

CSL ASX Announcement

3 November 2022

CSL Highlights Progress Across Strong R&D Pipeline

CSL Limited (ASX:CSL; USOTC:CSLLY) – CSL will today hold its annual Research and Development Investor Briefing.

Please find attached the presentation materials, including a news release outlining highlights across the portfolio.

The briefing for investors and analysts will be held at 9:00am Australian Eastern Daylight Time.

The 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 in the day.

Authorised by **Fiona Mead**, Company Secretary

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The CSL logo is a red square with the letters 'CSL' in white, bold, sans-serif font.A white rounded rectangular box containing the text 'Danielle, Living with Primary Immunodeficiency' in a black sans-serif font. The background of the slide is a photograph of a woman with long blonde hair, wearing a blue blazer, sitting at a table outdoors and talking to a man whose back is to the camera.

R&D Investor Briefing

November 3, 2022

Legal Notice

Important Notice and Disclaimer

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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.

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.

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The CSL logo is displayed in white, bold, sans-serif capital letters on a red square background in the top left corner of the image.

Inauguration of R&D innovation
hub in Marburg, Germany
13 September 2022



Introduction

William Mezzanotte MD

Executive Vice President, Head of R&D
Chief Medical Officer

CSL



Agenda

01 Welcome

— Mark Dehring

**02 Introduction, FY22
Retrospective & Highlights,
Combined CSL Portfolio**

— Bill Mezzanotte

03 Research

— Andrew Nash

04 Vaccines

— Jon Edelman

05 Development

— Steve Pascoe

06 Commercial

— Bill Campbell

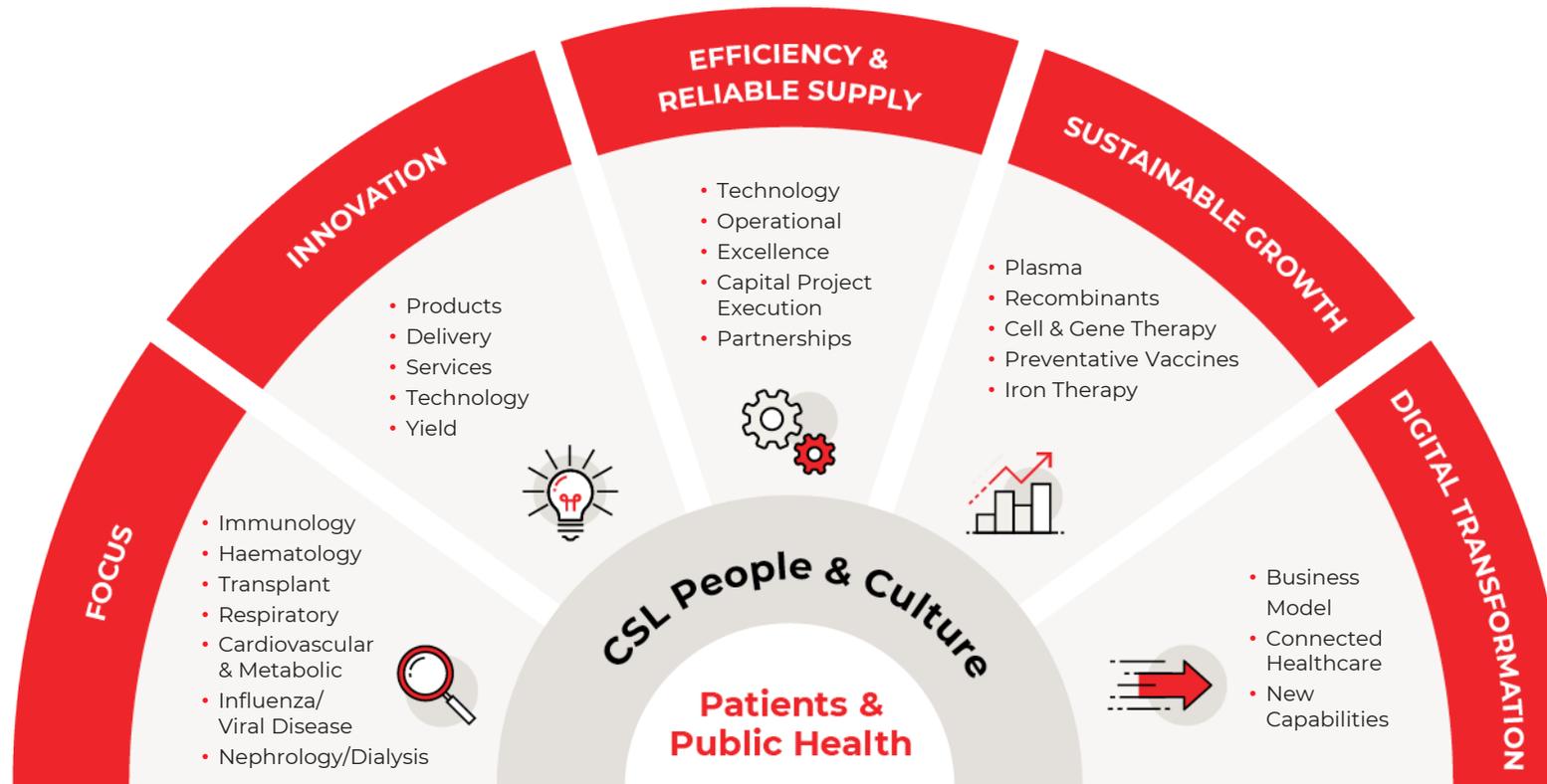
**07 Looking toward
FY23 & Summary**

— Bill Mezzanotte

08 Q&A

— Panel

R&D – Supporting CSL’s 2030 Strategy



R&D Highlights – FY22



Immunology

- **Garadacimab** (Anti-FXIIa) HAE
 - Phase III study enrolment completed (Last Patient In)
 - FDA confirmed Fast Track Eligibility
 - EMA Orphan Drug Designation granted
- **BERINERT®** SC HAE submitted to JP PMDA
- **HIZENTRA®**
 - Phase II SSc study enrolment completed (Last Patient Last Visit)
 - EU approval to expand SID indications



Haematology

- **CSL888** (Haptoglobin) SAH US Orphan Drug Designation granted
- **Etranacogene dezaparvovec**
 - Primary endpoint achieved in (Haem B gene therapy) HOPE-B study
 - MAA (EU) & BLA (US) submitted
- **KCENTRA® Trauma**
 - FDA approval to proceed with Phase III
- **IDELVION®** Haem B China CTA filed



Cardiovascular & Metabolic

- **CSLI12** (ApoA-1)
 - 80% enrolment achieved
 - 3rd interim analysis completed
- **CSL346** (Anti-VEGF-B) DKD Phase II POC study completed



Respiratory

- **Garadacimab** (Anti-FXIIa) IPF Phase II study initiated



Vaccines

- **aQIVc** (cell antigen + MF59®) Phase II study complete
- **FLUCELVAX®** Quadrivalent
 - US & Argentina approval 6M+ indication
 - AU 2yr+ extension
 - NZ 9yr+ extension approval
- **FLUAD®** Quadrivalent
 - Adults 50-64yr Phase III study enrolment completed
- **AUDENZ™** MDV US approval, triggering full ownership transfer of HS to CSL Seqirus



Partnerships & Alliances

- A joint venture founded by CSL, WEHI, & University of Melbourne secured State Government funding to create a biotech start-up incubator in CSL's new global headquarters, under construction, in Melbourne



R&D Capacity Expansion

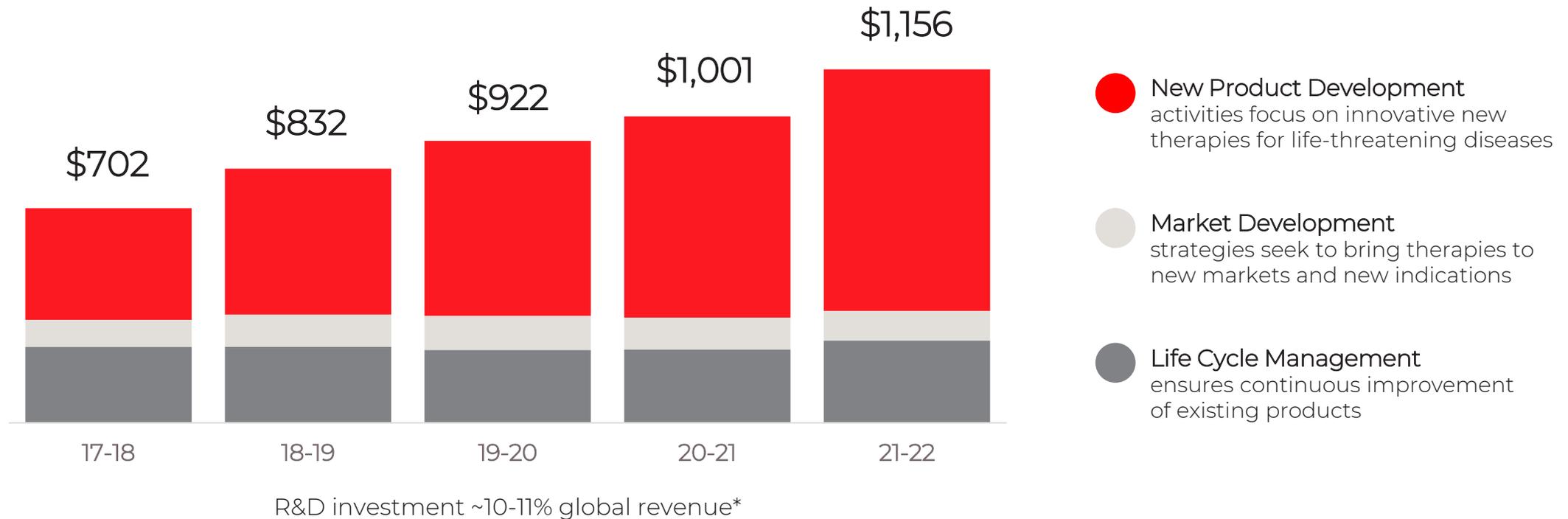
- Melbourne: New AU HQ and R&D facilities under construction to house ~800 employees; on track for completion early 2023
- Marburg: New R&D Campus to accommodate ~500 employees set to open Sep 2022
- Boston: New CSL Seqirus facility in Waltham to be operational in 2022; will host ~300 employees supporting CSL's R&D portfolio including sa-mRNA technology platform



Transplant

- **CSL964** (AAT) prevention of GvHD – MODULAATE Phase III study Part 2 initiated

Commitment to Research and Development



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

Expanding R&D's Global Footprint



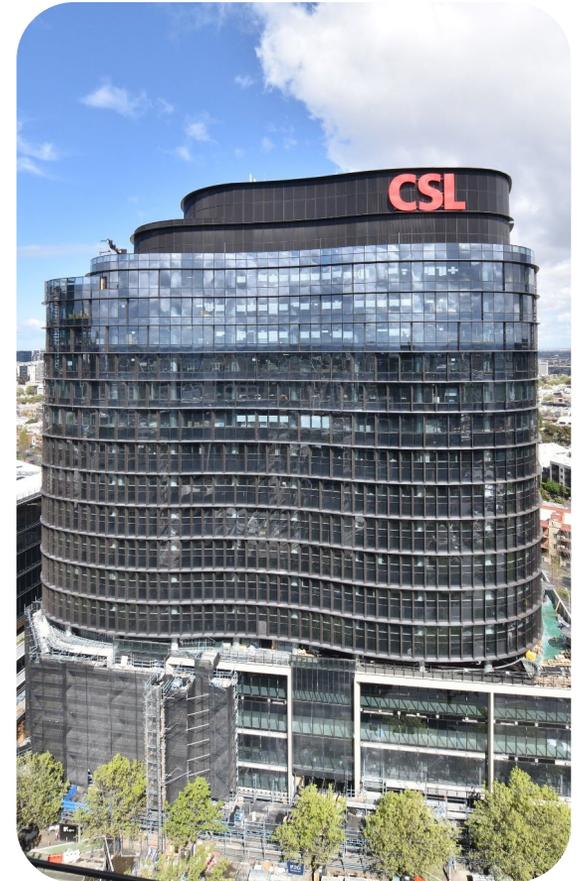
Tullamarine, AU



Marburg, DE

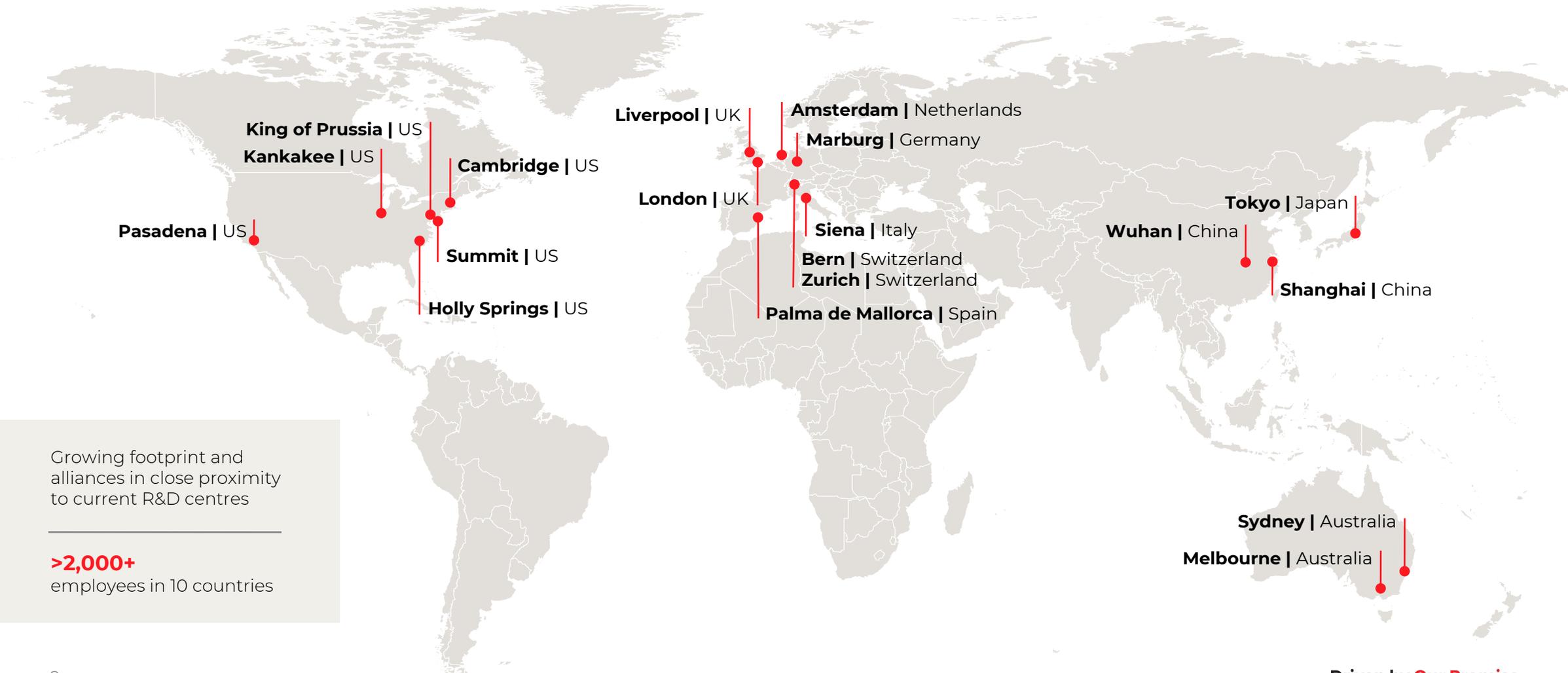


Waltham, MA, US



Melbourne, AU

Our CSL R&D Footprint - Key Global R&D Locations



Growing footprint and alliances in close proximity to current R&D centres

>2,000+
employees in 10 countries

Recent CSL News Aligned with R&D Strategy

Strengthen Our Core Competencies

Build Strategically and Scientifically in our TAs

Explore Disruptive Innovation

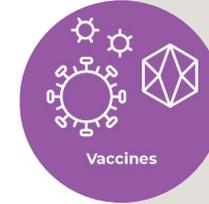
Expand into Complementary Disease Areas and Platforms

Embrace the External Environment



Haematology

License to TS23 from Translational Sciences



Vaccines

Strengthen sa-mRNA capabilities through partnership with Arcturus Therapeutics



Expanded R&D Infrastructure & Incubator



Advance of Internal Portfolio across Therapeutic Areas



CSL Vifor

Global Leadership in Nephrology

Empowered by Unique Partnership with Fresenius Medical Care

CSL Vifor

STRONG PHARMA EXPERTISE

- Development for commercialisation
- Clinical development
- Manufacturing, regulatory and market access



**FRESENIUS
MEDICAL CARE**

GLOBAL LEADER IN DIALYSIS

~350,000
Kidney disease
patients*



>54 million
dialysis
treatments p.a.*



>4,200
Clinics*



**VIFOR FRESENIUS MEDICAL CARE
RENAL PHARMA**



GLOBAL LEADERSHIP IN NEPHROLOGY THROUGH:

Close collaboration
on global scale



Access to patient data &
faster clinical trial
execution



**Disease
Insight and
Expertise**

Improving outcomes
via treatment algorithms



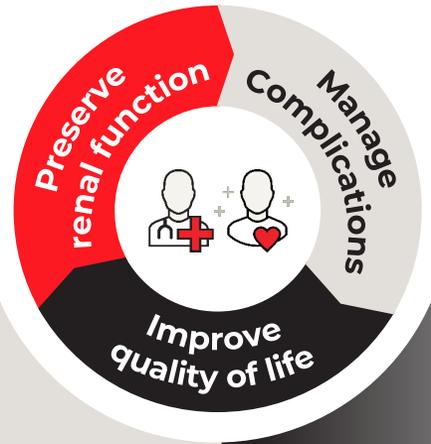
Attractive partner
for innovation



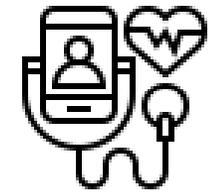
Supporting Chronic Kidney Disease Patients Along Their Journey



Chronic Kidney Disease Treatment



Dialysis Treatment



Transplant



CSL Immunology Portfolio

Sparsentan

CSL112

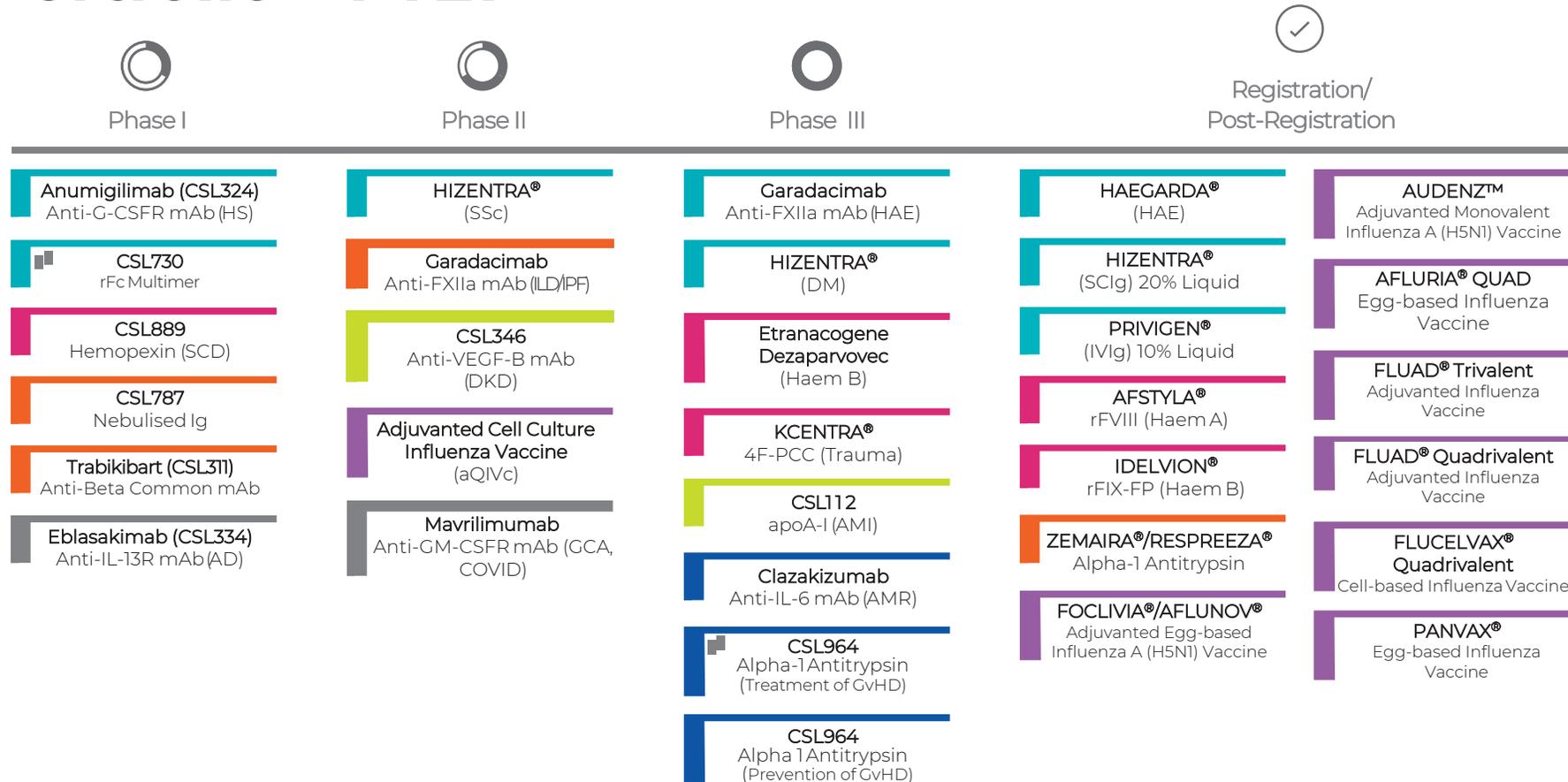
INS-3001

Clazakizumab

SNF472

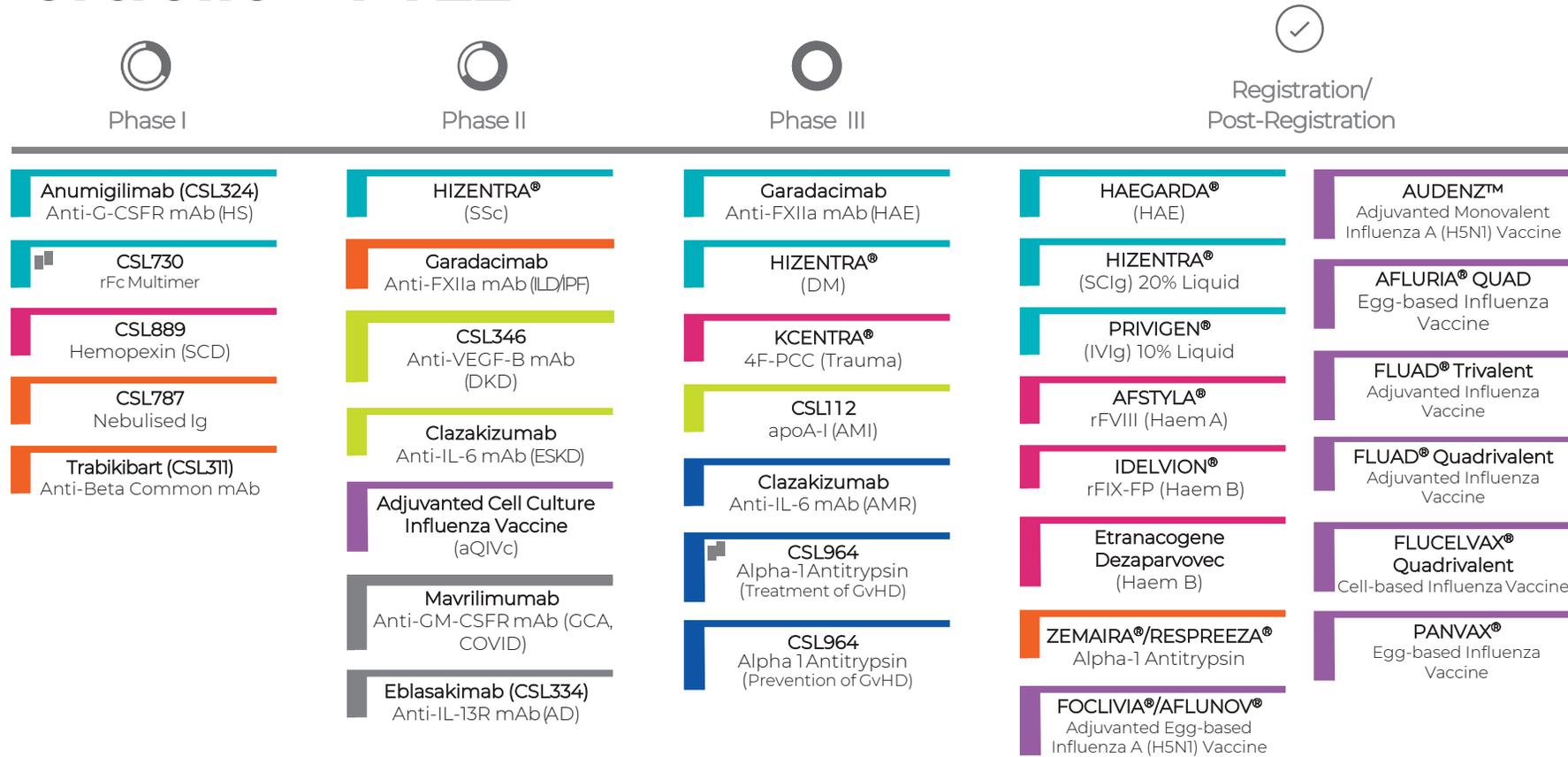
Clazakizumab

R&D Portfolio – FY21



■ Immunology
 ■ Haematology
 ■ Respiratory
 ■ Cardiovascular & Metabolic
 ■ Transplant
■ Vaccines
 ■ Outlicensed Programs
 ■ Partnered Projects

R&D Portfolio – FY22



■ Immunology
 ■ Haematology
 ■ Respiratory
 ■ Cardiovascular & Metabolic
 ■ Transplant
■ Vaccines
■ Outlicensed Programs
■ Partnered Projects

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Research

Pipeline Building Through External Innovator Engagement

Andrew Nash PhD

Senior Vice President, Research
Chief Scientific Officer

CSL





CSL External Innovator Engagement

Creating investable opportunities

- Early discovery/ Stage 0 portfolio
- Research Acceleration Initiative (RAI)
- WEHI / CSL Centre for Biologic Therapies

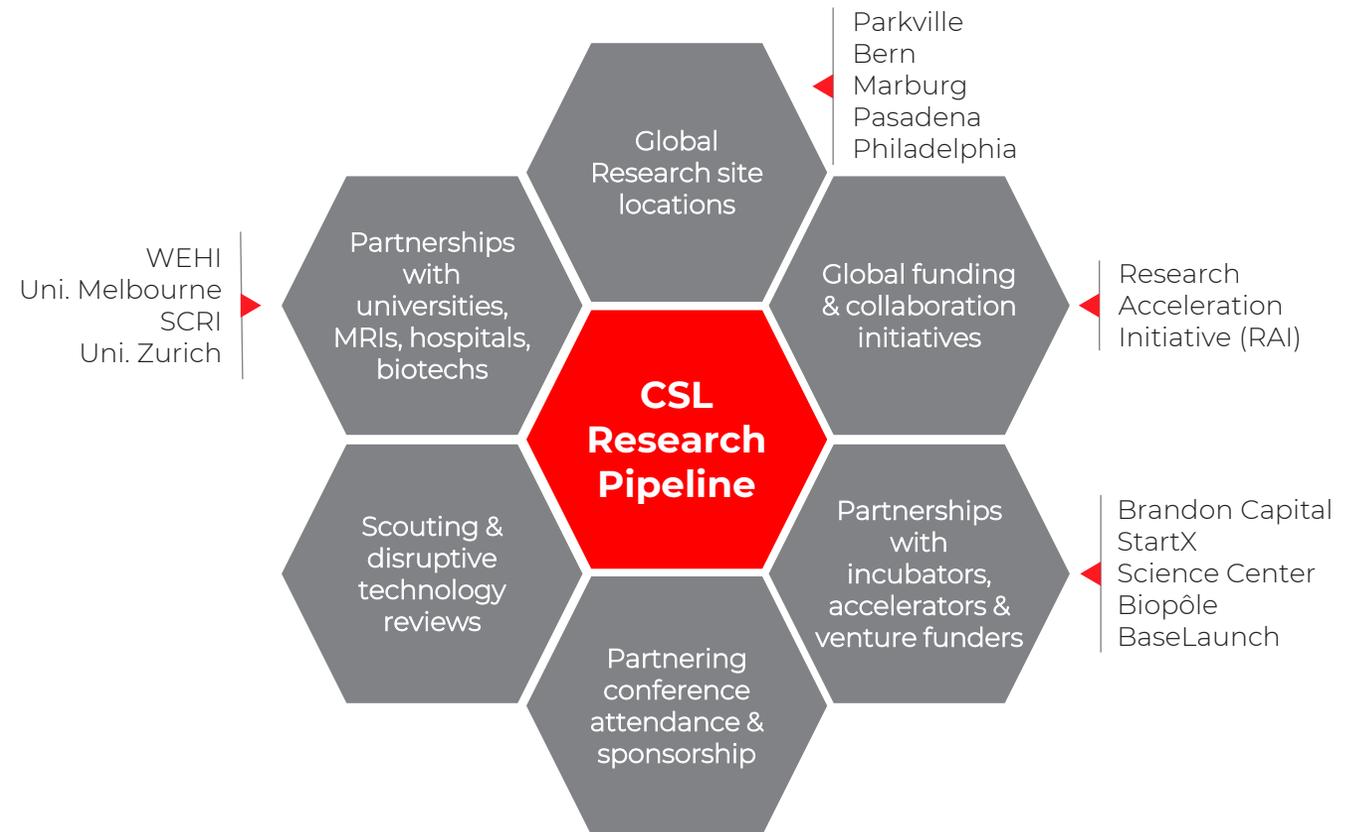
Direct investment

- VC / accelerator investment
- Investment in start-ups

Developing innovation ecosystem

- People & skills / Infrastructure & technology
- Bio21 Global Research Hub
- Biotech Incubator partnership
- CSL Melbourne & Tullamarine facilities

Research External Innovation Strategy



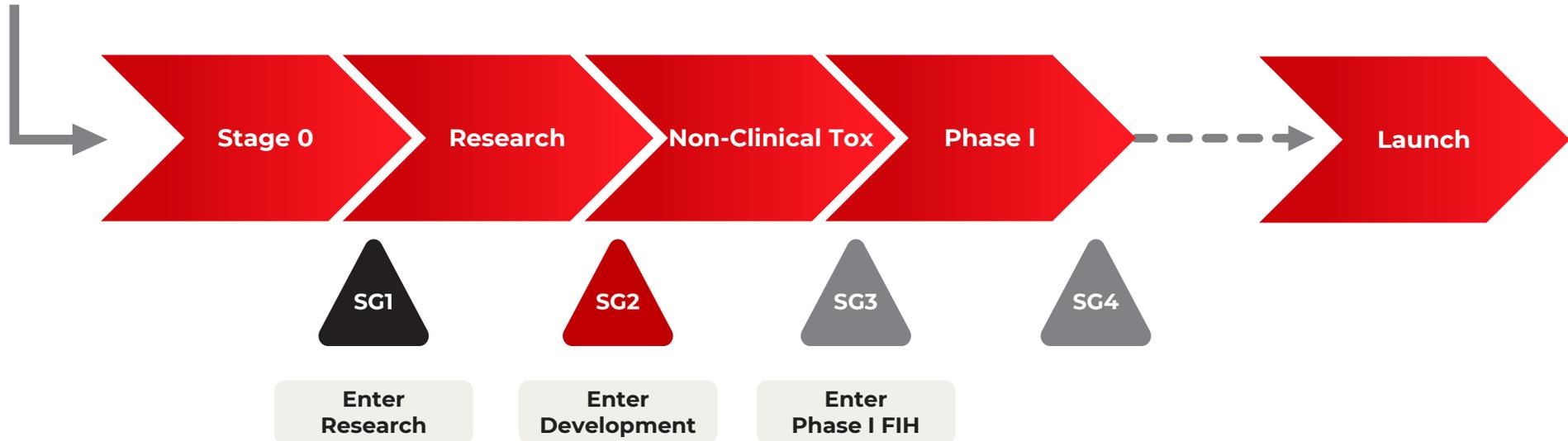
Abbreviations: MRI – Medical Research Institute; SCRI – Seattle Children’s Research Institute; VC – Venture Capital

CSL External Innovator Engagement

External collaboration and engagement delivers a robust and on-strategy Stage 0 portfolio



CSL Research Acceleration Initiative
Seeking Expressions of Interest from Research Organisations

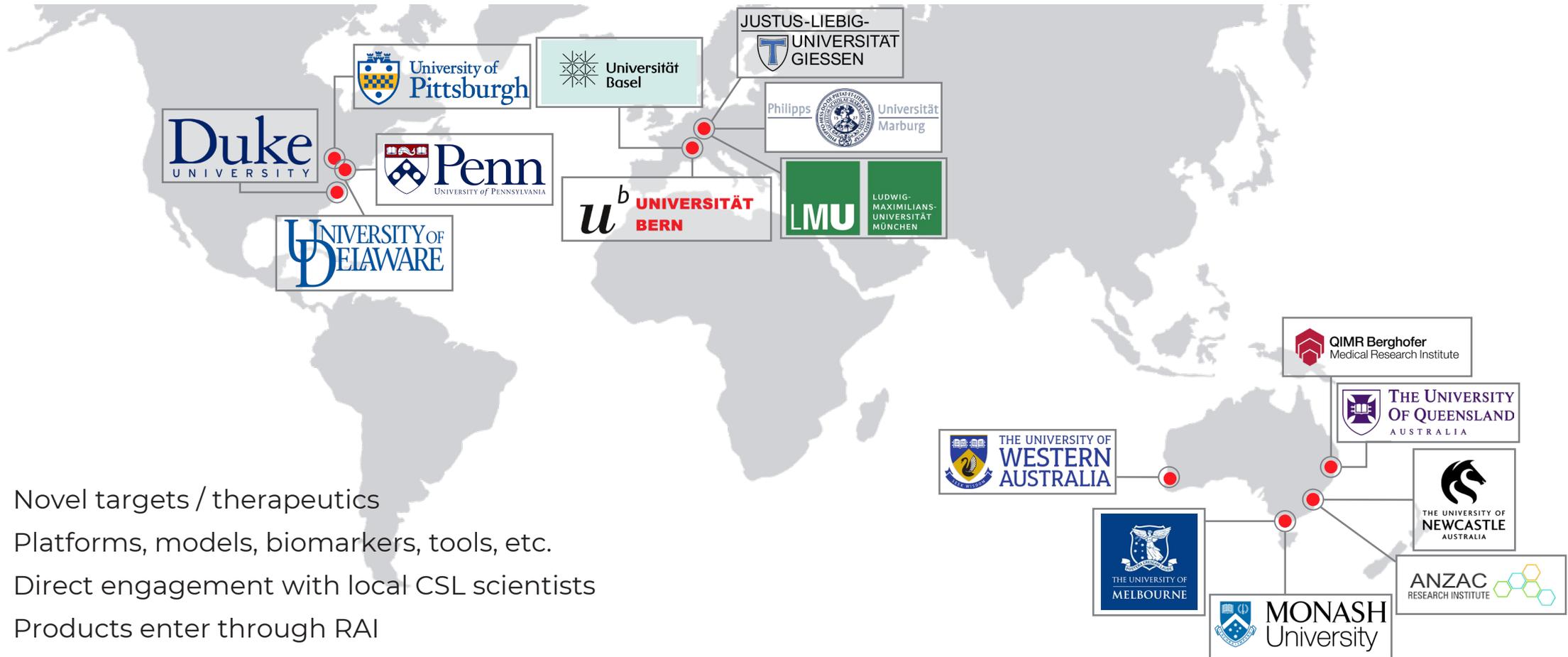


Abbreviations: FIH – First-in-Human; SG – Stage Gate; Tox – Toxicology



CSL External Innovator Engagement

Stage 0 Collaborations



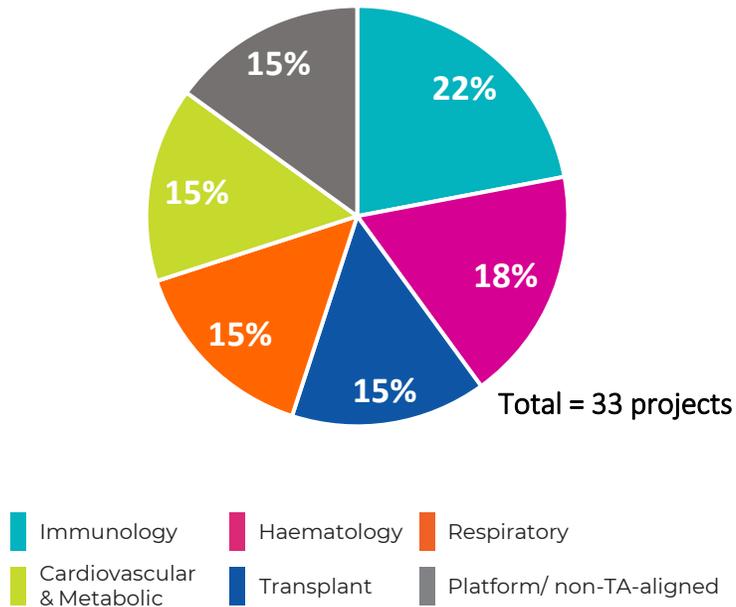
- Novel targets / therapeutics
- Platforms, models, biomarkers, tools, etc.
- Direct engagement with local CSL scientists
- Products enter through RAI

Abbreviations: RAI – Research Acceleration Initiative

CSL External Innovator Engagement

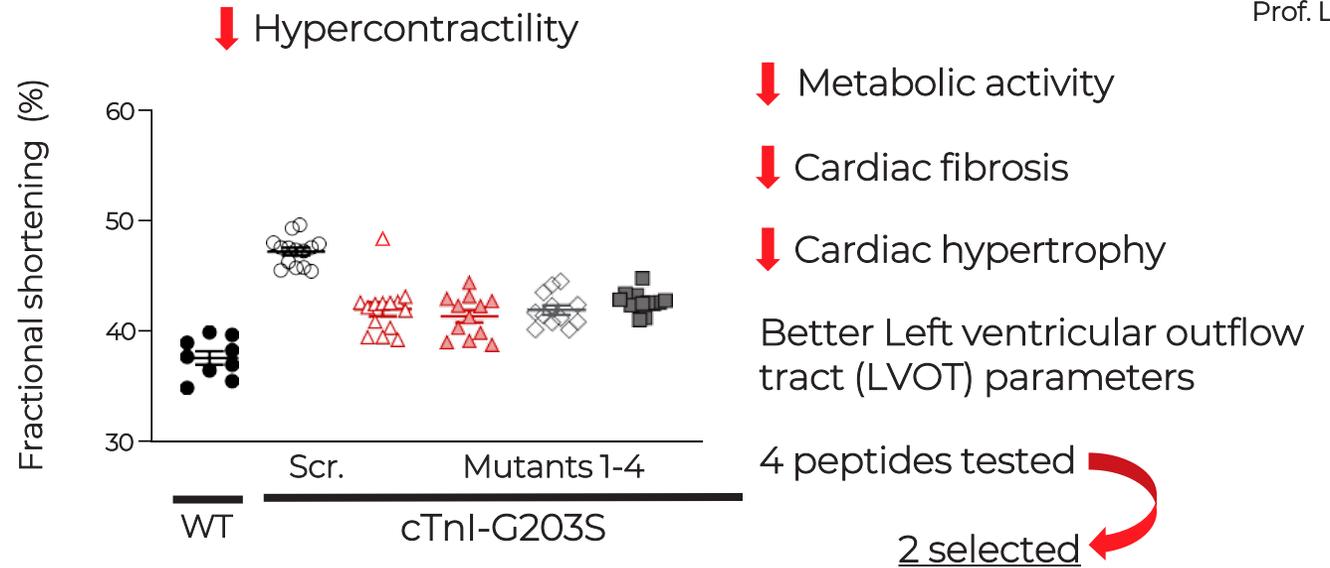
Stage 0 Portfolio

TA Classification of Stage 0 Projects (%)



An iCa-L peptide antagonist for familial HCM

Results preventive approach



THE UNIVERSITY OF
WESTERN
AUSTRALIA

Prof. Livia Hool

Abbreviations: HCM - Hypertrophic Cardiomyopathy; TA - Therapeutic Area; WT - Wild Type

CSL External Innovator Engagement

Biotech Incubator Partnership

- \$95m project housed across two floors located at CSL's new global corporate headquarters
- Run by independent, experienced operator
- Lab space, office space, suites, meeting rooms including board room, co-working spaces & event spaces
- Target launch date early 2024
- Expressions of interest: incubator@csl.com.au



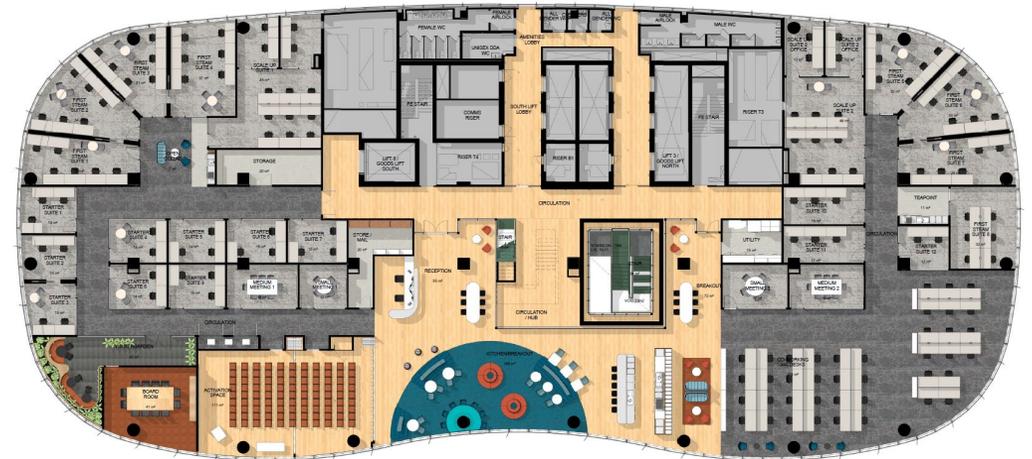
Space for up to 40 start-ups

- 1,400m² wet lab space (214 benches)
- 1,700m² office space (143 desks)



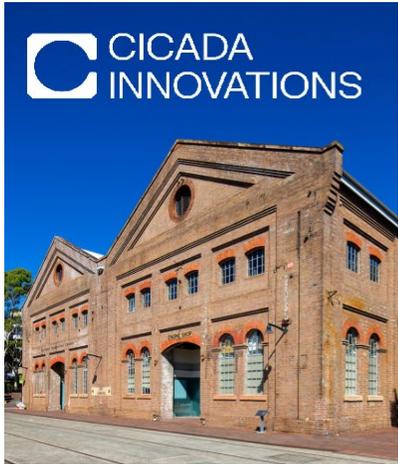
CSL External Innovator Engagement

Key Ingredients for a Successful Incubator	Biotechnology Incubator
Co-location with global, industry anchor	✓
Location in well-established hub of science & technology	✓
Affordable wet-lab & office space	✓
Access to support services & state-of-the-art equipment / facilities	✓
Facilitated introductions to investors (access to capital)	✓
Mentoring, commercialization, education & programming	✓
Proximity to Central Business District	✓
Proximity to public transport	✓



CSL External Innovator Engagement

Cicada Innovations Appointed as Incubator Operator



Australia's Flagship Deep Tech Incubator

- 20 years experience in developing ventures
- Sydney based incubator supports deep tech innovators with:
 - cutting edge labs & offices
 - training & mentoring
 - connection to investors, partners, policy makers

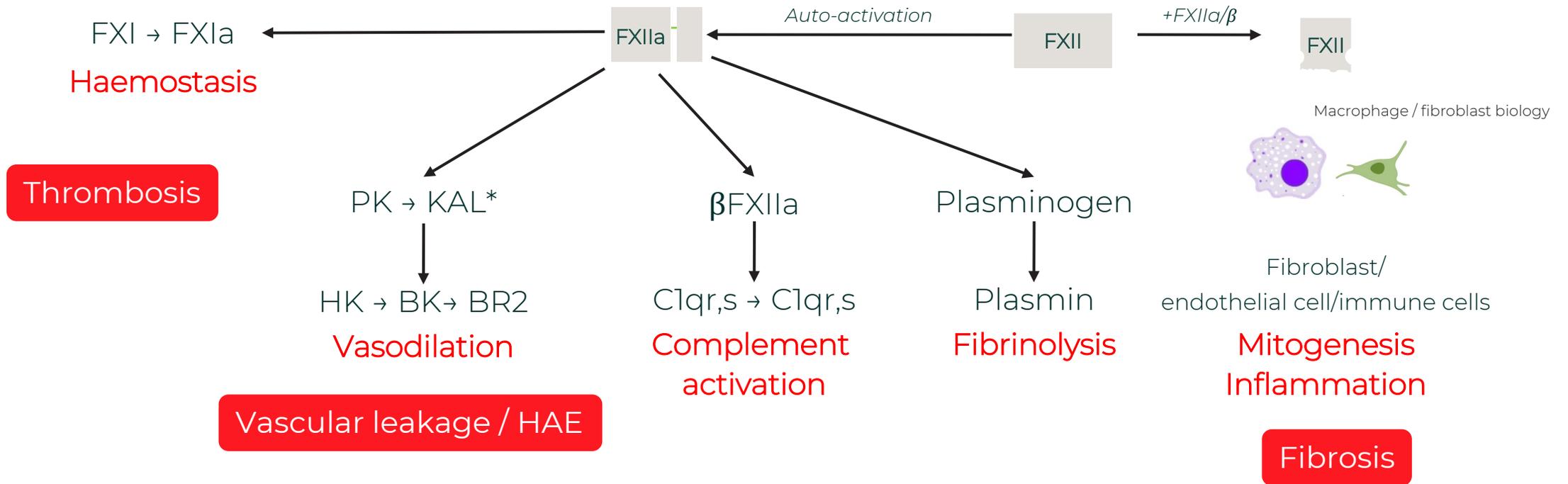


Two Decades of Impact

- 326+ Start-ups incubated
- \$1.5B Collectively raised by start-ups
- \$1.3B In exits from 6 deep tech ventures
- 500+ Patents & trademarks filed
- 1,000's Jobs created & people trained

Garadacimab (Discovery – Development – Medicine)

Garadacimab potently inhibits α FXIIa, shutting down multiple biological pathways

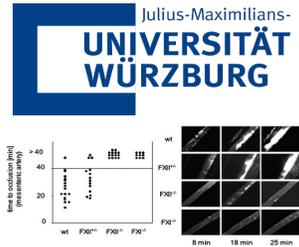


* Feedback loops removed for simplicity

Abbreviations: BK - Bradykinin; B2R – B2 Receptor; C1-INH – C1 Inhibitor; HAE – Hereditary Angioedema; HMWK – High Molecular Weight Kininogen; KAL – Kallikrein; PK – Plasma Kallikrein; PPK - Plasma Pre-kallikrein

Garadacimab (Discovery – Development – Medicine)

Uni. Würzburg: FXII / thrombosis, data & IP



Renné, T. et al., (2005) J. Exp. Med. 202(2):271-281



**Proof of concept
with Infestin**

**Human FXIIa blocking
mAb / **Garadacimab****

External Partners

FXIIa Antagonist mAb – thrombosis, ECMO



**Karolinska
Institutet**

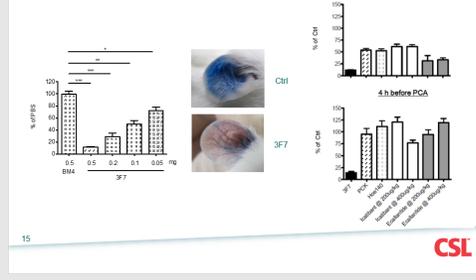


Previous R&D Investor Day

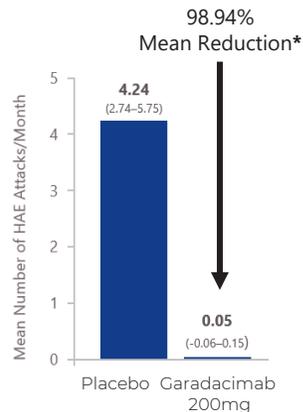
FXIIa Antagonist mAb - HAE

Percutaneous anaphylaxis, a mouse model of HAE

- anti-FXIIa mAb 3F7 inhibits edema



**CSL → global leader in
FXIIa therapeutics**



Initial focus on thrombosis

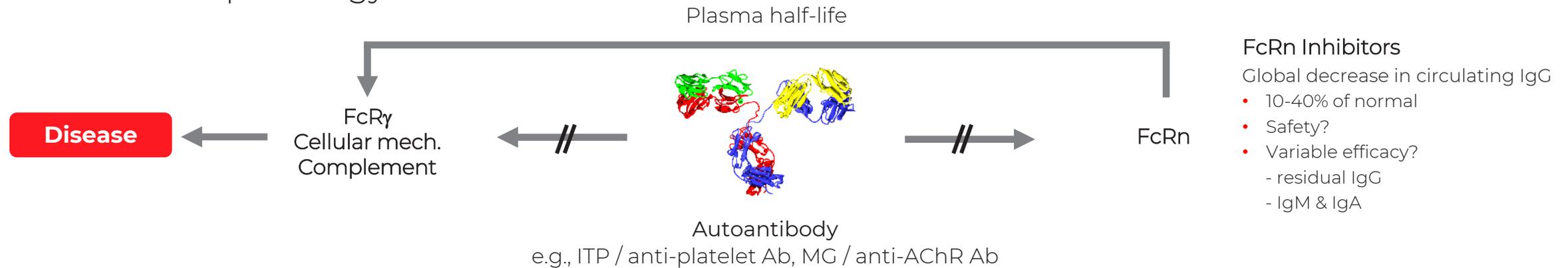
HAE as target indication



Abbreviations: ECMO – Extra Corporeal Membrane Oxygenation; IP – Intellectual Property; HAE – Hereditary Angioedema; mAb – Monoclonal Antibody

CIDP is a Complex Autoimmune Disease

- Role of IgG autoantibodies in disease onset & progression is unclear
- Response to FcRn inhibitors dependant on the central role of IgG autoantibodies in disease pathology



CSL IVIG	✓		✓
CSL Development	✓	CSL730 Ph I	
CSL Research	✓	FcRn inhibitors, dual FcR _γ / FcRn, Complement inhibitors	✓

Abbreviations: Ab – Antibody; Anti-AChR - Anti-acetylcholine Receptor; FcRn - Neonatal Fc Receptor; IgA – Immunoglobulin A; IgG – Immunoglobulin G; IgM – Immunoglobulin GM; ITP - Immune Thrombocytopenia; MG – Myasthenia Gravis

The CSL logo is a red square with the letters 'CSL' in white, bold, sans-serif font.

Vaccines

Targeting Unmet Need in Influenza & Beyond

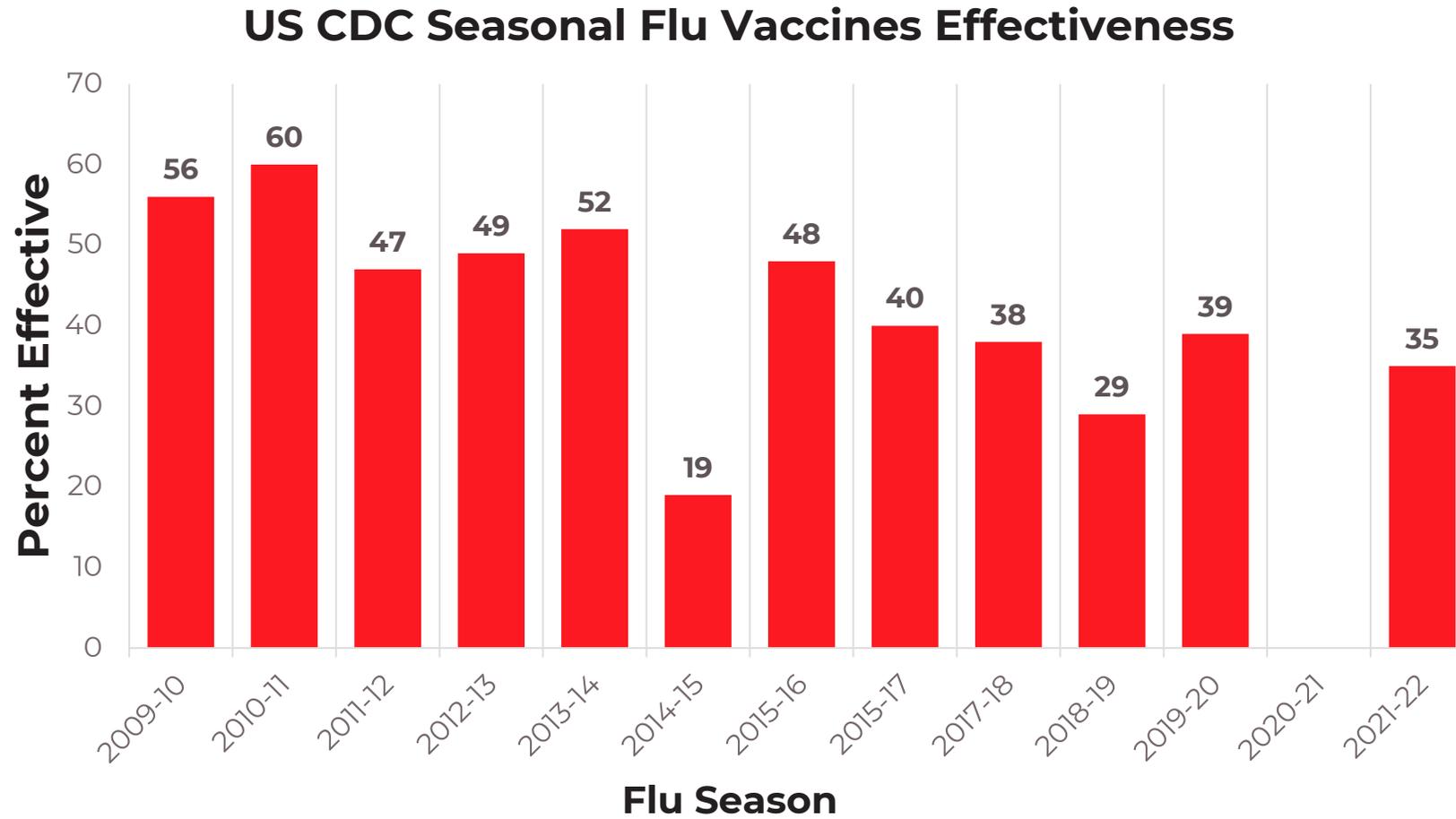
Jon Edelman MD

Vice President, Clinical Development
Interim Head, CSL Seqirus Vaccines
Innovation Unit

CSL



Influenza Vaccines are Inconsistently Effective Season to Season

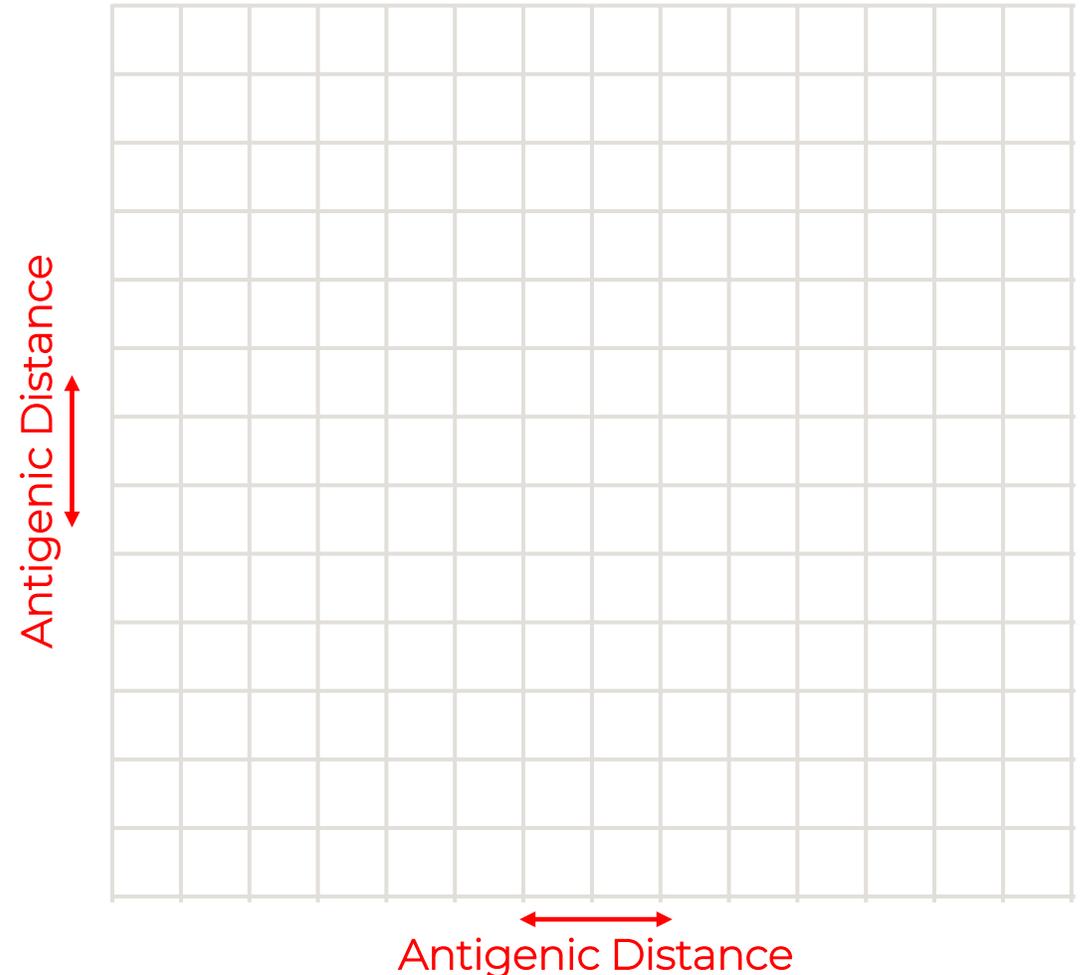


Source: [CDC Seasonal Flu Vaccine Effectiveness Studies | CDC https://www.cdc.gov/flu/vaccines-work/effectiveness-studies](https://www.cdc.gov/flu/vaccines-work/effectiveness-studies)

Abbreviations: CDC – Centre for Disease Control & Prevention

Recommended Vaccine Viruses May Not Match with Circulating Flu

- WHO continually isolate and characterize influenza viruses in circulation in humans
- WHO Collaborating Centers determine the antigenic relatedness of these strains
- Viruses are mapped to enable the selection of a candidate vaccine virus (CVV) for each flu subtype for each flu season
- Prior to 2016, all CVVs were grown in eggs

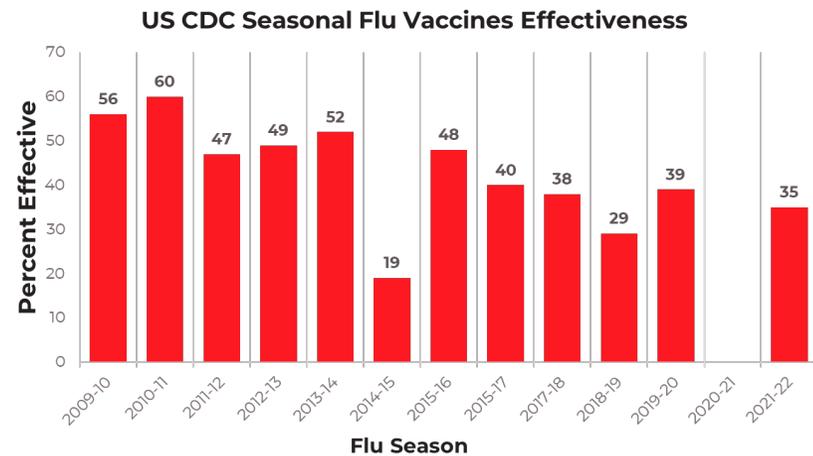


Recommended Vaccine Viruses May Not Match with Circulating Flu

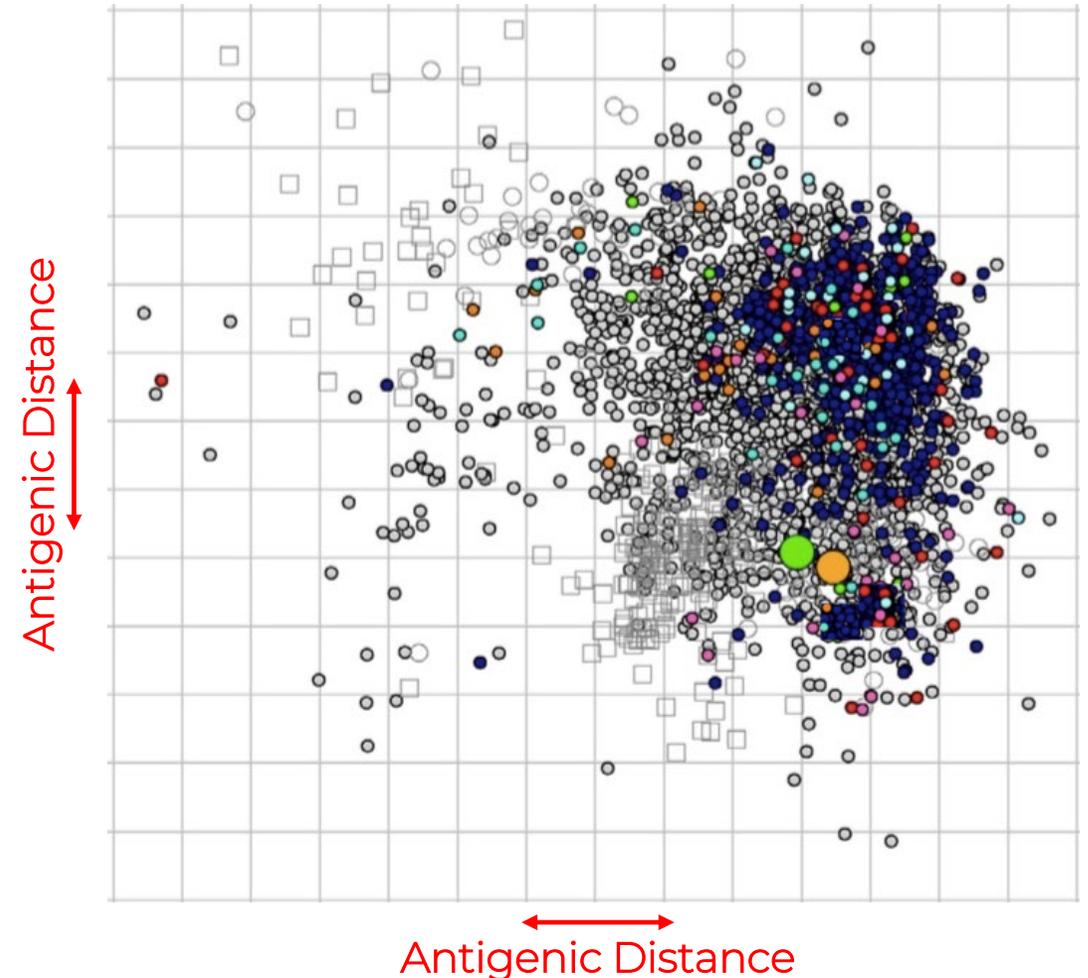
In 2012, the CVV that WHO chose was antigenically distant from the majority of circulating H3N2 viruses

EGG VACCINE VIRUSES

- A/Victoria
- A/Texas

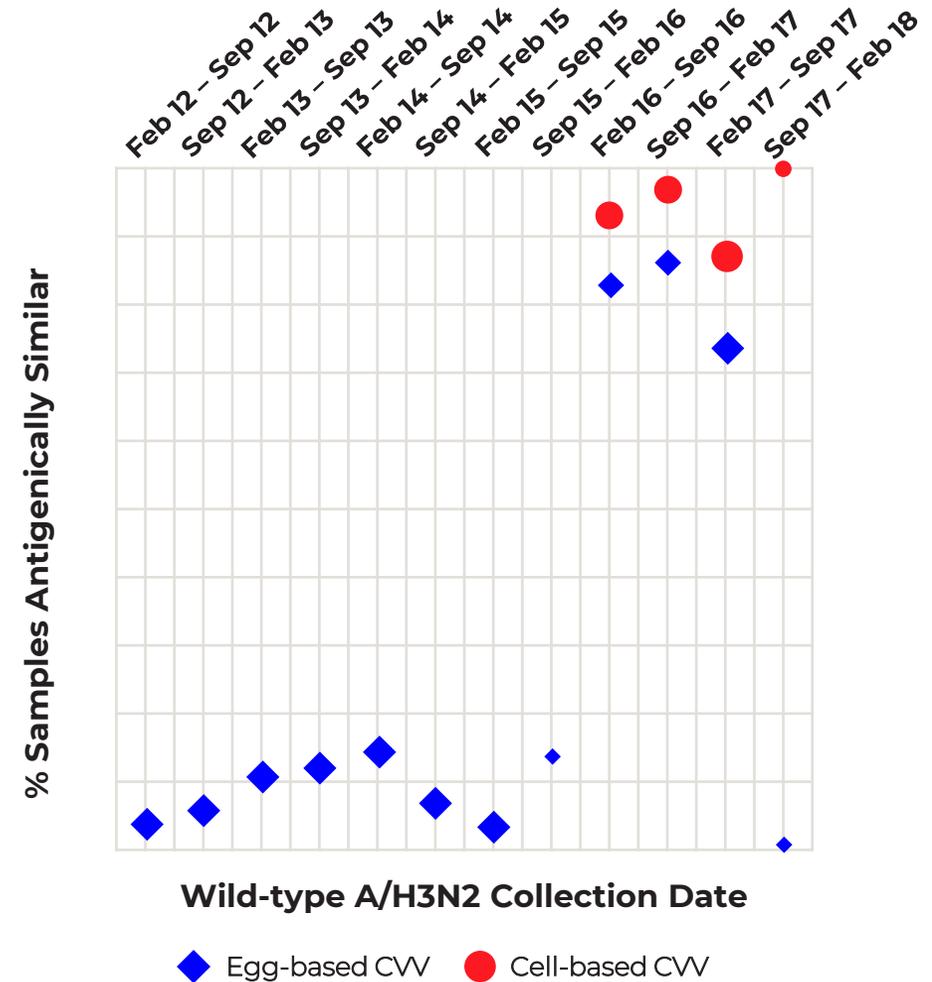


Abbreviations: CVV – Candidate Vaccine Virus; WHO – World Health Organisation



Frequency of H3N2 Egg-adaptation Mismatch over Time

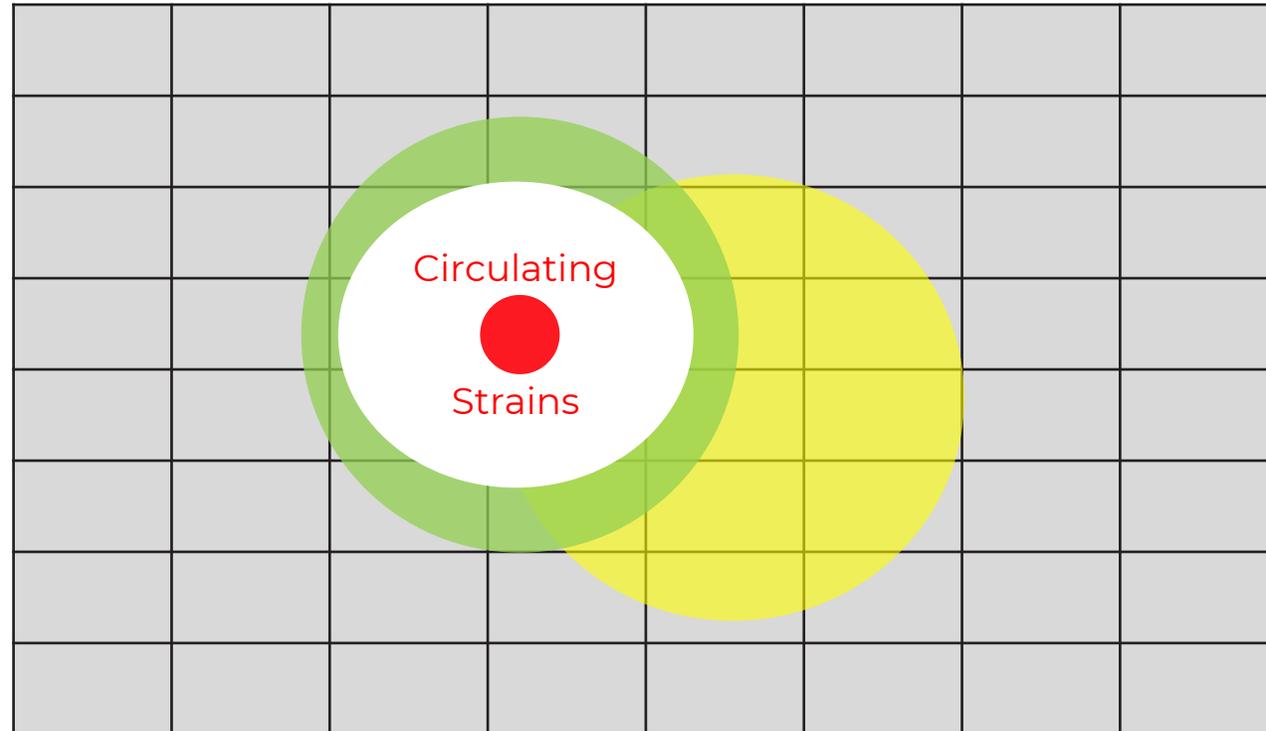
- Adaptation of viruses grown in eggs results in poorer antigenic match to circulating viruses compared to viruses grown in cells
- Since 2016, WHO makes separate cell and egg seed seasonal strain recommendations



Source: Rajaram, S. et al., (2020) *Int. J. Environ. Res. Public Health* 17(15): 5423. doi:10.3390/ijerph17155423

Cell-based Vaccines are Designed to Provide a Better Match to WHO-selected Flu Virus Strains

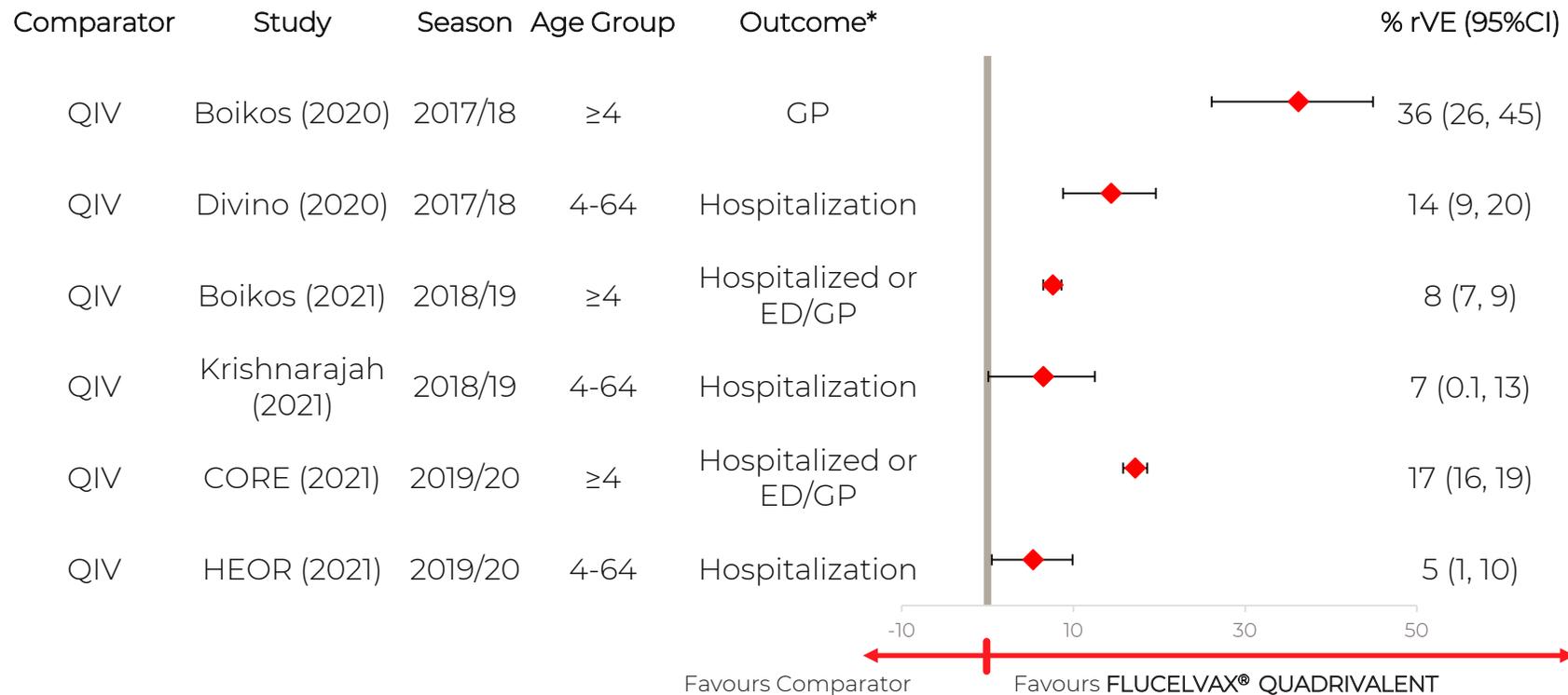
**Cell-Based
Vaccine**



**Egg-Based
Vaccine**

Real World Evidence – Showing Benefit of Cell-based Influenza Vaccines to Reduce Strain Mismatch

Flucelvax® QUADRIVALENT - Benefit of Cell Culture

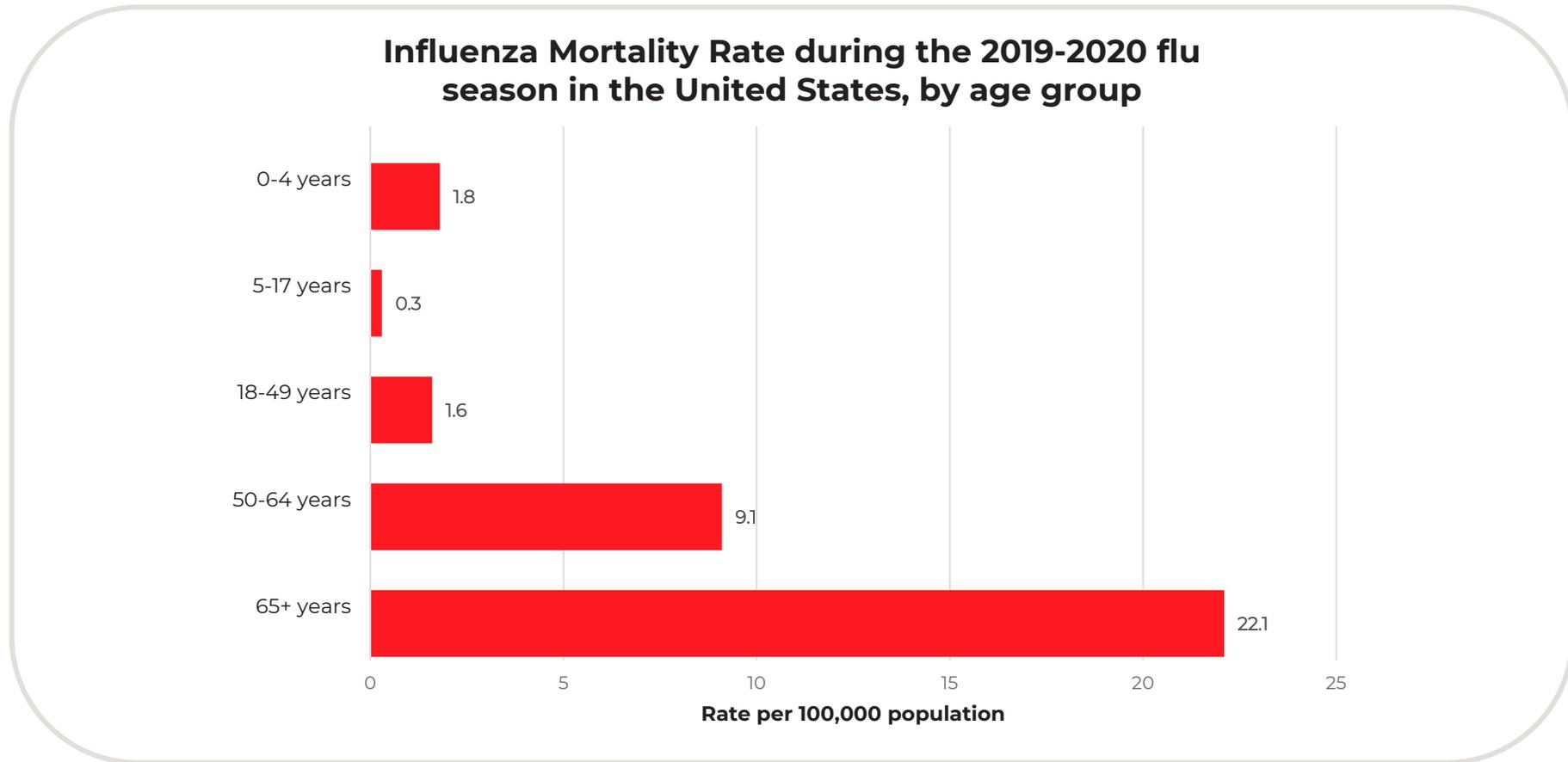


*Outcomes due to influenza or pneumonia

2017/18 was the first season a cell-based seed (H3N2) was included in FLUCELVAX® QUADRIVALENT. The outcomes reported in these publications contain information not included in the Prescribing Information. These studies provide data across 3 US influenza seasons with different study designs, outcomes, and study limitations comparing the relative vaccine effectiveness (rVE) of FLUCELVAX® QUADRIVALENT compared to traditional, egg-based influenza vaccines. In seasons where egg adaptation occurs, studies suggest FLUCELVAX® QUADRIVALENT has the potential to be more effective than traditional, egg-based vaccines.

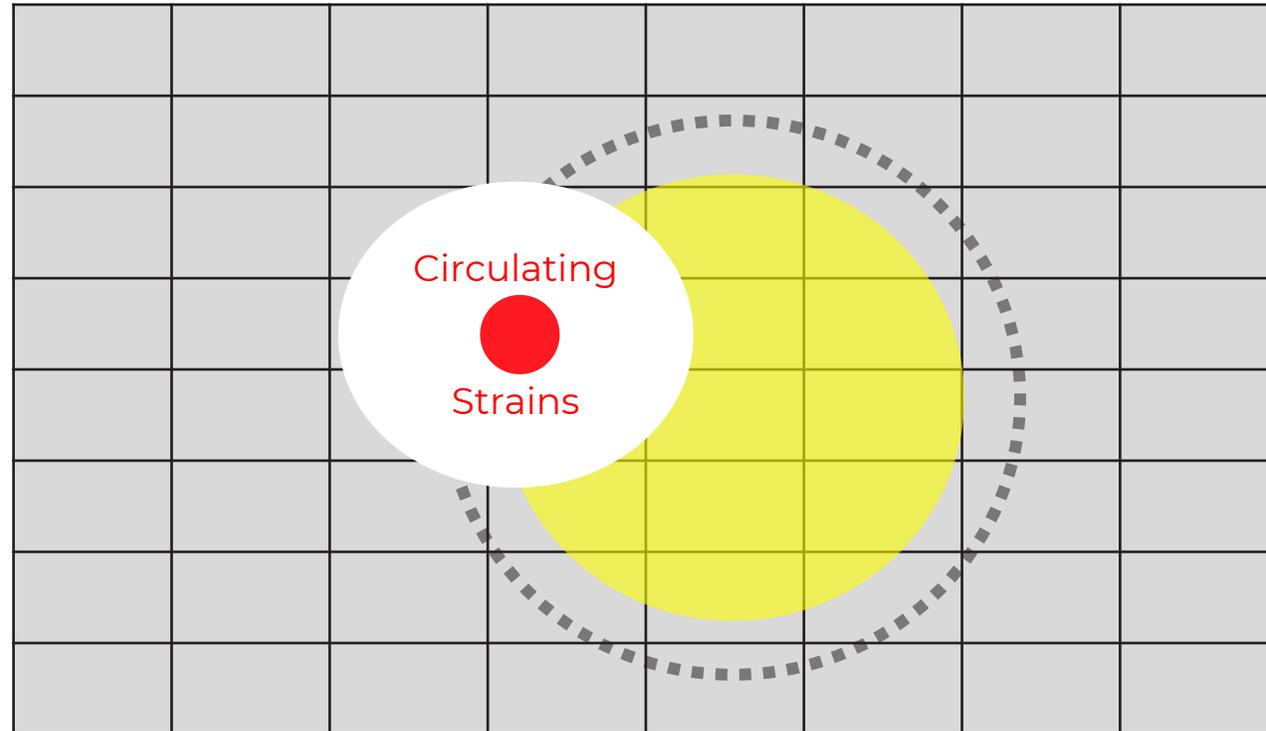
Source: Boikos, C. *et al.*, (2020) *CID* 73:816-823; CORE (2021): Presented at ECCMID 2021; HEOR (2021): Manuscript pending; RWE studies from across 4 US influenza seasons with different study designs, outcomes, and study limitations assessed the relative vaccine effectiveness of FLUAD compared to a high-dose influenza vaccine.

Immunosenescence and Comorbidities Contribute to Higher Mortality in Older Adults



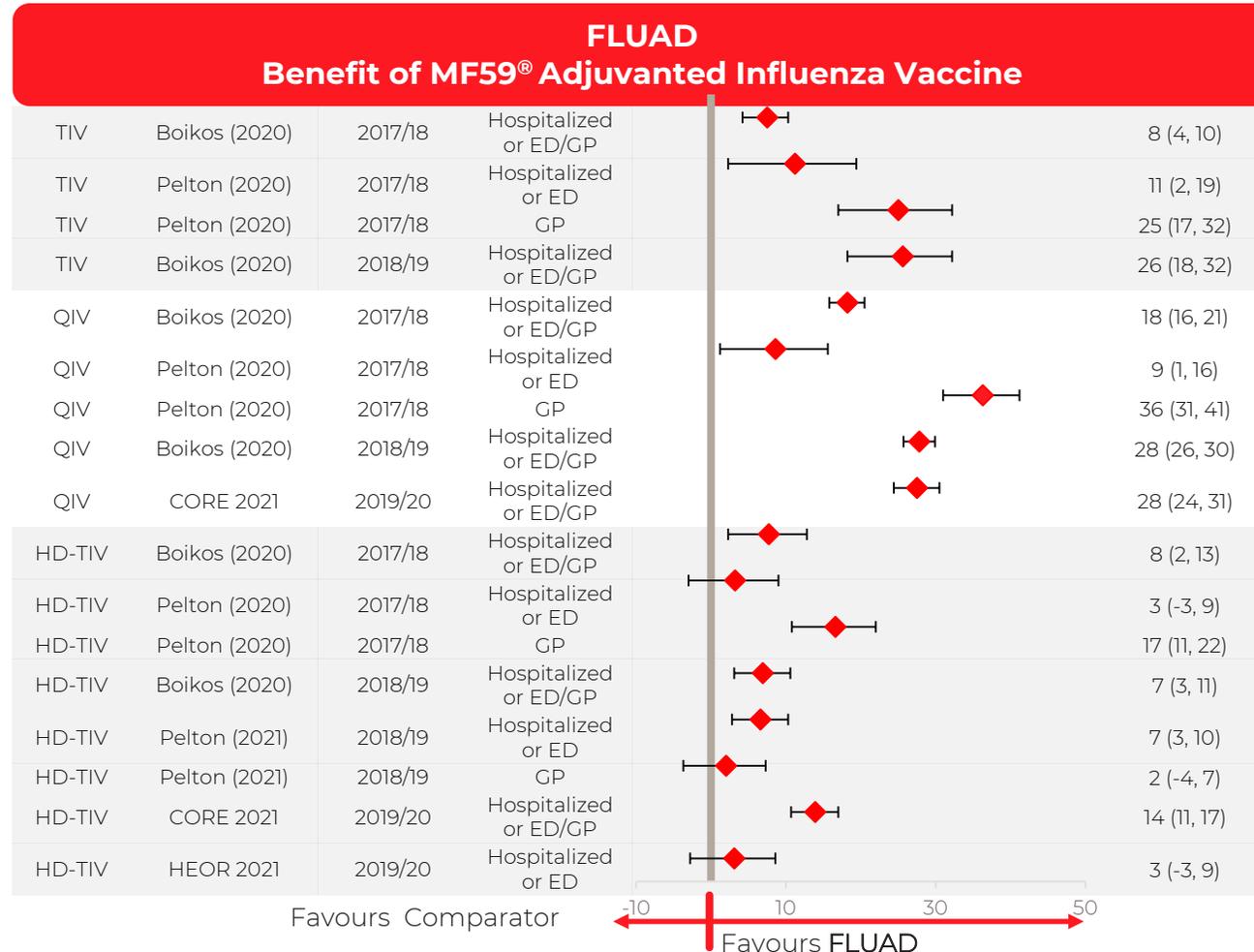
Source: CDC [(National Center for Immunization and Respiratory Diseases (NCIRD))] © Statista 2022; United States: CDC [(National Center for Immunization and Respiratory Diseases (NCIRD))] 2019-2020
Abbreviations: CDC – Centre for Disease Control & Prevention

Adjuvanted Vaccines Increase the Immune Response in Vulnerable Individuals

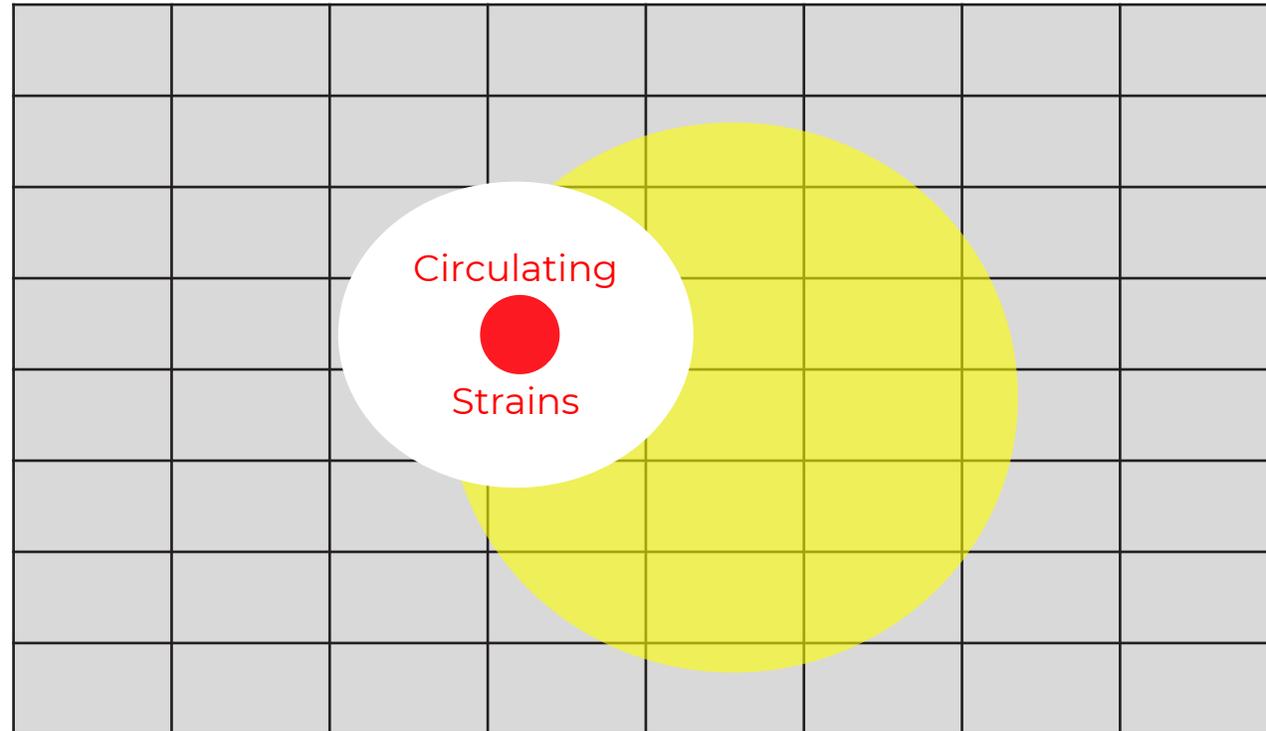


**MF59[®] Adjuvanted
Egg-Based Vaccine**

Real World Evidence – Benefit of MF59® Adjuvanted Influenza Vaccine



Higher Doses of Antigen Can Increase Immune Response in Older Adults

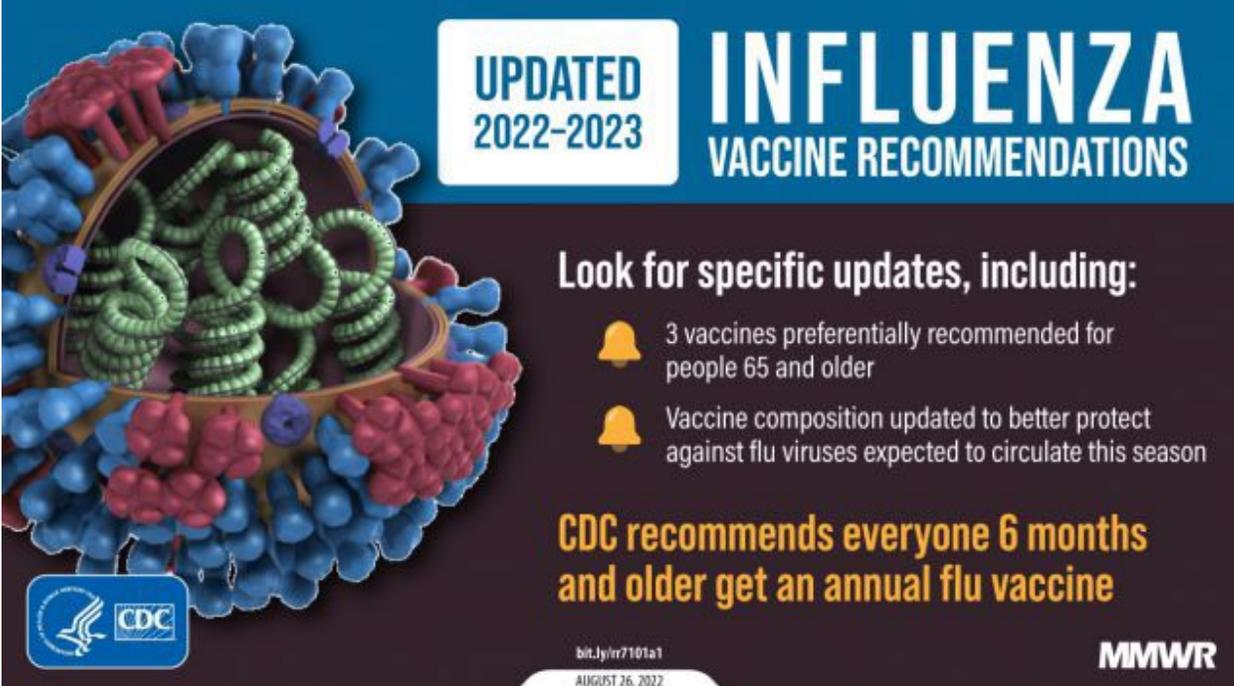


**Higher Dose
Egg-Based Vaccine**

Preferentially Recommended by CDC Over Standard-dose Influenza Vaccines

For persons 65 years and older:

- Adjuvanted egg-based vaccine
- Higher dose egg-based vaccine
- Recombinant-based vaccine



The graphic features a 3D illustration of an influenza virus particle on the left, showing its characteristic surface proteins and internal structure. The background is a dark blue gradient. In the top right, a white box contains the text 'UPDATED 2022-2023' and 'INFLUENZA VACCINE RECOMMENDATIONS' in large, bold, white letters. Below this, the text 'Look for specific updates, including:' is followed by two bell icons and two lines of text: '3 vaccines preferentially recommended for people 65 and older' and 'Vaccine composition updated to better protect against flu viruses expected to circulate this season'. At the bottom, a large orange and white text block states 'CDC recommends everyone 6 months and older get an annual flu vaccine'. The CDC logo is in the bottom left, and 'MMWR' is in the bottom right. A small URL and date are at the very bottom.

UPDATED 2022-2023

INFLUENZA

VACCINE RECOMMENDATIONS

Look for specific updates, including:

- 3 vaccines preferentially recommended for people 65 and older
- Vaccine composition updated to better protect against flu viruses expected to circulate this season

CDC recommends everyone 6 months and older get an annual flu vaccine

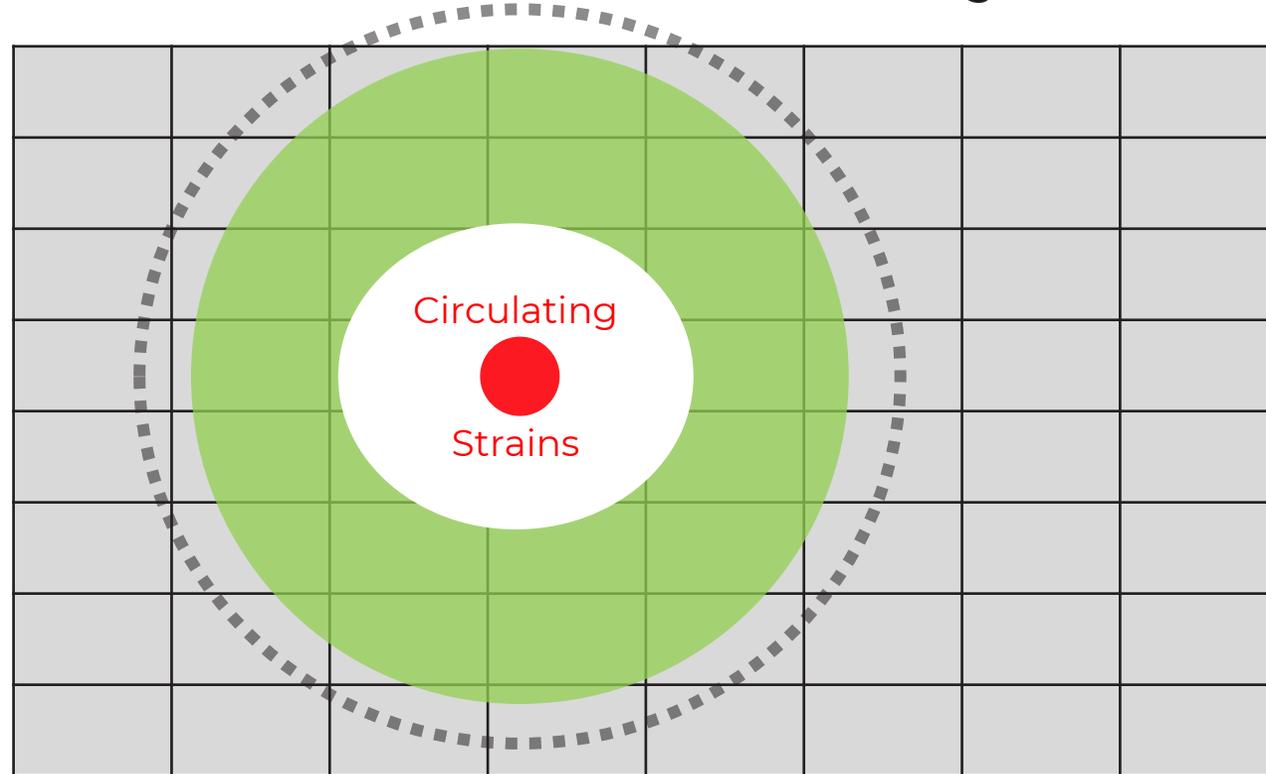
 **CDC**

bit.ly/r7101a1
AUGUST 26, 2022

MMWR

aQIVc - Combining Adjuvant & Cell Technologies & Boosting the Dose of Each to Improve Vaccine Effectiveness

3 Proven Flu Vaccine Technologies



High Dose MF59[®] Adjuvanted Cell-Based Vaccine



Phase III – NH 2023



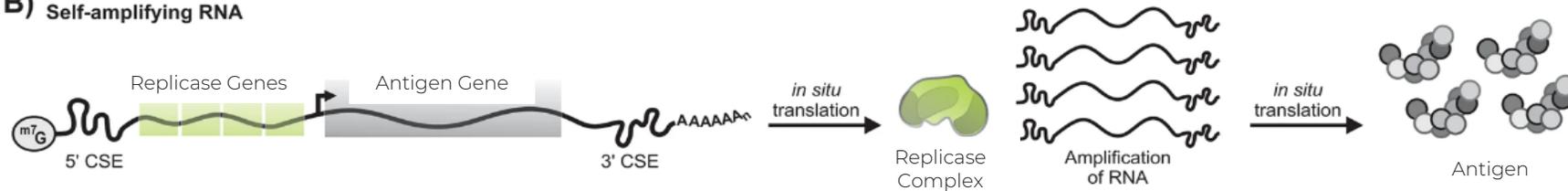
Continued Focus on Next Generation mRNA Vaccines

Next Generation mRNA Technology: Self-amplifying mRNA

A) Conventional mRNA



B) Self-amplifying RNA



Advantages over conventional mRNA vaccines

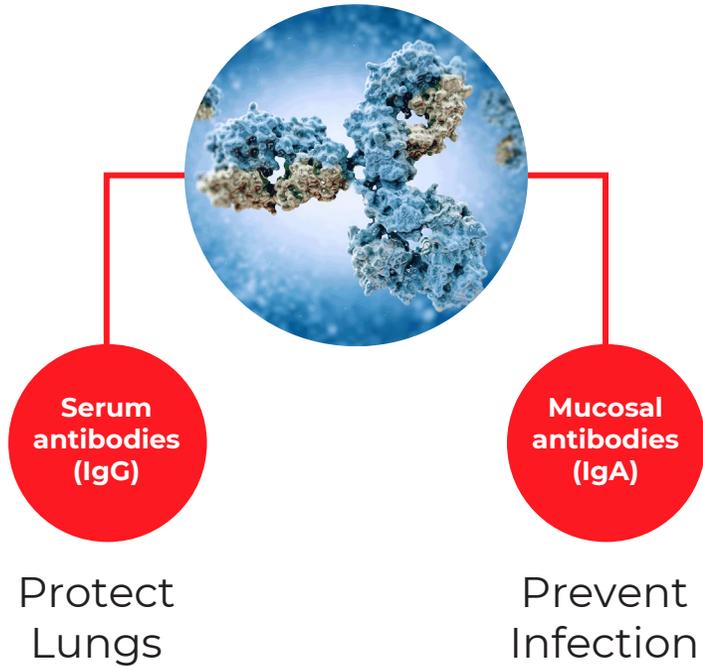
- Lower dose to achieve comparable antigen levels with potential for better tolerability
- Ability to entrain multiple antigens in one sa-mRNA
- More complete activation of immune system

Source: Bloom, K. et al., (2021) *Gene Ther.* 28: 117–129. <https://doi.org/10.1038/s41434-020-00204-y>

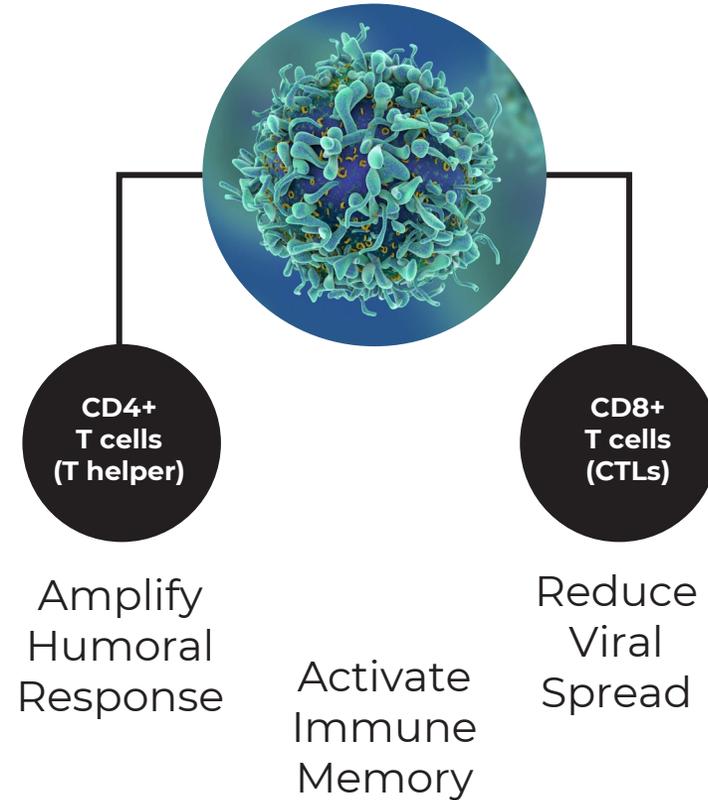
Abbreviations: CSE - Conserved Sequence Element; mRNA - Messenger RNA; RNA - Ribonucleic Acid; sa-mRNA - self-amplifying mRNA; UTR - Untranslated Region

Engaged Immune System = More Protection

Humoral

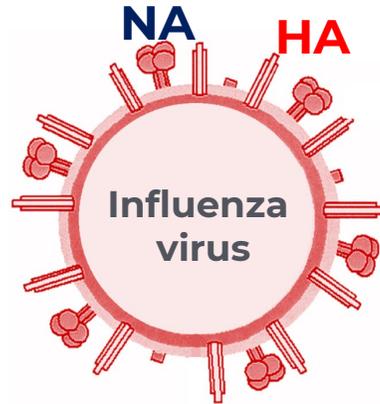


Cellular

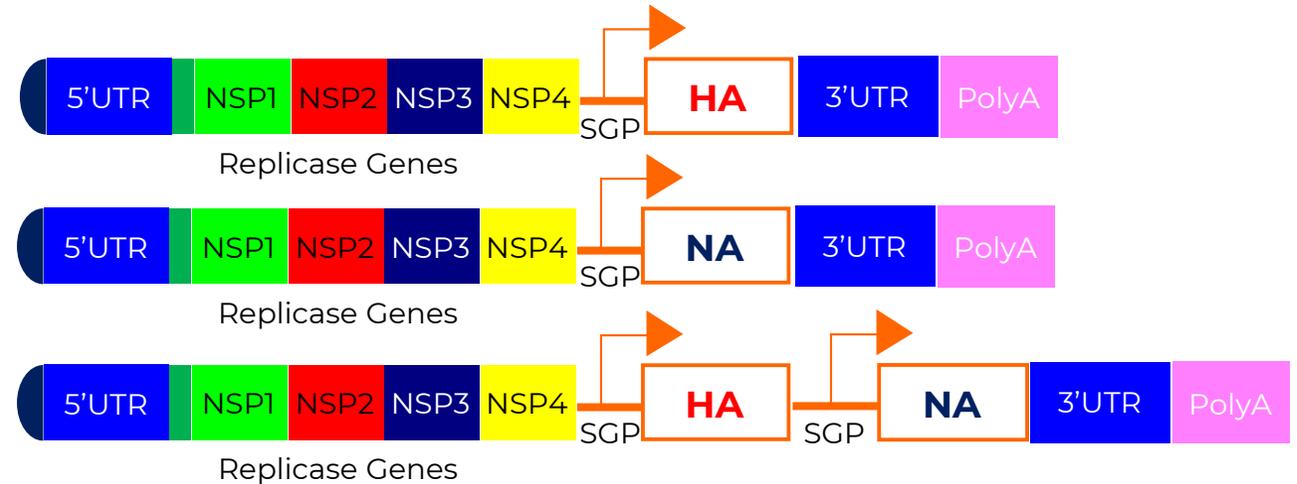


Abbreviations: IgA – Immunoglobulin A; IgG – Immunoglobulin G

sa-mRNA Bicistronic Vaccines Co-express HA & NA



sa-mRNA mono and bicistronic HA/NA vaccine



Haemagglutinin (HA) & Neuraminidase (NA) are two viral surface proteins

- HA –main antigen in most licensed influenza vaccines
- NA – more highly conserved than HA
- sa-mRNA monocistronic strategy expresses HA or NA antigens
- sa-mRNA bicistronic strategy co-expresses HA & NA antigens

Source: Chang, C. et al., (2022) *Mol. Ther. Meth. & Clin. Dev.* (27): 195-205

Abbreviations: NSP - Non-structural Protein; RNA - Ribonucleic Acid; SGP - Sub Genomic Promoter; UTR - Untranslated Region

Protection of Ferrets from Influenza Infection by sa-mRNA HA-NA Vaccines



1st IM/Prime



Day 1

2nd IM/Boost



22

Challenge Evaluate



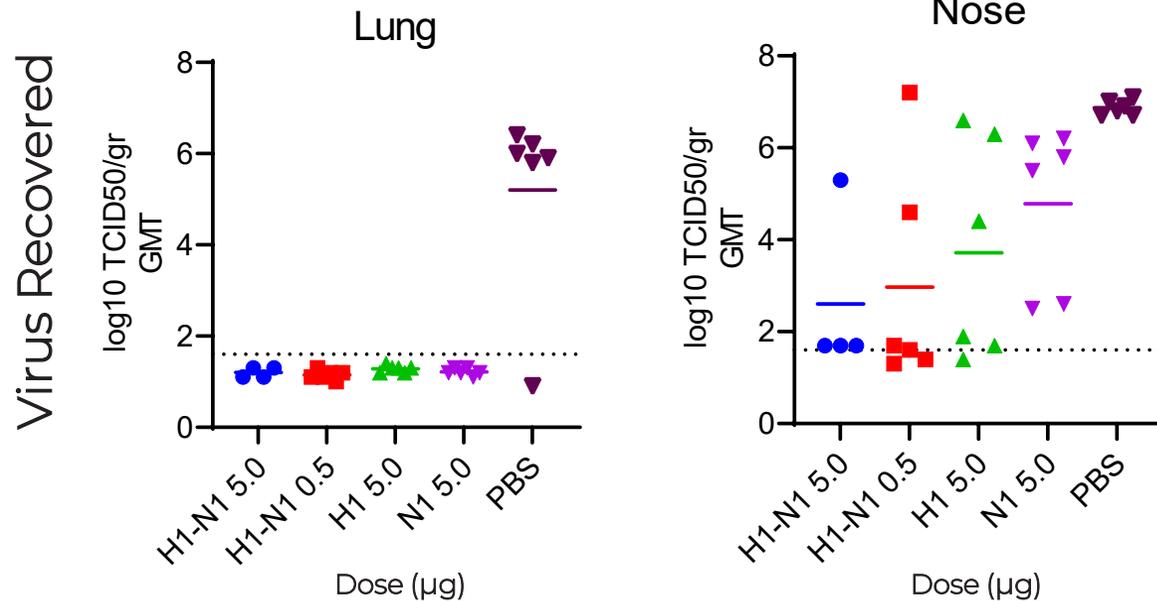
50

54

H1	Dose:
N1	5.0 µg
H1N1	0.5 µg

Dose:
5.0 µg
0.5 µg

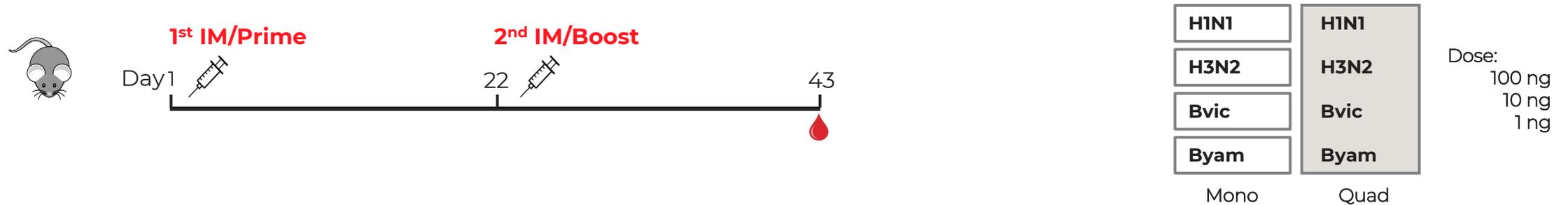
Vaccine and challenging viruses
A/Netherland/602/2009 (H1N1)



- Full protection of lung with mono- & bivalent HA-NA sa-mRNA vaccines
- Near complete protection with bivalent HA-NA at 1/10th dose of HA alone

Source: Chang, C. et al., (2022) *Mol. Ther. Meth. & Clin. Dev.* (27):195-205
Abbreviations: IM - Intramuscular

Robust Anti-HA and Anti-NA Neutralizing Antibody Against Seasonal Strains by Quadrivalent sa-mRNA HA-NA Vaccines



Both monovalent and quadrivalent bicistronic sa-mRNA vaccines

- Raised neutralizing antibodies against HA *and* NA in a dose dependent manner
- Doses as low as 1 ng were effective in generating measurable neutralization of each viral subtype



mRNA Phase I – initiating 2023

Source: Chang, C. et al., (2022) *Mol. Ther. Meth. & Clin. Dev.* (27):195-205

Abbreviations: IM - Intramuscular

Collaboration with Arcturus Therapeutics* - COVID-19 & More

Topline data from ongoing Phase I/II/III study evaluating ARCT-154 (Arcturus' sa-mRNA vaccine candidate against COVID-19 disease caused by SARS-CoV-2 virus)

- >19,000 adult subjects enrolled in Ph I/II/III registrational study
- >16,000 subjects enrolled in Ph III placebo-controlled efficacy portion of study
- Study conducted when Delta & Omicron variants were dominant in Vietnam

- Evaluation of vaccine efficacy demonstrated study met primary endpoint of prevention of virologically confirmed COVID-19 disease
 - 95% efficacy overall for prevention of severe COVID-19 disease including related deaths
 - 55% efficacy overall for preventing symptomatic COVID-19 disease
- Incidence of unsolicited adverse events with ARCT-154 similar to placebo; No reported cases of myocarditis or pericarditis
- ARCT-154 to advance into pivotal booster trial in major markets



Phase I/II/III – Ongoing

* Transaction with Arcturus Therapeutics is subject to customary regulatory clearances before closing

Source: Arcturus Therapeutics News Release April 2022 <https://ir.arcturusrx.com/news-releases/news-release-details/arcturus-announces-self-amplifying-covid-19-mrna-vaccine>

Arcturus Therapeutics Complements CSL Seqirus' Long-term Strategy in Vaccines

Benefits from Arcturus Therapeutics Collaboration*

Faster clinical development with higher probability of success

Application to additional pathogens, including those with pandemic potential

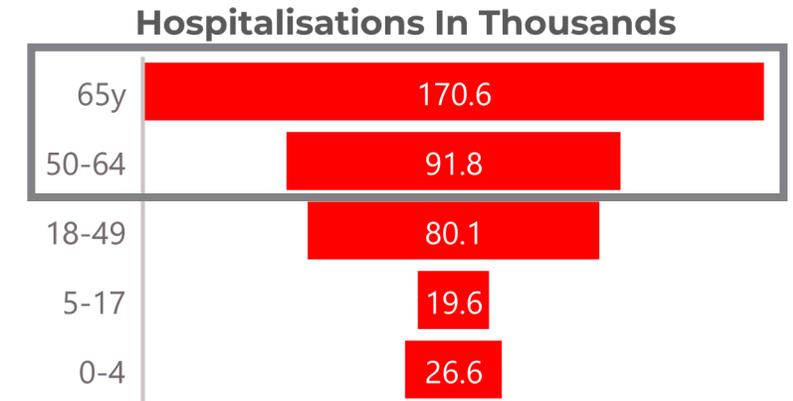
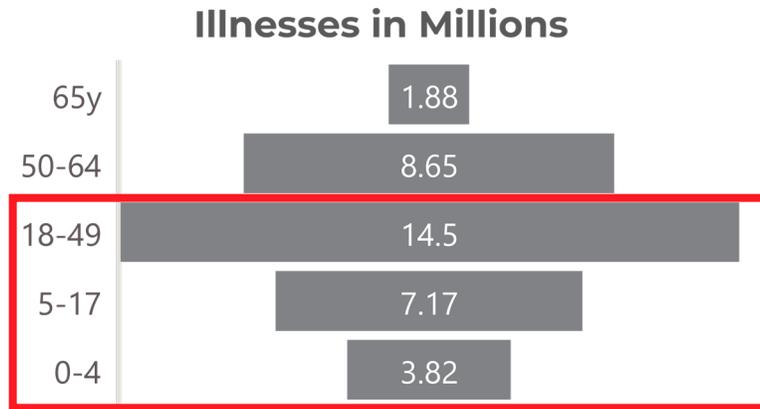
Access to an established manufacturing network

Access to LNP & lipid library with application across vaccines

* Transaction with Arcturus Therapeutics is subject to customary regulatory clearances before closing

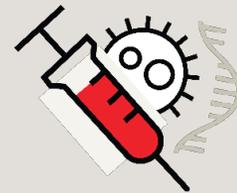
Abbreviations: LNP – Lipid nanoparticle

Future offerings of our Vaccine Programs Across the Spectrum of Need in Influenza and Beyond



Cell-based QIVc

Maximise coverage, reduce force of infection in all ages



Next generation mRNA

Efficacy, tolerability, speed of response
Flexibility for flu and beyond

Adjuvanted cell aQIVc

High efficacy, well tolerated, for at risk populations

The CSL logo is a red square with the letters 'CSL' in white, bold, sans-serif font.

Development

Key Program Updates

Steve Pascoe MD

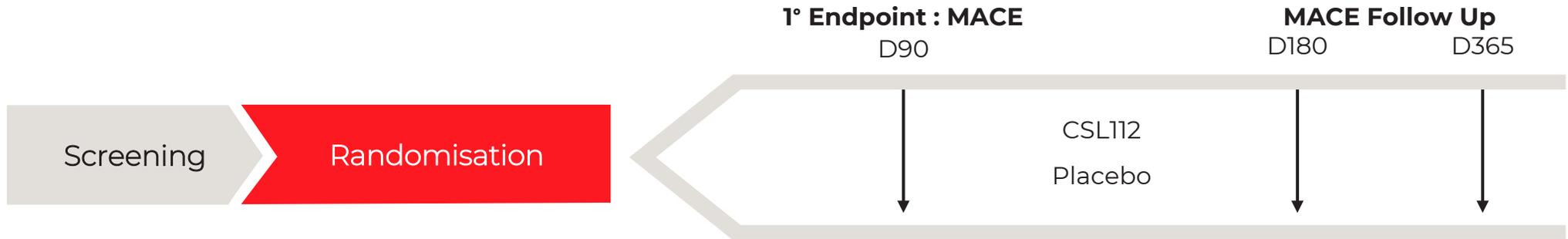
Senior Vice President,
Clinical & Therapeutic Area Strategy

CSL



CSL112 Apolipoprotein A-I (Human) - AEGIS-II

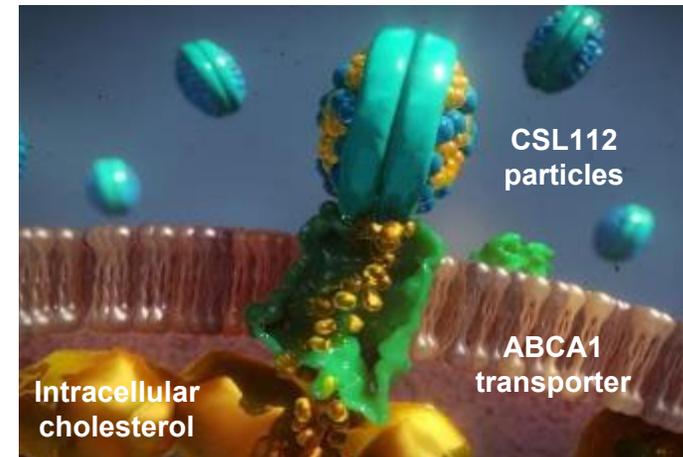
>18,000
Acute
Myocardial
Infarction
(AMI)



- Recruitment on track for LPI December 2022
- Launch on track for Q4 2025



Phase III – Ongoing



Garadacimab - Disruptive Innovation to Improve Treatment Options for HAE Patients



Phase III - Double-blind, placebo-controlled, randomised clinical study evaluating efficacy & safety of SC Garadacimab for the prophylaxis of HAE Attacks

- Primary & key secondary efficacy endpoints achieved with high degree of statistical significance & clinically meaningful differences vs. placebo
- Study results to be presented at upcoming congress & published in peer-reviewed journal

Differentiated, Patient-Focused Profile

- Differentiated profile
- Convenient administration (AI): Quick (<15 sec) & easy delivery
- True once-monthly treatment dosing
- Favorable safety & tolerability profile

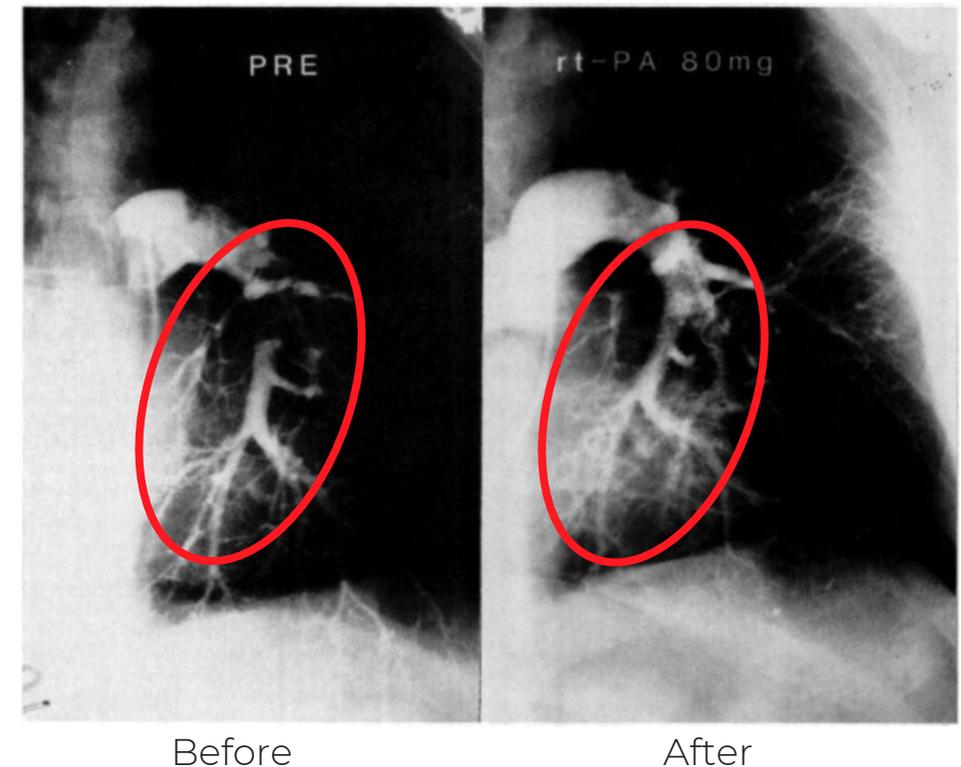


Global submissions targeted 2023

Pulmonary Embolism Affects Millions Worldwide and Remains a Major Cause of Death

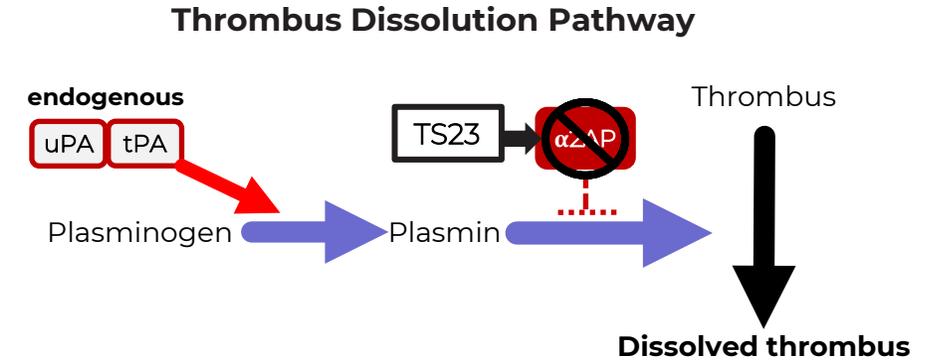
Submassive PE (sPE)

- Acute cardiovascular disorder where thrombus (blood clot) obstructs lung blood flow
- Causes acute strain of the right side of heart (RV:LV) w/o haemodynamic instability
- Mortality: 7% (≤ 30 days)
- SOC is anticoagulation only
- Current treatment with recombinant tissue plasminogen activator has unacceptable major bleeding risk (~6%)
- There is need for safer, effective treatment that dissolves thrombi and does not cause serious bleeding

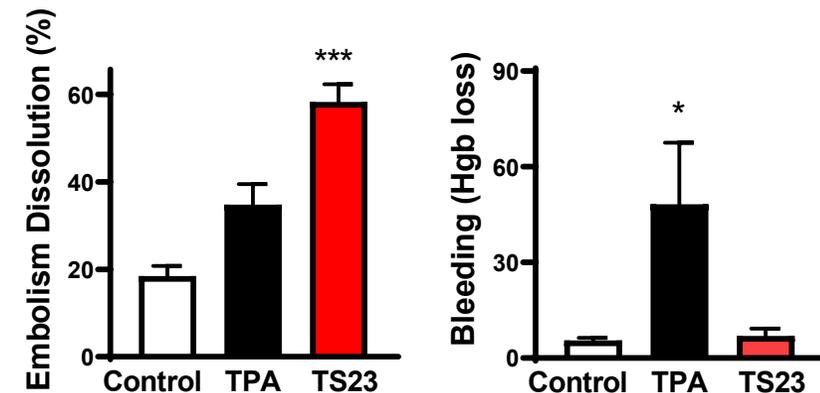


TS23 is a Novel, Proposed Safe, Effective Therapy for Dissolving Thrombosis with Minimal Bleeding Risk

- TS23 - first-in-class, therapeutic mAb targeting alpha-2-antiplasmin (α 2AP)
- α 2AP blocks dissolution of acute cardiovascular thrombi
- α 2AP inactivation allows endogenous (local) plasmin activity normally generated in a thrombus to dissolve it, thereby avoiding a systemic lytic state & associated bleeding risk
- TS23 - safe and effective in Phase I HV
 - Dose related inactivation α 2AP (up to 95%)
 - Thrombus dissolution *ex vivo* and inc. D-dimers *in vivo*



TS23 dissolves experimental pulmonary emboli without increasing bleeding



Phase II – Q4 2022

Source: Singh, S. *et al.*, (2017) *Circulation* 135(11):1011-1020. doi:10.1161/CIRCULATIONAHA.116.024421.
 Abbreviations: HV – Healthy volunteers; mAb – Monoclonal Antibody; tPA - tissue Plasminogen Activator; uPA – urokinase plasminogen activator



Etranacogene Dezaparvovec

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

Key Results from Phase III HOPE-B Trial

- Pivotal Phase III study (HOPE-B) showed superiority (annual bleeding rate, ABR) compared to standard of care
- Stable & durable FIX expression to near normal levels demonstrated following treatment:
 - At 18 months steady-state, total number of annual bleeds decreased by 64% compared
 - 24 month data are comparable



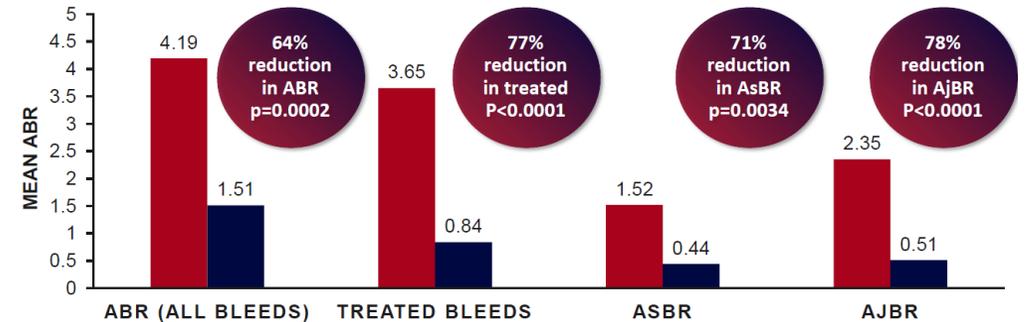
Launch – US & EU Q1 2023

* One-sided p-value ≤ 0.025 for post-treatment/lead-in < 1 is regarded as statistically significant

Source: Clinical trial AMT-061-02 2-year Clinical Study Report

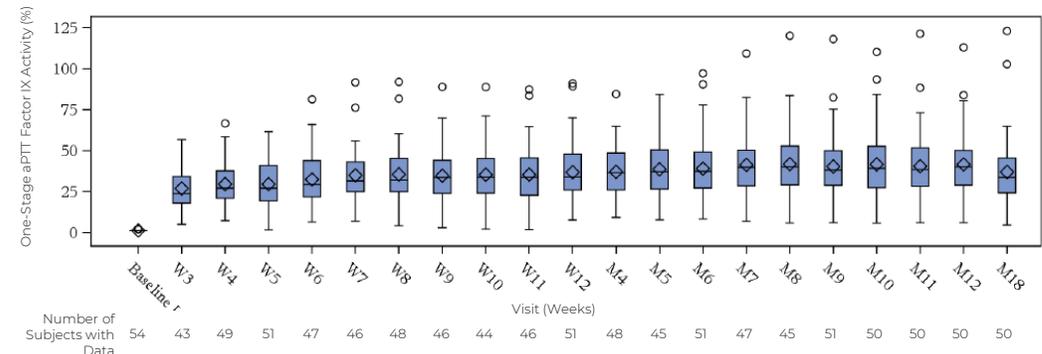
Abbreviations: ABR – Annual Bleeding Rate; AJBR – Annualised Joint Bleeding Rate; aPTT – Activated Partial Thromboplastin Time; ASBR – Annualised Spontaneous Bleeding Rate

Improvement in ABR of Specific Bleed Types



Etranacogene dezaparvovec reduced ABR by 64% and demonstrated superiority to prophylaxis*

Uncontaminated Central Laboratory One-Stage (aPTT-based) FIX Activity during Post-treatment Period





Etranacogene Dezaparvovec

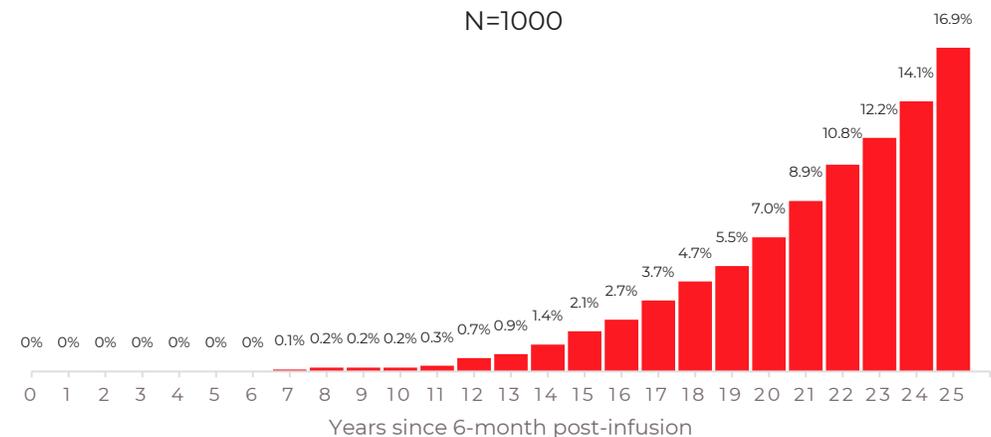
Gene Therapy (AAV5-Padua FIX) for Treatment of Haemophilia B

Etranacogene dezaparvovec is a result of CSL's ongoing commitment to further develop treatments for haemophilia B that address unmet medical needs

AAV5 vector gene therapy with key differentiating factors:

- Single dose gene therapy not requiring concomitant steroid therapy
- Effective in a broad set of patients
- Steady state FIX activity levels without peaks & troughs associated with prophylactic FIX infusions
- Improved quality of life, return to normal physical activities, & freedom from routine infusions
- ICER draft report on etranacogene dezaparvovec estimates durability at 23 years

Predicted Cumulative Proportion Of Participants With Factor IX Activity Levels



Source: Shah, J., et al. (2022) *Curr Med Res Opin.* 25: 1-11. doi: 10.1080/03007995.2022.2133492.

Abbreviations: AAV5 - Adeno-associated virus 5; ICER - Institute for Clinical and Economic Review; NAb – Neutralising Antibodies

Clazakizumab in AMR

50% of All Kidney Transplants Fail by Year 10; AMR Implicated in 57-63% of Graft Losses

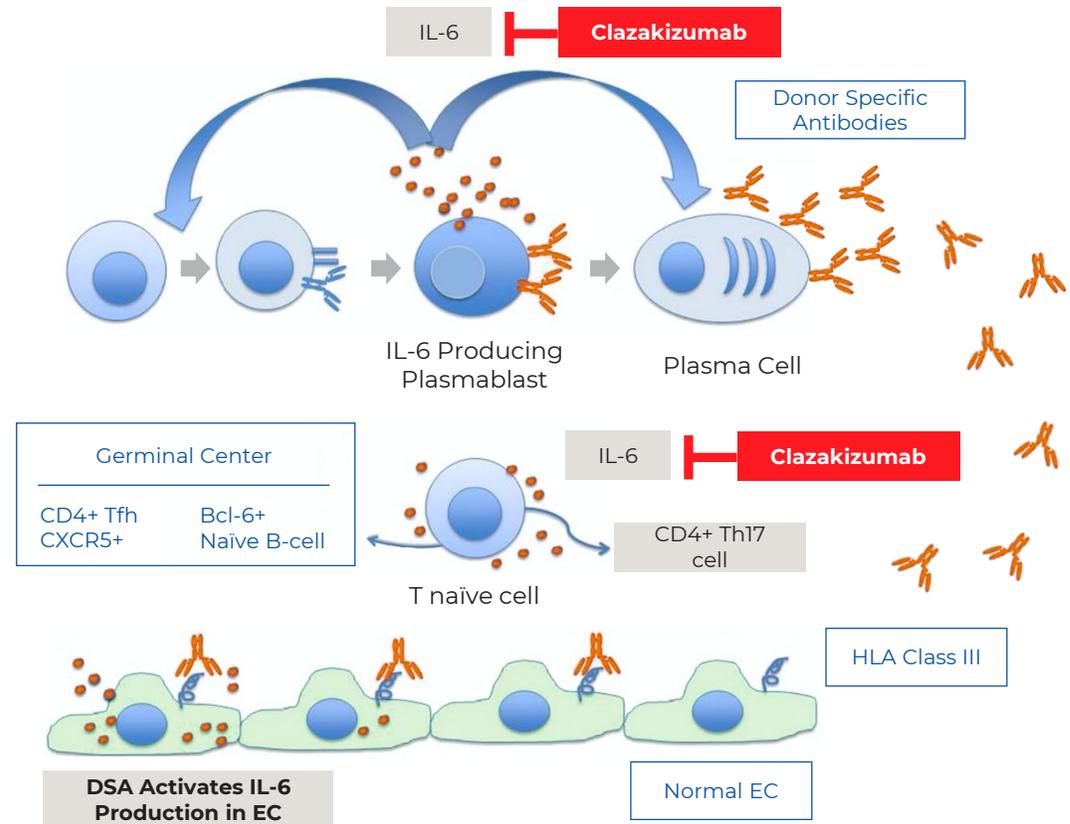
IL-6 induces donor-specific antibodies (DSAs) leading to renal tissue damage

Chronic AMR:

- Graft loss leads to low quality of life, dialysis, re-transplantation and/or death; high resource burden
- No approved treatments; clazakizumab would be first-line treatment

Anti-inflammatory and immune modulatory effects of IL-6 blockade:

- Reduces plasmablasts & proinflammatory T cells
- Increases Treg cells
- Decreases DSA production
- Reduces IL-6 production in activated ECs and subsequent reduction in vasculopathy



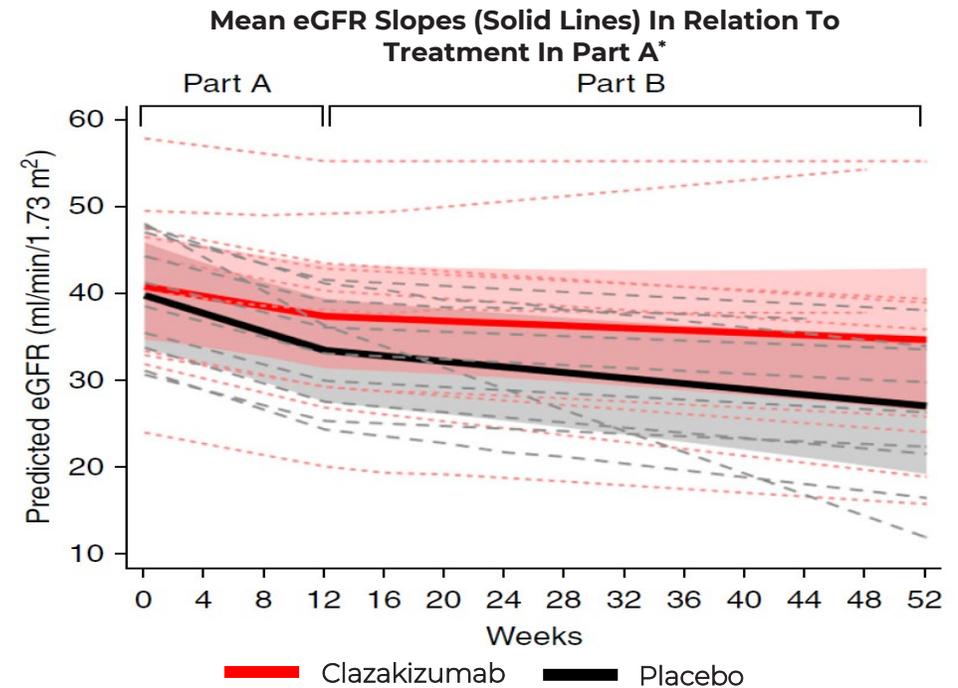
Source: Adapted from Jordan, S. et al., (2017) *Transplantation*. 101 (1): 32-44.

Abbreviations: AMR – Antibody-Mediated Rejection; EC – Endothelial Cells; HLA - Human Leukocyte Antigen; DSA – Donor Specific Antibodies

Clazakizumab Stabilizes Kidney Function & Improves Histologic Evidence of Rejection

Results from Phase II randomized, placebo-controlled trial in late AMR

- Clazakizumab slows eGFR decline by 60% after 12 weeks (model-based prediction)¹
- In 51 week biopsies, clazakizumab decreased molecular AMR and “all rejection” scores



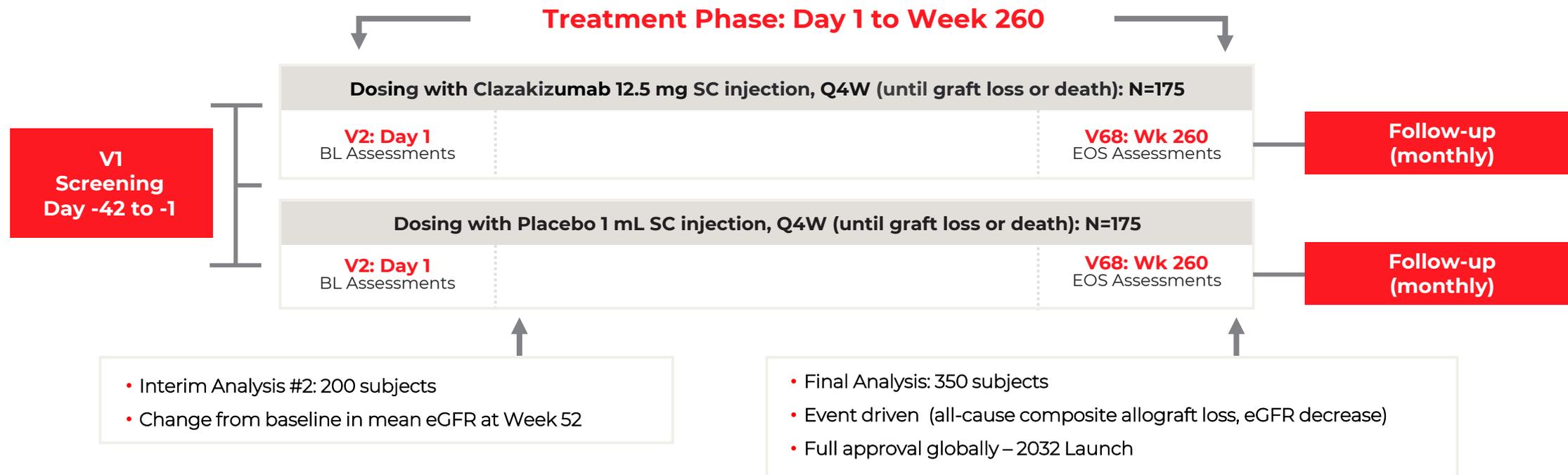
Part A: Mean eGFR decline in Clazakizumab group was slower compared with placebo

Source: 1. Doberer, K. et al., (2021) *J Am Soc Nephrol*. 32: 708-722.

Abbreviations: AMR – Antibody-Mediated Rejection; eGFR - estimated Glomerular Filtration Rate

IMAGINE

Clazakizumab for chronic AMR treatment study



Conditional Approval US - 2025



Clazakizumab in Dialysis

Dialysis is the most common treatment modality in ESKD



>550k

≈ 130k new cases annually



>370k

≈ 80k new cases annually

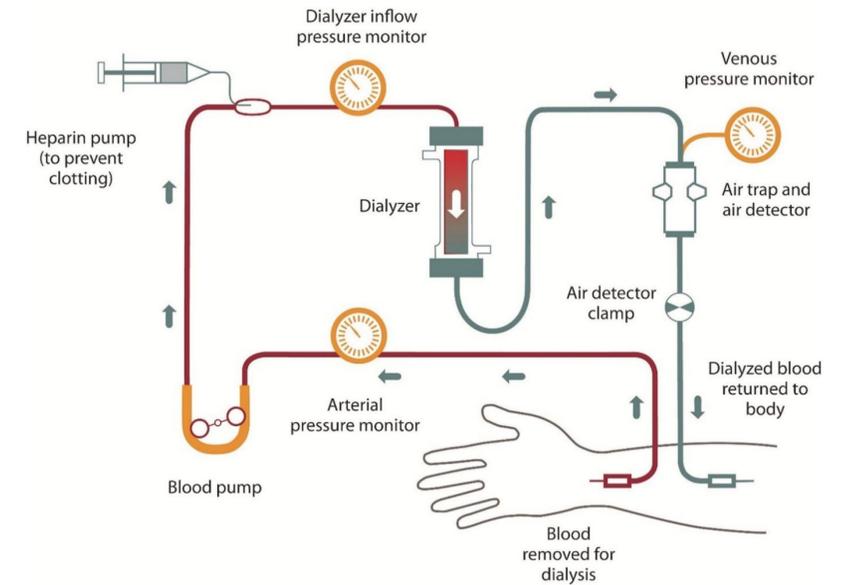


>350k

≈ 40k new cases annually

**Very High Unmet Need
160 deaths per 1,000 patients
annually**

Currently no proven treatments to reduce CV
events in dialysis



Role of inflammation

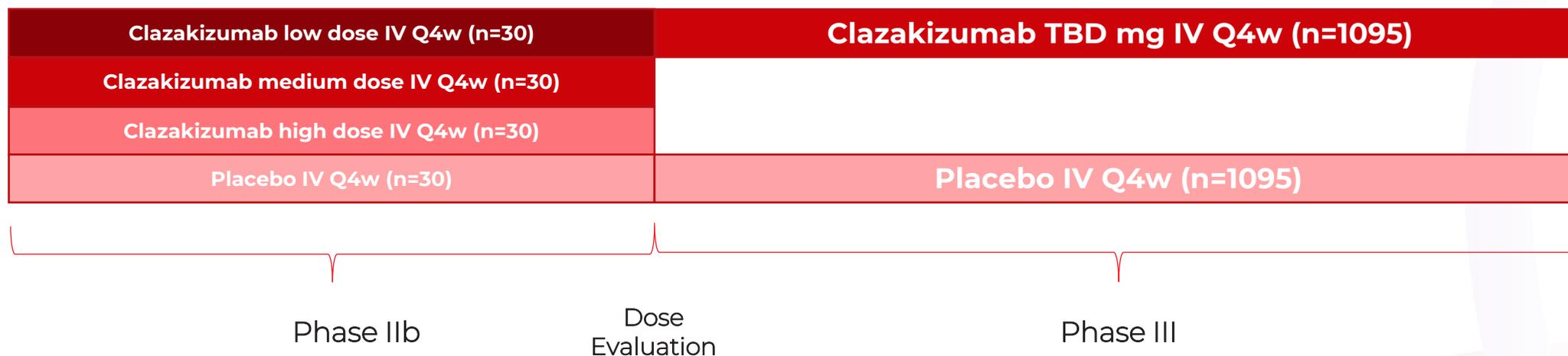
- Inflammation common in dialysis and strongly associated with CV events, central role of IL-6
- Strong science supporting link between IL-6 and CV events

CLAZAKIZUMAB in Dialysis



PREVENTION OF SERIOUS CARDIAC EVENTS
BY TARGETING IL-6 IN ESKD

- To demonstrate that IL-6 antagonism with clazakizumab will reduce CV events in dialysis patients
- An “Operationally Seamless” Phase IIb/III combined dose ranging (Phase IIb) and CV outcome trial (Phase III)
- Novel design to shorten development timeline received favorable feedback from FDA, EMA, PMDA
- Leverage Fresenius Medical Care study sites



Phase IIb/III – FPI Oct 2022

Abbreviations: CV – Cardiovascular; EMA – European Medicines Agency; FDA – Food & Drug Administration; FPI – First Patient In; PMDA – Pharmaceuticals & Medical Devices Agency; Q4w – every 4 weeks; TBD – To be determined



Haematology

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 haemostasis, stop bleeding quickly, and improve survival of Trauma patients with AMB



Data from preclinical and clinical studies¹⁻³ 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

*Among children, adolescents and young adults 1-44 years old.

Source: 1. Ghosh, S. et al., (2021) <https://doi.org/10.1371/journal.pone.0258192>; 2. Zeeshan, M. et al., (2019) *J Trauma Acute Care Surg.* 87(2): 274-281.; 3. Joseph, B. et al., (2014) *World J Surg* 38(8): 1875-8.

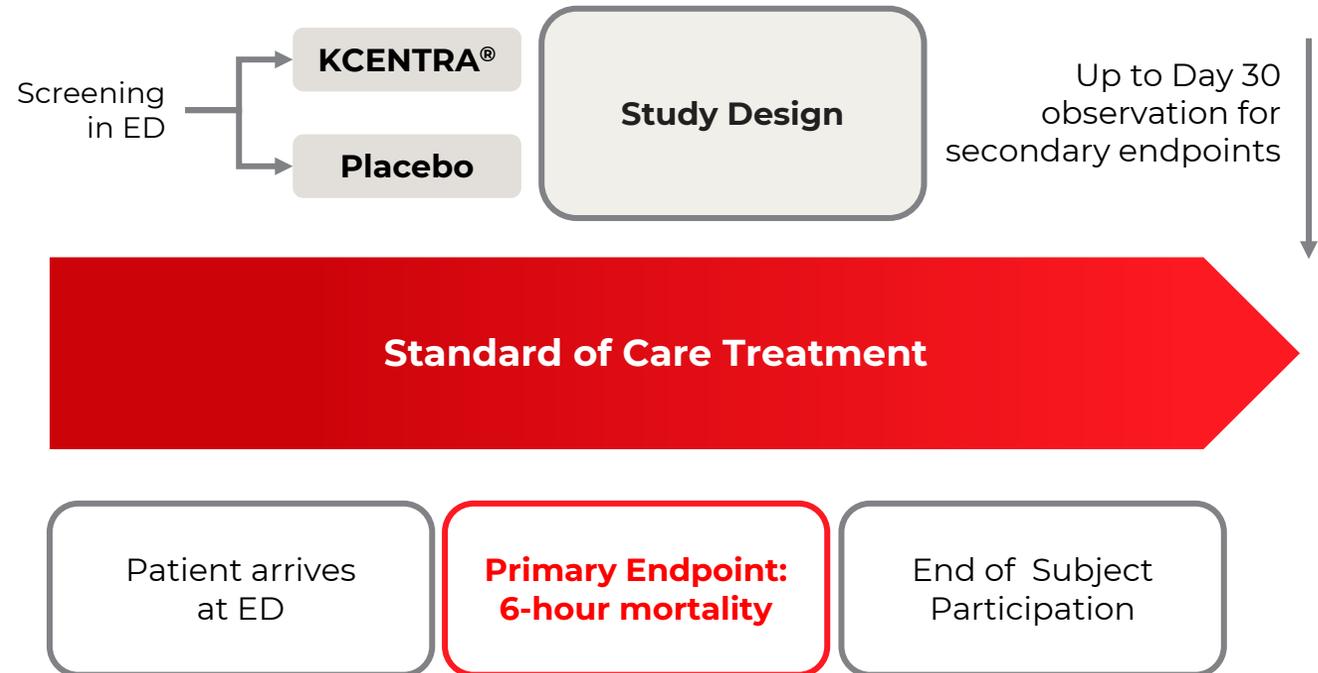
Abbreviations: 4-F PCC- Four-Factor Prothrombin Complex Concentrate



KCENTRA® Large Simple Study

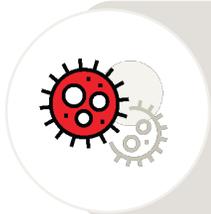
KCENTRA®

- Multimodal therapy containing multiple clotting factors that may be safe & effective in achieving haemostasis in patients with traumatic injury & confirmed or suspected acute major bleeding
- Enrollment starts: Feb 2023
- Study ends: Jul 2026
- Up to 8,000 subjects

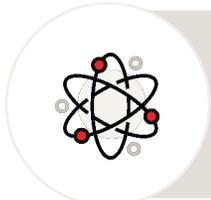


Phase III – initiating Q1 2023

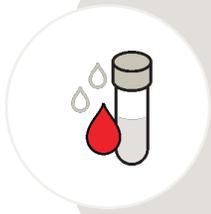
Sparsentan for IgA nephropathy and Focal Segmental Glomerulosclerosis (FSGS)



IgA nephropathy is the most prevalent type of primary glomerulonephritis worldwide and a major cause of kidney failure^{1,2}



**The incidence of FSGS is estimated to be:⁴
0.1/100,000/year in children 0.8/100,000/year in adults**



Despite having a good understanding of the pathophysiology and potential therapeutic targets, no non-immunosuppressive therapies are approved for the treatment of IgA nephropathy^{†,1,5,6}

**IgA
nephropathy
affects
3.5 in 10,000
people^{*,3}**

* The number of patients affected by the condition is estimated and assessed on the basis of data from the EU, Iceland, Liechtenstein, Norway, and the UK. This represents a population of 519,200,000 (Eurostat)³;

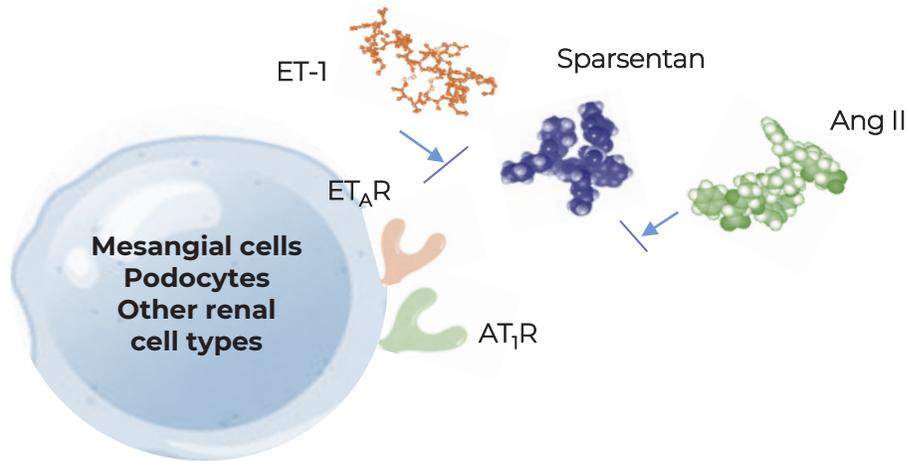
† Only one FDA-approved product, delayed-release budesonide, is indicated for the treatment of patients with primary IgAN at risk of rapid disease progression, approved by FDA on December 15, 2021, positive opinion for market authorization in Europe May 2022.⁷

Source: **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.** McGrogan, A. et al., (2011) *Nephrol Dial Transplant* 26:414–430; **5.** Barratt, J. & Feehally, J. (2005) *J Am Soc Nephrol.* 16: 2088–97; **6.** Tarpeyo US PI 2021 (accessed July 2022)

Abbreviations: EU - European Union; FDA - Food & Drug Administration; IgA - Immunoglobulin A; IgA - IgA Nephropathy

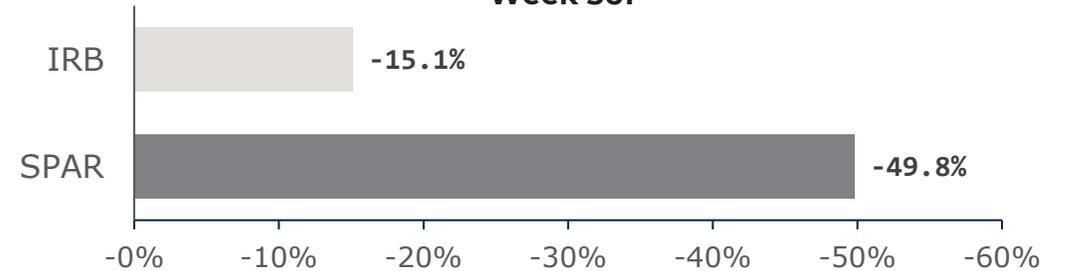
Sparsentan is a Novel Dual Endothelin Angiotensin Receptor Antagonist in Development for IgAN & FSGS*

Sparsentan is being developed in partnership with Traverre Therapeutics, a US biotechnology company. CSL Vifor territories include EU, AU & NZ.

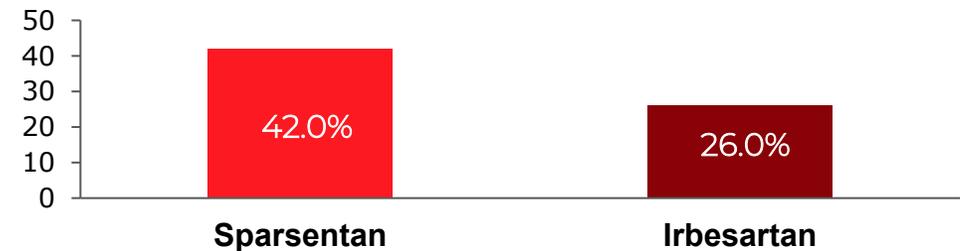


Sparsentan has been shown to reduce proteinuria in Immunoglobulin A nephropathy (IgAN) and in FSGS

IgAN: Mean Change in Proteinuria from Baseline at Week 36¹



FSGS: Partial Response Endpoint at Week 36²



IgAN Conditional approval – H2 2023
FSGS Submission – Q4 2023

* Sparsentan is an investigational compound for treatment of primary or genetic FSGS and IgAN. It is not approved by any regulatory agency.

Source: 1. Traverre Therapeutics press release: <https://ir.traverre.com/news-releases/news-release-details/traverre-therapeutics-announces-positive-topline-interim-results> (accessed May 2022); 2. Traverre Therapeutics press release: <https://ir.traverre.com/news-releases/news-release-details/traverre-therapeutics-announces-achievement-interim-proteinuria> (accessed July 2022) Figure © 2022 Traverre Therapeutics, Inc. All rights reserved.

Abbreviations: Ang II - Angiotensin II; AT₁R - Angiotensin II Receptor Type 1; ET_AR - Endothelin Receptor Type A; ET-1 - Endothelin 1; IgAN - Immunoglobulin A Nephropathy

Key Research with FERINJECT®/ INJECTAFER® in Heart Failure (HF)

	HEART-FID ¹	FAIR-HF2 ²
POPULATION	Patients (N=3014) with HFrEF and ID	Patients (N=1200) with full HF spectrum and ID
INTERVENTION	Ferric Carboxymaltose	Ferric Carboxymaltose
PRIMARY ENDPOINT	Treatment response over 12 months for incidence of death, hospitalisation for HF and change in 6MWT over 6 months	Composite of recurrent hospitalisations for HF and CV death after ≥12 months of follow-up
SPONSOR	American Regent, a Daichii Sankyo Company	University Hospital Hamburg, Germany
DATA AVAILABILITY	Q2 2023	Q1 2024

Source: 1. <https://clinicaltrials.gov/ct2/show/NCT03036462>; 2. Kalra, P.R. et al., (2022) *Heart* 0:1–7. doi:10.1136/heartjnl-2022-321304

Abbreviations: CV – Cardiovascular; HF - Heart failure; HFrEF - Heart Failure with Reduced Ejection Fraction; ID - Iron Deficiency; 6MWT - 6-minute Walk Test

SNF472 - Calciphylaxis/Calcific Uremic Arteriopathy (CUA): Orphan Disease with High Morbidity and Mortality

Extreme form of vascular calcification in skin arterioles affecting mostly patients with end stage renal disease

- No approved treatments; standard of care limited to palliative options
- Characterized by intensely painful ischemic/necrotic wounds
- Rapid disease progression leads to extreme pain, infection and death

~10k

patients in US & Europe¹

~55%

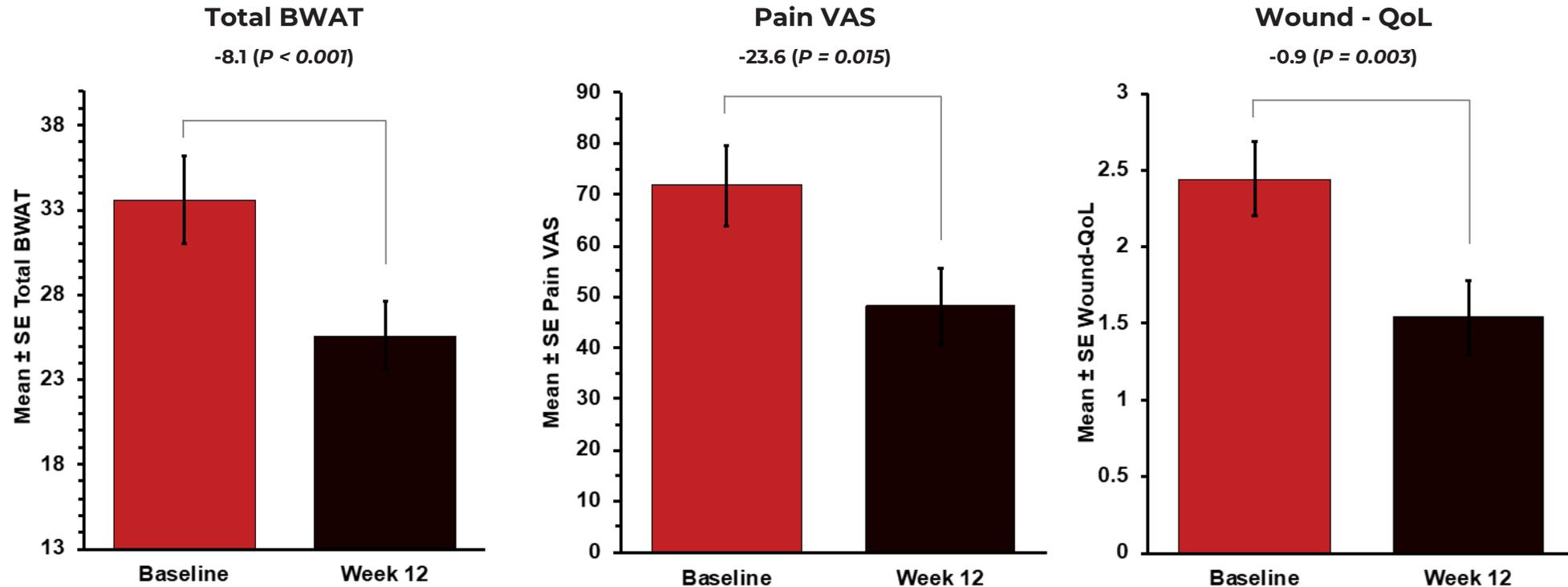
1-year mortality²

*SNF472 blocks hydroxyapatite (HAP) surfaces, the **final common pathway** of vascular calcification*



Source: 1. Company market research: survey conducted with 100 practicing nephrologists and dialysis clinicians in December 2017. Figure extrapolated from US prevalence, National kidney foundation – ESRD in the US, European Renal Association – European Dialysis and Transplant Association (2016 Annual Report). US + Europe prevalence estimated at 9.8K; 2. Weenig, R.H. et al., (2007) *J Amer Acad Derm.* 56(4): 569-579; Nigwekar, S. U. et al., (2018) *N Engl J Med.* 378: 1704-1714; 3. Shetty, M. et al., (2018) *Cleveland Clin J Med.* 85(8): 584-585. doi: <https://doi.org/10.3949/ccjm.85a.18009>.

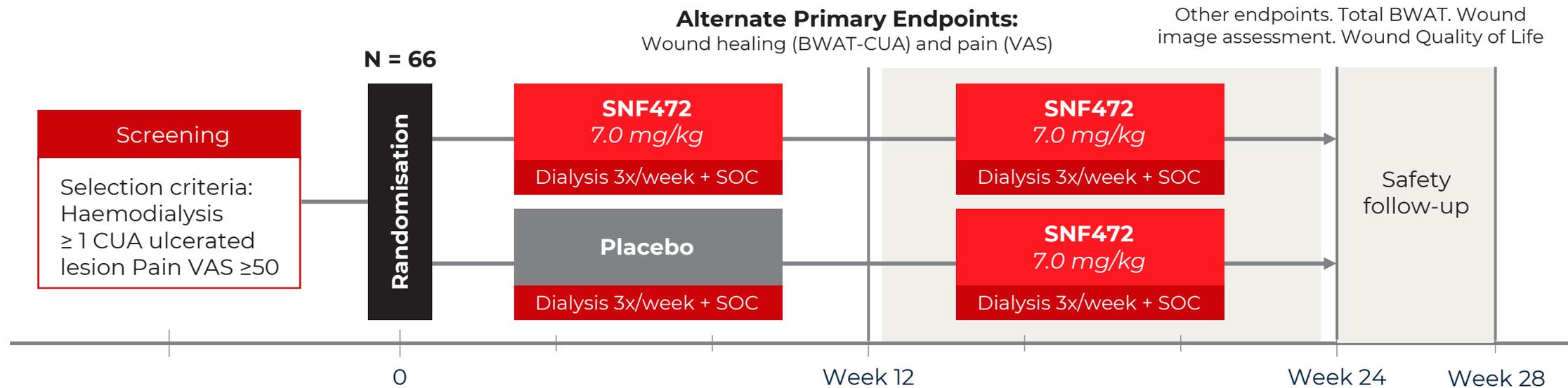
Phase II in CUA: Wounds and Pain Improved During SNF472 Treatment



Abbreviations: BWAT - Bates-Jensen Wound Assessment Tool; VAS - Visual Analog Scale; QoL - Quality of Life; Range of possible values: Total BWAT, 13–65; Pain VAS, 0–100; Wound QoL 0–4.

CALCIPHYX – Phase III Pivotal Study in CUA

Design and Alternate Primary Endpoints Agreed to by FDA/EMA



Phase III – Top Line Data 1H 2023

Abbreviations: BWAT - Bates-Jensen Wound Assessment Tool; CUA - Calcific Uremic Arteriolopathy; EMA – European Medicines Agency; FDA – Food & Drug Administration; QoL - Quality of Life; SOC - Standard of Care; VAS - Visual Analog Scale

Patients and Public Health: **Our Promise**

- Expanding late-stage portfolio
- High unmet need
- Many CSL products entering Phase III & market



Aidan and his mother, Amy,
Living with Primary Immunodeficiency



Logan,
Living Haemophilia B

Commercial

Bill Campbell

Executive Vice President
Chief Commercial Officer
CSL Behring



FY22 Commercial Highlights



Performance

- Global revenue \$8.4Bn
- Delivering on our promise to patients during time of uncertainty
- Investment in infrastructure, technology & market conditioning to support growth



Immunology

- Despite supply constrained environment, PRIVIGEN® & HIZENTRA® remained market leaders
- Continued CIDP expansion



Haemophilia

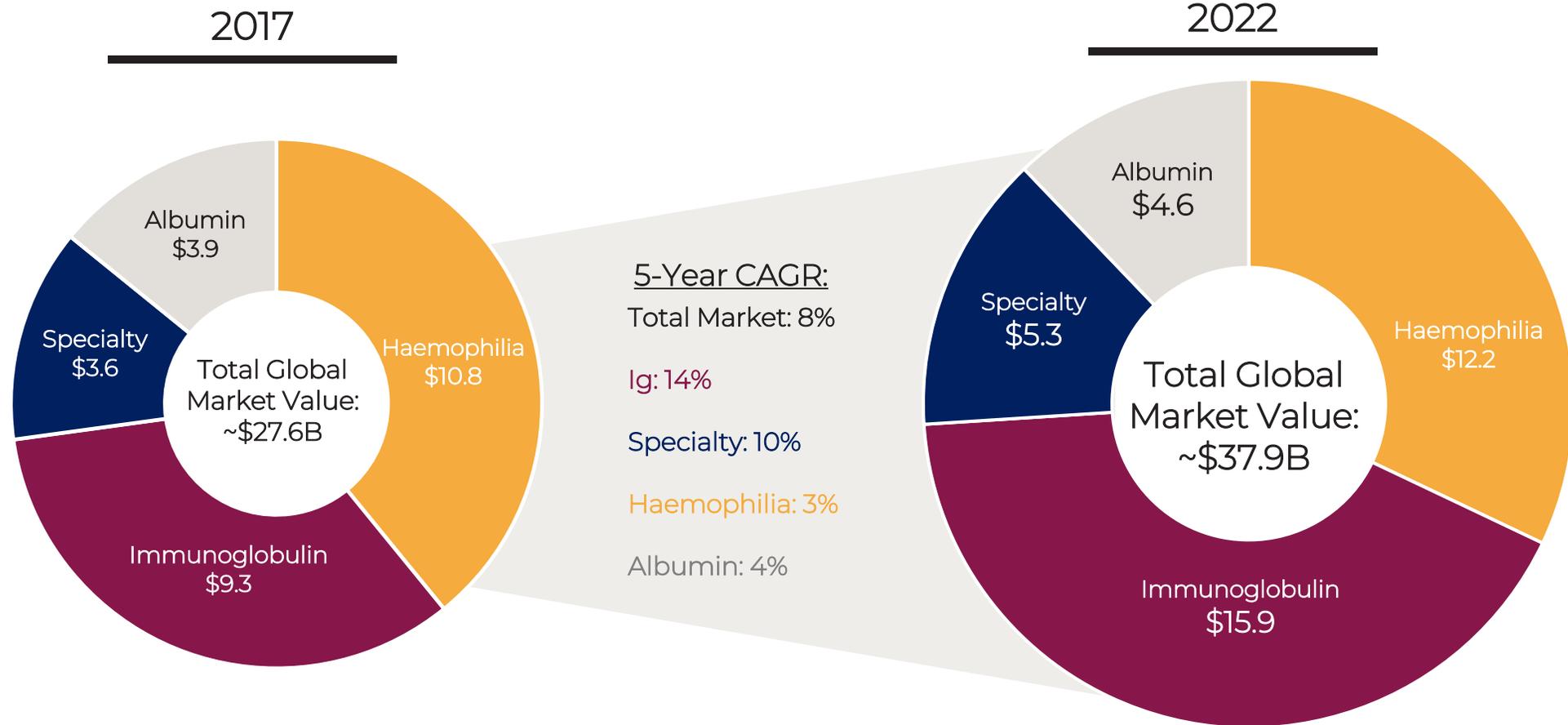
- Maintained IDELVION® leadership in key markets
- Successful launches in France and Argentina
- Etranacogene dezaparvovec (Haem B gene therapy) market readiness



Specialty

- Strong growth from HAEGARDA and KCENTRA®
- Zemaira / Respreeza supply challenges behind us

Targeted Protein Therapeutic Market Continues to Grow



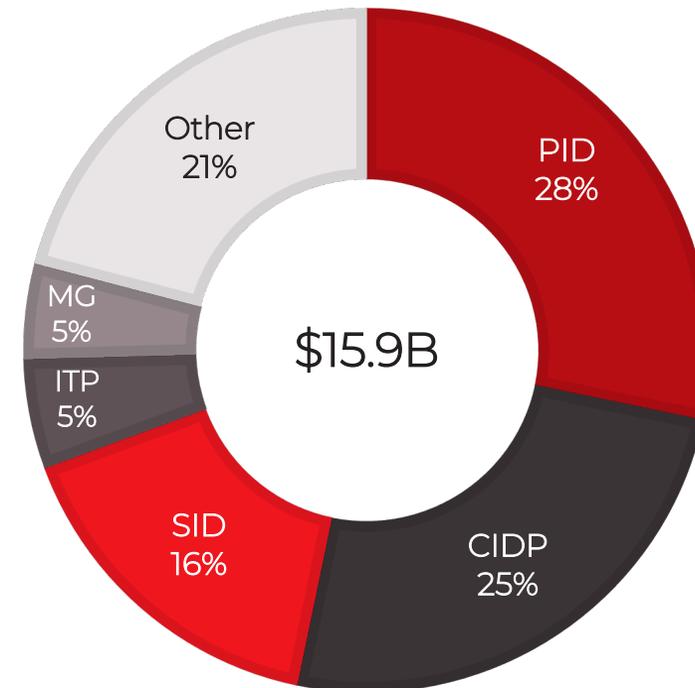
Source: CSL Actuals FY17 and FY22; Market based on internal TA forecast models, competitor annual reports, situation analysis, CI reports 2022 Market: Immunoglobulins market include Hyperimmunes; Haemophilia market include Factor XIII and non-factor(Hemlibra); Specialty includes AAT, HAE, Fibrinogen, PCC, ATT markets
Abbreviations: CAGR – Compound Annual Growth Rate

Immunoglobulin Market

Market Dynamics

- Growth limited by COVID constrained plasma collections
- Underlying Ig demand remains robust
- FY22 CSL Plasma collections increased 24% YOY
 - Investment in plasma collection centers during COVID
- Leading indicators of disease diagnosis returning to pre-covid levels

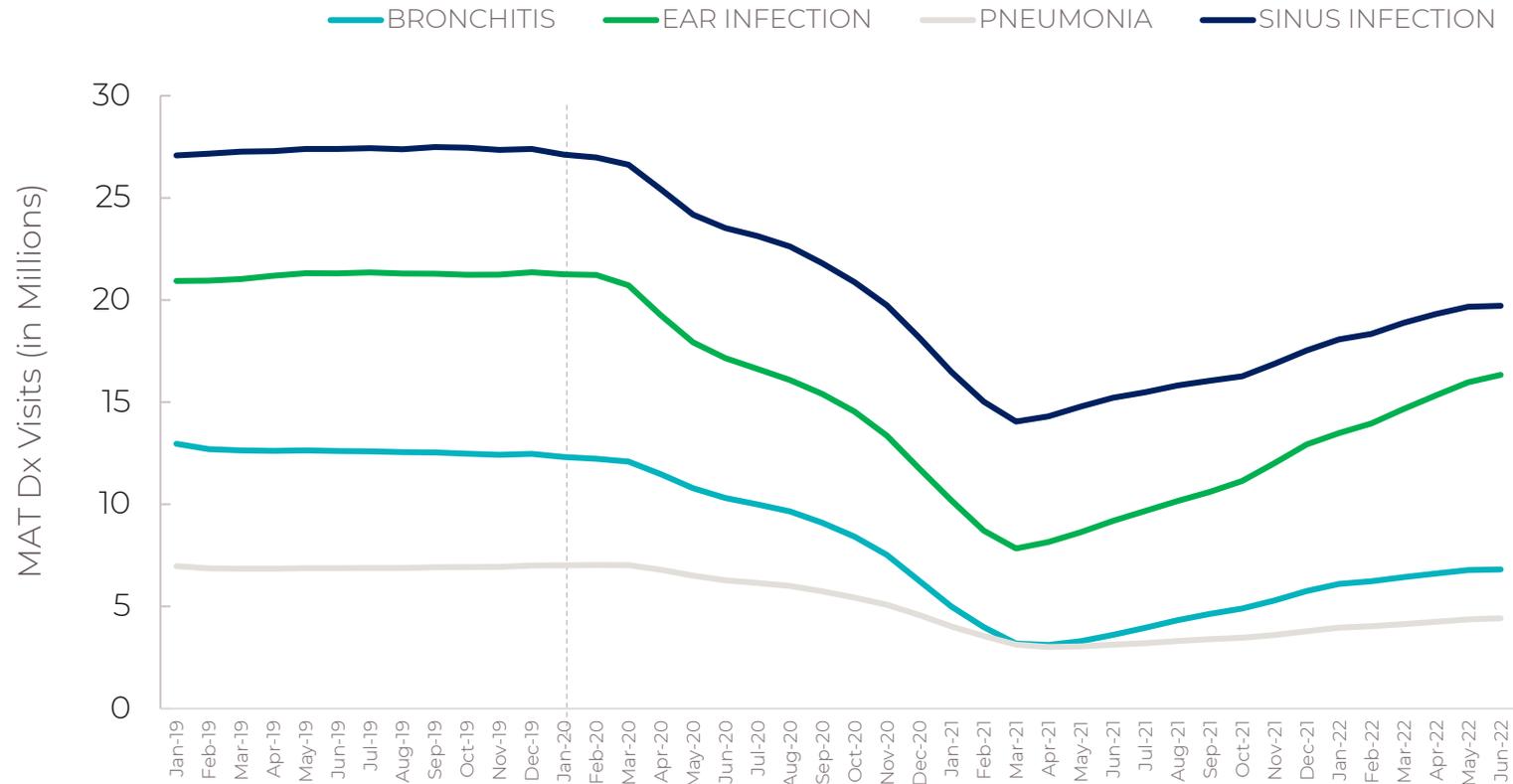
Global Ig Volume by Indication



Source: Data on file for 2021

Abbreviations: CIDP - Chronic Inflammatory Demyelinating Polyneuropathy; ITP - Idiopathic Thrombocytopenic Purpura; MG - Myasthenia Gravis; PID - Primary Immune Deficiency; SID - Secondary Immune Deficiency; YOY - Year on Year

Infection rates leading to a PID diagnosis at ~70% of pre-COVID levels



- Lead indicators declined starting March 2020
- Trough level in Mar-21
- PID patient diagnosis continuing to increase in recent months

“Patients will return to a normal pre-Covid life and have the same risks and exposures, plus the immune system will need practice.” – Immunologist

Source: Data on File – Represents US market only
 Abbreviations: PID - Primary Immune Deficiency

Immunoglobulins

FY22 Sales: \$4,024M¹

Down 3%²

- HIZENTRA®, >10 years as worldwide market leader
 - 75% of targeted physicians using HIZENTRA® to treat CIDP
 - >50% of HIZENTRA® starts in the US are newly diagnosed patients
 - Increased preference for home treatment as a result of the pandemic
-
- Patient focused supply continuity strategy executed
 - PRIVIGEN® patient share⁴ in US up +3% YOY
 - PRIVIGEN® maintained market leadership in key global markets

“We see a lot more PID patients. It seems to have gone up even into July and August.... I think its a combination of diagnosis and patients realizing the value of prophylaxis...” Immunologist

Source:

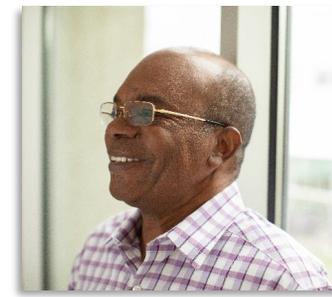
¹ Excludes Ig hyperimmunes

² Growth percentages shown at constant currency to remove the impact of exchange rate movements, facilitating comparability of operational performance.

³ Combination - updated Peripheral Nerve Society (PNS) treatment guidelines, PATH extension data

⁴ Date on file - Represents US market in core indications; PID, CIDP, SID

Abbreviations: CIDP - Chronic inflammatory demyelinating polyneuropathy; YOY - Year on Year



Patients report favorable treatment experience with HIZENTRA[®]

At least **97%** were very/somewhat satisfied with:¹ (n=33)

- Ability to personalize treatment
- Overall convenience
- Overall ease of administration
- Ability to fit treatment into their lifestyle

Online Harris Poll survey, sponsored by CSL Behring LLC, of 104 U.S. adults with PI who ever received IVIg (n=65), SCIg in glass vials (n=65), and/or SCIg in prefilled syringes (n=33)

1 Ig

Prescribed for PID and the only SCIg approved for use in CIDP¹

Proven

Long-term protection with >10 yrs. of real-world experience

>3.5

Years of clinical efficacy and tolerability evidence

New

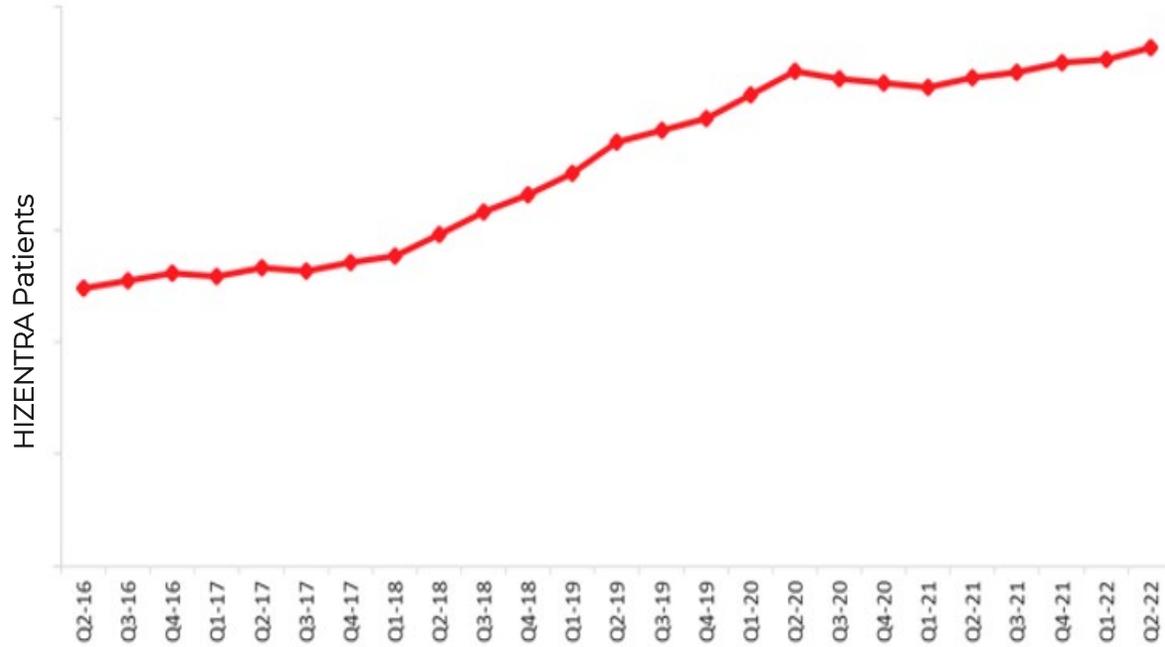
Personalized treatment option with prefilled syringes

Source: ¹Data on File – Represents US market only

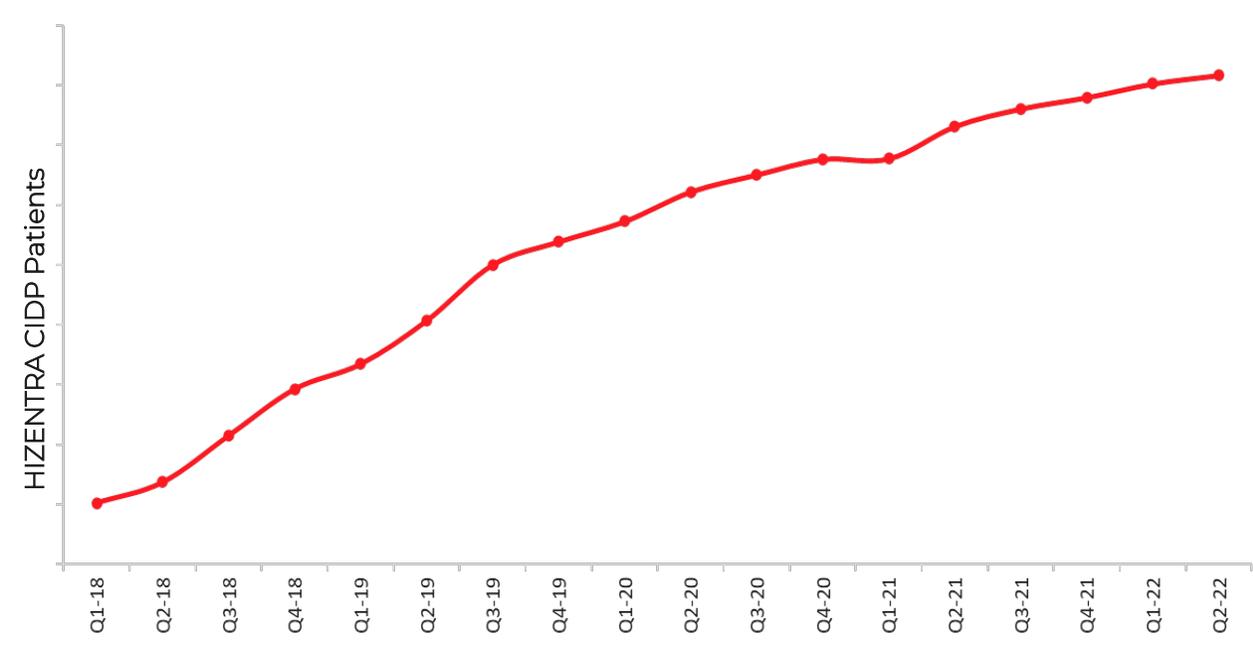
Abbreviations: CIDP - Chronic inflammatory demyelinating polyneuropathy; PID – Primary Immune Deficiency

HIZENTRA® Sustained Market Leadership: US

Patient Growth: All Indications



CIDP Patient Growth



Source Represents US market only
Abbreviations: CIDP - Chronic Inflammatory Demyelinating Polyneuropathy

Haemophilia

FY22 Sales: \$1,166M

Up 8%¹



- IDELVION[®] +20%¹ YOY revenue growth
 - Standard of care in Haemophilia B with compelling clinical profile
 - Market leadership² in key markets, including US, Germany, Italy, Spain, Switzerland and Japan
 - Strong launches during pandemic
-
- AFSTYLA[®] holding patient share in competitive Haem A segment
 - pdFVIII maintained market leadership globally in vWD with 55% patient share^{2,3}
 - HUMATE[®] revenue growth of +4%¹ YOY

Source:

¹ Growth percentages shown at constant currency to remove the impact of exchange rate movements, facilitating comparability of operational performance.

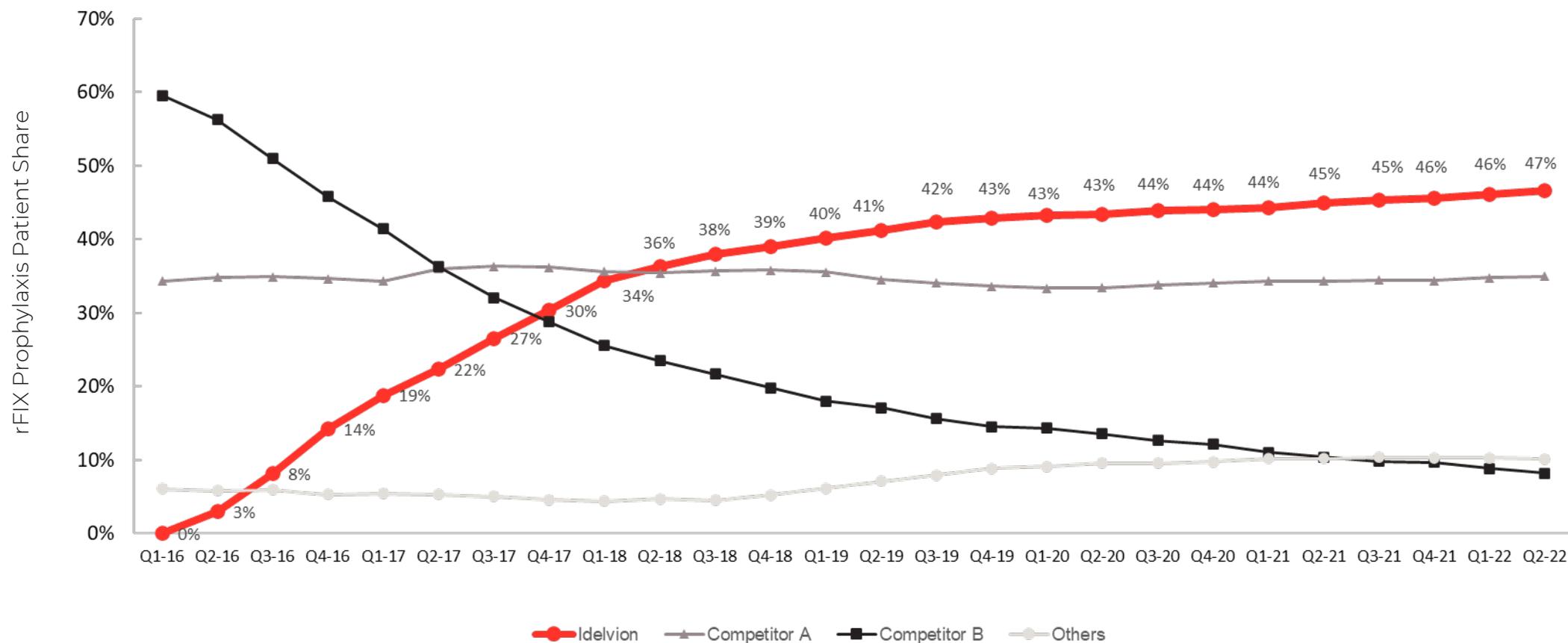
² Data on file

³ Includes HUMATE[®]/HAEMATE[®] and VONCENTO[®]

⁴ Data on file – Represents US market in core indications; PID, CIDP, SID

Abbreviations: vWD – von Willebrand Disease; YOY – Year on Year

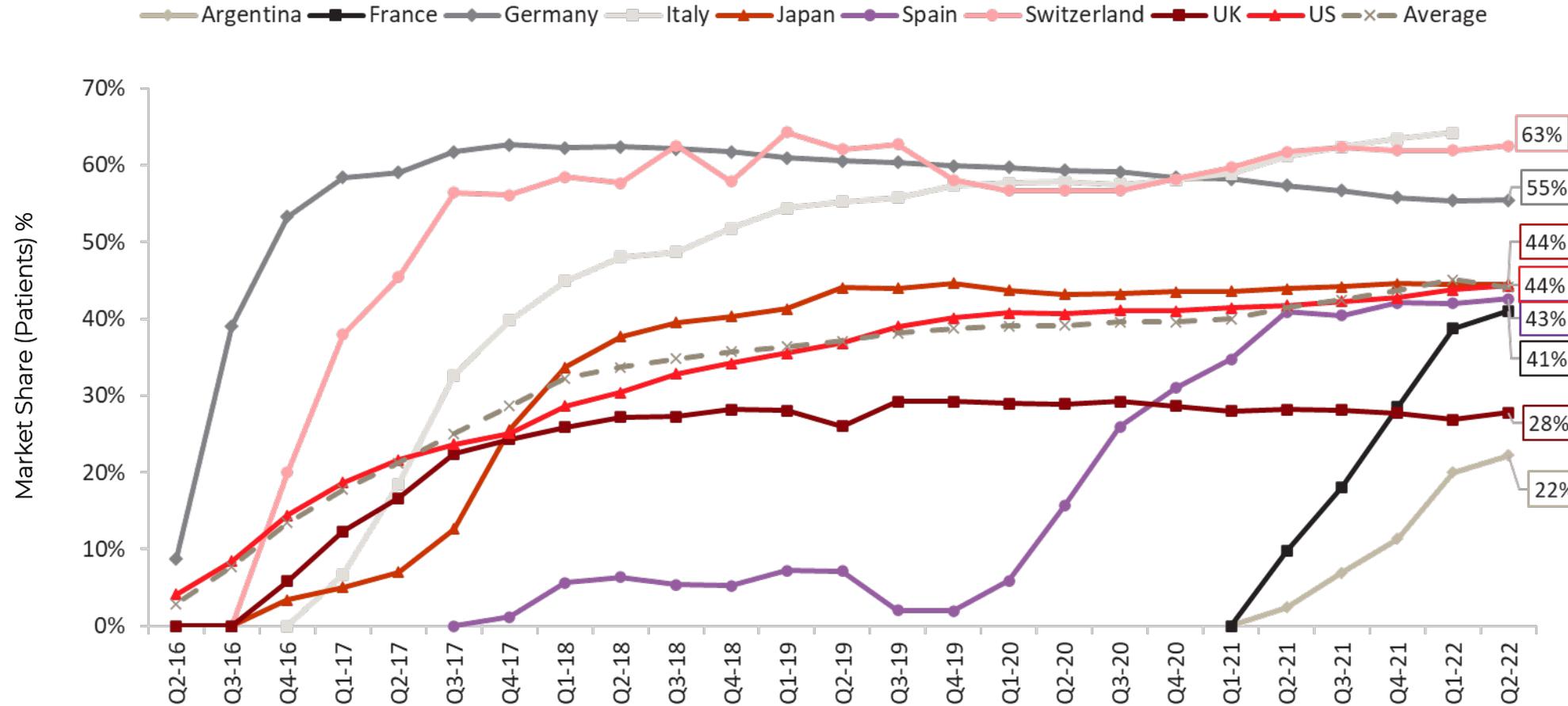
IDELVION® - Maintaining Market Leadership



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



Source: Data on file

Gene Therapy in Haem B: Patients' unmet needs include achieving greater freedom from the burden of the disease



 **Durable Protection:** Patients crave more durable treatments, to help protect them from the spontaneous bleeds and joint damage.

 **Psychological and Social Impact:** Patients face anxiety, depression, and social issues as a part of managing their Haem B. Patients experience challenges with living a “normal” life.

 **Infusion Burden:** Patients report feeling like managing their Haem B is time-consuming and restricts their ability from living their life.

“I want more **freedom from my infusions** so that I can spend time **living life to the fullest** [...] I **don't want to receive injections anymore**” (Patient)



Specialty Products

FY22 Sales: \$1,792M

Up 3%¹

- KCENTRA[®] +18%¹ YOY revenue growth; exceeded pre-pandemic levels
- Remains the gold standard for warfarin reversal in the US
- Substantial growth opportunities, with FFP still used in ~40% of patients² in the US

- HAEGARDA[®] +5%¹ YOY revenue growth
- Launches in EU and Australia exceeding expectations
- Treatment paradigm shifts further from on-demand to long-term prophylaxis
- Pipeline expansion opportunity with Garadacimab

- ZEMAIRA[®] / RESPREEZA[®] supply challenges behind us

Source:

¹ Growth percentages shown at constant currency to remove the impact of exchange rate movements, facilitating comparability of operational performance.

² Data on file

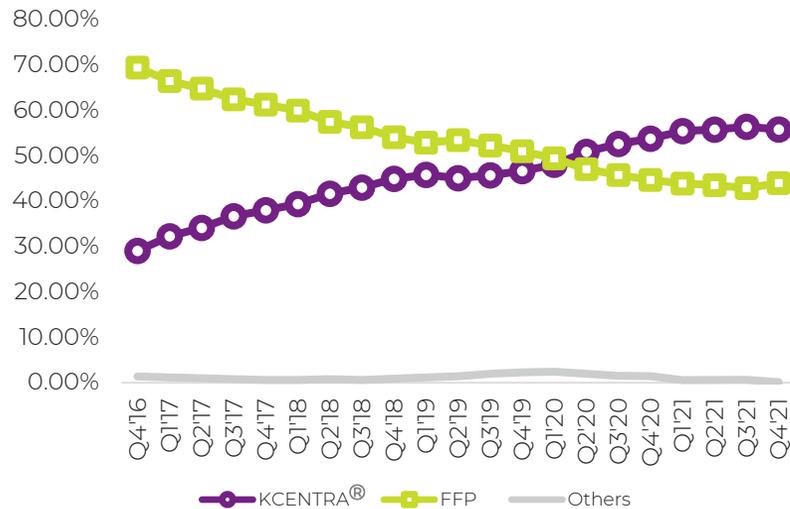
Abbreviations: FFP – Fresh Frozen Plasma; YOY – Year on Year

KCENTRA® - Growth in the US

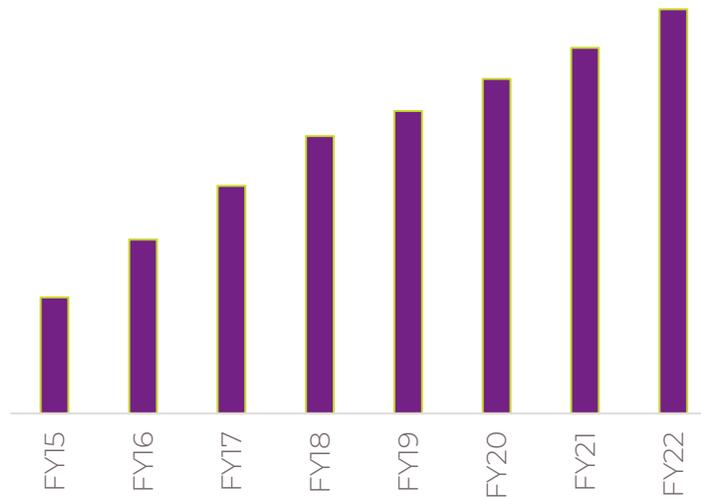
US Clinical practice guidelines recommend KCENTRA® over FFP to reverse the effects of Warfarin*

- ~1.4M patients on warfarin, with ~18k new patient starts per month¹
- Growth drivers: Superior efficacy data versus fresh frozen plasma and penetration within hospital systems

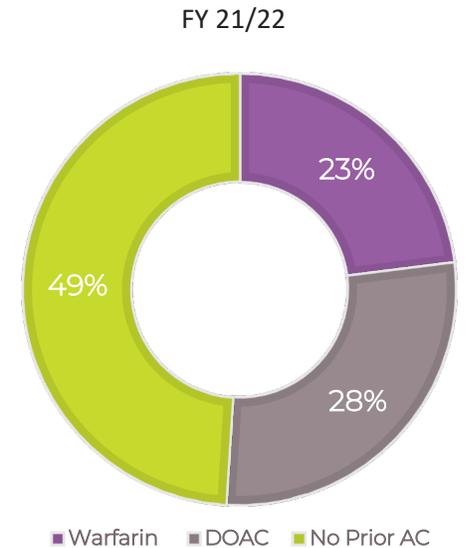
Warfarin Urgent/Major Bleed Reversal Shares



KCENTRA® Demand



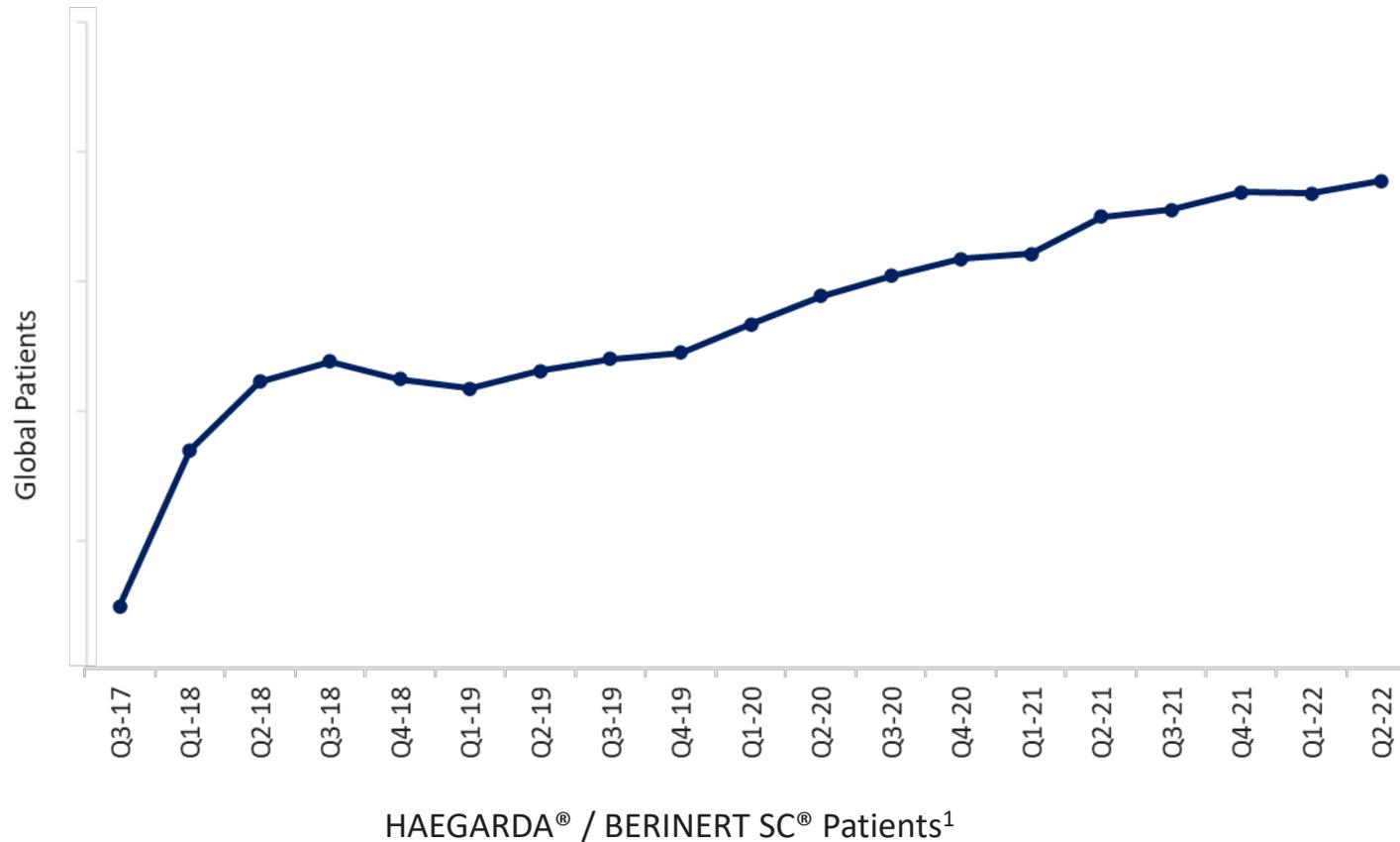
KCENTRA® Source of Business by Segment



Source: All data represents US market only
 * 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
¹ Data on file – represents US market only
Abbreviations: DOAC - Direct-acting Oral Anticoagulants; FFP - Fresh Frozen Plasma; YOY - Year on Year

HAEGARDA[®] / BERINERT[®] SC

Patient Growth Amidst Increased Competition



Regional Progress

- US: New patient growth in competitive market
- EU: Recent launches exceeding expectations
- Australia achieved +70% patient share^{1,2} within a year of launch
- Three additional launches planned by end of 2022

Source:

¹ Data on file

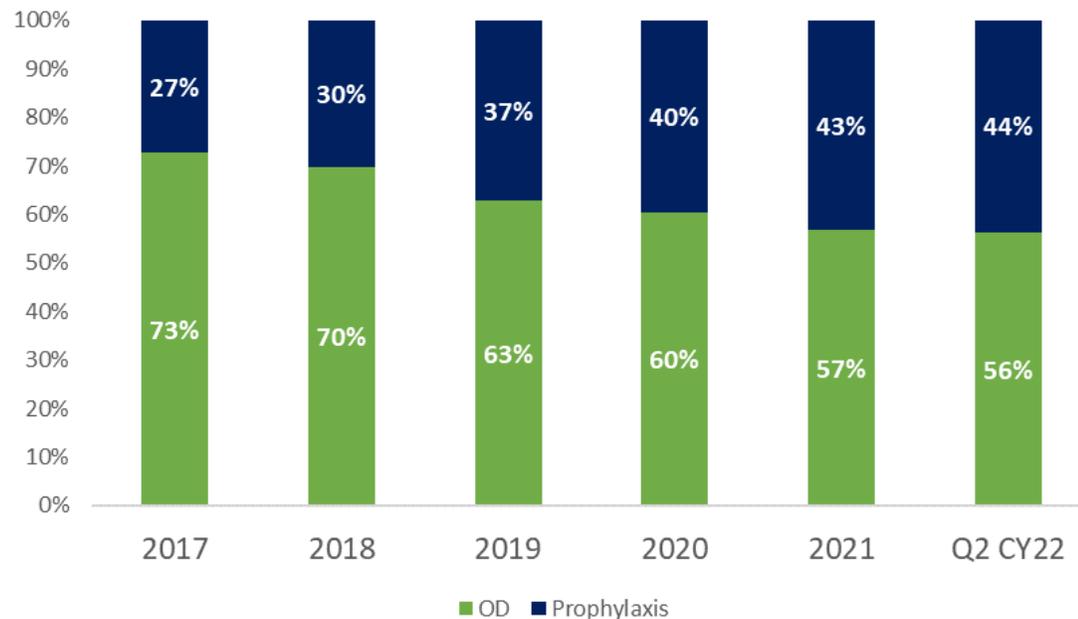
² Patient share in the non-steroidal prophylaxis segment

Abbreviations: SC – Subcutaneous

HAEGARDA[®] /BERINERT[®] SC Efficacy Drives Potential

Proven Record Of High Efficacy And Safety²

HAE Market Share (Patients) by Regimen¹



- Prophylaxis segment continues to grow; reducing patients on acute therapy to ~55%
- >50% of HAEGARDA[®] patients have been on therapy for more than a year
- Continue to see patients switch back from competing products to the benefits of HAEGARDA[®] /Berinert[®] SC¹

Source:

¹ Data on file – Represents US, DE & ES. Includes all HAE markets, split on long term prophylaxis vs. on-demand

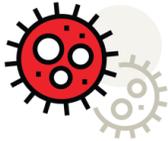
² In the clinical trial, 95% median reduction in number of attacks in patients receiving 60 IU/kg of HAEGARDA[®] vs placebo, and a >99% median reduction in rescue medication use in patients receiving 60 IU/kg of HAEGARDA[®] vs placebo.

Abbreviations: SC – Subcutaneous

Commercial Summary



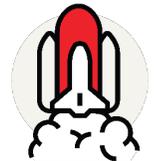
Executing on Long-Range plan



Pivoted from COVID constrained approach to demand generation



Anticipate strong growth in FY23



Preparing for transformational new launches



Sustained track record of delivering long-term growth

The CSL logo is displayed in white, bold, sans-serif capital letters on a red square background in the top left corner.

Michael,
Living with Haemophilia B



Summary

William Mezzanotte MD

Executive Vice President, Head of R&D
Chief Medical Officer

CSL



Combined CSL & CSL Vifor R&D Portfolio – FY22



Phase I



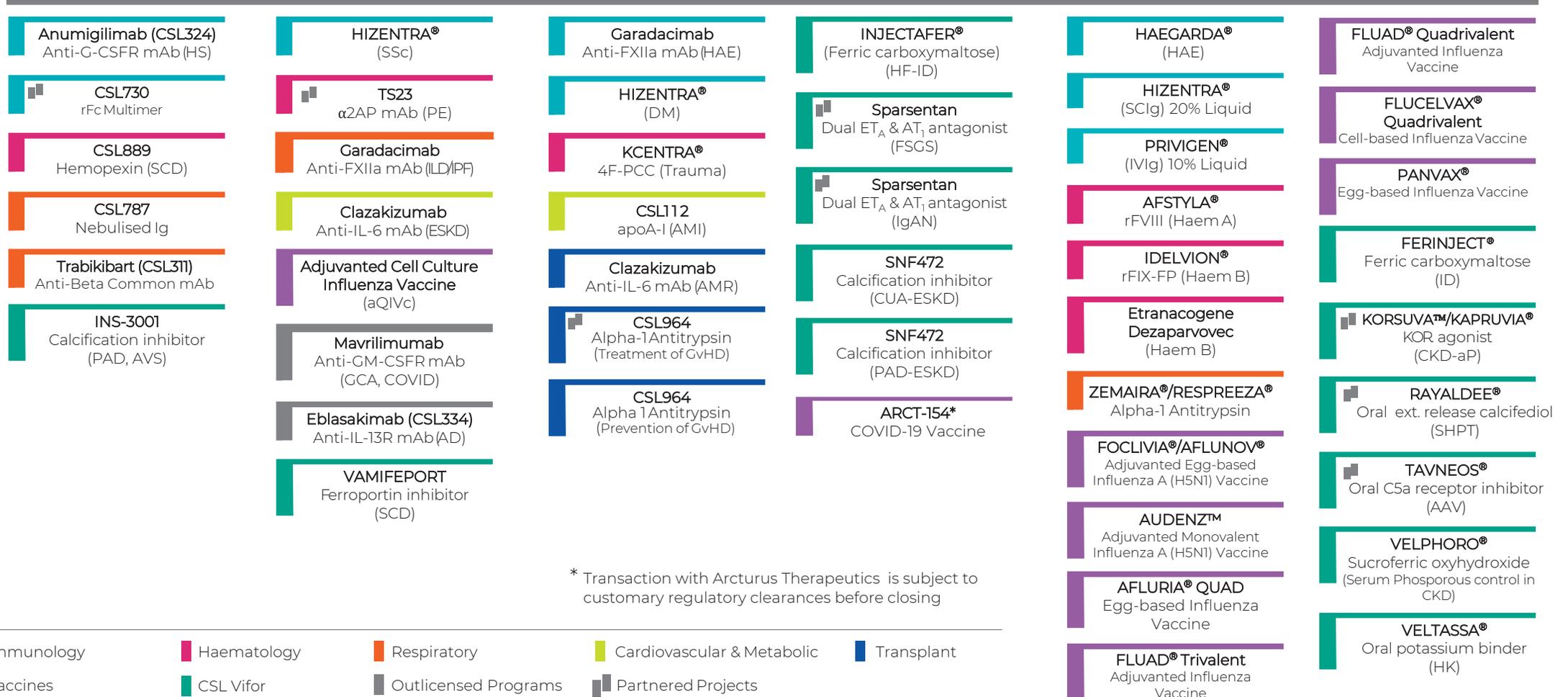
Phase II



Phase III



Registration/Post-Registration



Immunology

Haematology

Respiratory

Cardiovascular & Metabolic

Transplant

Vaccines

CSL Vifor

Outlicensed Programs

Partnered Projects

Forward-Looking Portfolio Highlights – FY23



Immunology

- **Garadacimab** (Anti-FXIIa) HAE
 - Phase III study data announced
 - Global submissions started
- **Anumigilimab** (CSL324; G-CSFR antagonist) Phase Ib study last patient out
- **BERINERT®** SC HAE JP PMDA approval



Haematology

- **CSL889** (Hemopexin) Phase I study last patient out
- **Etranacogene dezaparvovec** US & EU launch
- **KCENTRA®** Trauma Phase II study first patient in



Respiratory

- **Garadacimab** (Anti-FXIIa) IPF Phase II study enrolment complete
- **CSL787** (Neb Ig) Phase I study enrolment complete



Cardiovascular & Metabolic

- **CSL112** (ApoA-1) Phase III study enrolment complete
- **Clazakizumab** (ESKD) Phase IIb/III study first patient in



Transplant

- **CSL964** (AAT) treatment of GvHD – Phase III study last patient in



Vaccines

- **aQIVc** (cell antigen + MF59®) Phase IIb study results available
- **ARCT-154** COVID vaccine global submissions started

CSL Vifor

- **INS-3001** (AVS) Phase I study first patient in
- **FERINJECT®** (ferric carboxymaltose) ID China approval
- **INJECTAFER®** (ferric carboxymaltose) HF-ID Phase III data available
- **KORSUVA™/KAPRUVIA®** (difelikefalin) multiple country approvals
- **SNF472** CUA Phase III Top Line Data
- **Sparsentan** (IgAN) CMA EU
- **VELPHORO®** (sucroferric oxyhydroxide) China approval
- **Vamifeport** (SCD) Phase IIa study recruitment complete

R&D Strategic Investments Coming to Fruition

**Strengthen Our
Core Competencies**

**Build Strategically and
Scientifically in our TAs**

**Explore Disruptive
Innovation**

**Expand
into Complementary
Disease Areas and
Platforms**

**Embrace the External
Environment**

- **Continued improvements in manufacturing processes**
- **Progression of our clinical internal portfolio**
 - Plasma – CSL112, KCENTRA[®], AAT (GvHD), HIZENTRA[®], CSL787 & CSL889
 - MAb – CSL730, Clazakizumab, Anumigilimab
 - Vaccines – aQIVc+
 - Small molecules – SNF472, Sparsentan
- **Exciting near-term launches for disruptive new therapies**
 - Etranacogene dezaparvovec
 - Garadacimab
- **Embracing the External Environment**
 - New Research Partnerships
 - Biotech Incubator
- **Strategic Additions in Complementary Platforms and Therapy Areas**
 - Translational Sciences – Thrombosis reduction – Haematology
 - Arcturus – next generation mRNA technology
 - CSL Vifor – Strengthen our CardioRenal Portfolio, New Core Competency in Nanomedicines/Iron
- **Leading Commercial expertise to bring these therapies to patients**

The CSL logo is a red square with the letters 'CSL' in white, bold, sans-serif font.

Leah, Living with
Hereditary Angioedema

Panel Q&A Session

Next-Generation mRNA, Gene Therapy, Plasma Products, Monoclonal Antibodies, and Recent Acquisitions and Collaborations Highlight CSL R&D Day 2022

Pipeline advancements and investment in innovation and disruptive technologies to help fuel sustainable, profitable growth for CSL's three businesses, CSL Behring, CSL Seqirus and CSL Vifor, in the decades ahead

MELBOURNE, Australia and KING OF PRUSSIA, Pennsylvania – 03/02 November

22 -- At its annual R&D investor briefing today, global biotechnology leader CSL (ASX:CSL; USOTC:CSLLY) demonstrated how its growing, innovative pipeline is well-positioned to meet the current and future needs of patients and public health. CSL revealed progress and plans in advancing assets that have the potential to disrupt current standards of care in its areas of focus (immunology, haematology, respiratory, cardiovascular and metabolic, transplant, nephrology, vaccines) using its strategic scientific platforms (plasma protein technology, recombinant technology, cell and gene therapy, and sa-mRNA, adjuvanted, cell-based and egg-based vaccines).

Among the highlights presented were the following:

Late-Stage Development Includes Disruptive Innovation and New Additions to the CSL Portfolio

- Etranacogene dezaparvovec (also known as CSL222), an investigational gene therapy for the treatment of adults with haemophilia B has been accepted for priority review by the United States (US) Food and Drug Administration (FDA) and standard review by the European Medicines Agency (EMA). If approved, etranacogene dezaparvovec would be the first-ever gene therapy treatment option for the haemophilia B community. The regulatory filings are supported by results from the pivotal HOPE-B trial, the largest gene therapy trial in haemophilia B to date. The multi-year clinical development program for etranacogene dezaparvovec was led by uniQure (Nasdaq: QURE) and sponsorship of the clinical trials has transitioned to CSL after acquiring global rights to commercialize the investigational treatment.
- Top-line Phase III results for garadacimab (CSL312, anti-FXIIa), an investigational first-in-class monoclonal antibody being developed as a long-term preventive treatment for patients with hereditary angioedema, demonstrated that the study met its primary and secondary efficacy objectives and showed favourable safety and tolerability. CSL aims to begin filing for approval with global regulatory authorities next calendar year. Garadacimab was discovered and optimised by scientists at CSL's Bio21-based Research site, with formulation and manufacturing for the clinical programs completed at the CSL Broadmeadows Biotech Manufacturing Facility.

- CSL Vifor brings a leading portfolio of therapies in nephrology, dialysis and iron deficiency. New late-stage assets to the pipeline include Sparsentan for IgA nephropathy and focal segmental glomerulosclerosis (FSGS) and SNF472 for calciphylaxis and calcific uremic arteriopathy (CUA).

R&D Portfolio Progress Across Areas of Focus and Scientific Platforms

- Clazakizumab, an anti-IL6 monoclonal antibody, intended for the treatment of chronic active antibody-mediated rejection (AMR) in kidney transplant recipients continues to progress in the Phase III IMAGINE trial. This is CSL's leading program for clazakizumab, which will also be investigated in a Phase IIb/III study for improvement of cardiovascular (CV) outcomes in dialysis patients. CSL plans to engage Fresenius Medical Care dialysis centres in the study.
- AEGIS-II, a Phase II, multicenter, double-blind, randomised, placebo-controlled, parallel-group study to evaluate the efficacy and safety of CSL112, compared to placebo, in reducing the risk of major adverse CV events (MACE) in patients following a heart attack, will enrol the last patient by the end of 2022, with completion of the trial expected towards the end of 2023.
- CSL is advancing the Phase IIb study for its adjuvanted, cell-based high-dose quadrivalent influenza vaccine (aQIVc). This study will help CSL further build the body of clinical evidence to support the optimal formulation for when the company moves into the Phase III immunogenicity and safety study for aQIVc.
- Published results from the preclinical studies of CSL's self-amplifying messenger RNA (sa-mRNA) influenza vaccine candidates, the next generation of mRNA vaccines, indicate a potent, cross-reactive immune response against pandemic and seasonal influenza strains, A(H5N1) and A(H1N1). CSL's sa-mRNA candidate is expected to enter clinical trials in 2023.

Recently Announced

- Collaboration and license agreement with Arcturus Therapeutics aims to accelerate next-generation mRNA capabilities in influenza, pandemic preparedness and other selected respiratory viral pathogens -- including a near term COVID-19 vaccine that has recently reported interim results from a large Phase III efficacy study, meeting its primary and secondary endpoints of prevention of infection and severe disease with a favourable safety profile.
- A strategic option and license agreement with Translational Sciences to license TS23, a first-in-class anti- α 2-antiplasmin monoclonal antibody. TS23 is being developed to dissolve thrombi that cause serious conditions such as pulmonary embolism (PE) and acute ischemic stroke (AIS). The treatment candidate is soon to be evaluated in the US in the NAIL-IT Phase II study, which has been designed to evaluate the safety and thrombolytic effect of ascending doses of TS23 in patients with sub-massive (intermediate risk) PE.

“CSL is on the leading-edge of innovation in areas we know well and we have strategically and methodically built a pipeline that has never been more robust with

diverse sources of innovation, from in-house and external sources, that include the disruptive scientific platforms of gene therapy and sa-mRNA,” said Dr. Bill Mezzanotte, Executive Vice President, Head of R&D, and Chief Medical Officer for CSL. “Our enhanced capabilities across all of our scientific platforms and therapeutic focus areas will help us in our relentless pursuit to deliver on our promise to help patients lead full lives, protect public health and sustainably grow our business in the decades ahead, while providing promising futures for our employees.”

In fiscal year 2021-2022, CSL invested approximately \$1.16 billion in R&D. This includes growing CSL R&D’s footprint in Melbourne, Australia; Marburg, Germany; throughout Switzerland and Waltham, Massachusetts – helping to create an integrated global organization that can conveniently collaborate with institutions everywhere -- offering scientists a wide array of opportunities for professional development and enhancing access to external innovation.

Advancing External Innovation: The Biotechnology Incubator at CSL’s Global Headquarters in Melbourne, Australia Names Its Operator

CSL, WEHI and The University of Melbourne have appointed Cicada Innovations as the independent operator of the new biotech incubator which will be located in CSL’s new global headquarters currently under construction in the Melbourne Biomedical Precinct. The appointment follows the project partners joining forces to create an incubator for biotech start-up companies, with the Victorian Government’s landmark Breakthrough Victoria Fund providing funding to support the AU\$95 million project. It will be Australia’s first and only incubator that is co-located with a leading biopharmaceutical company and will have space for up to 40 start-ups.

“Incubator residents will be working in an innovation-driven environment alongside a large and focused CSL R&D team, enabling opportunities for peer-collaboration, learning and sharing of ideas,” said Dr. Andrew Nash, CSL’s Chief Scientific Officer and Senior Vice President, Research. “The strong collaboration between CSL, the University of Melbourne, WEHI, Breakthrough Victoria and now Cicada Innovations has been critical to bring the incubator to fruition and reflects CSL’s values and desire to deliver on our promise to patients worldwide.”

For more about the incubator, <https://www.csl.com/news/2022/20221103-cicada-innovations-to-operate-new-biotech-incubator>.

For more on CSL’s R&D Investor Briefing, please visit <https://www.csl.com/>.

About CSL

[CSL Limited](#) (ASX: CSL; USOTC: CSLLY) is a leading global biotechnology company with a dynamic portfolio of lifesaving medicines, including those that treat haemophilia and immune deficiencies, as well as vaccines to prevent influenza. Since our start in 1916, we have been driven by our promise to save lives using the latest technologies. Today, CSL – including our three businesses, CSL Behring, CSL Seqirus, and CSL Vifor – provides lifesaving products to patients in more than 100 countries and employs more than 30,000 people. Our unique combination of



FINAL: 02 November 22

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commercial strength, R&D focus, and operational excellence enables us to identify, develop and deliver innovations so our patients can live life to the fullest. For inspiring stories about the promise of biotechnology, visit [CSLBehring.com/Vita](https://www.cslbehring.com/Vita) and follow us on [Twitter.com/CSL](https://twitter.com/CSL).

For more information visit www.csl.com.

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