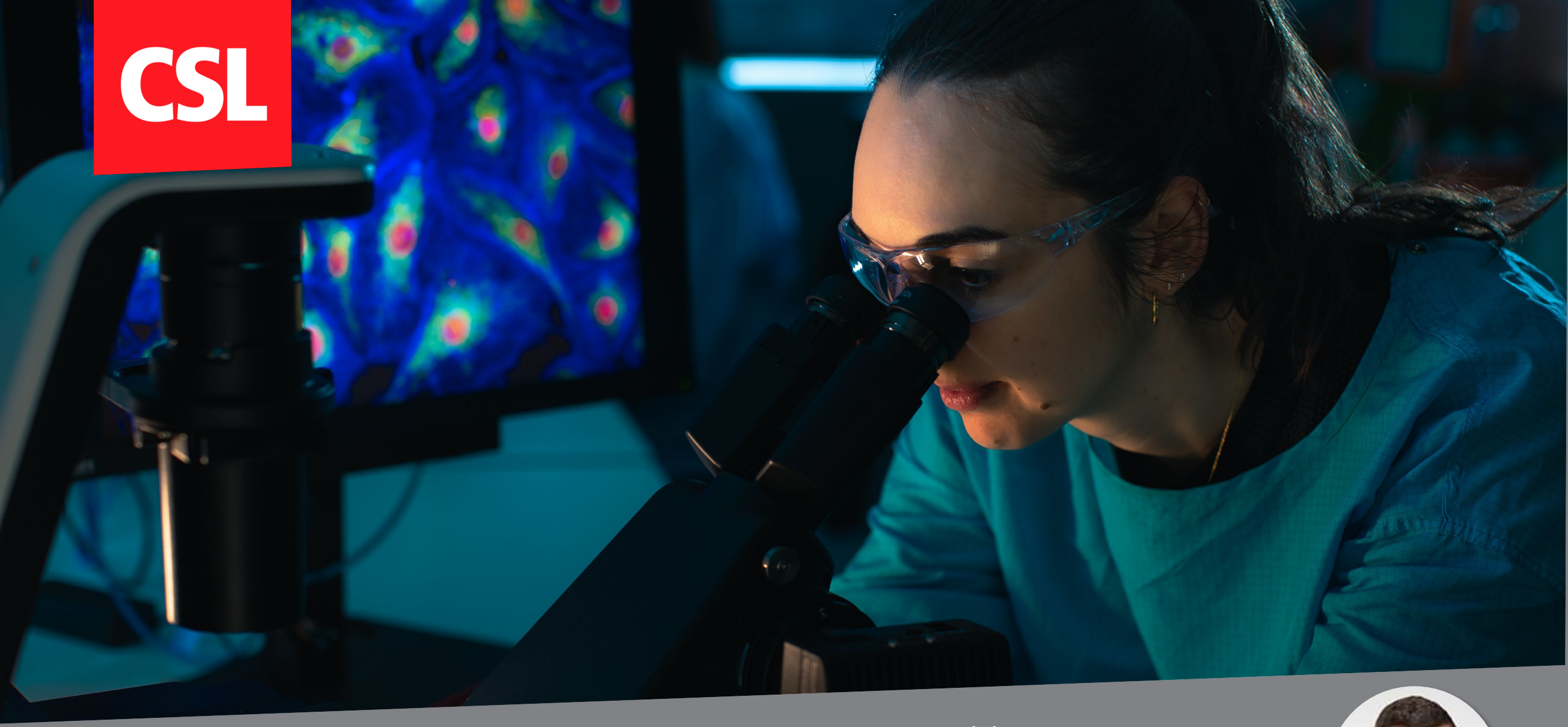


Introduction

William Mezzanotte MD, MPH
Executive Vice President
Head of R&D

CSL

Agenda

01 **Welcome**

Chris Cooper
Head Investor Relations

02 **Introduction & Portfolio Highlights**

Bill Mezzanotte MD, MPH
Executive Vice President
Head of R&D

03 **Plasma Products & Immunoglobulins**

Douglas Lee PhD
Senior Vice President
Plasma Product Development

04 **Therapeutic Development**

Marie-Pierre Hellio MD, PhD
Senior Vice President
Strategic Development

05 **Vaccines Development**

Jon Edelman MD
Senior Vice President
Vaccines Innovation Unit

07 **Innovation & Sustainability**

Deirdre BeVard
Senior Vice President
R&D Strategic Operations

08 **Looking Forward & Summary**

Bill Mezzanotte

09 **Q&A**

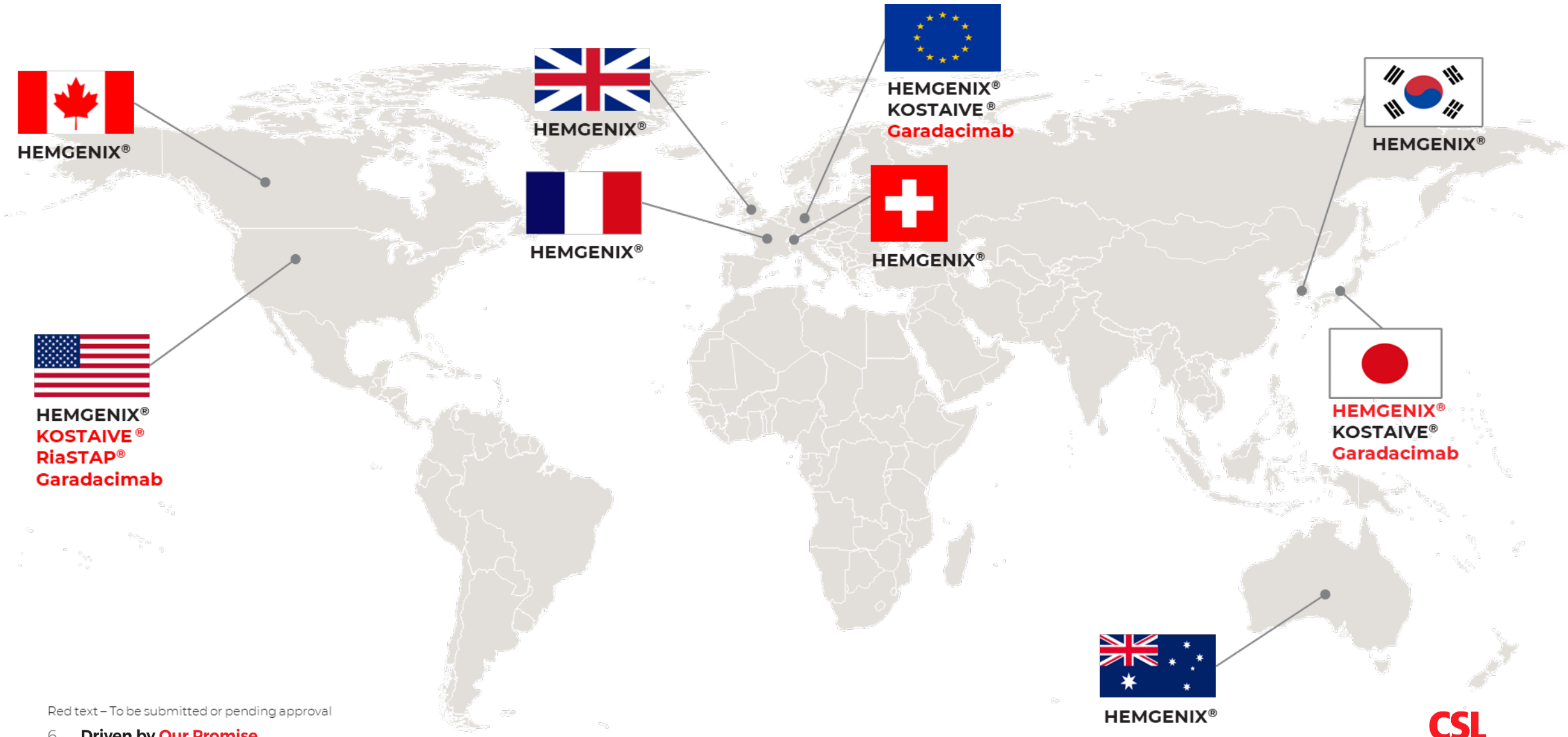
Panel

Dates are all Calendar Years unless otherwise noted

Key Takeaways

- **R&D continues to invest and innovate** (SID, Nebulised Ig, Horizons 1 & 2, sa-mRNA) in our core Ig, plasma & vaccine platforms to support future growth
- We are **relentlessly focused on rapid advancement** of our research & early development programs towards late-stage development & registration
- **HEMGENIX®, KOSTAIVE®, RiaSTAP® & garadacimab** are all advancing toward registration & approval for key indications in key regions
- We have experienced a few late-stage setbacks (KCENTRA® Trauma, HIZENTRA® DM, clazakizumab AbMR), however each of these products have promising follow-on indications which we are actively pursuing
- We have **exciting, novel Phase II** (e.g. Vamifeport, Hemopexin) and **Phase III programs** (e.g. aTIVc, CSL964, clazakizumab, HIZENTRA® POTS) to add incremental value to patients & CSL

Key Submissions and Approvals



Red text – To be submitted or pending approval

R&D Portfolio Highlights – FY24

Cardiovascular & Metabolic

- **CSL112 (ApoA-1) AMI** Phase III top line results
- **Clazakizumab (ESKD)**
  - Phase IIb complete
  - Phase III first patient in

Immunology

- **Garadacimab (Anti-FXIIa) HAE**
  - EU, US & JP submissions
- **HIZENTRA® DM** Phase III enrolment complete
- **HIZENTRA® PFS 50mL**
  - US Launch
  - EU submission
- **Anumigilimab (Anti-G-CSFR) HS** Phase II study first patient in*

CSL Behring Horizon 2

- Ongoing pre-clinical studies with pilot plant materials
- Ongoing HA engagement

Haematology

- **IDELVION® China** Phase III first patient in
- **Vamifeport (SCD)** last patient out
- **CSL889 (Hemopexin) SCD** Phase I top line results

Nephrology & Transplant

- **Clazakizumab (Anti-IL-6) ca-AbMR** Phase III study 200 patients enrolled*
- **CSL964 (Treatment of aGvHD)** Phase III top line results
- **FILSPARI® (sparsentan) (IgAN)** EU CMA
- **VELPHORO®** China launch
- **VELTASSA®**
  - AU Launch
  - US & EU paediatric approval

Respiratory

- **Trabikibart (Anti-Beta Common) ASTH** Phase I study complete
- **Garadacimab (Anti-FXIIa) IPF/ILD** Phase IIa study complete
- **CSL787 (Neb Ig)** Phase I study complete

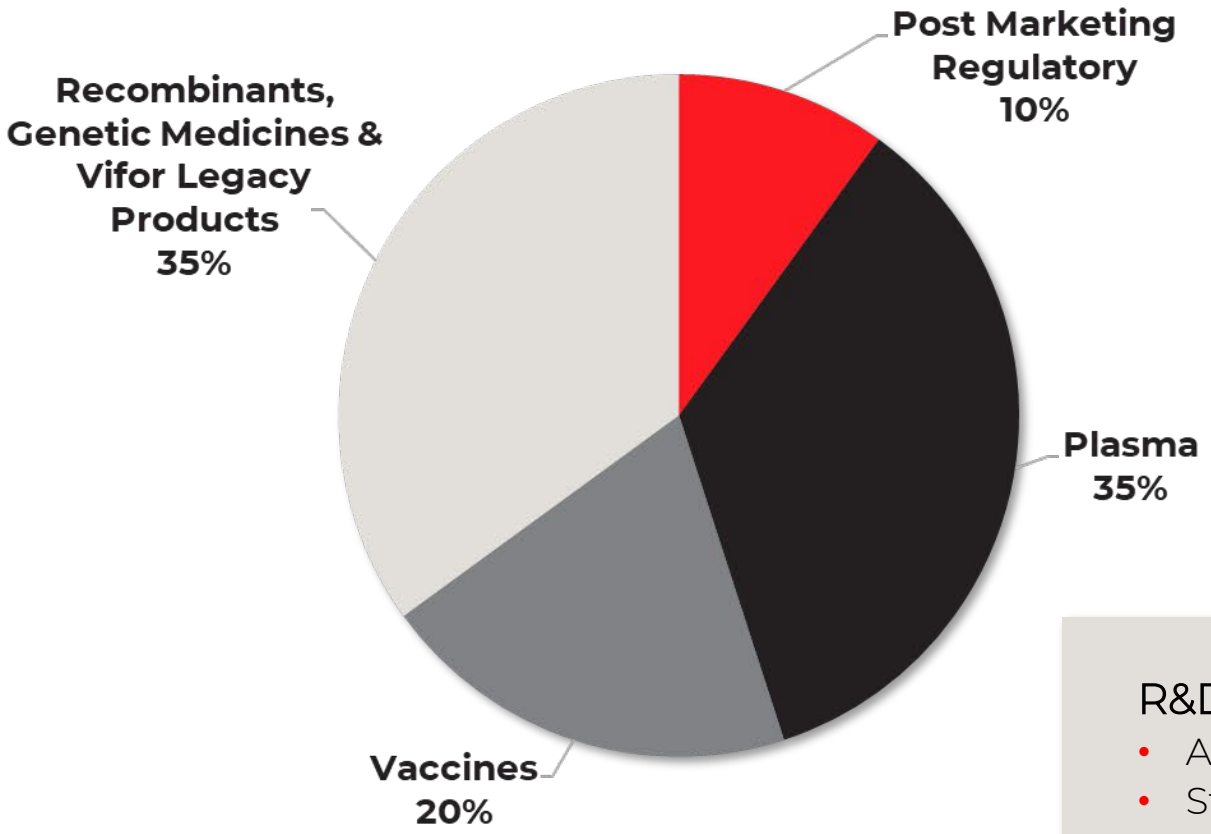
Vaccines

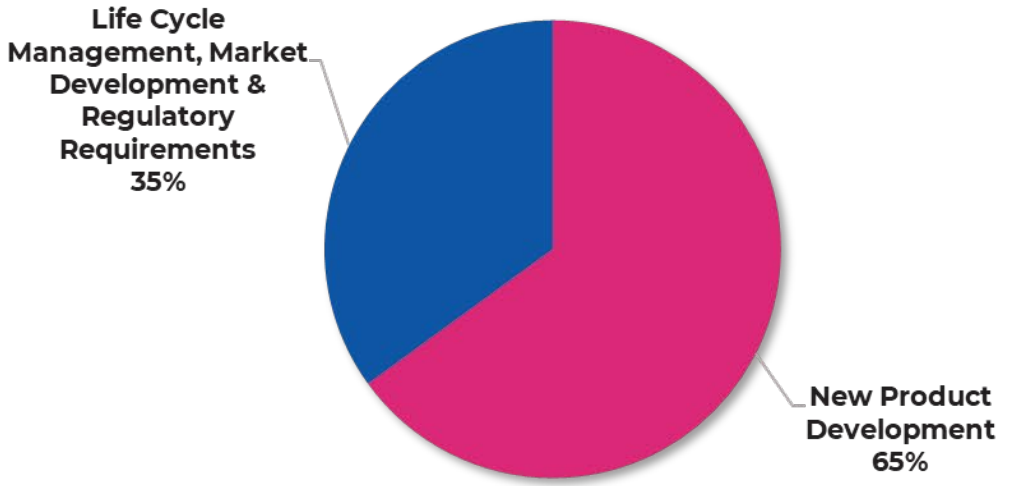
- **aQIVc (Adjuvanted Cell-based Quadrivalent Influenza Vaccine)** Phase III study 50yr+ first patient in
- **KOSTAIVE® sa-mRNA** (COVID)
  - JP approval
  - US† & EU submissions
- **CSL406 sa-mRNA (H5N1) Flu** Phase I first patient in
- **CSL400 sa-mRNA Quad Flu** Phase I first patient in
- Transition of **QIV to TIV** in US

* Program stopped; † Delayed to FY25

Abbreviations: AU – Australia; aGvHD acute Graft versus Host Disease; ca-AbMR - Chronic Active Antibody-Mediated Rejection; DM – Dermatomyositis; ESKD – End Stage Kidney Disease; EU – Europe; HA – Health Authority; HAE – Hereditary Angioedema; HS – Hidradenitis Suppurativa; IgAN - IgA Nephropathy; ILD – Interstitial Lung Disease; IPF - Idiopathic Pulmonary Fibrosis; JP – Japan; Neb Ig - Nebulised Ig; PFS – Pre-Filled Syringe; sa-mRNA – Self-Amplifying messenger RNA; RNA – Ribonucleic Acid; SCD – Sickle Cell Disease; US – United States

R&D Investment Allocations





R&D Financial Stewardship

- Active Portfolio Management
- Strategic Partnerships
- Productivity Gains
- Gated spend in development and in large trials (futility analyses)

Streamlining Our Therapeutic Areas and Platforms

Therapeutic Areas

- Immunoglobulins
- Transplant & Immunology
- Haematology
- Cardiovascular & Renal
- Vaccines

Platforms

- Plasma Protein Technology
- Recombinant Protein Technology
- Genetic Medicine
- Vaccines Technology

Plasma Proteins & Immunoglobulins

Douglas Lee PhD
Senior Vice President
Plasma Product Development
CSL

Focus on Immunoglobulins (Ig) and Plasma Product Development

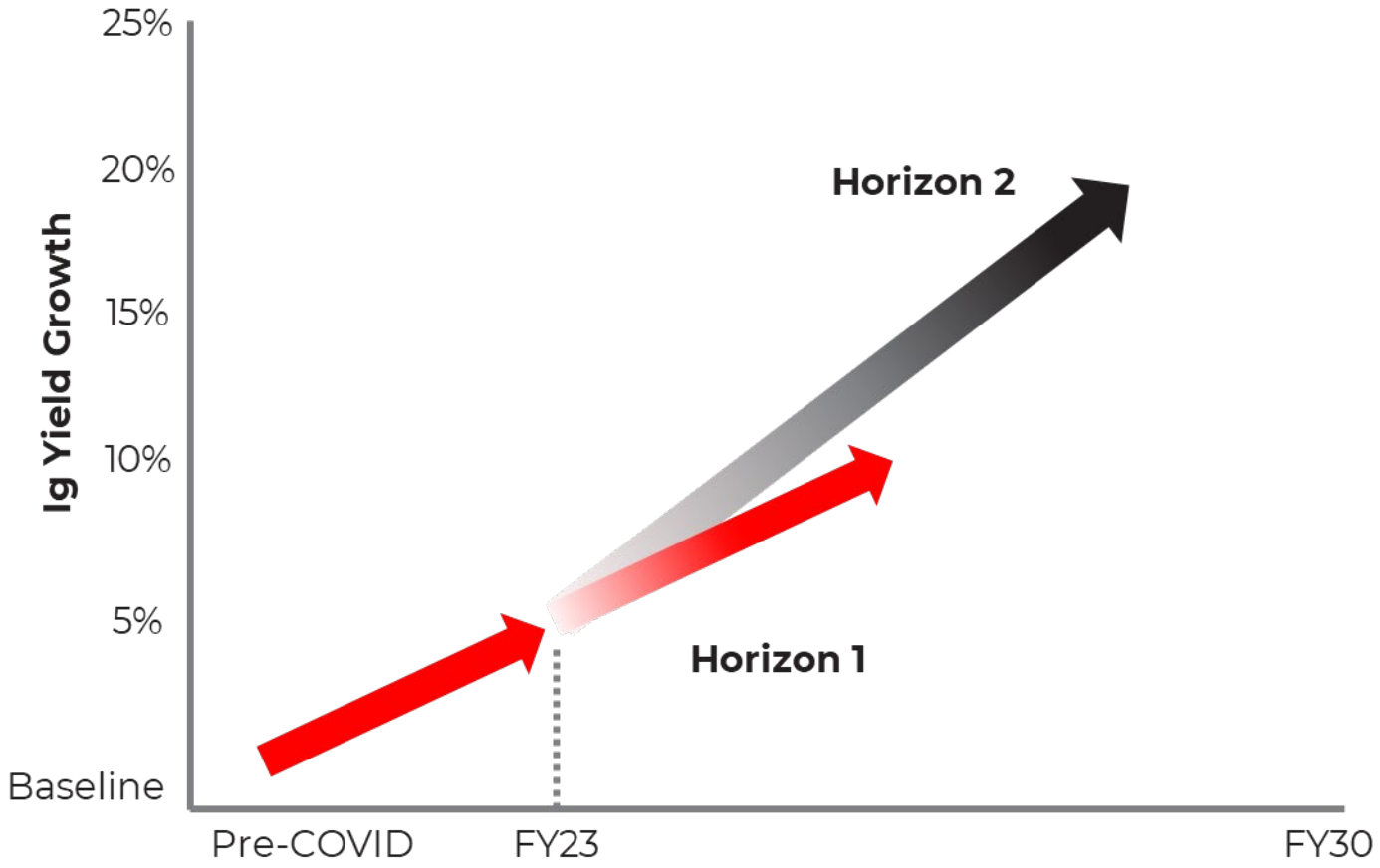
Growing on a Strong IgG Foundation

- Strengthen Our Core
- Sustainable Growth

Continuing to invest in Plasma Product Development

- New Products
- Product Lifecycle
- Process Science driving Continuous Innovation

Ig Yield Maximisation Strategy*



Horizon 1

- Continuous Improvement: Yield and capacity improvement initiatives focusing on current PRIVIGEN® & HIZENTRA® process

Horizon 2

- Industry Leadership: Proprietary and industry disruptive Ig process providing for greater yield improvements

* Illustrative only. Subject to success and timing of R&D activities and decisions of HAs

Horizons 1 & 2 – Meeting Patients' Future Ig Needs

Strengthen Our Core

Horizon 1 - Gaining with our Current Processes

- Target maximising yields with minimal changes to current process
- Leverage process analytics to identify new opportunities for improvement
- Reduce regulatory complexity

privigen®
Immune Globulin Intravenous (Human), 10% Liquid

Hizentra®
Immune Globulin Subcutaneous (Human) 20% Liquid

FY25 R&D Deliverables
- Complete toxicology package
- Process robustness package
- Health Agency interactions

Horizon 2 - The Future of Ig Processing

- Novel proprietary process - high Ig yields
- Complements current process
- Provide product comparable to current PRIVIGEN® & HIZENTRA® products
  - Safety
  - Purity
  - Quality
- Smaller footprint
- Requires new regulatory filing
- Multi-year phased introduction

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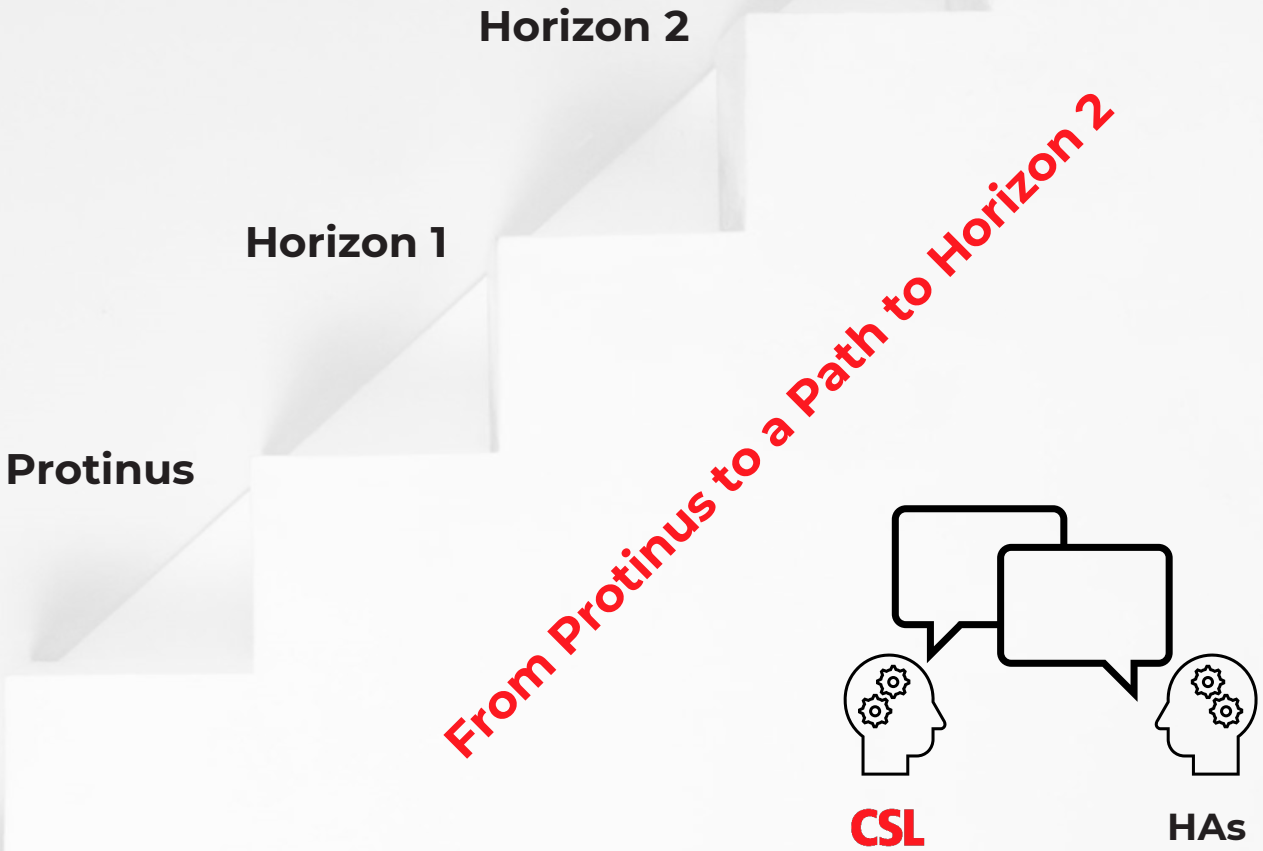
Horizons 1 & 2 - A Purposeful, Collaborative Regulatory Path

- Partner with Health Authorities (HAs) by providing robust analytical programs & non-clinical data packages
- Leverage state-of-the-art analytics to deliver robust process control strategies
- Listen to HAs to understand their potential concerns early in development process and address them proactively



Improving Patient Options – HIZENTRA® Pre-Filled Syringe (PFS)

Product Lifecycle

Fast, simple and convenient for patients

- First & only PFS available for patients using SCIg
- Ease of Use - no vial transfer or preparation needed
- Convenience – patients can self-administer
- Flexible – patients can tailor treatment to their schedules & needs
- Fewer supplies may reduce steps, effort, and product waste
- Less risk of contamination or breakage
- Available in multiple volumes to fit patients' individual needs*
  - 1g/5mL, 2g/10mL, 4g/20mL, 10g/50mL

2024					2025			
January	March	April	May	August	January	February	April	July+
North America (full launch)	Denmark Mexico	Argentina	Norway	Japan	Germany	Italy Greece	United Kingdom	Additional International Markets

* Not all PFS options will launch in every affiliate
Abbreviations: SCIg – Subcutaneous Immunoglobulin

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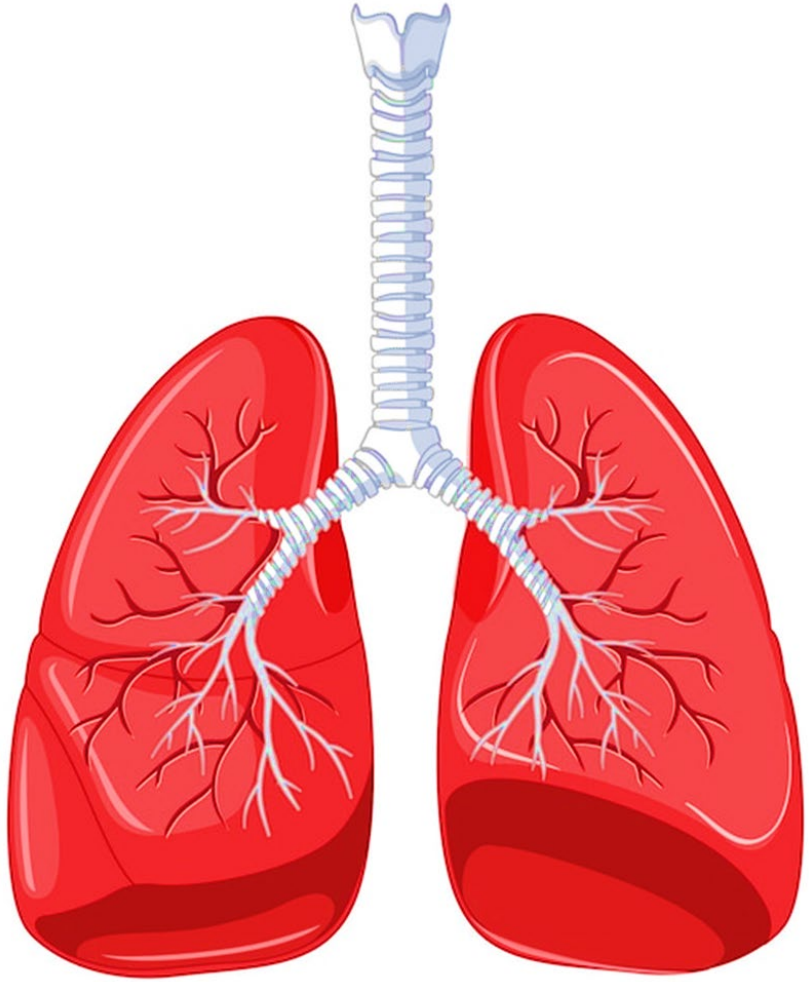
Nebulised IgG (CSL787)

Strengthen Our Core

CSL787 combines advanced plasma-based therapy with cutting-edge delivery technology

- Unique formulation designed for lung delivery
- State-of-the-art nebuliser to deliver this new product
- Innovative combination of IgG composition & inhalation technology
  - Maintains IgG molecular integrity to ensure IgG retains natural binding properties
  - Provides appropriate physicochemical properties of the nebulised particle for effective drug delivery



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New Products from Plasma

Growing on a Strong IgG Foundation

- Strengthen Our Core
- Sustainable Growth

Continuing to Invest in Plasma Product Development

- New Products
- Product Lifecycle
- Process Science driving Continuous Innovation

Optimising RiaSTAP® (CSL511) & Hemopexin (CSL889)

Product Lifecycle

RiaSTAP® (CSL511)

- Introduction of 2nd virus reduction step
- Established GMP-ready commercial facility for new CSL511 manufacturing process & validated improved process
- Process changes submitted as Type II variation for RiaSTAP® & Haemocomplettan® P
- First commercial manufacturing campaign completed confirming robustness of process

CSL511 Process EU Approved – Sep 2024

Hemopexin (CSL889)

- New plasma protein characterised by CSL Research
- Phase II manufacturing in progress
- State-of-the-art proprietary process with small operational footprint
- Current development focused on final commercial process for Phase III clinical study materials

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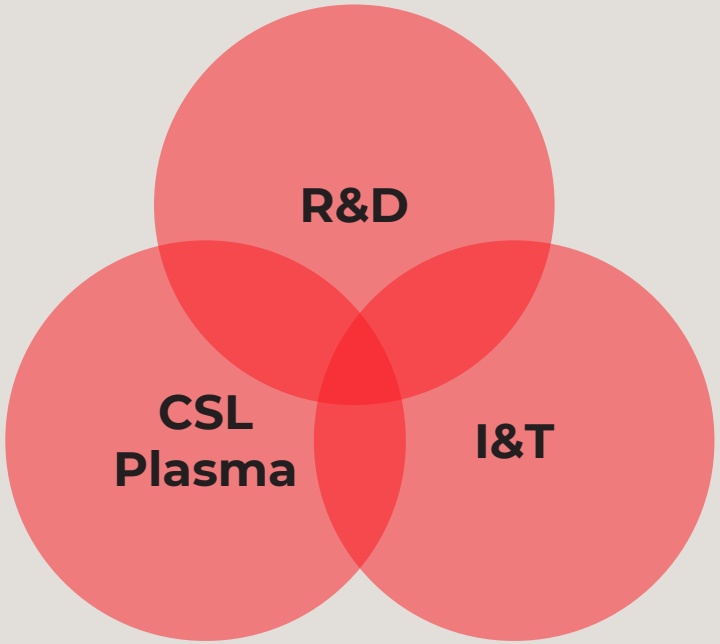
Plasma Innovation Platform Strategy Group (PSG)

Enterprise Collaboration for Innovation

Process Science driving Continuous Innovation

Re-imagining plasma donation through a progressive lens of digitisation, science, and regulatory policy to provide for the needs of our donors & patients while driving value for CSL

- Drive breakthrough innovation, unconstrained by industry norms
- PSG champions for delivery teams, removing roadblocks & managing relevant cross-organisational stakeholders



- Optimise plasma protein collection allowing for yield growth
- Drive development strategies to improve donor safety & experience
- Help CSL to improve the donor experience

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Plasma Product Development: Continuous Innovation

- **Building on a Legacy of Innovation:** Strong Foundation for Future Growth in Plasma Products
- **Immunoglobulins:** Vital for Patients and Key to CSL's Future Growth with **New Innovation Opportunities**
- **Novel Technological Innovations:** Cutting-Edge Technologies for Existing Products
- **Our R&D Efforts:** Demonstrating Our Commitment to Patients & Donors

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Pete, Living with Haemophilia B

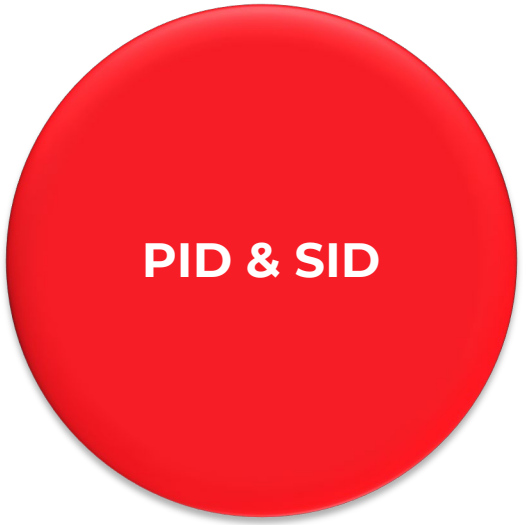
Therapeutic Development

Marie-Pierre Hellio MD, PhD
Senior Vice President
Strategic Development
CSL

Immunoglobulin Replacement and Immunomodulation

IVIg & SCIg Usage

Immuno-replacement



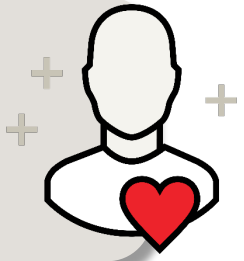
Immuno-modulation

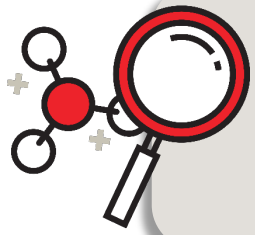
Abbreviations: IVIg – Intravenous Immunoglobulin; PID – Primary Immune Deficiency; SCIg – Subcutaneous Immunoglobulin; SID – Secondary Immune Deficiency

HIZENTRA® in Secondary Immune Deficiency (SID)

Significant unmet needs persist in SID

- Hematologic cancer & therapy reduces B-cells & antibodies
  - Leading to SID and serious or recurrent infections
- Infections major cause of death among CLL & MM patients





New approaches required

- Infection prevention by IgRT well documented
- Supported by clinical guidelines worldwide & non-US indications
- Placebo use complicates randomised trials in patients with high unmet need

Sustainable development

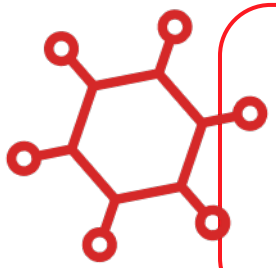
- Actively discussing novel data generation approaches with HAs
- New clinical development avenues

Abbreviations: CLL –Chronic Lymphocytic Leukaemia; IgRT– Immunoglobulin Replacement Therapy; MM – Multiple Myeloma

HIZENTRA® in Post-COVID POTS – a Debilitating "Long COVID" Disease

Postural Orthostatic Tachycardia Syndrome (POTS)

- Dysregulation of autonomic nervous system
- Symptoms include lightheadedness, palpitations, fatigue, "brain fog", GI dysfunction
- No approved therapies; only symptomatic treatments available

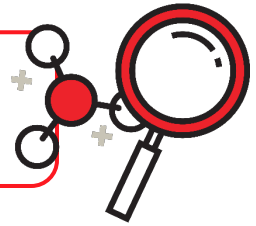


COVID-19 has dramatically changed POTS epidemiology

- Post-COVID sequalae experienced by 2-14% of patients[1]
  - Mostly in younger women with no prior comorbidities[1]
- Disability similar to COPD & heart failure limiting employment & ADLs[2]

IgG is a promising potential treatment for post-COVID POTS

- Aetiology hypothesised to be immune dysregulation & autoantibodies[3]

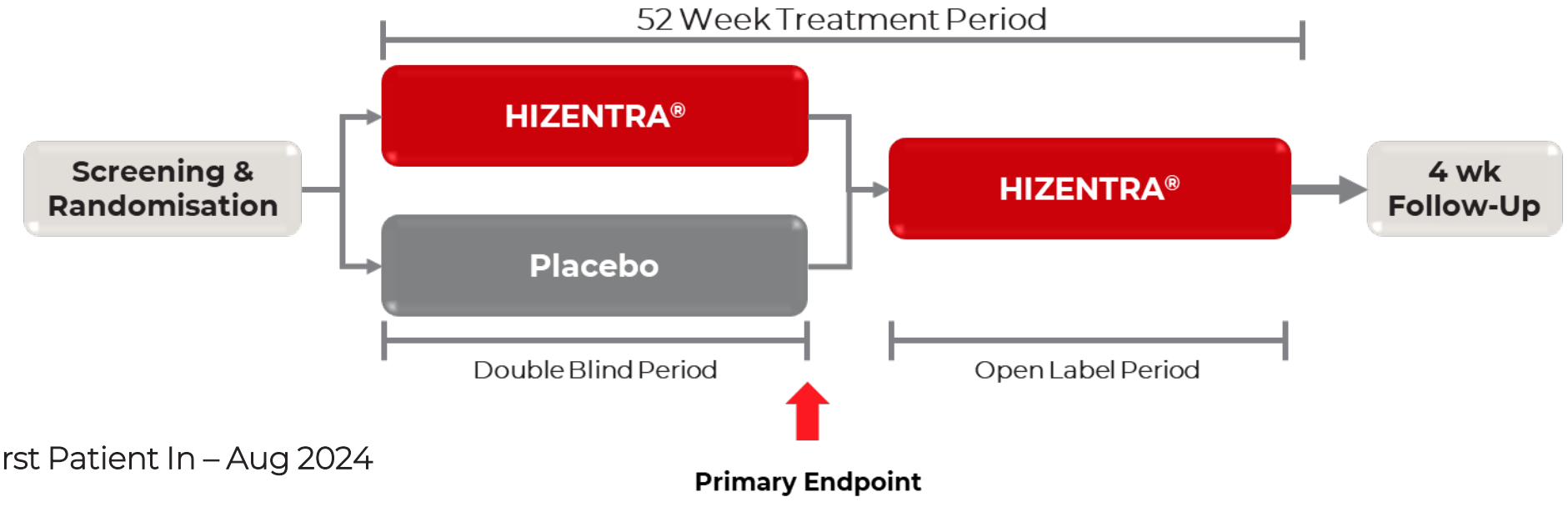


Abbreviations: ADLs – Activities of Daily Living; COPD – Chronic Obstructive Pulmonary Disease; GI- Gastrointestinal

Sources: 1. Ormiston C.K. *et.al.*, (2022) *Heart Rhythm* 19(11):1880-1889; 2. Benrud-Larson, L.M. *et al.*, (2002) *Mayo Clin Proc* 77(6):531-537; 3. Wallukat, G. *et al.*, (2021) *J Trans Autoimm* 4

HIZENTRA® Phase III Study in Patients with Post-COVID POTS

- Adult patients (n=177) with post-COVID POTS
- **Primary Endpoint:** Proportion of patients not meeting POTS diagnostic criteria
- **Key Secondary Endpoints:** Absolute HR change, COMPASS 31 total, COMPASS 31 orthostatic intolerance symptoms

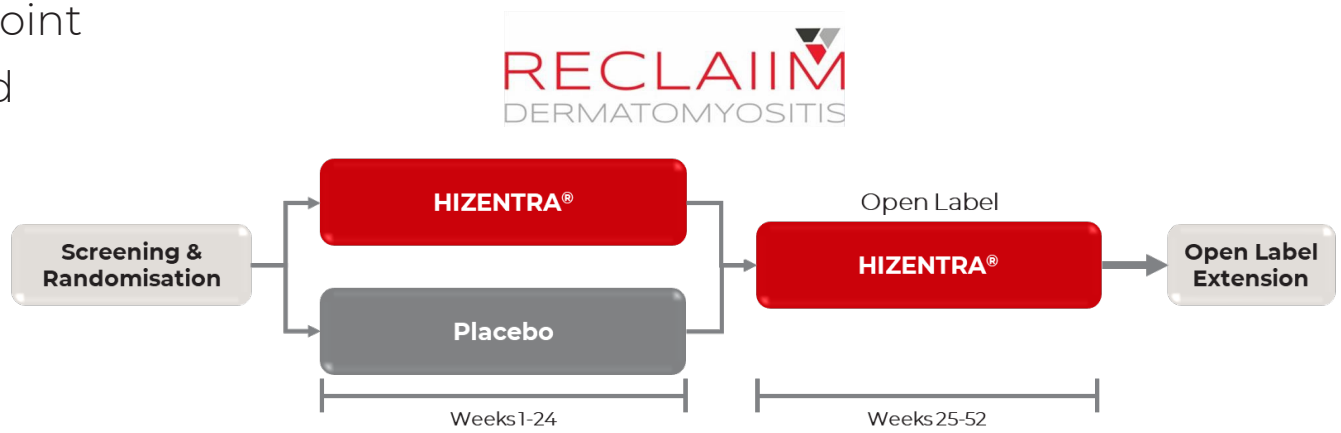


Phase III First Patient In – Aug 2024

Abbreviations: COMPASS - Composite Autonomic Symptom Score; HR – Heart Rate

HIZENTRA® Phase III Study in Patients with Dermatomyositis

- 134 treatment-experienced adult patients with dermatomyositis enrolled & reached primary endpoint
- **Primary endpoint:** responder rate (%) of HIZENTRA® recipients vs. placebo
  - Responder defined by TIS of ≥ 20 points* at 2 timepoints up to week 25 & completed 24 weeks of randomised treatment without use of rescue corticosteroid treatment
- Study did not meet primary efficacy endpoint
- HIZENTRA® response rate within expected range; unexpected high response rate in placebo group
- No new safety findings
- Plans to terminate study are underway

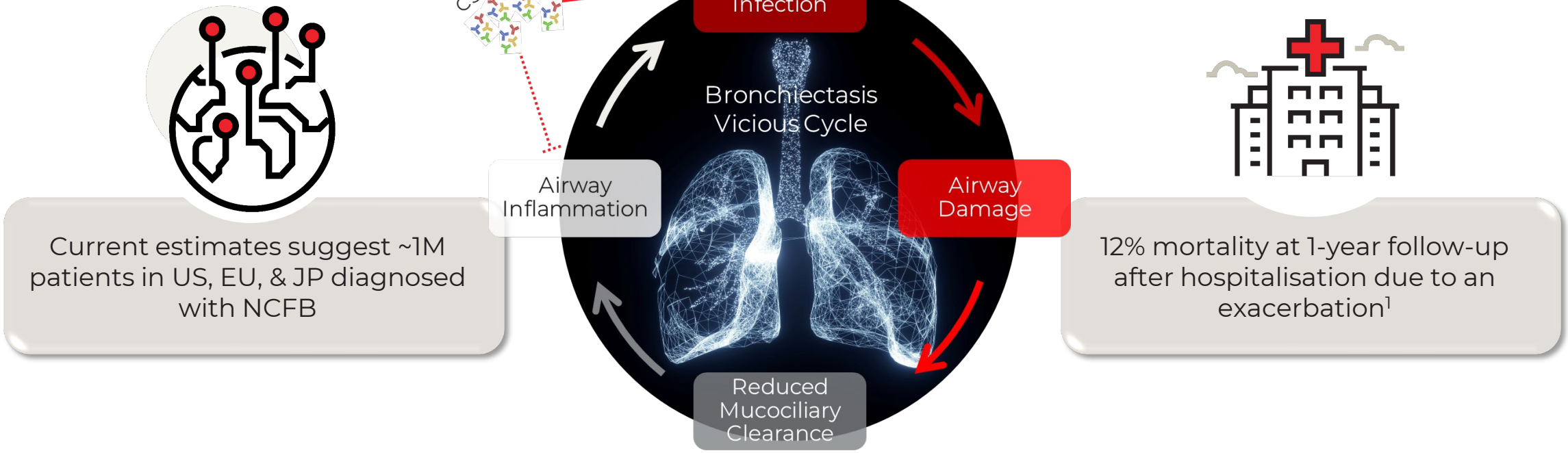


Phase III Study Completed

* Minimum TIS improvement threshold
Abbreviations: TIS – Total Improvement Score

Nebulised IgG (CSL787) in Non-Cystic Fibrosis Bronchiectasis (NCFB)

High unmet need in NCFB for patients with limited treatment response to Standard of Care who suffer severe and frequent exacerbations



Current estimates suggest ~1M patients in US, EU, & JP diagnosed with NCFB

12% mortality at 1-year follow-up after hospitalisation due to an exacerbation[1]

Sources: 1. Scioscia, G., *et.al.*, (2022) *Archivos de Bronconeumologia* **58(11):**773-775

CSL787 - Nebulised IgG in Non-Cystic Fibrosis Bronchiectasis

CSL787 combines advanced plasma-based therapy with cutting-edge delivery technology

Phase I in healthy subjects & subjects with mild NCFB

- Included subjects with mild NCFB with largely preserved lung function & tested positive for presence of ≥ 1 of 6 types bacteria (including *pseudomonas aeruginosa)*
- Antibacterial effects observed following 15 days of once daily dosing in all 18 treated subjects with 3 active doses

Phase II First Patient In – Q1 2025

Garadacimab - Disruptive Innovation to Improve Treatment Options for HAE Patients

Phase III study evaluating efficacy & safety of SC Garadacimab for prophylaxis of HAE Attacks

- Primary & key secondary efficacy endpoints achieved with high degree of statistical significance & clinically meaningful differences vs. placebo
- Pivotal data releases at AAAAI2023 and primary results published in The Lancet journal[1]

Differentiated, Patient-Focused Profile

- Differentiated profile
- Autoinjector - Convenient administration
- Once-monthly treatment dosing
- Favorable safety & tolerability profile

EU, US, JP Expected Approvals - 1H 2025
Phase III Paeds Study Completion – Q4 2025

Abbreviations: AAAAI – American Academy of Allergy, Asthma & Immunology; AI – Autoinjector; HAE – Hereditary Angioedema; SC – Subcutaneous
Sources: 1. Craig, T.J. *et al*., (2023) *Lancet* 401:1079–1090

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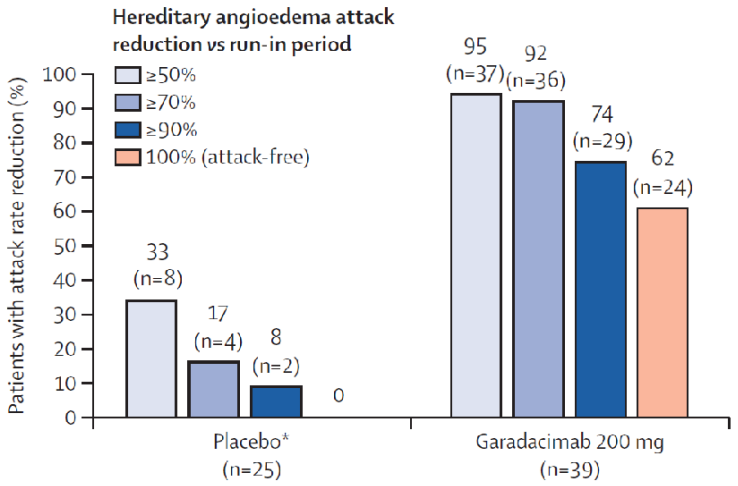
Phase III Study Evaluating Efficacy and Safety of SC Garadacimab for Prophylaxis of HAE Attacks

Durable efficacy, providing sustained protection from HAE attacks over median exposure of 13.8 months

- ≥94% reduction in number of attacks vs. run-in - sustained throughout OLE
- 85% patients had ≥90% attack reduction vs. run-in; 60% patients attack-free
- 88% patients attack-free at end of observation period (months 13–15)

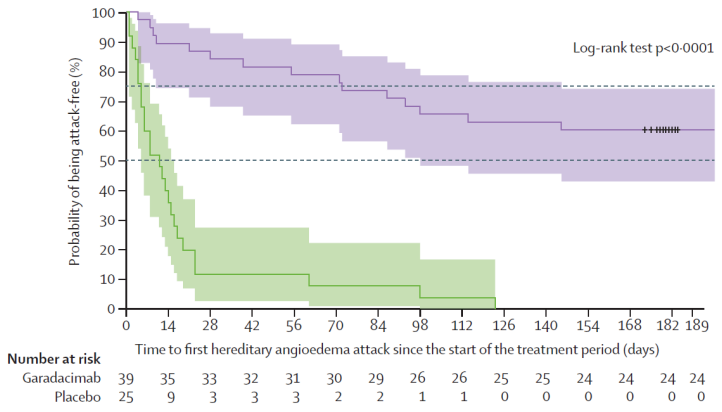
Favourable long-term safety profile

Hereditary angioedema attack reduction vs. run-in period

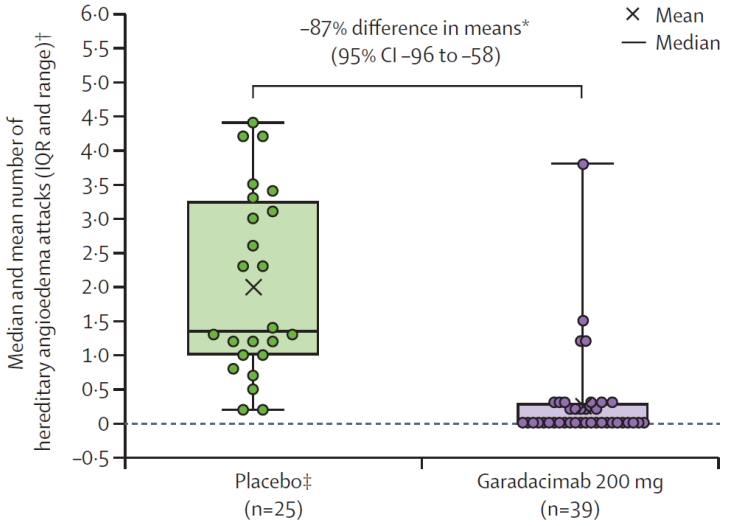


THE LANCET

Time to first hereditary angioedema attack



Mean and median number of monthly attacks during 6-month treatment period



Abbreviations: OLE – Open Label Extension
Sources: Craig, T.J. *et al.*, (2023) *Lancet* 401:1079–1090

Fibrinogen - Coagulation Factor Critical for Clot Stability

AFD (hypofibrinogenemia) - known risk factor for haemorrhage in many perioperative surgical settings, including cardiovascular surgery, obstetrics, & trauma

1st
coagulation factor to drop to critically low levels in acute bleeding situations[1]

50%
of patients experience low levels during complex cardiac surgery[2]

Fibrinogen

10-25%
of patients require fibrinogen supplementation with cryoprecipitate during complex cardiac surgery in US[3]

50%
higher need for ≥5 units RBC when fibrinogen levels fall below[4]

- Blood transfusions associated with increased morbidity, mortality, & hospital costs[5,6]

CSL's Patient Blood Management (PBM) vision:

- Reduce perioperative bleeding
- Reduce need for blood transfusions
- Improve patient outcomes and cost effectiveness

Abbreviations: RBC – Red Blood Cell
Sources: ; 1. Franchini, M. *et al.*, (2012) *Blood Trans* 10(1): 23–27; 2. Nishi, T. *et al.*, (2020) *Gen Thor Cardio Surg* 68: 335–341; 3. D'Agostino, R.S. *et al.*, (2019) *Ann Thor Surg* 107:24; 4. Karkouti, K. *et al.*, (2013) *Anesth Analg* 117:14–22; 5. Mehaffey, J.H. *et al.*, (2018) *J Thor Cardio Surg* 155(3):875-88; 6. Koch, C.G. *et al.*, (2006) *Ann Thor Surg* 81(5):1650-7.

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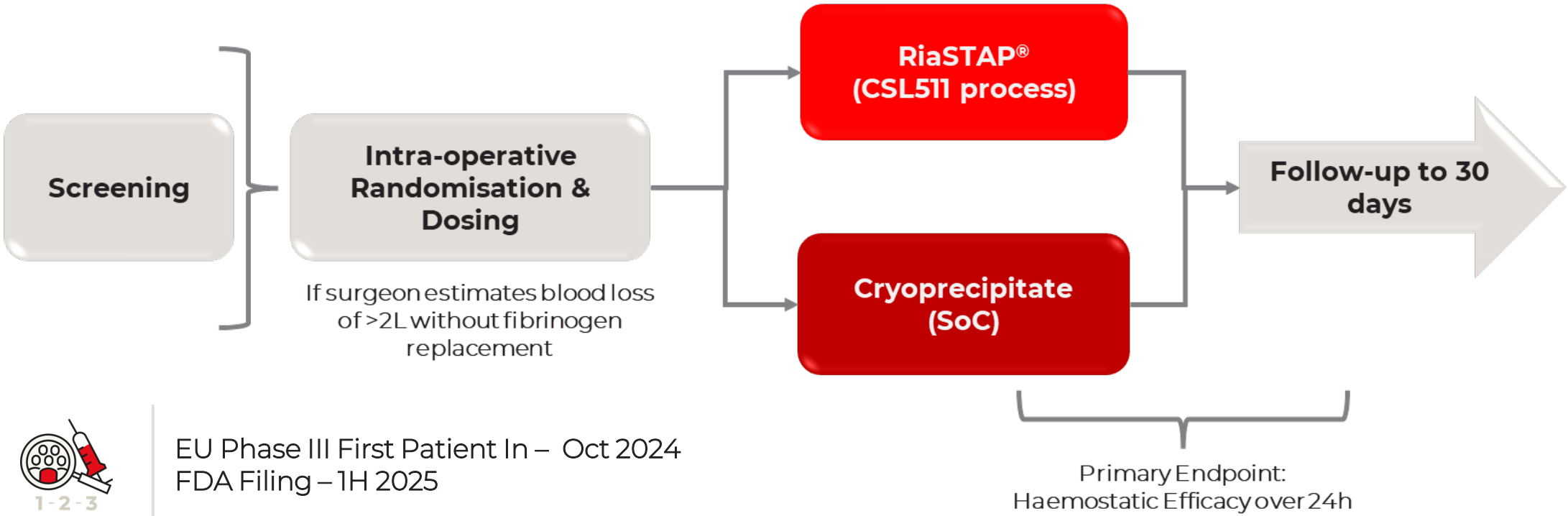
RiaSTAP® Phase III Study – Comparison to SoC

Patients with pseudomyxoma peritonei (PMP) undergoing cytoreductive surgery with hyperthermic intraperitoneal chemotherapy

- Single centre study
- Non-inferiority comparison between RiaSTAP® & cryoprecipitate (SoC)



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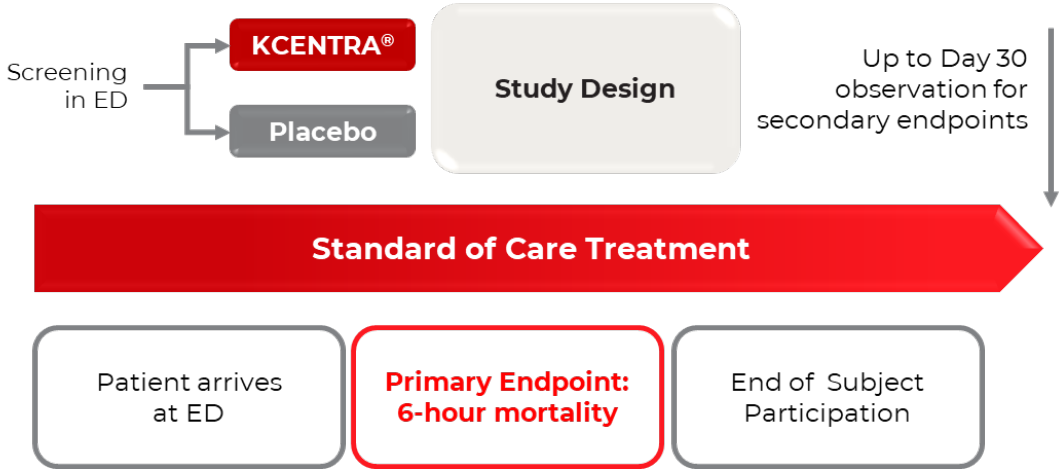
EU Phase III First Patient In – Oct 2024
FDA Filing – 1H 2025

Abbreviations: SoC – standard of care

KCENTRA® - Trauma and PCC Trial

Enrolling and dosing patients (with highest risk of mortality) in hospitals according to clinical trial standards is challenging, impacting both feasibility & sample size

- First patient enrolled in March 2023
- More than 1400 patients enrolled across 84 sites in 3 countries (US, UK, AU)
- No major safety or tolerability concerns with KCENTRA®
- Lower than expected mortality in the trial with sample size implications
- Highlights the importance of early KCENTRA® administration to target patients with highest risk of mortality



Abbreviations: ED – Emergency Department; PCC - Prothrombin Complex Concentrate

KCENTRA® Opportunities

Expanding use of CSL's Four-Factor Prothrombin Complex Concentrate (4F-PCC)

Perioperative Coagulopathy

- **Increased Surgical Bleeding**: Leads to more allogeneic blood transfusions, higher morbidity, mortality, & costs
- **Coagulation Factor Concentrates**: Use in PBM protocols reduces transfusions & mortality
- **PCC Usage**: Growing use in various surgeries, including cardiac, liver transplant, & trauma
- **PCC is part of international guidelines** for perioperative bleeding treatment

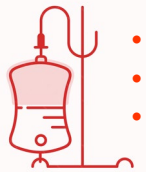
DOACs: a leading factor in reducing morbidity & mortality in atrial fibrillation patients

>15m
patients globally on DOACs for treatment of AFib or VTE

~2-4%
acute major bleeding is most common side effect of DOACs

7-20%
all-cause mortality within 30d of major DOAC-related bleeding

Current treatments include:



- Specific antidotes
- 4F-PCC (off-label use)
- Fresh frozen plasma

Phase III Clinical Studies in discussion with HAs

Abbreviations: AFib – Atrial Fibrillation; DOAC – Direct Oral Anti-Coagulant; VTE – Venous Thromboembolism

Sources: Spahn, D.R. & Goodnough, L.T. (2013) *Lancet* 381(9880):1855–65; Raphael, J. *et al.,* (2019) *Anesth. Analg.* 129(5):1209-1221. Erdoes, G. *et al.,* (2021) *Anaesthesia* 76(3):381-392; Kietaibl, S. *et al.,* (2023) *Eur. J. Anaesthesiol. 40(4):226-304;* National Blood Clot Alliance.

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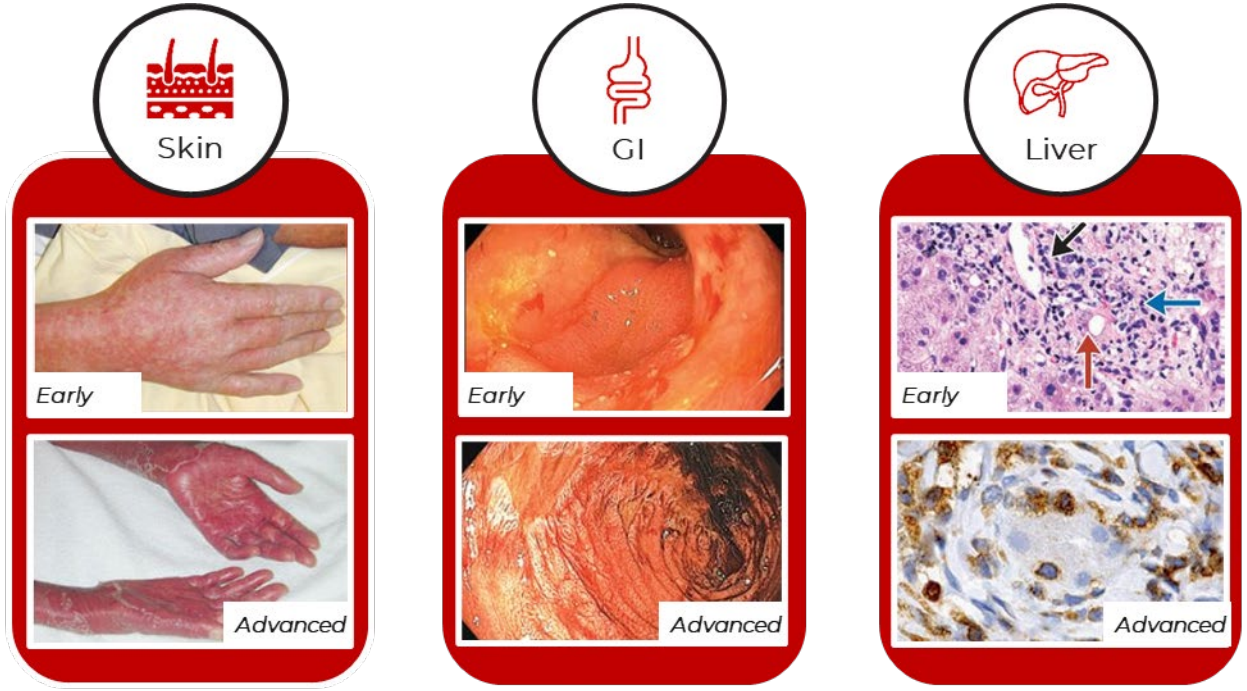
Graft versus Host Disease (GvHD)

Frequent Post-Transplantation Complication with High Morbidity and Mortality

- Up to 50% of patients develop GvHD after allogeneic HSCT despite current prophylactic regimens
- Of those who develop acute GvHD, only 50% respond to treatment[1] (termed “steroid-refractory”)
- Severity of acute GvHD varies: Grades III & IV are most severe
- Mortality associated with grade III and grade IV one year after transplant is 75% & 95%, respectively[2]

Clinical Manifestations[3]



- Maculopapular rash

- Upper GI: nausea, vomiting
- Lower GI: profuse watery diarrhoea; bloody diarrhoea or ileus

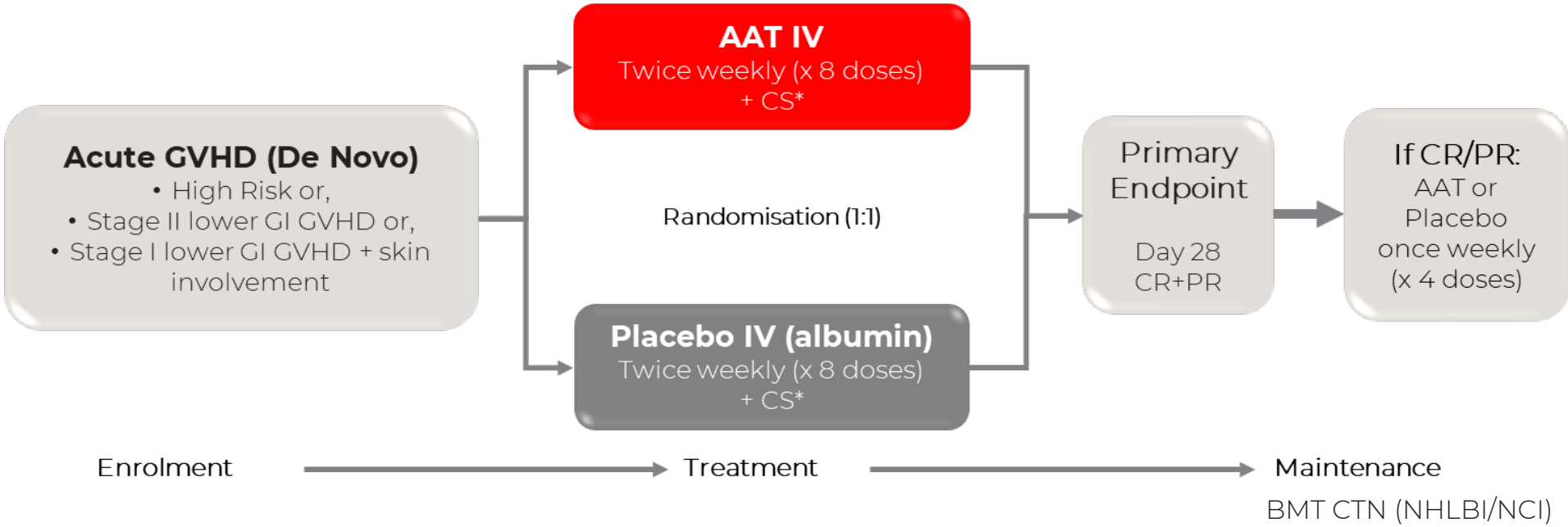
- Cholestatic jaundice
- Hyperbilirubinemia

Abbreviations: HSCT – Haematopoietic Stem Cell Transplant

Sources: 1. Ferrara, J. & Chaudry, M. (2018) *Blood Adv.* 2(22):3411-3417; 2. Hill, L. *et al.*, (2018) *Ther Adv Hematol.* 9(1):21-46; 3. Zeiser, R. & Blazar, B.R. (2017) *N Engl J Med.*377(22):2167-2179

Alpha-1 Antitrypsin (AAT) for Acute GvHD Treatment Study: BMT-CTN 1705

Collaboration with Blood & Marrow Transplant Clinical Trials Network



Primary Endpoint: Overall (complete or partial) response to aGVHD treatment at Day 28

Phase III Results Public Presentation – 1H 2025

Abbreviations: CR – Complete response; PR – Partial response.
*Corticosteroids (CS) = Methylprednisolone starting dose equivalent to prednisone 2 mg/kg/day. (Tapering at discretion of treating physician)

Clazakizumab in Chronic Antibody Mediated Rejection (AbMR)

- Futility analysis enabled clear decision to terminate study based on eGFR
  - Study unlikely to meet ultimate primary efficacy outcome (time to composite all-cause allograft loss or irreversible loss of allograft function) upon completion
  - Results disappointing & unexpected given Phase II eGFR data
- Full data disclosure planned at American Society of Nephrology October 2024

Largest placebo-controlled study conducted in AbMR

First Health Authority agreement on surrogate endpoint

Leadership and trust with academic & regulatory stakeholders

Abbreviations: eGFR – estimated Glomerular Filtration Rate

Clazakizumab in Patients with End Stage Kidney Disease (ESKD) on Dialysis

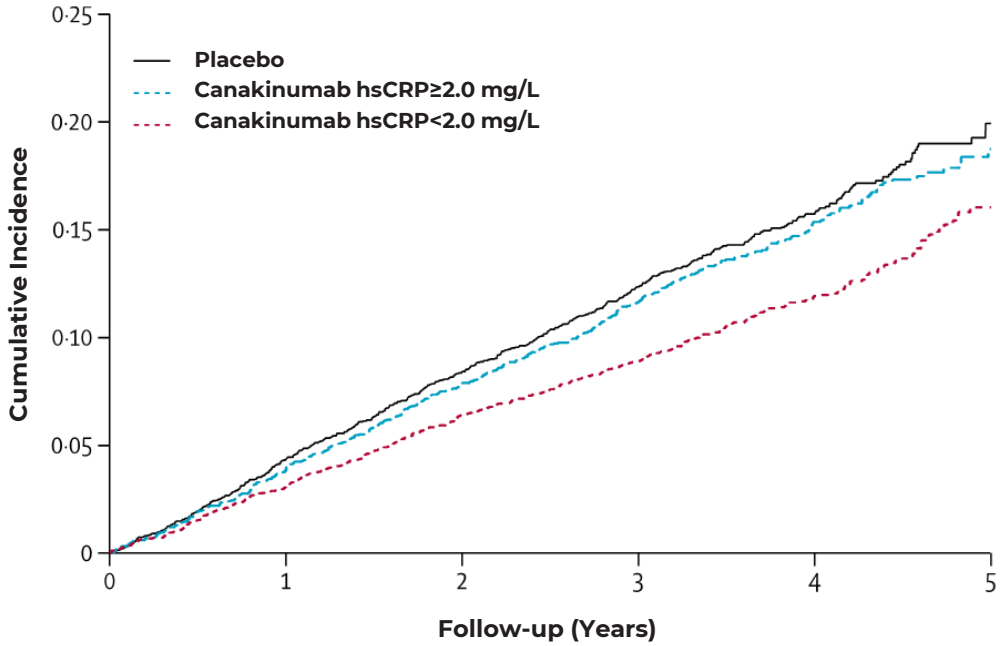
Dialysis is the most common treatment modality in ESKD

- Very high unmet need - 188 deaths per 1,000 patients annually[1]
- Mortality primarily caused by CV disease is higher than in most common cancers
- Currently no proven treatments to reduce CV events in dialysis

Role of inflammation

- Inflammation common in dialysis and strongly associated with mortality and morbidity, central role of IL-6
- Strong science supporting link between IL-6 and CV events

Reduction of hsCRP with canakinumab leads to reduced MACE and CV mortality[2]

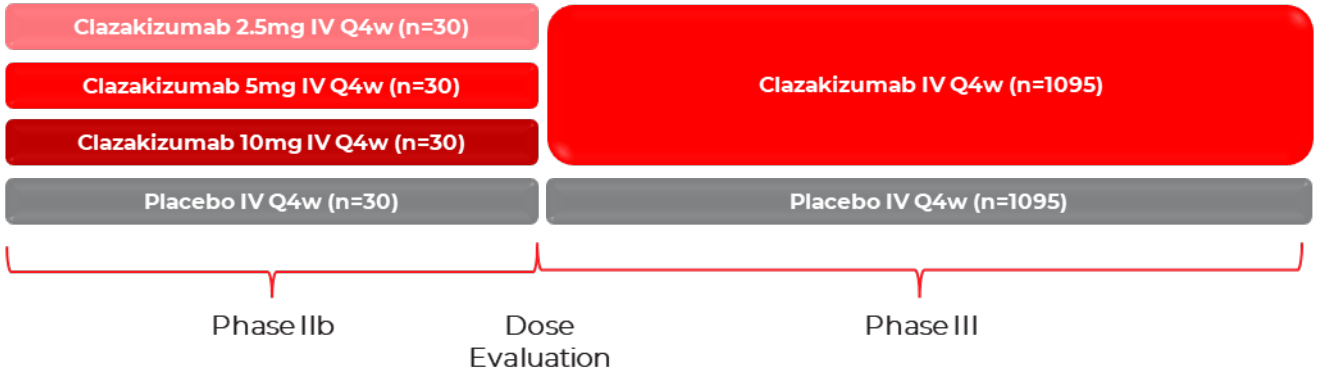


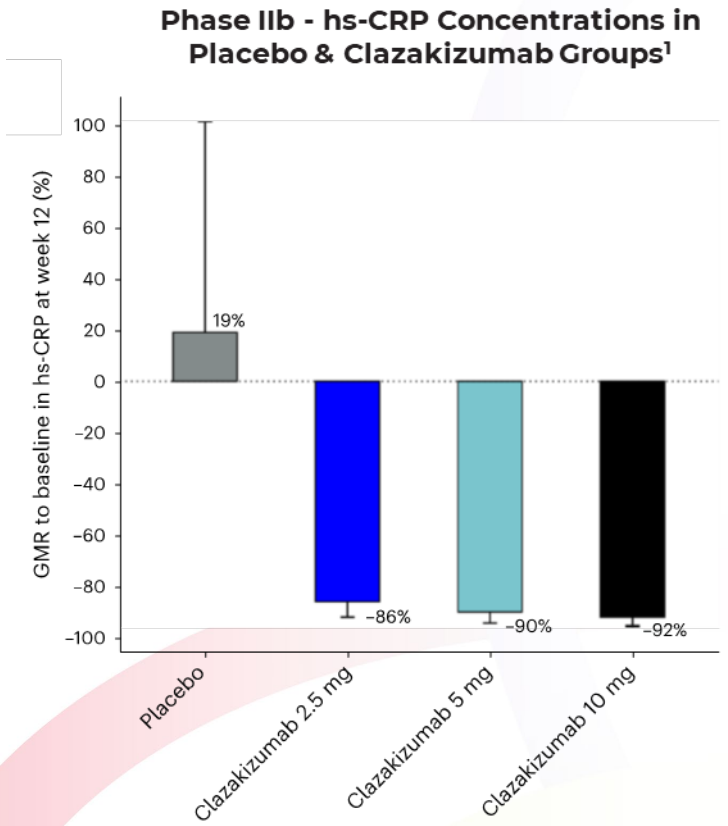
Abbreviations: CV – Cardiovascular; ESKD – End Stage Kidney Disease

Sources: 1. United States Renal Data System (USRDS) 2023 Annual Report; 2. Reproduced from: 2. Ridker et al., Lancet 2018; 391: 319–28.

Phase III Study of Clazakizumab to Evaluate Cardiovascular Events in ESKD Patients

- Phase IIb/III combined dose ranging (Phase IIb) and CV outcome trial (Phase III)
- To demonstrate that IL-6 antagonism with clazakizumab will reduce CV events in dialysis patients





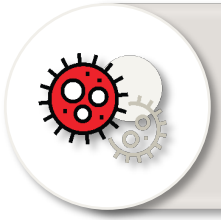
- Phase IIb part completed; primary data reported at European Renal Association Meeting & published in Nature Medicine
- Clazakizumab at low doses associated with dramatic improvement of key inflammatory biomarker predictors of CV risk and was well tolerated

1-2-3

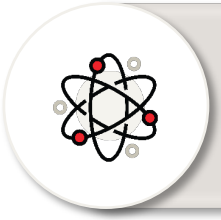
Phase III Last Patient In - H1 2026

Abbreviations: CRP – C-reactive Protein; CV – Cardiovascular; ESKD – End Stage Kidney Disease
Source: 1. Chertow, G.M. *et al.*, (2024) *Nat Med* 30: 2328-2336

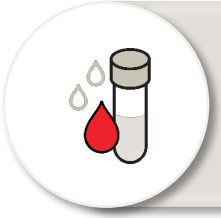
Unlocking New Horizons: Launching FILSPARI® for Treatment of IgA Nephropathy (IgAN)



Most prevalent type of primary glomerulonephritis worldwide & major cause of kidney failure[1,2], affecting 3.5 in 10,000 people*[,3]



Detected in 19–51% of kidney biopsies performed in glomerular diseases in EU and frequently diagnosed during 3rd & 4th decade of life



Despite good understanding of pathophysiology & potential therapeutic targets, no non-immunosuppressive therapies are approved for treatment of IgAN†[,1,4,5]

Developed in partnership with Travere Therapeutics, a US biotechnology company

FILSPARI® (sparsentan) tablets 200 mg/400 mg

Novel, non-immunosuppressive, dual endothelin angiotensin receptor antagonist (DEARA) with high selectivity for endothelin A receptor (ET_AR) & angiotensin II subtype 1 receptor (AT_1R)

* Number of patients affected by the condition is estimated & assessed on basis of data from EU, Iceland, Liechtenstein, Norway, and UK. This represents population of 519,200,000 (Eurostat)[3];
† Only one FDA-approved product, delayed-release budesonide, is indicated for treatment of patients with primary IgAN at risk of rapid disease progression, approved by FDA on December 15, 2021, positive opinion for market authorisation in Europe May 2022.

Sources: 1. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group (2021) *Kidney Int.* 100(4S): S1–S276; 2. Yeo, S.C. *et al.,* (2018) *Pediatr Nephrol.* 33: 763–77; 3. EU/3/20/2336: Orphan designation for the treatment of primary IgA nephropathy. Available at: https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu3202336 (accessed: July 2022); 4. Barratt, J. & Feehally, J. (2005) *J Am Soc Nephrol.* 16: 2088–97; 5. Tarpeyo US PI 2021 (accessed July 2022)

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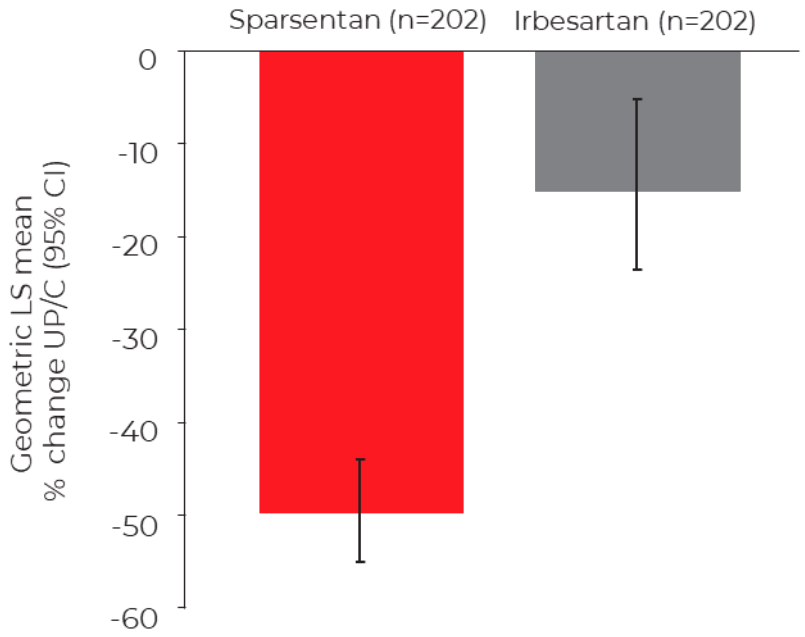
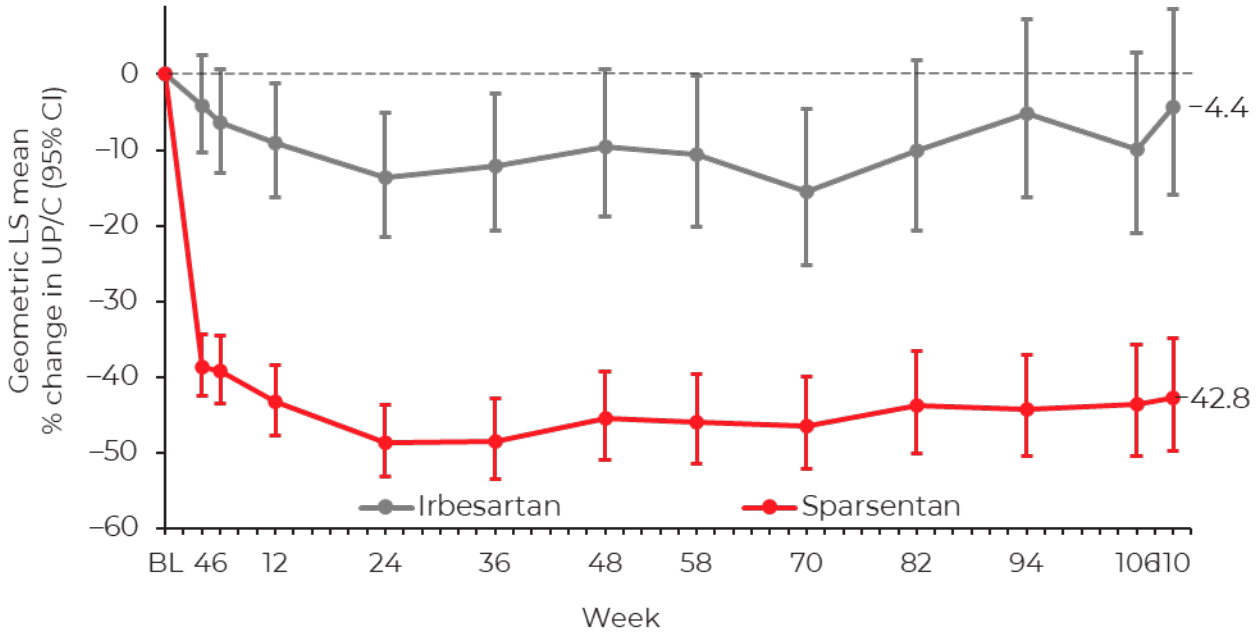
FILSPARI® Significantly Reduced Proteinuria Over 110 Weeks in Phase III (PROTECT) Study in Adults with Primary IgAN

% Change from baseline in UP/C at Week 36[1]
(Prespecified primary endpoint)



% Change from baseline in UP/C to Week 110[2]
(Prespecified secondary endpoint)



Primary Endpoint met at 36-week interim analysis,
with a between group relative reduction in proteinuria of 41% (P<0.0001)

Abbreviations: BL, baseline; CI, confidence interval; LS, least squares; UP/C, urine protein-creatinine ratio.
Sources: 1. Heerspink, H.J.L. *et al.*, (2023) Lancet 401;1584–94; 2. Rovin, B.H. et al., (2023) Lancet 402:2077–90.

Vamifeport (CSL624) for Hereditary Haemochromotosis (HH)

Genetic disorder characterised by increased intestinal absorption of iron leading to iron overload and eventually causing end organ damage

~150-200k

diagnosed symptomatic patients in US

~20%

subjects are non-responders or intolerant to phlebotomy

~10%

subjects have high disease & treatment burden requiring better pharmacological options

Phase II – In planning stage

High unmet need in patients refractory from or phlebotomy intolerance due to lack of approved therapies

Iron removal by phlebotomy is poorly tolerated or contraindicated in refractory patients; restoring regulation of iron could be effective

Vamifeport (from CSL Vifor acquisition) mimics effects of hepcidin on ferroportin (FPN), restoring normal regulation of iron & preventing excessive iron absorption

Sources: EASL Clinical Practice Guidelines on haemochromatosis. *J Hepatol.* 2022, 77:479-502.

Sickle Cell Disease (SCD) – A Complex Systemic Disease

Genetic disorders associated with hereditary haemolytic anaemia or vaso-occlusive crisis (VOC) with rigid red cells & adhesive blood cells occluding circulation

~120k
diagnosed patients in US

~40-50%
poor efficacy of current prophylaxis treatment options

No pharmacological treatment exists for treatment of VOC

Current Treatment Options

- Non-opioid analgesics & opioids
- Gene therapy adoption is expected to be limited

Role of Hemopexin in SCD

- Heme toxicity major component of SCD
- Vaso-occlusive crisis (VOC) & hemolytic anemia most common manifestations of SCD
- VOC can result in severe daily pain, ultimately potential organ failure & reduced life expectancy
- Hemopexin - natural heme scavenger with potential to reverse VOC

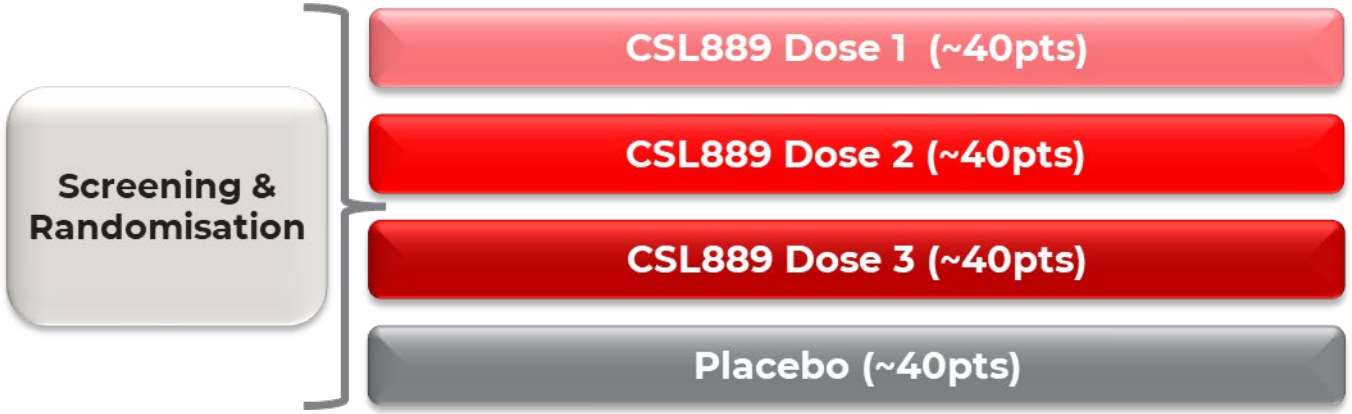
Demonstrating effectiveness in reducing/eliminating VOCs & associated complications will transform treatment paradigm

Hemopexin (CSL889) for Acute VOCs in Sickle Cell Disease

Phase I Study in Adult Patients with Sickle Cell Disease

- CSL889 well tolerated at all dose levels
- No serious adverse events attributed to CSL889

Phase II Study to Evaluate Efficacy & Safety of CSL889 in Patients with SCD Experiencing VOC

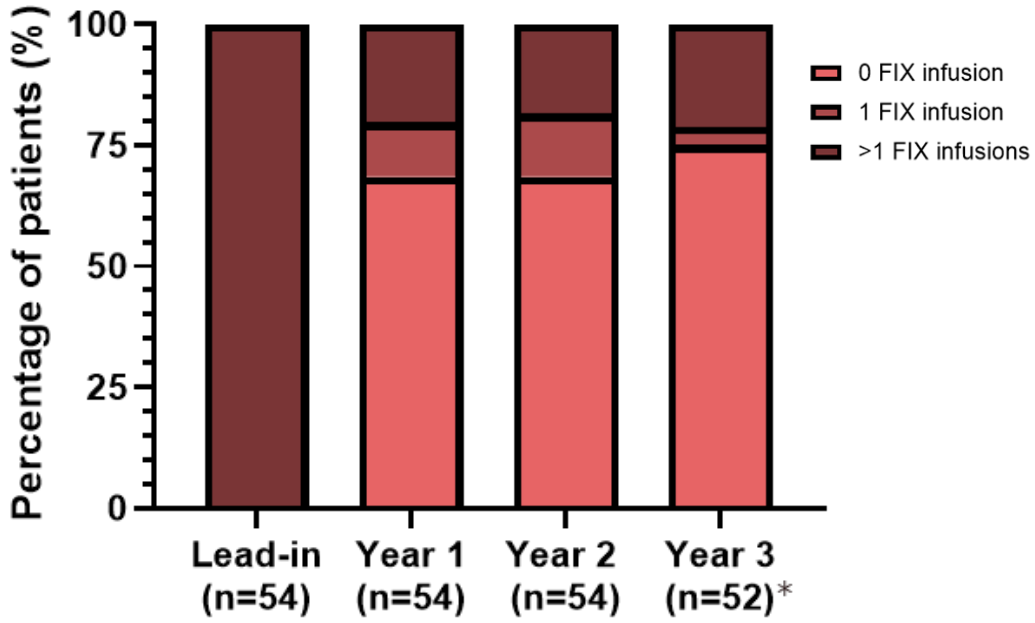


Adults & Adolescents

Phase II First Patient In – Q1 2025

HEMGENIX® for Treatment of Haemophilia B

HEMGENIX® has consistently favourable safety profile, with no treatment-related SAEs reported, and no new safety events reported through 3 years post-treatment



- After 36 months of follow up:
  - mean FIX levels remained elevated & sustained consistent with 24-month data showing ongoing durable effect[1]
  - 94% of participants did not require continued prophylaxis
  - 46% of participants received no FIX infusion over 3-year period
- 48-month analysis confirmed:
  - sustained Factor IX activity levels at 37.4%, with superior bleed protection compared to FIX prophylaxis,
  - decrease of exogenous Factor IX consumption by 96%
- No serious adverse events (AE) related to treatment
- Overall safety profile remained favorable & consistent with previous observations

Registration/Launch/Post Registration Studies – Ongoing
Phase III JP Last Patient In – Achieved Oct 2024

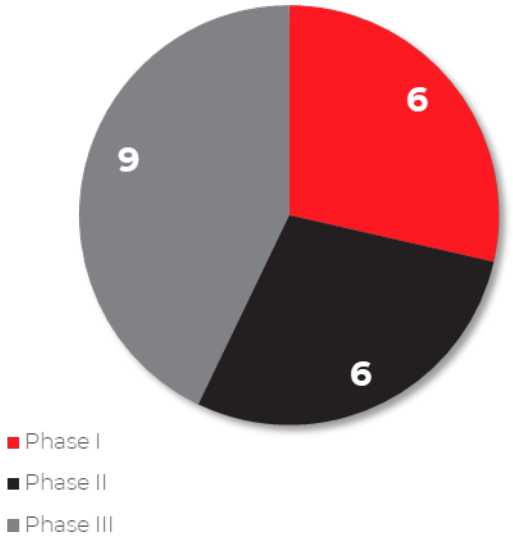
*One patient died (prophylaxis free); one patient who remained on prophylaxis withdrew consent for efficacy assessment

Source: 1. Pipe S.W. *et al.*, (2023) N Engl J Med 388(8):706-718.

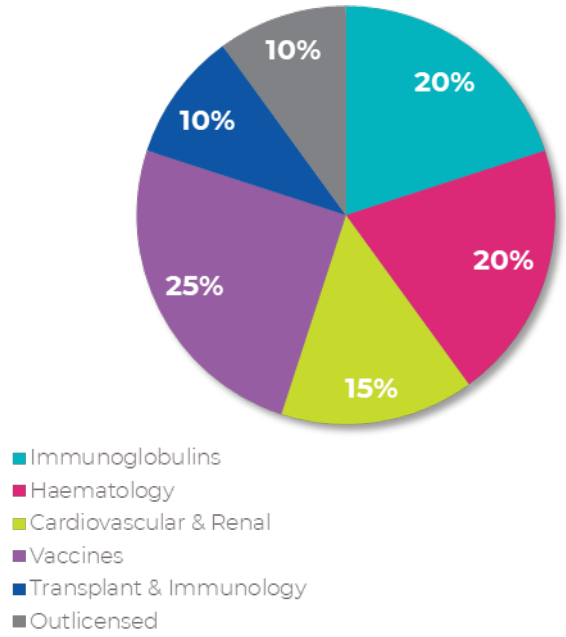
A Robust Pipeline for the Future

Developing a robust portfolio of therapeutic area opportunities across our platform capabilities

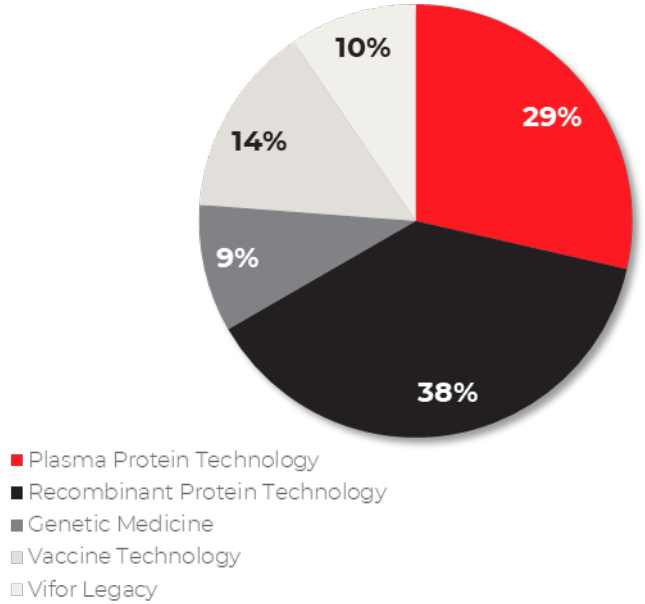
21
programs in clinical development



TA balanced
across R&D portfolio



Leveraging all
Platforms



Vaccines Development

Targeting Unmet Need in Influenza & COVID

Jon Edelman MD
Senior Vice President
Vaccines Innovation Unit
CSL

Progress and Challenges in Influenza Continue to Inform CSL R&D Efforts in Vaccines

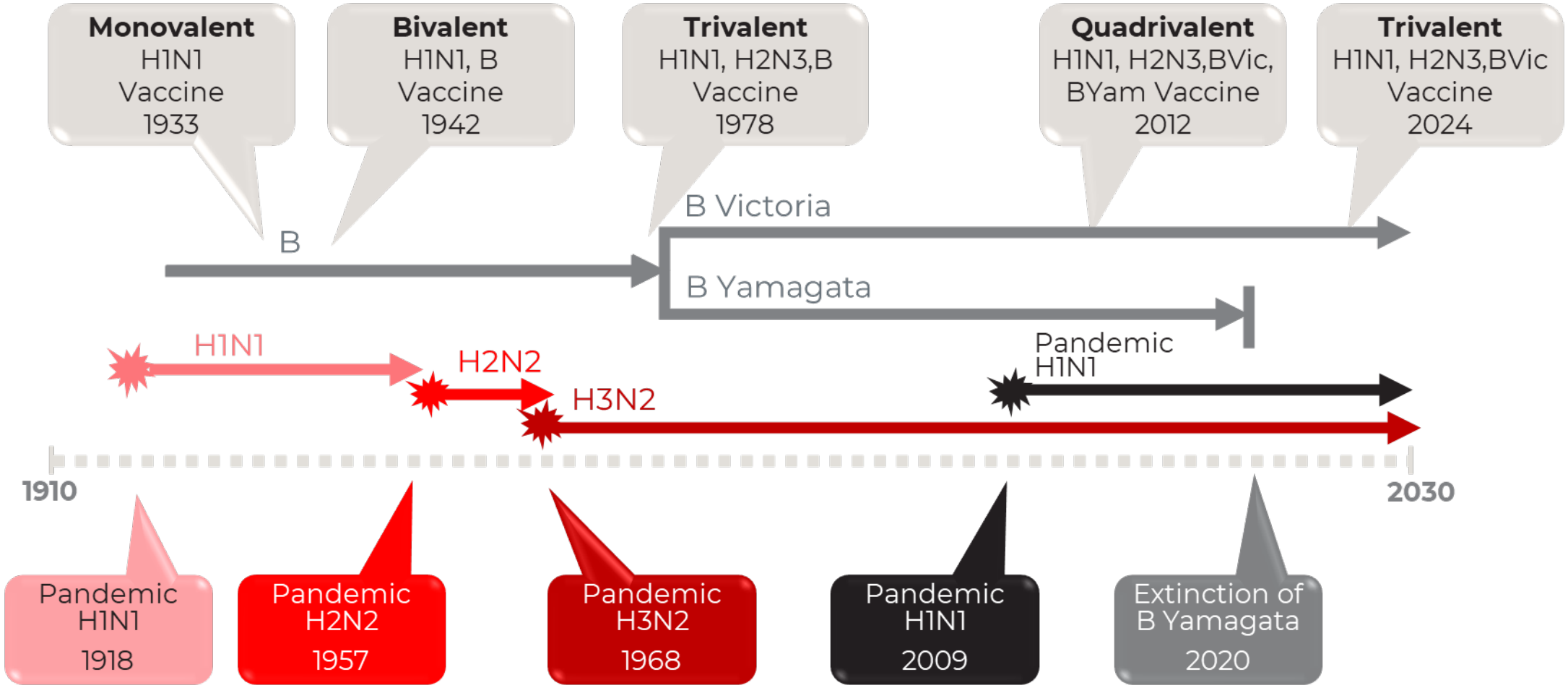
Over the past we have seen positive impacts of influenza vaccination:

- Avoidance of morbidity
- Extinction of B Yamagata

However, scientific challenges remain:

- Inconsistent effectiveness of standard vaccines
- Highly pathogenic avian influenza H5N1

Influenza Vaccines Have Evolved to Keep Up with Changes in Circulating Viruses



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Transition From Quadrivalent Influenza Vaccines (QIV) to Trivalent Influenza Vaccines (TIV)

As CSL transitions to TIV formulations, we are committed to maintaining the protection, safety, reliability, and value of our differentiated seasonal influenza vaccine portfolio

CSL Seqirus played key role in shaping landscape to ensure smooth transition to TIV

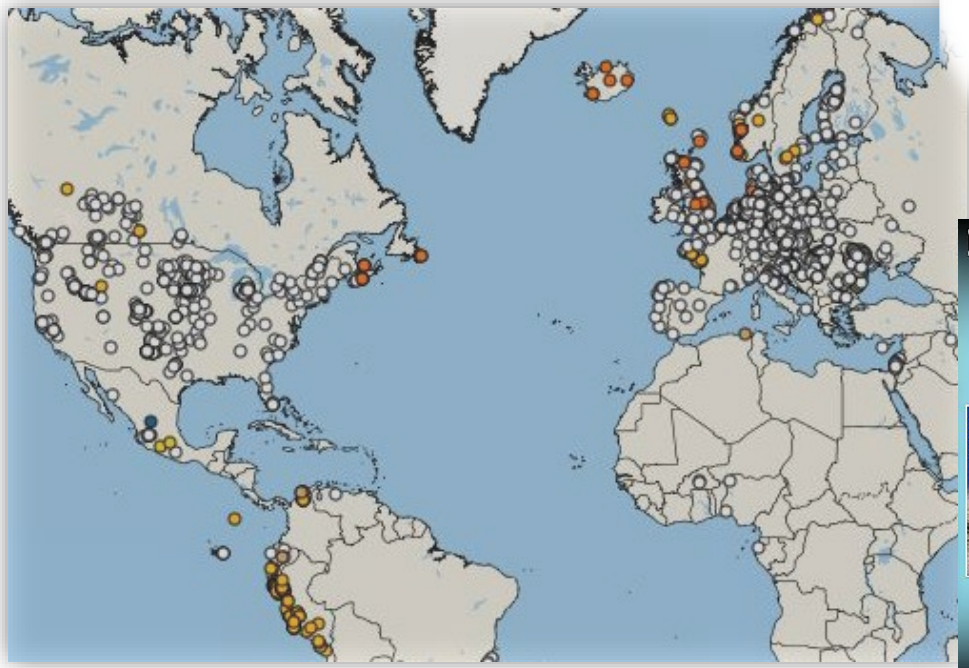
CSL's NH24/25 vaccines in US are all TIV

Transitioning ROW to TIV over next year

- ✓ US FDA - All TIV **released** Jul 24 for NH24/25
- ✓ UK MHRA - **approved** on Jul 24 for NH25/26
- ✓ EU EMA – **on track** for approval by NH25/26
- ✓ ROW – anticipate transition by SH26

Worldwide Spread of H5 Avian Influenza Now Affecting Dairy Cows

Cumulative weekly avian flu reports in FAO EMPRES-I database from 01 Aug 23 to 30 Jul 24[1]



The New York Times

U.S. Considers Vaccinating Chickens as Bird Flu Kills Millions of Them

The largest outbreak of avian influenza in U.S. history has driven up egg prices and raised concerns about a human pandemic, though C.D.C. experts say the risk of that is low.

University of Minnesota

CIDRAP

Avian flu detected in Idaho dairy cows

Lisa Schnirring, Today at 9:48 a.m.

Topics: Avian Influenza (Bird Flu)

shironosov/iStock

Abbreviations: FAO EMPRES-I Food and Agriculture Organization of the United Nations Emergency Prevention System-i;
Source: 1. FAO EMPRES-I Global Animal Disease Information System [Accessed 30 July 2024]

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Pandemic Strategy - Innovation at Industrial Scale

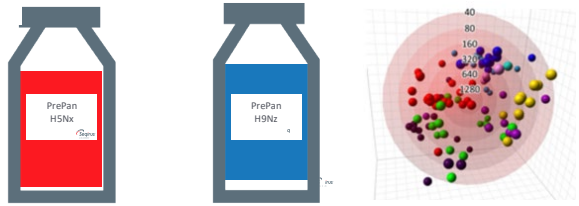
As an Expert, Responsive and Proven Partner to 30 Governments

Cell-Culture Technology
Greater match & effectiveness
Next gen technology today, at scale & speed

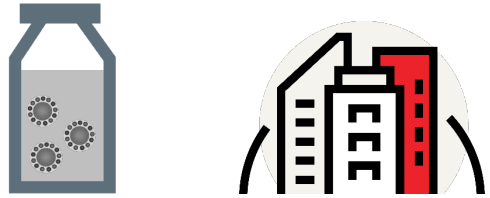
MF59® Adjuvant
Dose sparing
Breadth of protection
300mds+ safety database

sa-mRNA (future)
Potential for higher effectiveness, durability multi pathogen, speed, dose sparing (vs mRNA)

Global access for governments to MF59®-adjuvanted, cell & egg-based APA's / pandemic vaccine for population wide coverage



Pre-pandemic stockpiles afford ability to combine with different pandemic antigens of concern, permitting dose-sparing and further reach of early supply.
MF59® adjuvant can be used in other products



Selected technology partnerships
(MF59® & investment in cell-based capacity, R&D

BARDA
Australian Government
HM Government

Abbreviations: MDS – Minimum Data Set

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CSL Seqirus Pandemic Portfolio

Panvax®
Pandemic Influenza Vaccine
(split virion, inactivated), adjuvanted

Influenza A (H5N1)
Monovalent Vaccine,
Adjuvanted
AUDENZ®

AFLUNOV®
Prepandemic Influenza vaccine (H5N1)
(surface antigen, inactivated, adjuvanted)*

H5N8 zoonotic vaccines offers protection against the current H5N1 clade 2.3.4.4b

H5N8
Alum adj, egg

Oct 2023 - TGA approval

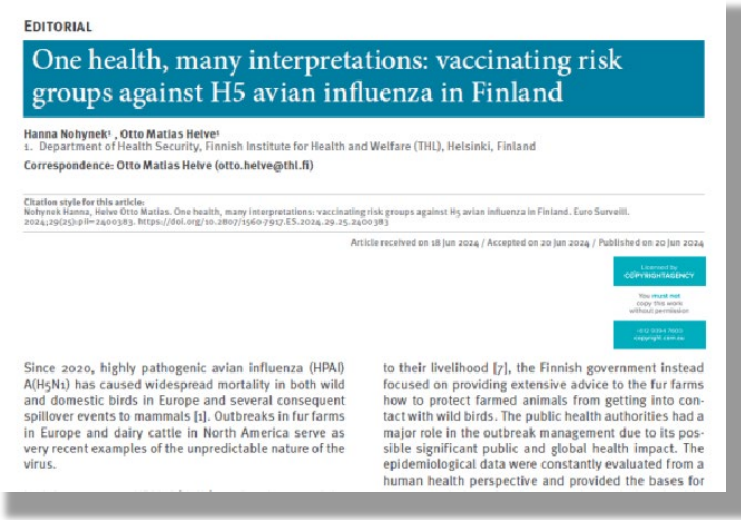
H5N8 & H5N1
MF59® adj, cell

Under review with FDA

H5N8
MF59® adj, egg

Mar 2024 - MHRA Approval
Apr 2024 - EMA approval

First avian influenza vaccination program: FINLAND



EDITORIAL

One health, many interpretations: vaccinating risk groups against H5 avian influenza in Finland

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Correspondence: Otto Matias Helve (otto.helve@thl.fi)

Citation style for this article:
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Article received on 18 Jun 2024 / Accepted on 20 Jun 2024 / Published on 20 Jun 2024

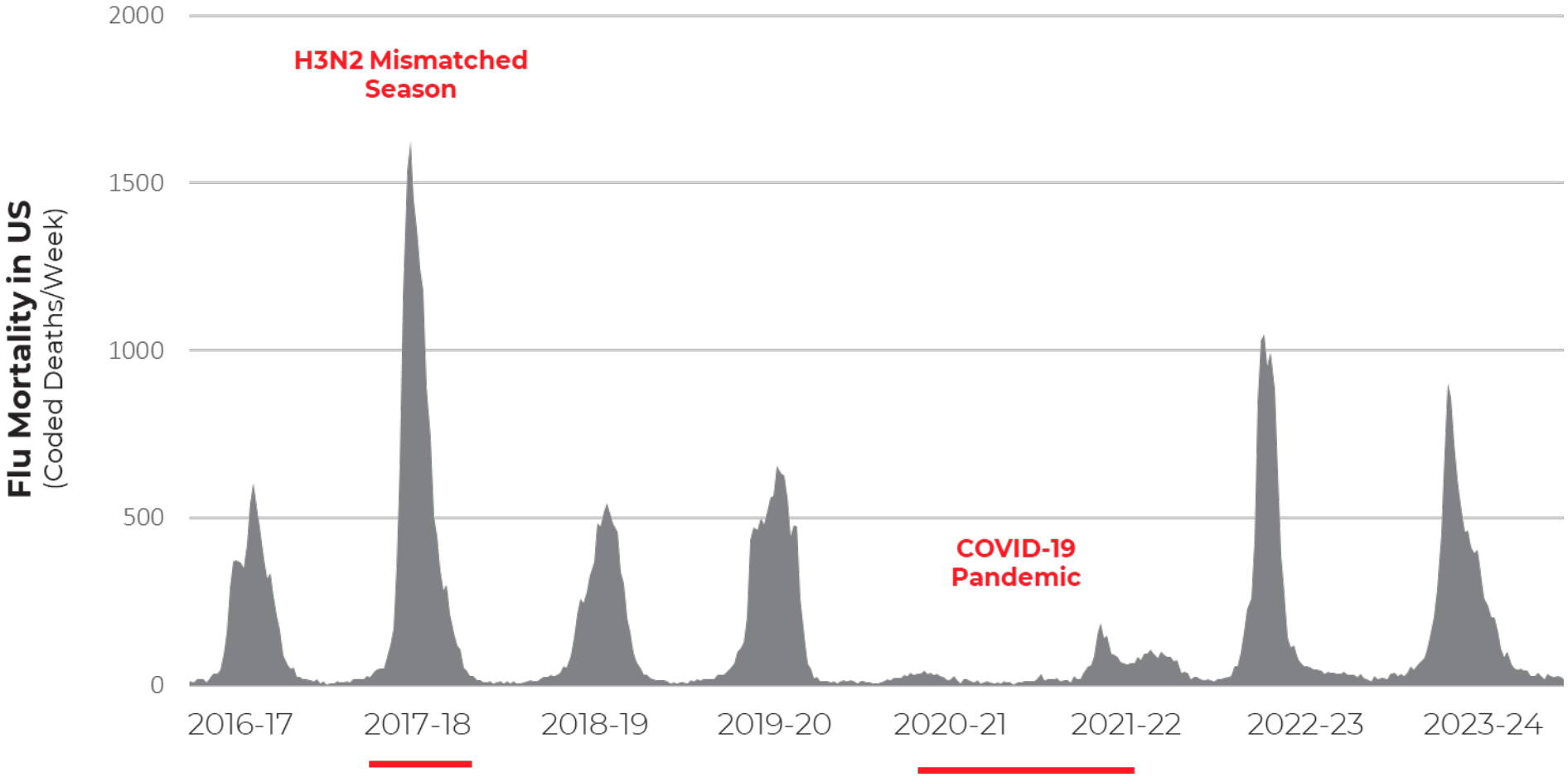
Since 2020, highly pathogenic avian influenza (HPAI) A(H5N1) has caused widespread mortality in both wild and domestic birds in Europe and several consequent spillover events to mammals [1]. Outbreaks in fur farms in Europe and dairy cattle in North America serve as very recent examples of the unpredictable nature of the virus.

to their livelihood [7], the Finnish government instead focused on providing extensive advice to the fur farms how to protect farmed animals from getting into contact with wild birds. The public health authorities had a major role in the outbreak management due to its possible significant public and global health impact. The epidemiological data were constantly evaluated from a human health perspective and provided the bases for

* In EU and UK, approved as CELLDEMIC® (zoonotic), INCELLIPAN® (pandemic)

Sources: 1. FOCLIVIA® SmPC. 2. Panvax® Approved Product Information. 3. AUDENZ® PI. 4. AFLUNOV® SmPC. 5. Panvax® H5N8 pre-pandemic Approved Product Information. 6. Zoonotic Influenza Vaccine H5N8 SmPC. 7. CSL Seqirus Press Release 29th May 2024. 8. Clinicaltrials.gov

Influenza-related Mortality in US is Rising Post-COVID



Source: CDC MMWR – Centers for Disease Control and Prevention
Morbidity and Mortality Weekly Report

CSL

Renewed Efforts to Increase Influenza Vaccinations

A Key Public Health Priority

Ad Council, AMA, and CDC Urge Americans to "Play Defense Against Flu" with New Vaccination Campaign

NEWS PROVIDED BY
The Ad Council →
Oct 10, 2024, 00:01 ET

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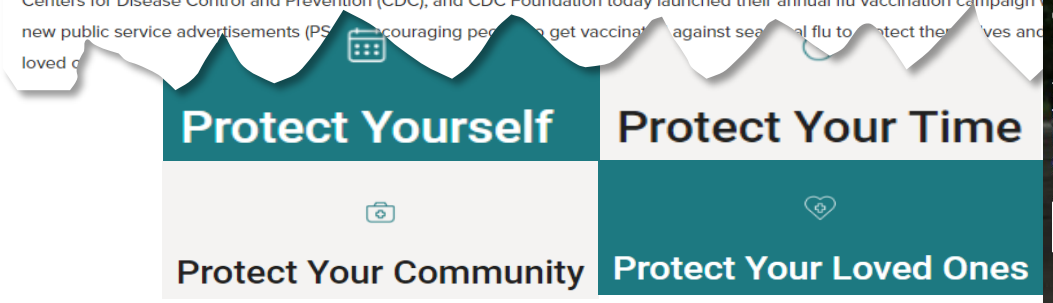
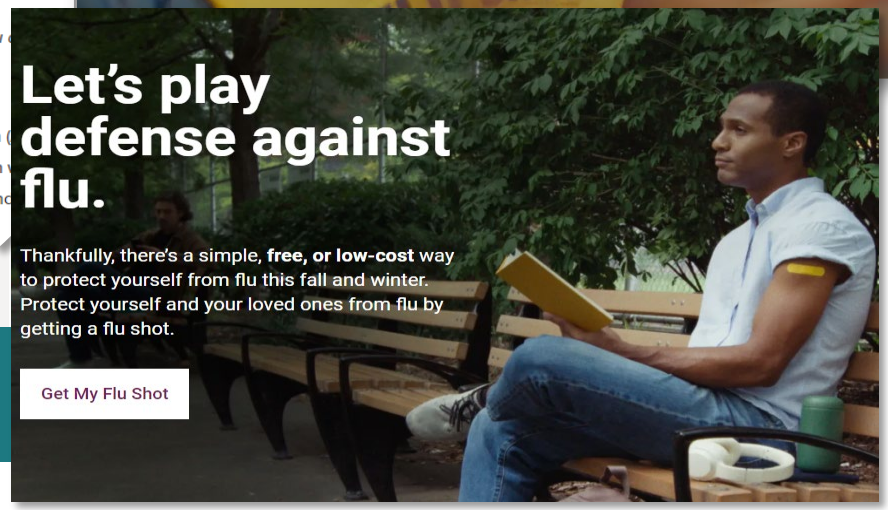
New PSAs remind audiences to receive their annual flu shot to protect themselves and their communities from the risk of flu [illegible] potentially serious complications.

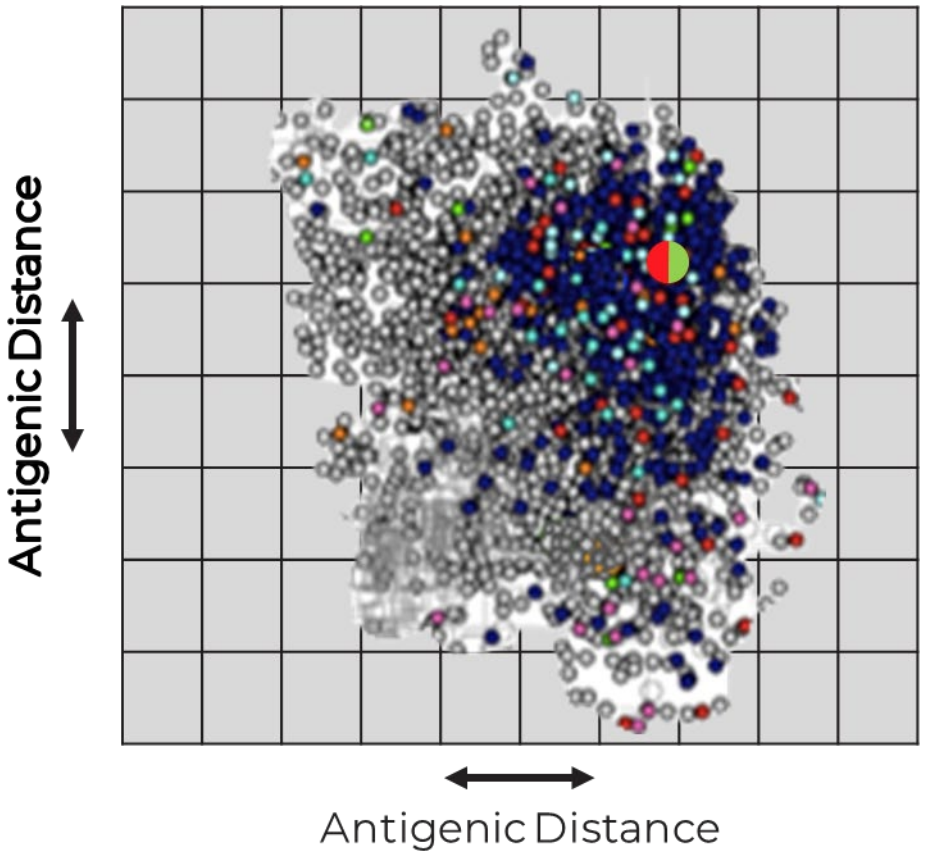
NEW YORK, Oct. 10, 2024 /PRNewswire/ -- As cold and flu season approaches, The Ad Council, American Medical Association [illegible] Centers for Disease Control and Prevention (CDC), and CDC Foundation today launched their annual flu vaccination campaign [illegible] new public service advertisements (PS[illegible]couraging peo[illegible]n get vaccina[illegible] against sea[illegible]l flu to [illegible]tect the[illegible]ves and loved o[illegible]





CSL's Three-Pronged Approach to Improving Current Egg-based Vaccine Technology

WHO recommended **Cell** & **Egg** CVVs are antigenically matched

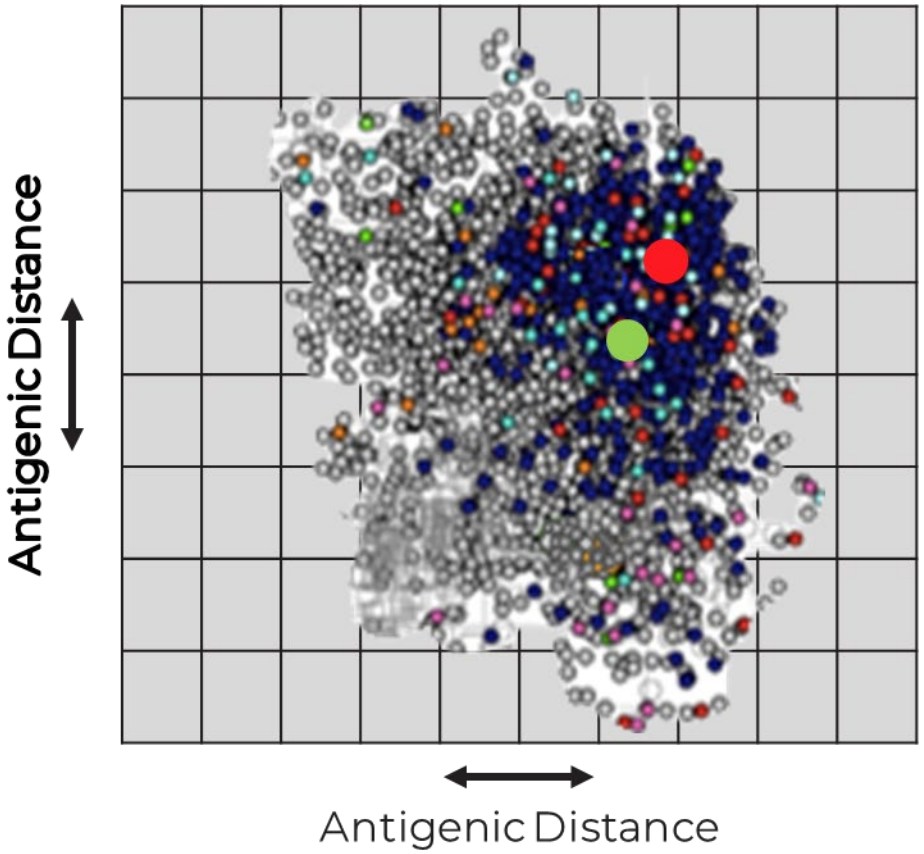


1. Adjuvant
   - Boost & broaden response
2. Cell-based
   - Exact match to target
3. Optimised Dose
   - Further increase response

Abbreviations: CVV – Candidate Vaccine Virus; WHO – World Health Organisation

CSL's Three-Pronged Approach to Improving Current Egg-based Vaccine Technology

WHO recommended **Cell** & **Egg** CVVs are antigenically different



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Abbreviations: CVV – Candidate Vaccine Virus; WHO – World Health Organisation

MF59® Adjuvant Offers an Enhancement for Egg-based Vaccines

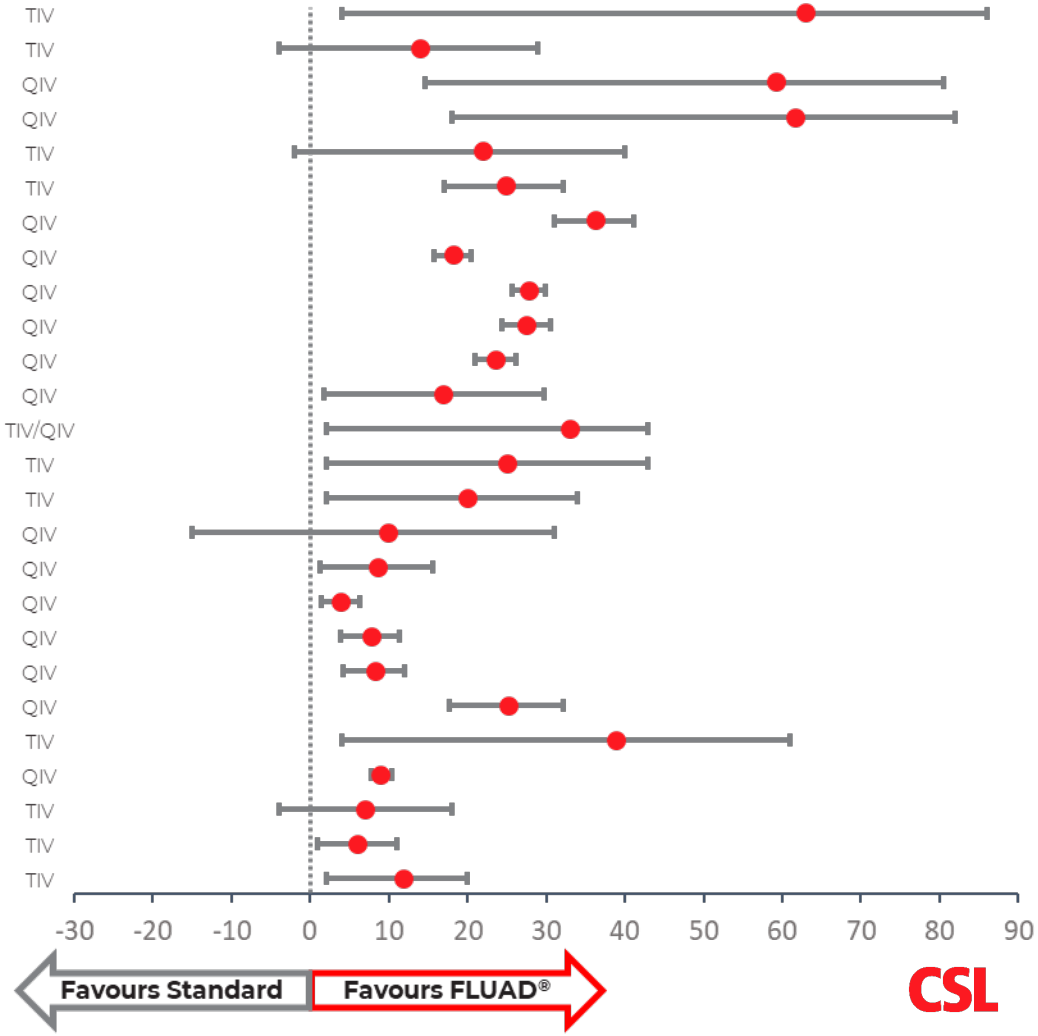
FLUAD®

Adjuvant MF59®

Immune boosting impact of MF59® adjuvant

FLUAD® vs Standard Egg – Benefit of MF59®

Study	Season(s)	aTIV/aQIV vs.
Van Buynder et al. 2013	2011/12	TIV
Pott et al. 2023	2012/13-2014/15	TIV
Domnich et al. 2022	2018/19, 2019/20	QIV
Ku et al. 2024	2022/23	QIV
Gravenstein et al. 2021	2016/17	TIV
Pelton et al. 2020	2017/18	TIV
Pelton et al. 2020	2017/18	QIV
Boikos et al. 2021	2017/18	QIV
Boikos et al. 2021	2018/19	QIV
Imran et al. 2022	2019/20	QIV
Imran et al. 2024	2019/20	QIV
Ku et al. 2024	2022/23	QIV
Cocchio et al. 2020	2011/12–2016/17	TIV/QIV
Mannino et al. 2012	2006/07–2008/09	TIV
McConeghy et al. 2020	2016/17	TIV
Machado et al. 2021	2012/13–2017/18	QIV
Pelton et al. 2020	2017/18	QIV
Izurieta et al. 2019	2017/18	QIV
Izurieta et al. 2020	2018/19	QIV
Izurieta et al. 2020	2019/20	QIV
Imran et al. 2022	2019/20	QIV
Lapi et al. 2019	2001/02–2016/17	TIV
Imran et al. 2024	2019/20	QIV
McConeghy et al. 2020	2016/17	TIV
McConeghy et al. 2020	2016/17	TIV
Lapi et al. 2022	2002–2019	TIV



Abbreviations: QIV - Quadrivalent Influenza Vaccine; TIV - Trivalent Influenza Vaccine

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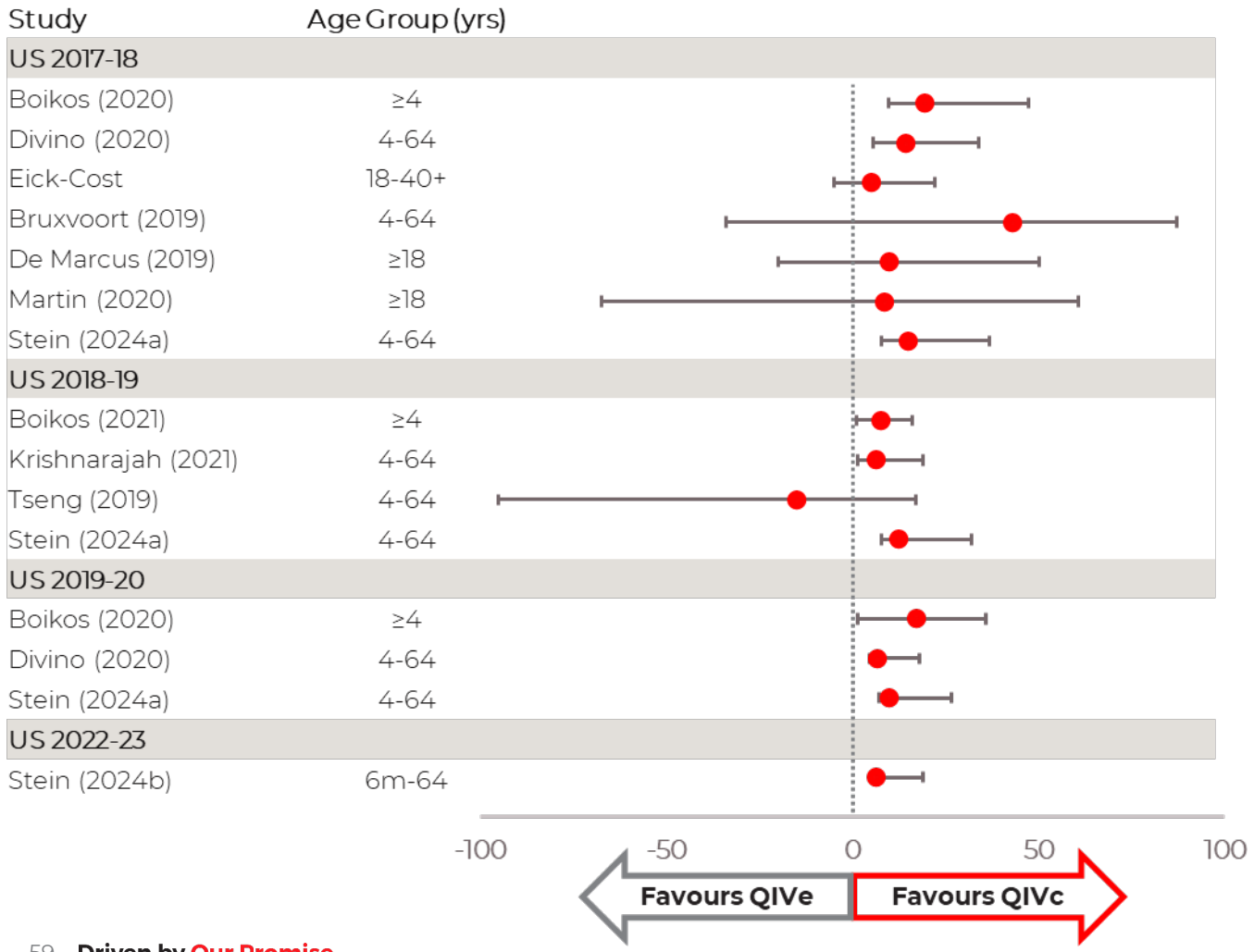
Real World Evidence: Cell-Based Vaccine Showed Improved rVE versus Egg-Based Vaccines Across 4 NH Seasons



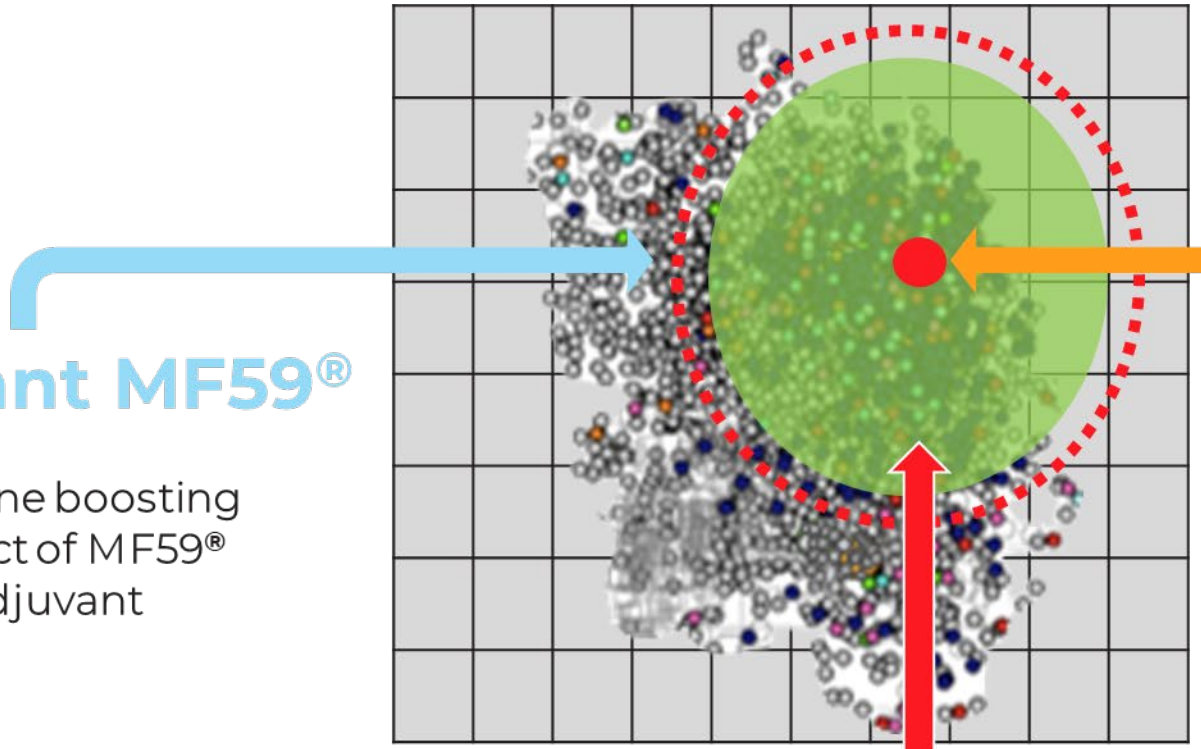
FLUCELVAX®

Cell

Cell Technology provides an exact antigenic match to recommended viral strain

CSL

aTIVc Combines Two Proven Vaccine Technologies and an Optimised Dose of Antigen



Adjuvant MF59®

Immune boosting impact of MF59® adjuvant

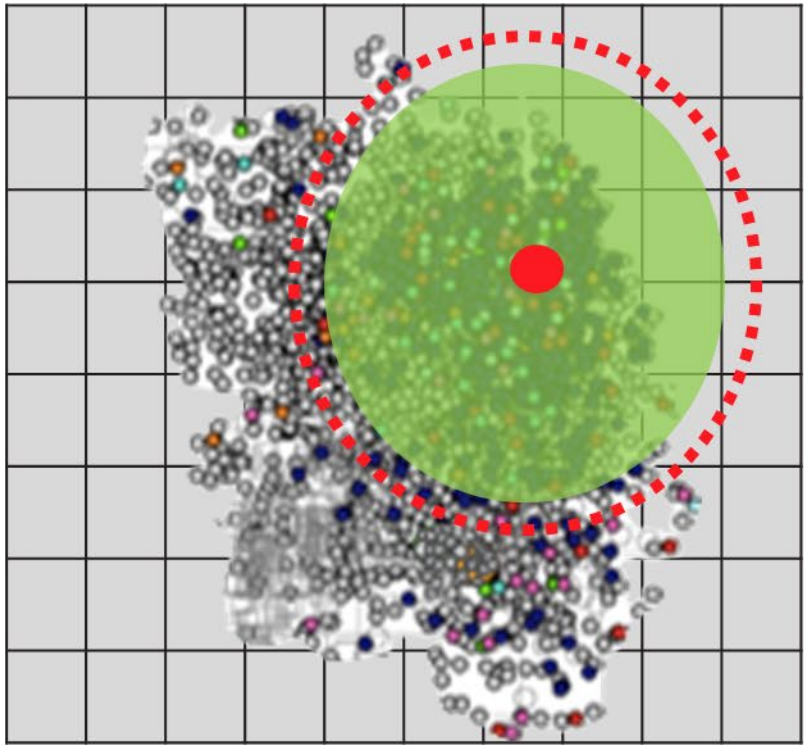
Cell

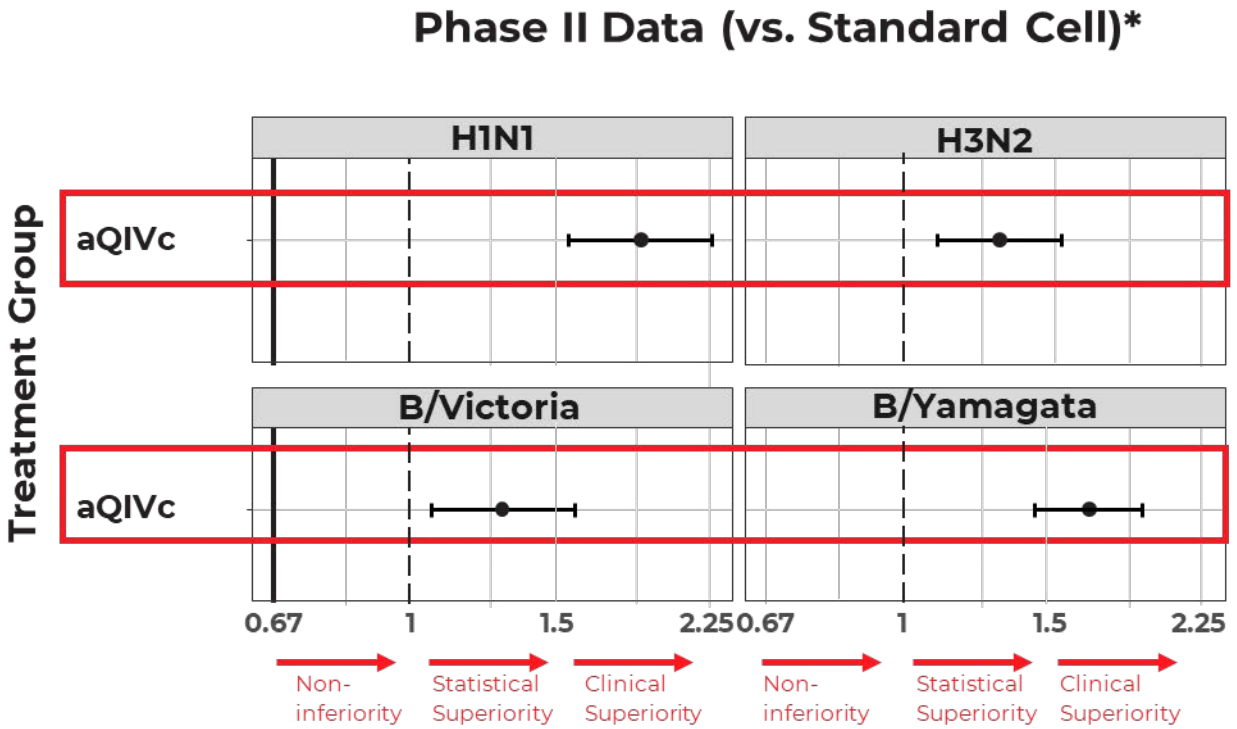
Cell Technology provides an exact antigenic match to recommended viral strain

Optimised dose of cell-based flu antigens

Abbreviations: aTIVc - adjuvanted trivalent cell-based influenza vaccine

aTIVc – Phase II Data Support the Advantages of Combining These Three Technologies

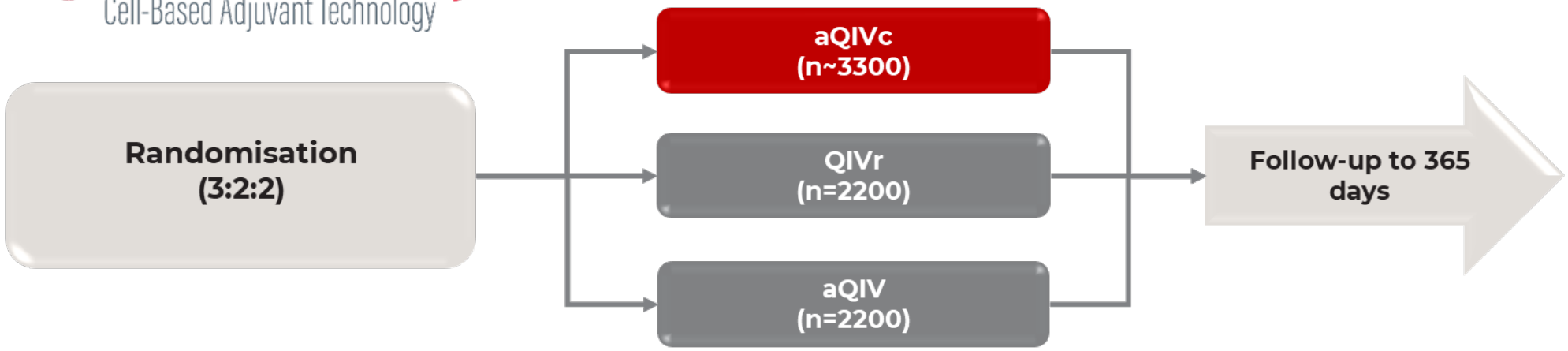




* aQIVc data will support registration of aTIVc

Phase III (V201_03) Immunogenicity & Safety Study in Adult Subjects ≥ 50 years

Celljuvant Study™
Cell-Based Adjuvant Technology



1-2-3

Phase III Data Readout – 1H 2025

Abbreviations: aQIV- adjuvanted quadrivalent influenza vaccine; aQIVc - adjuvanted cell-based quadrivalent influenza vaccine; QIVr - recombinant quadrivalent influenza vaccine

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Conventional mRNA Vaccines – While Promising, Limitations Remain

COVID-19

- Significant reactogenicity
- Waning effectiveness over time
- Frequent boosting required to maintain protection

RSV

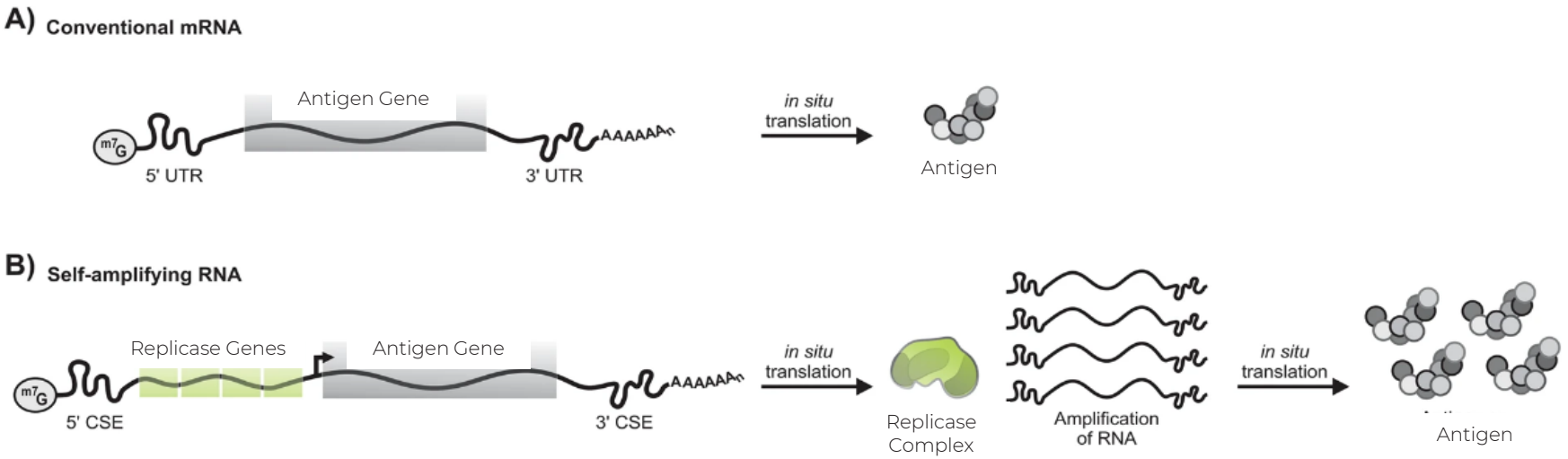
- Lower efficacy compared to protein-based vaccines (with or without adjuvant)

Influenza

- Higher reactogenicity than current influenza vaccines
- Inconsistent immunogenicity against B-strains
- Inconsistent efficacy in older adults

Abbreviations: RSV – Respiratory Syncytial Virus

Self-amplifying mRNA Vaccine Technology



Potential Advantages over Conventional mRNA Vaccines

Superior Immune Response
Increased clinical protection

Durable Immune Response
Less frequent boosters

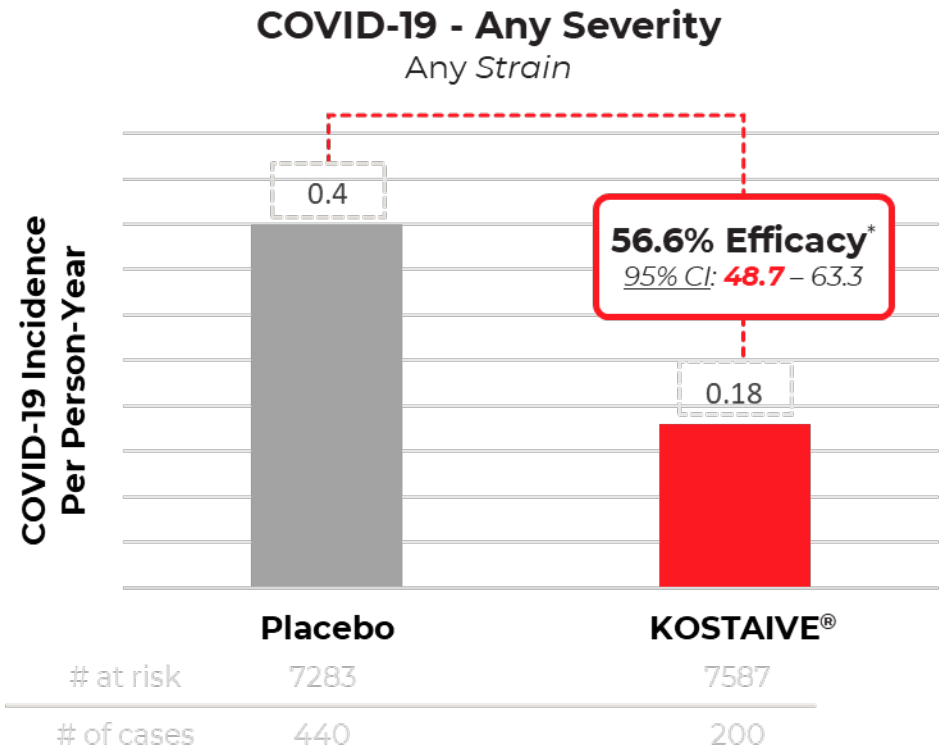
Broad Immune Response
Protection against antigenic escape viruses

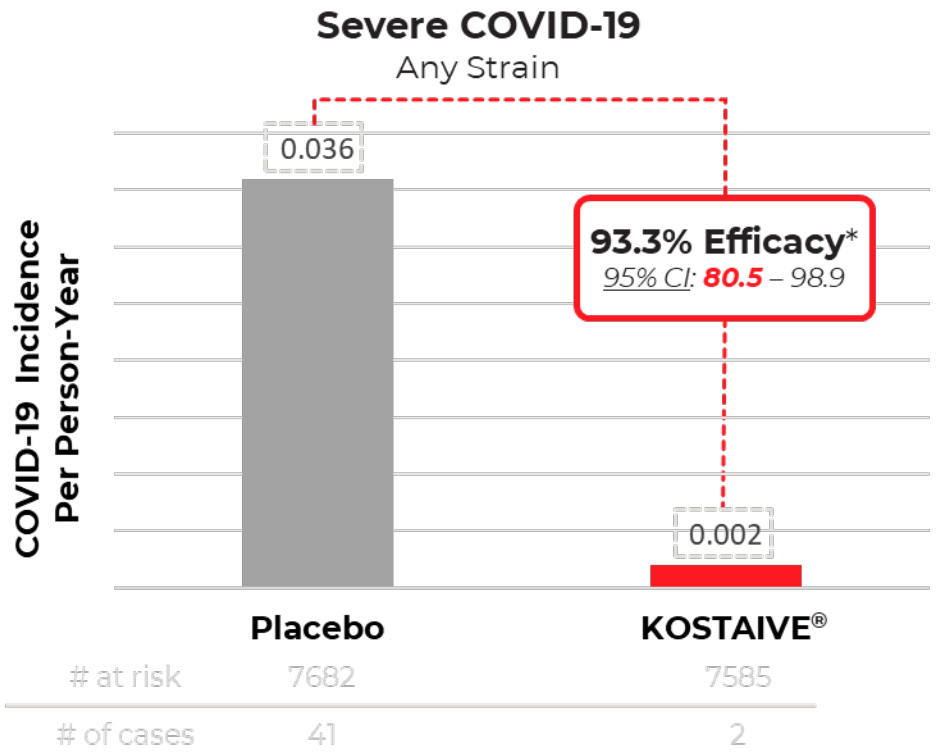
Lower mRNA dose
High potential for development of combined vaccines

Abbreviations: CSE - Conserved Sequence Element; mRNA – Messenger RNA; RNA - Ribonucleic Acid; sa-mRNA – self-amplifying mRNA; UTR - Untranslated Region
Source: Bloom, K. *et al.*, (2021) *Gene Ther.* 28: 117–129.

KOSTAIVE® (sa-mRNA) - Clinical Efficacy Against COVID-19

- Primary Endpoint met: VE against COVID-19 of any severity is 56.6%*
- Key Secondary Endpoint met: VE against severe COVID-19 is 93.3%†

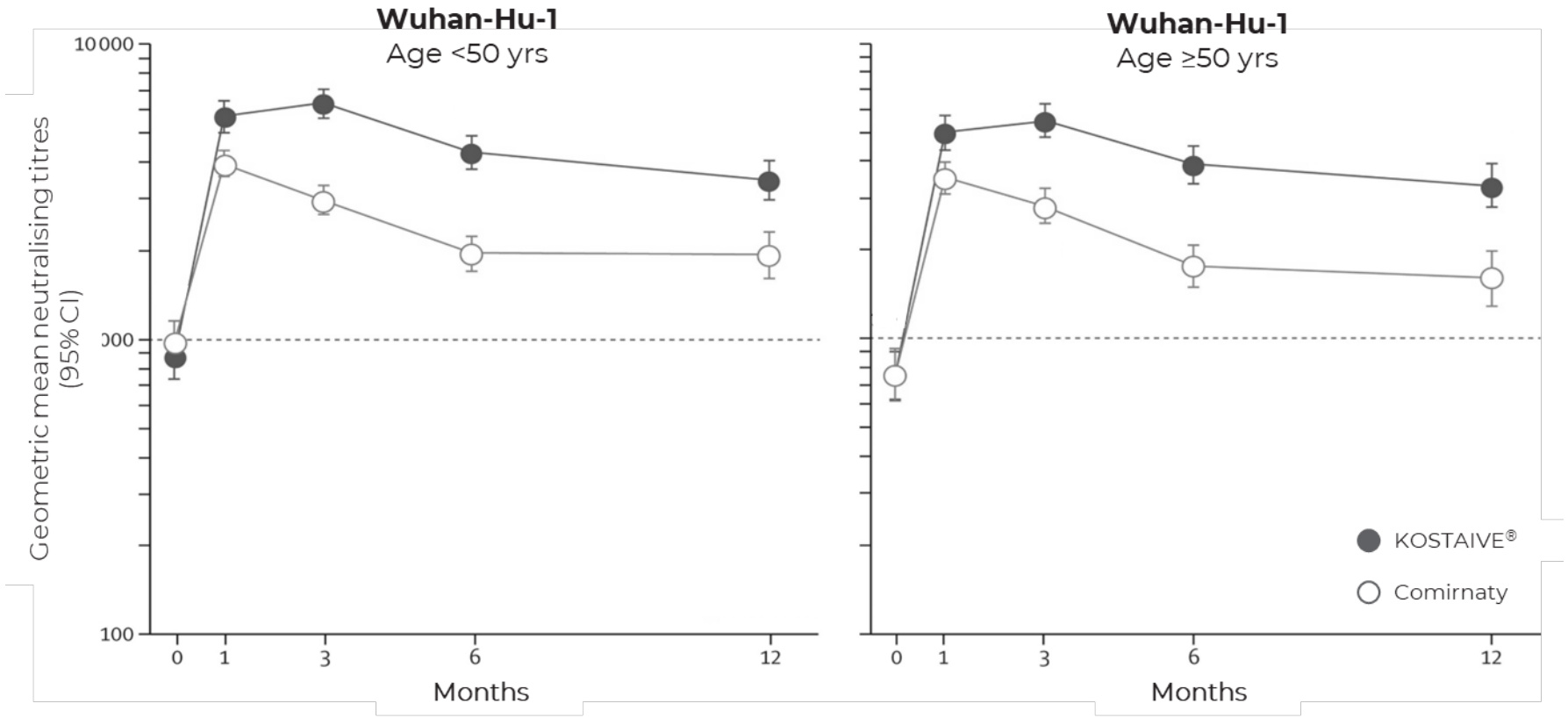




* Predefined success criteria for primary endpoint: Lower Limit of 95% confidence interval exceeds 30%
† Predefined success criteria for key secondary endpoint: Lower Limit of 96% confidence interval exceeds 0%
Figures show data for virologically-confirmed COVID-19 from 7 days after second dose up to Day 92.
Abbreviations: VE – Vaccine Effectiveness
Source: Reproduced from Hồ, N.T., *et al.*(2024) *Nat Commun* 15(4081)

KOSTAIVE® - More Durable Post-booster Response at 12 Months than a Leading mRNA Vaccine

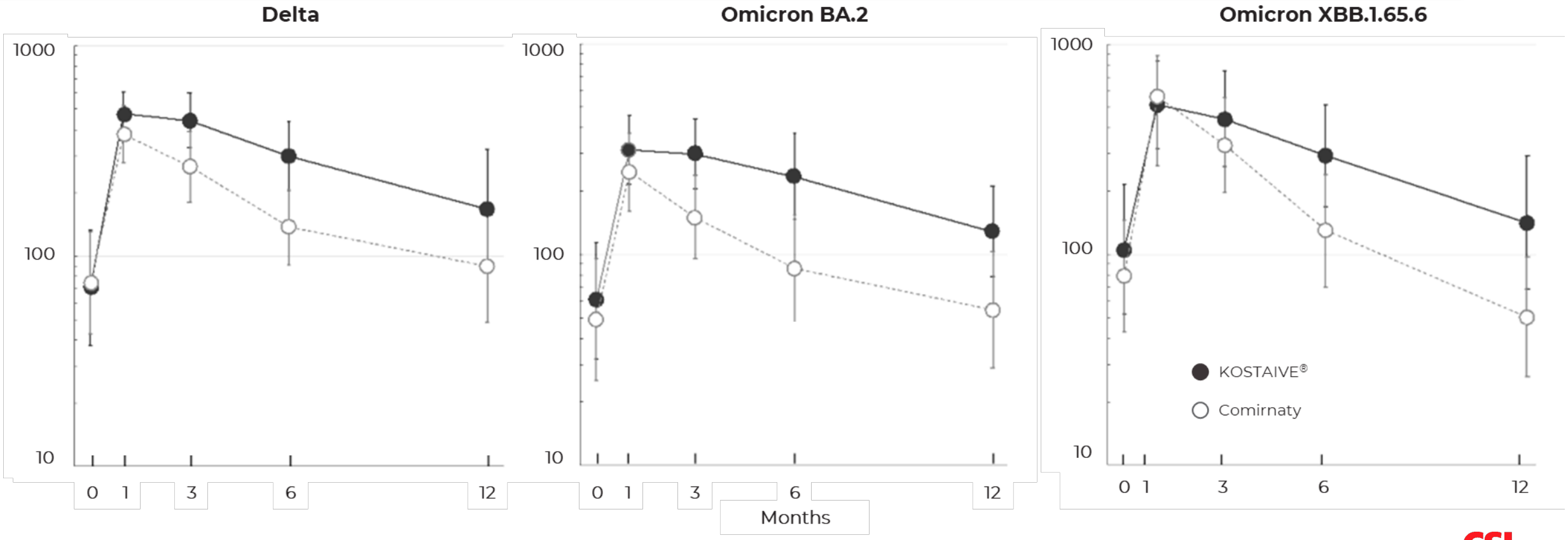
KOSTAIVE® (ARCT-154) induced higher immune response compared to conventional mRNA vaccine over 12 months post-booster in both young (18-49 years) & older (≥50 years) adults



Source: Oda, Y., *et al.*, (2024) *Lancet Infectious Diseases*, Published online

KOSTAIVE® - Broader Post-booster Response at 12 Months than a Leading mRNA Vaccine

KOSTAIVE® (ARCT-154) induces higher immune response to evolving variants of concern compared to a conventional mRNA vaccine over 12 months post-booster



Source: Oda, Y., *et al.*, (2024) *Lancet Infectious Diseases*, Published online

KOSTAIVE® - First Approved sa-mRNA Vaccine Against COVID-19

- Approved in Japan October 2024
- Under review in EMA
- US filing with updated formulation anticipated 2025

Innovation & Sustainability

Deirdre BeVard
Senior Vice President
R&D Strategic Operations
CSL

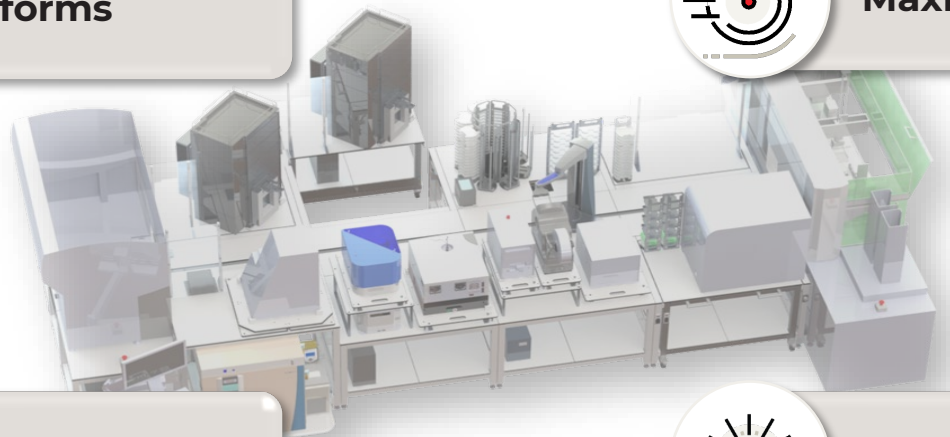
Delivering on Our Promise

More than a century ago, CSL made a promise to protect the health of those stricken with a range of serious medical conditions. Today, that promise has never been stronger

Digital Advances in Product Development

Autonomous labs linked with AI-powered data analysis, enable a new era of automated, more efficient & effective Product Development across all of our scientific platforms

- Scalable Technology Platforms
- Maximising Experimental Throughput

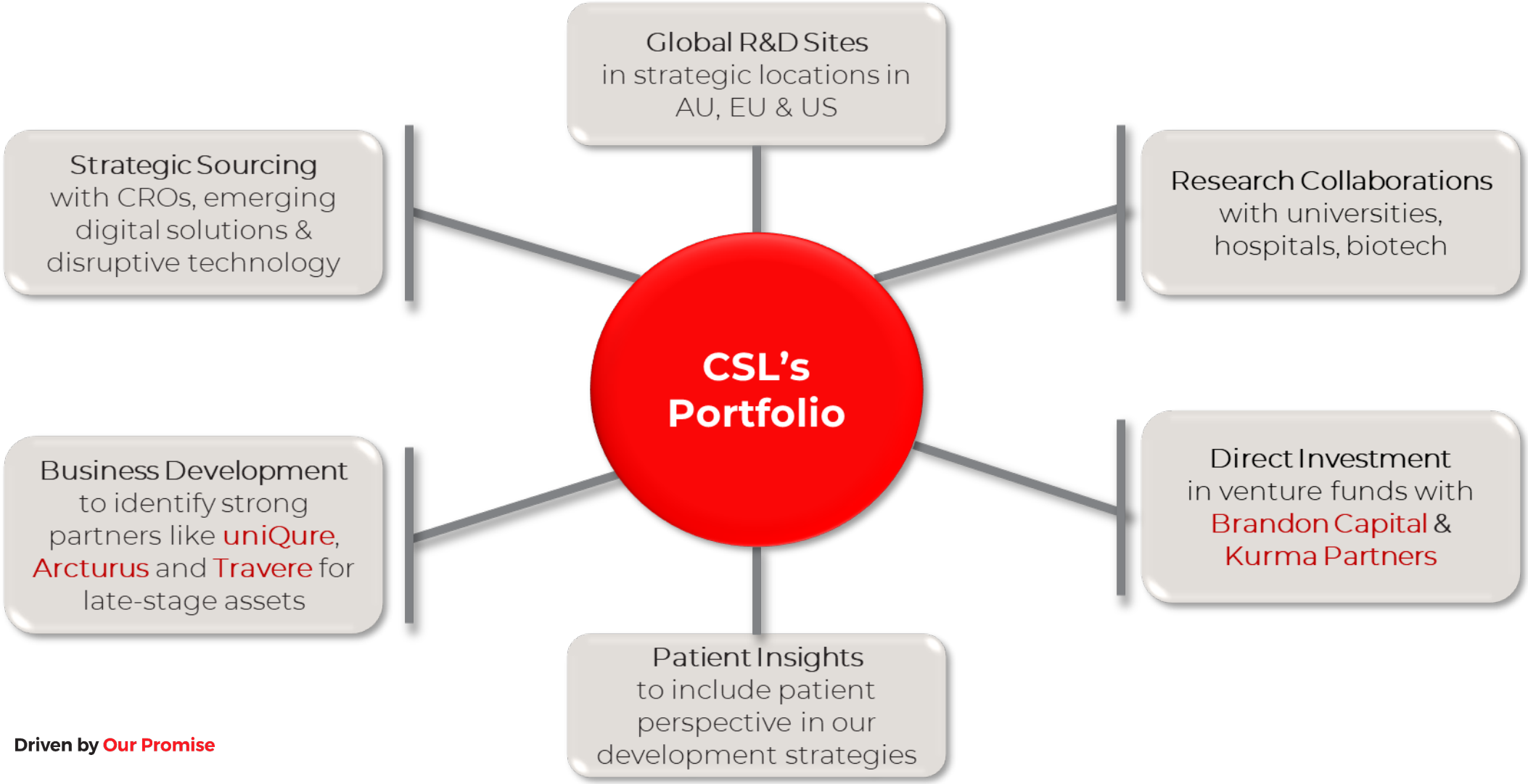


- Data Reproducibility & Robustness
- Accelerated Analysis & Reporting

Process development, formulation and drug product development all benefit from these advances which are applicable to all our scientific platforms

CSL R&D External Engagement for Innovation

Driving strategic partnering to amplify our research capabilities and advance our pipeline



Collaboration Leads to Innovative Growth and Patient Impact

CSL and uniQure awarded 2023 Prix Galien USA Award in the category of Best Product for Rare/Orphan Diseases for HEMGENIX®

CSL uniQure

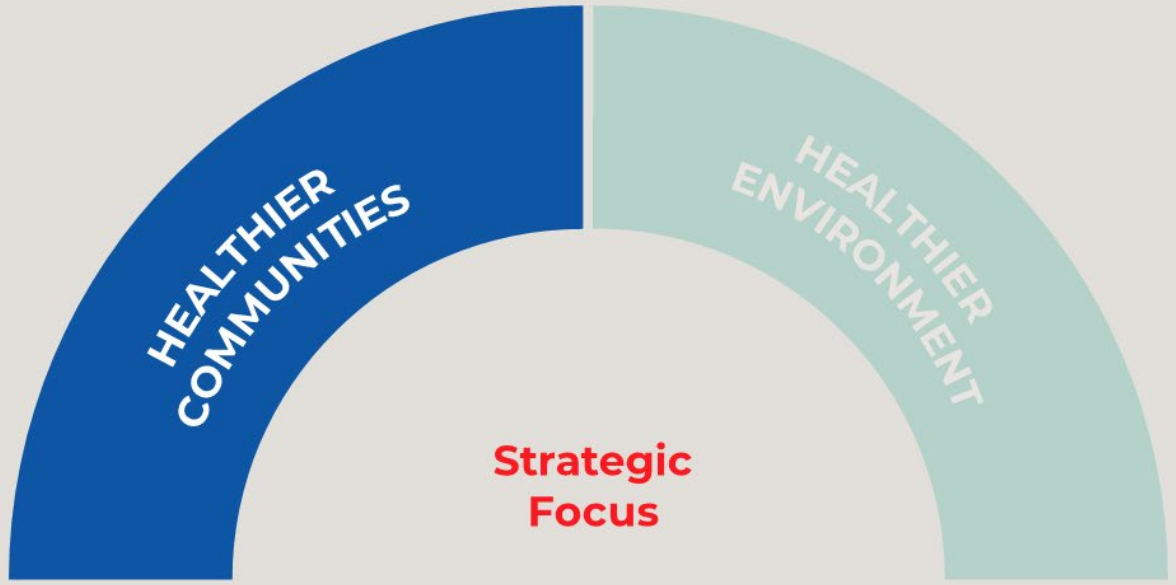
CSL

CSL's Sustainability Strategy

CSL's Sustainability Vision

CSL is committed to a **healthier world**.

Its vision is a sustainable future for its employees, communities, patients and donors, inspired by innovative science and a values-driven culture.



HEALTH EQUITY & EMPOWERMENT

Everyone deserves the opportunity to achieve and maintain their highest level of health and well-being

INCLUSION & BELONGING

Embed an inclusive culture where all backgrounds and perspectives belong, develop, and thrive

Partnerships Help Us Advocate for Patients

CSL actively works with organisations to develop programs & activities for patients

We partner to improve and expand educational and outreach efforts about these diseases and the importance of plasma donation

Medical/Pharma

Biotechnology Innovation Organization (BIO)

Pharmaceutical Research and Manufacturers of America (PhRMA)

European Federation of Pharmaceutical Industries and Associations (EFPIA)

Haemophilia Organisations

National Bleeding Disorders Foundation (NBDF) & locally based chapters

Hemophilia Federation of America (HFA) & locally based member organisations

World Federation of Hemophilia (WFH)

Rare Disease Organisations

National Organization for Rare Diseases (NORD)

Alpha-1 Foundation

GBS|CIDP Foundation

US Hereditary Angioedema Association (HAEA)

Immune Deficiency Organisations

Immune Deficiency Foundation (IDF)

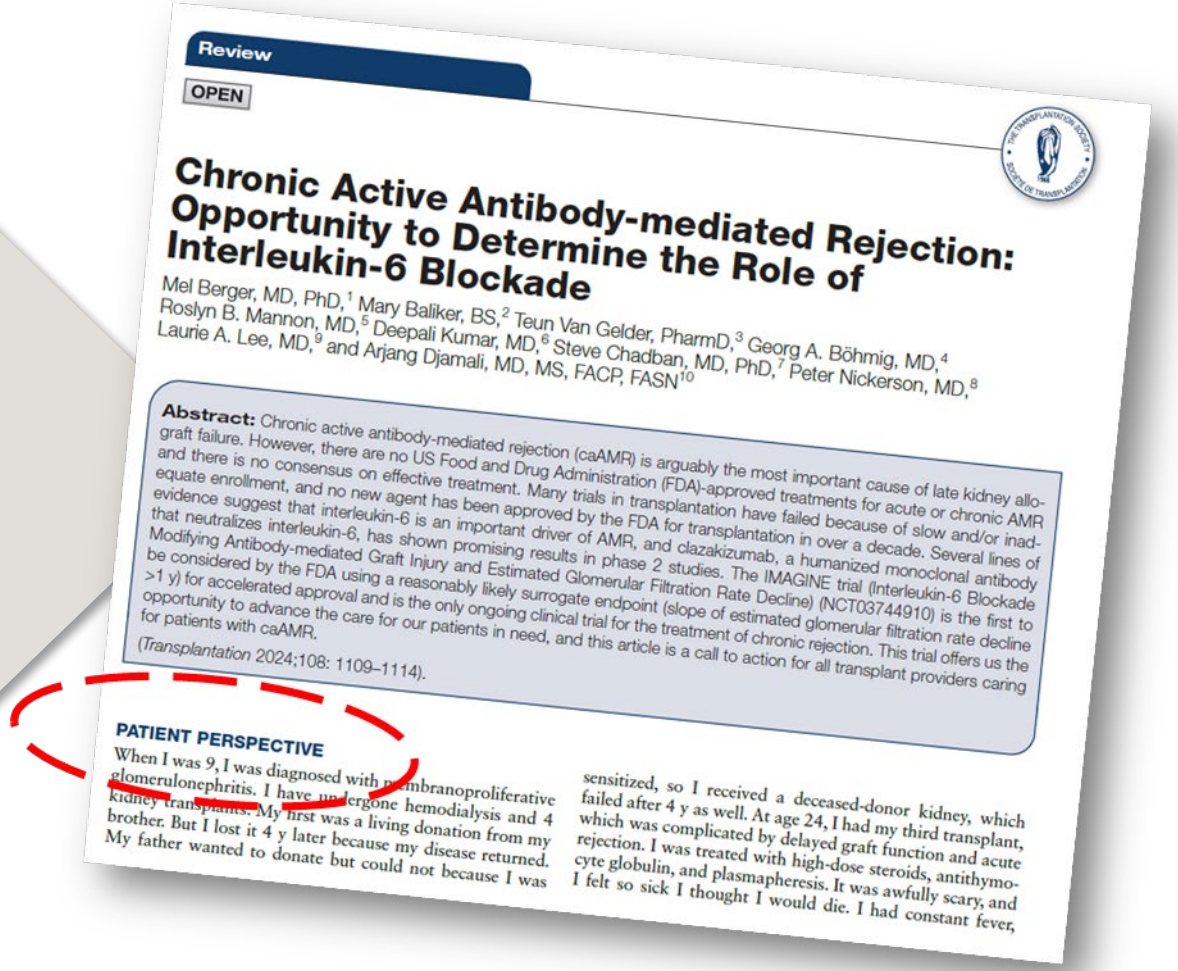
International Patient Organisation for Primary Immuno-deficiencies (IPOPI)

Jeffrey Modell Foundation (JMF)

Clazakizumab AbMR: Prioritising Patient Perspectives

CSL is committed to addressing the unmet needs of patients living with transplantation

CSL's clazakizumab AbMR team **utilised unique patient-focused efforts to recruit patients** in the Phase III IMAGINE study including publishing a peer-reviewed paper during study recruitment which uniquely **included a patient commentary as a call to action** for all transplant providers to consider clinical trials as an option for patients in their care.



Review

OPEN

Chronic Active Antibody-mediated Rejection: Opportunity to Determine the Role of Interleukin-6 Blockade

Mel Berger, MD, PhD,[1] Mary Baliker, BS,[2] Teun Van Gelder, PharmD,[3] Georg A. Böhmig, MD,[4] Roslyn B. Mannon, MD,[5] Deepali Kumar, MD,[6] Steve Chadban, MD, PhD,[7] Peter Nickerson, MD,[8] Laurie A. Lee, MD,[9] and Arjang Djamali, MD, MS, FACP, FASN[10]

Abstract: Chronic active antibody-mediated rejection (caAMR) is arguably the most important cause of late kidney allograft failure. However, there are no US Food and Drug Administration (FDA)-approved treatments for acute or chronic AMR and there is no consensus on effective treatment. Many trials in transplantation have failed because of slow and/or inadequate enrollment, and no new agent has been approved by the FDA for transplantation in over a decade. Several lines of evidence suggest that interleukin-6 is an important driver of AMR, and clazakizumab, a humanized monoclonal antibody that neutralizes interleukin-6, has shown promising results in phase 2 studies. The IMAGINE trial (Interleukin-6 Blockade Modifying Antibody-mediated Graft Injury and Estimated Glomerular Filtration Rate Decline) (NCT03744910) is the first to be considered by the FDA using a reasonably likely surrogate endpoint (slope of estimated glomerular filtration rate decline >1 y) for accelerated approval and is the only ongoing clinical trial for the treatment of chronic rejection. This trial offers us the opportunity to advance the care for our patients in need, and this article is a call to action for all transplant providers caring for patients with caAMR.

(*Transplantation* 2024;108: 1109–1114).

PATIENT PERSPECTIVE

When I was 9, I was diagnosed with membranoproliferative glomerulonephritis. I have undergone hemodialysis and 4 kidney transplants. My first was a living donation from my brother. But I lost it 4 y later because my disease returned. My father wanted to donate but could not because I was sensitized, so I received a deceased-donor kidney, which failed after 4 y as well. At age 24, I had my third transplant, which was complicated by delayed graft function and acute rejection. I was treated with high-dose steroids, antithymocyte globulin, and plasmapheresis. It was awfully scary, and I felt so sick I thought I would die. I had constant fever,

Berger, M., *et al.*, (2024) 108(5): 1109-1114.

Garadacimab Paediatric Trial: Empowering Patient Participation

Gathering patient insights into clinical development designs to help patients take control of their care and treatment

Meet our Clinical Companions from Empath Labs; helping our youngest clinical trial participants by providing a tool to engage, educate, and retain paediatric clinical trial participants while creating world class experiences for caregivers and sites.

CSL is the **first** company to use Clinical Companions in a clinical trial

Delivering on Our Promise

Our efforts to forge a healthier future for patients have been made possible through embracing the evolution of medicine, listening to patient voices and collaborating with purpose

Logan, Living with Haemophilia B

Stacy, Living with Primary Immunodeficiency

Summary

William Mezzanotte MD, MPH
Executive Vice President
Head of R&D
CSL

CSL R&D Portfolio – FY25

Phase I

- **Anumigilimab** – Anti-G-CSFR mAb (SCD)
- **CSL040** – Complement R1 Inhibitor
- **CSL405** – Cell-based Influenza (H2N3) Vaccine
- **CSL406** – sa-mRNA Influenza (H5N1) Vaccine
- **CSL400 (TIV)** – sa-mRNA Trivalent Influenza Vaccine
- **LASN01** – Anti-IL-11R mAb (IPF,TED)

Phase II

- **Horizon 2** – Ig Yield
- **CSL787** – Nebulised Ig
- **Hemopexin** – (VOC in SCD)
- **Vamifeport** – Ferroportin inhibitor (HH)
- **CSL301** – Anti-α2AP mAb (sPE)
- **CSL525 (SNF472)** – Calcification inhibitor (CUA-ESKD)
- **Eblasakimab (CSL334)** – Anti-IL-13R mAb (AD)

Phase III

- **HIZENTRA®** – (SCIg) 20% Liquid (CLL)
- **HIZENTRA®** – (SCIg) 20% Liquid (POTS)
- **RiaSTAP®** – Fibrinogen Concentrate (AFD)
- **Clazakizumab** – Anti-IL-6 mAb (ESKD)
- **CSL964** – Alpha 1 Antitrypsin (Treatment of aGvHD)
- **CSL964** – Alpha 1 Antitrypsin (Prevention of aGvHD)
- **FLUAD® Trivalent Efficacy** – Adjuvanted Egg-based Influenza Vaccine
- **CSL403 (aTIVc)** – Adjuvanted Cell-based Trivalent Influenza Vaccine

Registration/Post-Registration

- **HIZENTRA®** – (SCIg) 20% Liquid
- **PRIVIGEN®** – (IVIg) 10% Liquid
- **ZEMAIRA®/RESPREEZA®** – Alpha 1 Antitrypsin
- **HAEGARDA®** – C1 Inhibitor (HAE)
- **Garadacimab** – Anti-FXIIa mAb (HAE)
- **AFSTYLA®** – rFVIII (Haem A)
- **IDELVION®** – rFIX-FP (Haem B)
- **HEMGENIX®*** – (Haem B)
- **FILSPARI® (Sparsentan)** – Dual ET_A & AT_1 antagonist (IgAN)
- **KORSUVA®/KAPRUVIA®** – KOR agonist (CKD-aP)
- **RAYALDEE®** – Oral ext. release calcifediol (SHPT)
- **TAVNEOS®** – Oral C5a receptor inhibitor (AAV)
- **VELPHORO®** – Sucroferric oxyhydroxide (Serum P control in CKD)
- **VELTASSA®** – Oral potassium binder (HK)
- **AUDENZ®/CELLDEMIC®** – Adjuvanted Cell-based Monovalent Influenza A (H5N1) Vaccine
- **FOCLIVIA®/AFLUNOV®** – Adjuvanted Egg-based Influenza A (H5N1) Vaccine
- **FLUAD® Trivalent*** – Adjuvanted Egg-based Influenza Vaccine
- **FLUCELVAX® Trivalent** – Cell-based Influenza Vaccine
- **KOSTAIVE®** – sa-mRNA Vaccine (COVID)

* Ongoing Post-Marketing Studies

Immunoglobulins | Haematology | Cardiovascular & Renal | Transplant & Immunology
Vaccines | Outlicensed Programs | Partnered Projects

CSL

Forward-Looking Portfolio Highlights – FY25

Immunoglobulins

- HIZENTRA® POTS
  - Phase III first patient in
- HIZENTRA® PFS 50mL
  - JP submission
  - EU approval
- CSL787 (Neb Ig) Phase IIb first patient in
- Horizon 2
  - Toxicology package complete
  - Process robustness package complete

Cardiovascular & Renal

- Clazakizumab (MACE in ESKD)
  - Phase III 50% enrolment
- FILSPARI® (Sparsentan) IgAN Full EU approval
- VELTASSA®
  - US launch patients 12-<18yrs
  - Phase II Paeds 0-<12 yrs first patient in

Haematology

- HEMGENIX® Japan Phase III last patient in
- AFSTYLA® China Phase III first patient in
- RiaSTAP® AFD
  - Phase III first patient in
  - US submission
- CSL889 (Hemopexin) VOC in SCD Phase II first patient in
- Anumigilimab SCD Phase II first patient in

Transplant & Immunology

- Garadacimab (Anti-FXIIa) HAE
  - EU, US & JP approvals
- CSL964 (Treatment of aGvHD)
  - Data presentation
  - FDA interaction
- CSL040 (Complement R1 Inhibitor) Phase I complete

Vaccines

- CSL403 (aTIVc; Adjuvanted Cell-based Trivalent Influenza Vaccine)
  - 12 mo data
  - HA interactions
- aQIV to aTIV Transition EU approval
- KOSTAIVE® sa-mRNA (COVID)
  - EU approval
  - US submission
  - JP launch
- CSL400 (ARCT2138) sa-mRNA Quad Flu
  - Phase I complete
- CSL406 sa-mRNA (H5N1) Flu
  - Phase I complete

Abbreviations: *AFD – Acquired Fibrinogen Deficiency; aGvHD – Acute Graft versus Host Disease; aTIVc- Adjuvanted Cell-Based Trivalent Influenza Vaccine; aQIV – Adjuvanted Quadrivalent Influenza Vaccine; ESKD – End Stage Kidney Disease; EU – Europe; HA – Health Authorities; HAE – Hereditary Angioedema; JP – Japan; IgAN – Immunoglobulin A Nephropathy; MACE - Major Adverse Cardiac Events; Neb Ig - Nebulised Ig; PFS – Pre-Filled Syringe; POTS* - Postural Orthostatic Tachycardia Syndrome; *sa-mRNA – Self-Amplifying messenger RNA; RNA – Ribonucleic Acid; SCD – Sickle Cell Disease; US – United States; VOC – Vaso-occlusive Crisis*

Key Takeaways

- **R&D continues to invest and innovate** (SID, Nebulised Ig, Horizons 1 & 2, sa-mRNA) in our core Ig, plasma & vaccine platforms to support future growth
- We are **relentlessly focused on rapid advancement** of our research & early development programs towards late-stage development & registration
- **HEMGENIX®, KOSTAIVE®, RiaSTAP® & garadacimab** all advancing toward registration & approval for key indications in key regions
- We have experienced a few late-stage setbacks (KCENTRA® Trauma, HIZENTRA® DM, clazakizumab AbMR), however each of these products have promising follow-on indications which we are actively pursuing
- We have **exciting, novel Phase II** (e.g. Vamifeport, Hemopexin) and **Phase III programs** (e.g. aTIVc, CSL964, clazakizumab, HIZENTRA® POTS) to add incremental value to patients & CSL

Thank You / Questions