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# ASX Announcement

**For immediate release**

19 October 2021

## CSL's Annual R&D Day - 2021

**CSL Limited (ASX:CSL; USOTC:CSLLY)** – CSL will hold its annual Research and Development briefing today; the presentation is attached for the information of investors.

Amongst other achievements, CSL is pleased to highlight the following:

- CSL's Seqirus business advances first-of-its-kind adjuvanted, cell-based seasonal influenza vaccine (aQIVc) and increases work on its self-amplifying mRNA (sa-mRNA) development program. Earlier this month, the Biomedical Advanced Research and Development Authority (BARDA) awarded Seqirus a multi-year contract to provide clinical development services to evaluate the safety, immunogenicity, and dose-sparing capability of two H2Nx influenza vaccine candidates: one using a combination of Seqirus' FDA-licensed cell-based and adjuvanted technologies, and the other using its next generation sa-mRNA platform.

- New collaboration with the Walter and Eliza Hall Institute for Medical Research (WEHI), one of the most prominent medical research and medicine development organisations in Australia, to create a Centre for Biologic Therapies.

- Phase III study of 4-Factor Prothrombin Complex Concentrate to improve survival in traumatic injury and acute major bleeding will be initiated and the VANGUARD Phase III clinical trial for Garadacimab, a treatment in hereditary angioedema (HAE), enrolled its last patient – two months ahead of schedule. Additionally, recruitment from the AEGIS-II Phase III study of CSL112 (ApoA-1) for treatment of acute coronary syndrome is progressing despite COVID-19 impact on clinical trial sites and patients. More than 14,000 people have been enrolled in this study to date.

- Preparations are underway for EtranaDez, a gene therapy for haemophilia B, to submit a Biologics Licensce Application for the US and Marketing Authorisation Application for the EU.

- Overall, R&D investment was more than $1 billion in the past fiscal year -- across six therapeutic areas (immunology, haematology, respiratory, cardiovascular and metabolic, transplant, influenza), four scientific platforms (plasma fractionation, recombinant technology, cell and gene therapy, vaccines) and two businesses (CSL Behring and Seqirus).

"We continue to evolve as a leading plasma-based biotechnology company with purposeful diversity in therapeutic areas, scientific platforms and strategic alliances," said Dr. Bill Mezzanotte, Executive Vice President, Head of R&D, Chief Medical Officer for CSL. "We are continuing to invest in our core plasma business while also enhancing our other scientific platforms to better deliver on our promise to discover, develop and provide innovations that save and improve lives around the world."

Shareholders can access the briefing through CSL's website at CSL.com.au.

**Approved for Release**

Fiona Mead
Company Secretary

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# R&D Investor Briefing 2021

October 19, 2021

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# Introduction

## William Mezzanotte MD

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

CSL Behring

# Agenda

**01**

**Welcome**

Mark Dehring

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**Introduction – FY21 Retrospective & Highlights**

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**Research**

Andrew Nash

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Russell Basser &
Ethan Settembre

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**Looking toward FY22 & Summary**

Bill Mezzanotte

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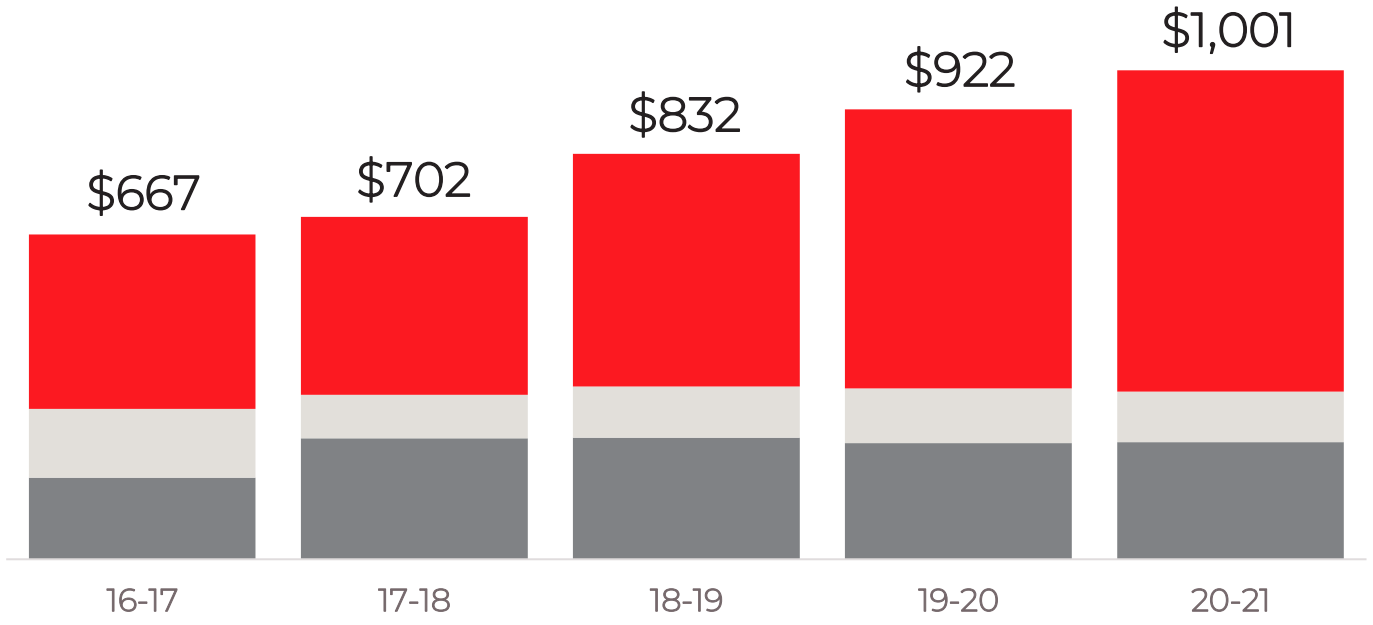
**Q&A**

Panel

# Commitment to Research and Development




R&D investment ~10-11% global revenue*

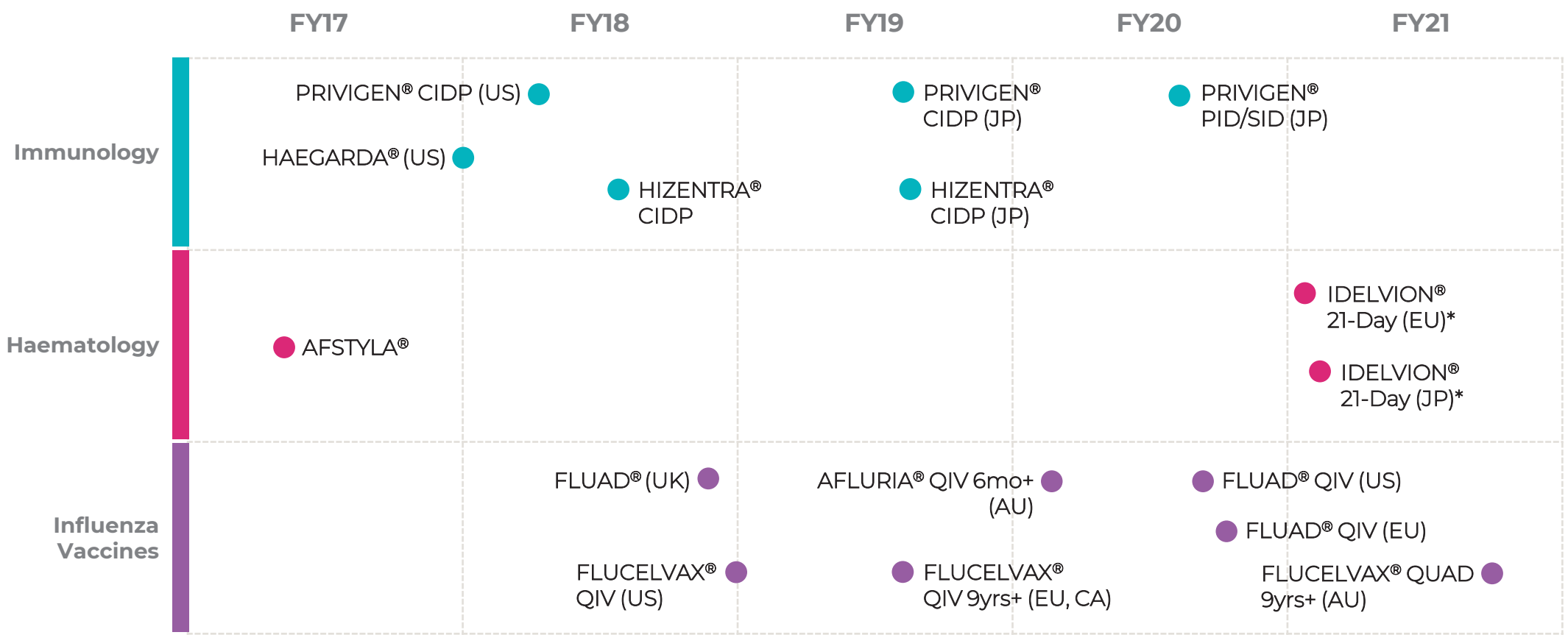
**New Product Development**
activities focus on innovative new therapies for life-threatening diseases

**Market Development**
strategies seek to bring therapies to new markets and new indications

**Life Cycle Management**
ensures continuous improvement of existing products

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

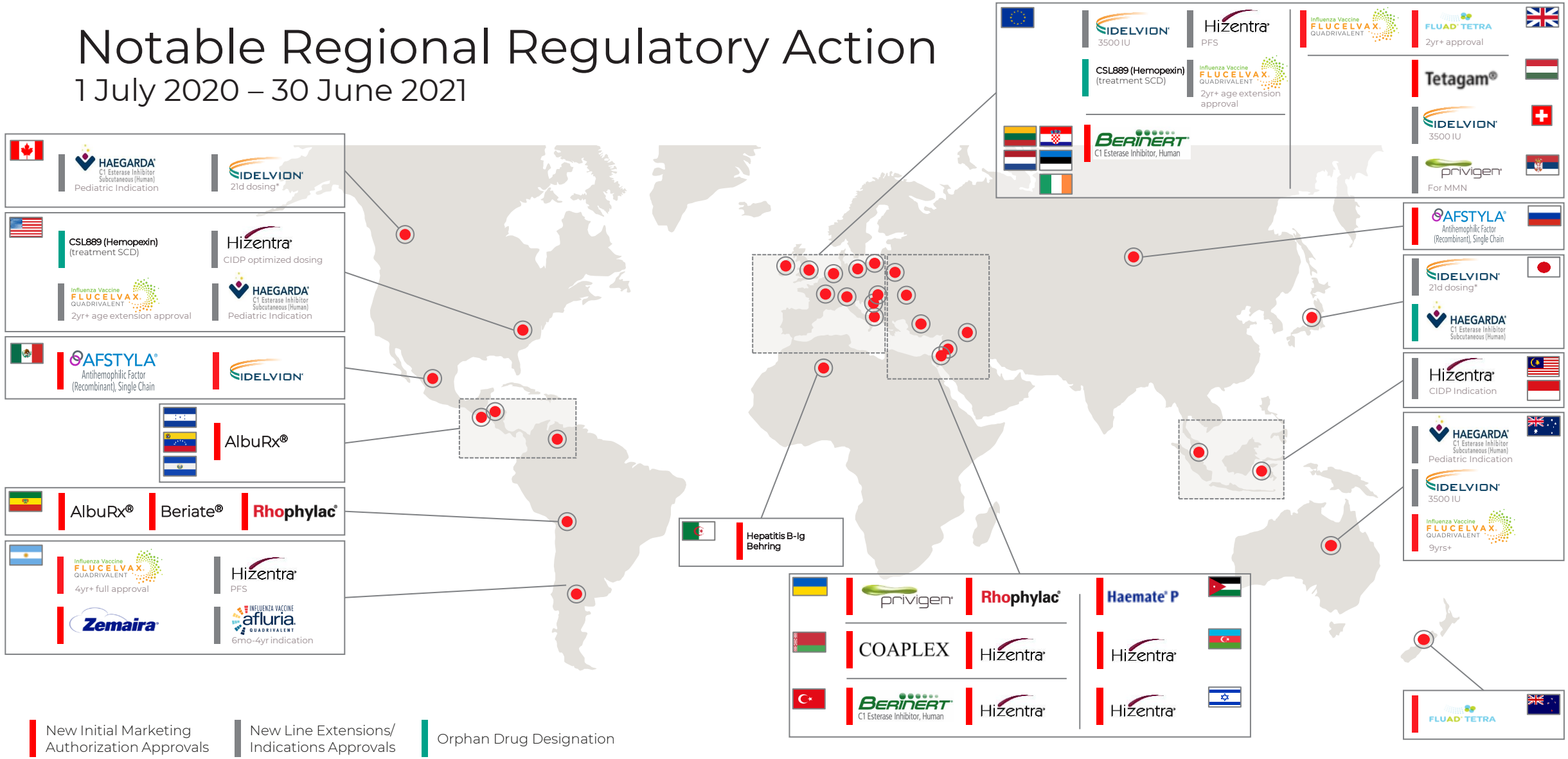
# Key Past Launches from R&D Portfolio




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

# Notable Regional Regulatory Action

## 1 July 2020 – 30 June 2021




New Initial Marketing Authorization Approvals

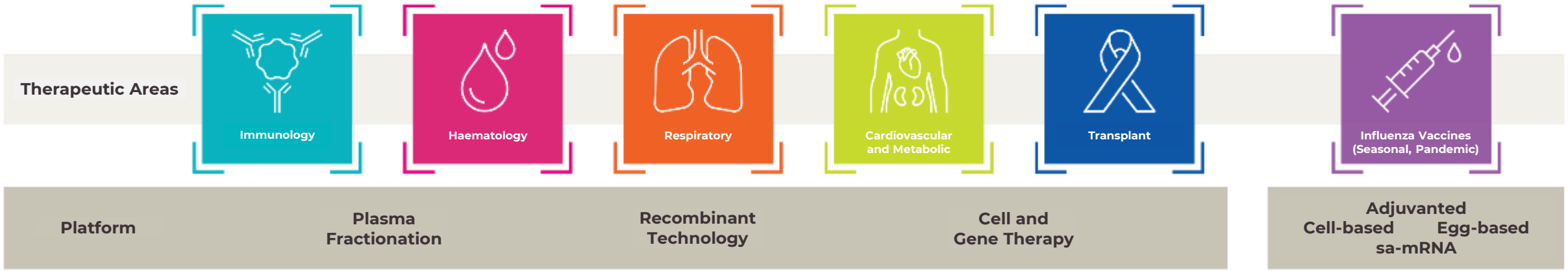
New Line Extensions/ Indications Approvals

Orphan Drug Designation

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

**Abbreviations:** SCD - Sickle Cell Disease; PFS - Pre-filled Syringe; MMN - Multifocal Motor Neuropathy; CIDP - Chronic Inflammatory Demyelinating Polyneuropathy

# Focus Through Our Therapeutic Areas and Platforms



# R&D Highlights – FY21


## Immunology

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


## Cardiovascular & Metabolic

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


## Haematology

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


## Respiratory

- First patient enrolled in CSL787 Nebulised Ig Phase I study


## Transplant

- Last patient dosed in Part 1 of CSL964 for prevention of GvHD study


## Influenza Vaccines

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

# R&D Portfolio – October 2020

Research

- Gene Therapy Treatments PID
- Discovery Projects
- Discovery Projects
- Discovery Projects
- Discovery Projects
- Discovery Projects

Pre-Clinical

- CSL888 Haptoglobin (SAH)
- CSL510 Modified Fibrinogen
- CSL040 Novel Complement Inhibitor
- sa-mRNA Influenza Vaccine
- LASN01 Anti-IL-11R
- P. Gingivalis (Periodontal Disease)

Phase I

- CSL324 Anti-G-CSFR mAb (HS)
- CSL730 rFc Multimer
- CSL889 Hemopexin (SCD)
- CSL200 CAL-H (SCD)
- CSL787 Nebulised Ig
- CSL311 Anti-Beta Common mAb
- UQ/CSL V451 (aCoV2)
- CSL334/ASLAN004 Anti-IL-13R mAb (AD)

Phase II

- HIZENTRA® (SSc)
- CSL630 pdFVIII Ruide
- CSL346 Anti-VEGF-B mAb (DKD)
- Garadacimab Anti-FXIIa mAb (ILD/IPF)
- Garadacimab Anti-FXIIa mAb (ARDS)
- Adjuvanted Cell Culture Influenza Vaccine (aQIVc)
- Mavrilimumab Anti-GM-CSFR mAb

Phase III

- HIZENTRA® (DM)
- HAEGARDA® Japan
- Garadacimab Anti-FXIIa mAb (HAE)
- EtranaDez* Etranacogene dezaparvovec
- KCENTRA® 4F-PCC (Trauma)
- CSL112 ApoA-1 (ACS)
- Clazakizumab Anti-IL-6 mAb (AMR)
- CSL964 Alpha-1 Antitrypsin (Treatment of GvHD)
- CSL964 Alpha-1 Antitrypsin (Prevention of GvHD)
- COVID-19 Hyperimmune Therapy

Registration/ Post-Registration

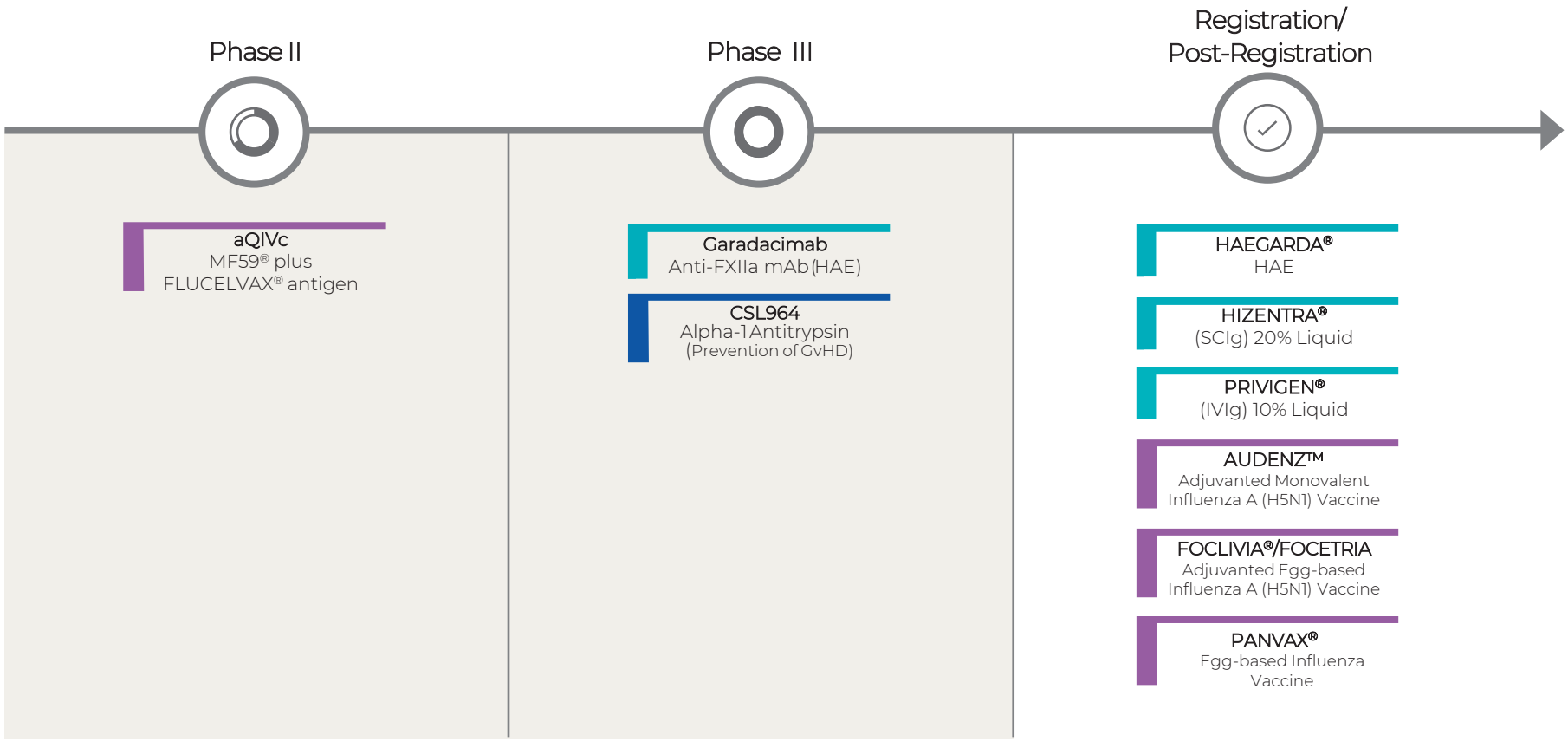
- PRIVIGEN® (PID) JP
- IDELVION® rFIX-FP (Haem B)
- AFSTYLA® rFVIII (Haem A)
- ZEMAIRA®/RESPREEZA® Alpha1-Proteinase Inhibitor
- AFLURIA® QUAD Egg-based Influenza Vaccine
- FLUCELVAX® Quadrivalent Cell-based Influenza Vaccine
- FLUAD® Quadrivalent Adjuvanted Influenza Vaccine
- AUDENZ™ Adjuvanted Monovalent Influenza A (H5N1) Vaccine

* Transaction with uniQure is subject to customary regulatory clearances before closing

Immunology | Haematology | Respiratory | Cardiovascular & Metabolic | Transplant

Influenza Vaccines | COVID | Outlicensed Programs | Partnered Projects

# R&D Product Progression in FY21




Immunology  Transplant  Influenza Vaccines

# Kcentra® in Trauma

Haematology

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

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

**~880k**

patients suffer traumatic injury annually in US

**~85%**

of haemorrhagic deaths occur within 6 hours

**35-40%**

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

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

Data from preclinical and clinical studies[1-3] 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
- Up to 8,000 patients



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

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


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):1875-81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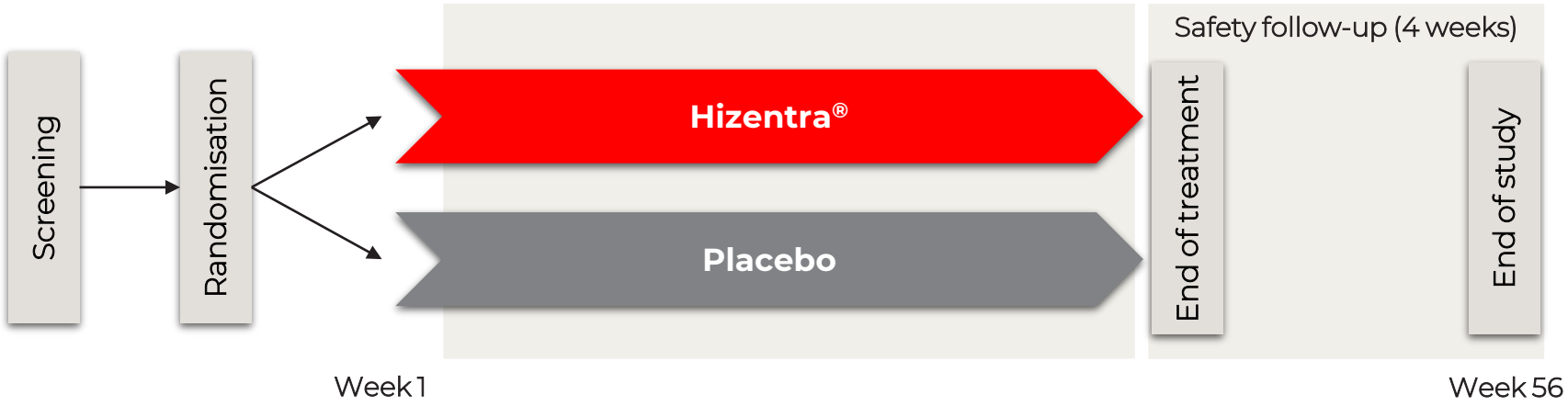
# Hizentra® Secondary Immune Deficiency (SID)

Immunology

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

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




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



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# Research

## Andrew Nash PhD

Senior Vice President, Research and Chief Scientific Officer

CSL Behring

# CSL Behring Research

**CSLB Global Research**

**Research / Candidate Discovery & Optimisation**

**Toxicology**
- Enabling-toxicology

**Research & Clinical Bioanalytics**
- GLP & GCLP assays

Research External Innovation (REI)

TA Leaders & Teams
- Research Strategy
- Project Portfolio


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



**Abbreviations:** GLP – Good Laboratory Practice; GCLP – Good Clinical Laboratory Practice

# CSL Behring Research – Strategy & Focus

**TA Research Strategy**

- Therapeutic discovery (internal & external)
- Extend existing Research assets
- MoA and LCM for clinical/ on market assets
- Develop and expand core platforms
- Identify & validate external clinical stage assets

Plasma

Recombinant Proteins

Cell & Gene Therapy

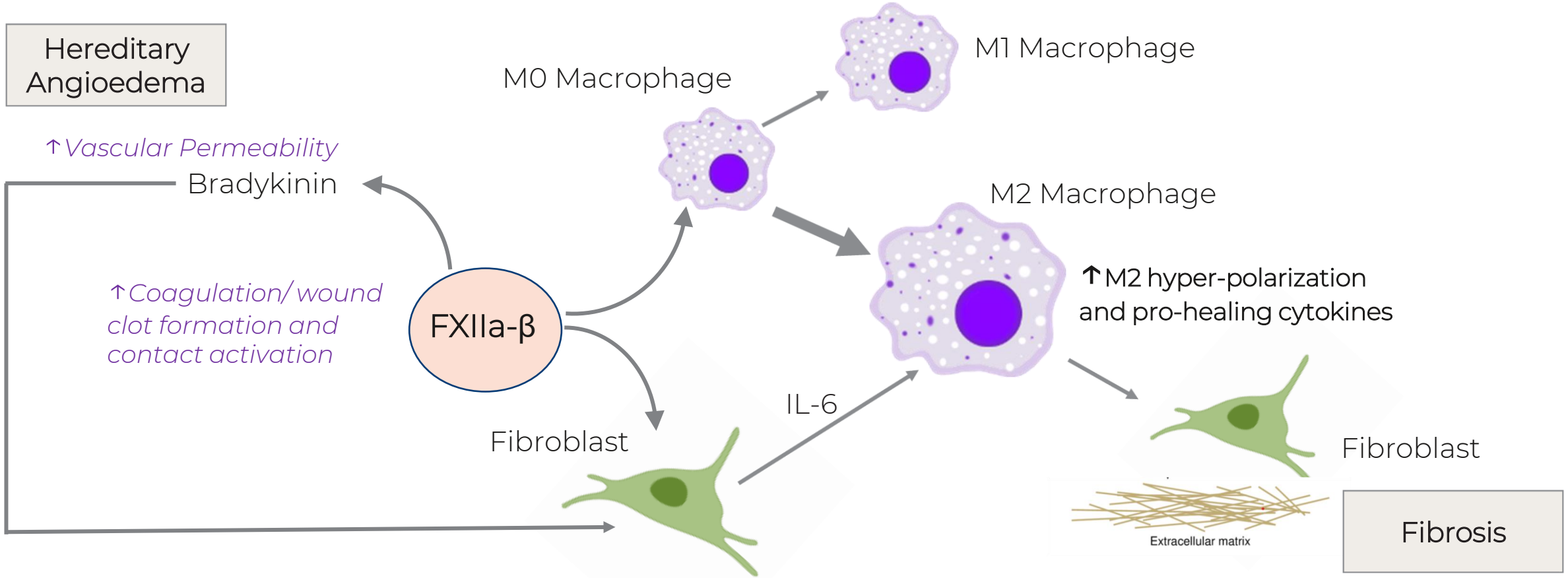
- **Lead** strategically aligned discovery research through:
  - Internal & external innovation
  - External asset procurement
- **Translate** forward and reverse to better understand opportunities and reduce risk
- **Accelerate** discovery outcomes through to FIH
- **Extend** current Research assets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

Individual Therapeutic Area (TA) Research Strategies


**Abbreviations:** FIH – First-in-Human; MoA – Mechanism of Action; LCM – Life Cycle Management

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

## Role of FXII in Fibrogenesis




↑ pro-inflammatory, pro-fibrotic, anti-fibrinolytic molecules, proliferation, migration, wound scratch healing, chemotaxis

# Development of Garadacimab for PF-ILD/IPF

## Summary of Key Supportive Research Data

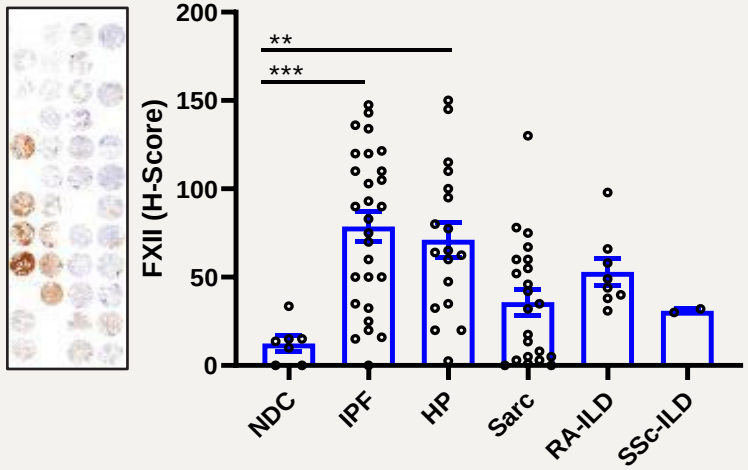
### Clinical Data

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

### Experimental Data

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

FXII Staining is Increased in PF-ILD Lungs – Tissue Microarray




Phase II – expected to commence H2 FY22

* Parental Monoclonal Antibody (mAb) of Garadacimab

# Research External Innovation & Collaboration Strategy

## The Competition for Innovation

Seattle Children's Research Institute

ASLAN PHARMACEUTICALS

KINIKSA

Lassen THERAPEUTICS

Denteric

WEHI brighter together

Seattle Children's Research Inst.
ASLAN
Kiniksa
Lassen
Denteric
WEHI

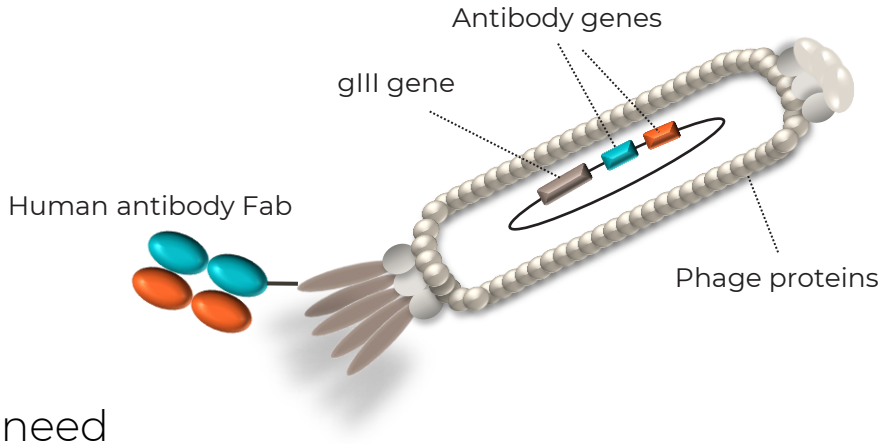

Abbreviations: MRI – Medical Research Institute

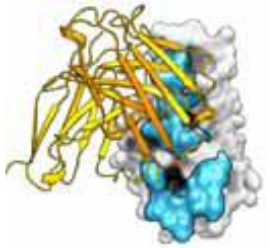
# Research External Innovation & Collaboration Strategy

## Centre for Biologic Therapies

CSL™ + WEHI brighter together

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



WCSL129 αCOVID-19 mAb from CSL library*

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



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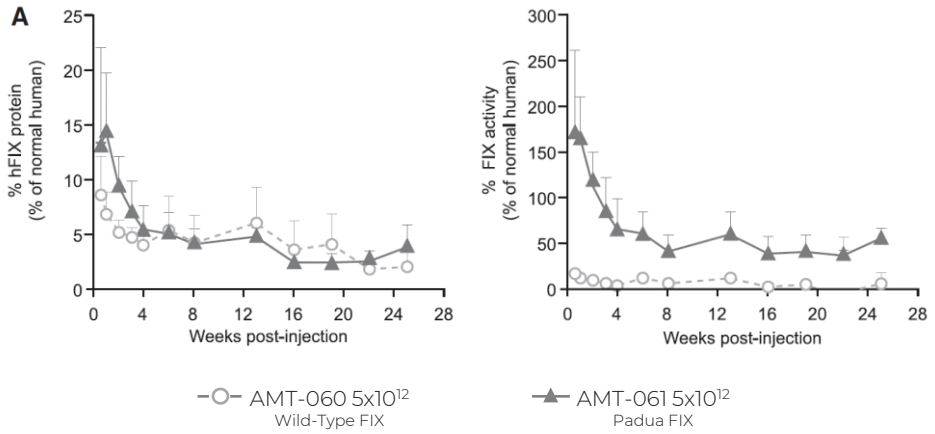
# Gene Therapy Technologies

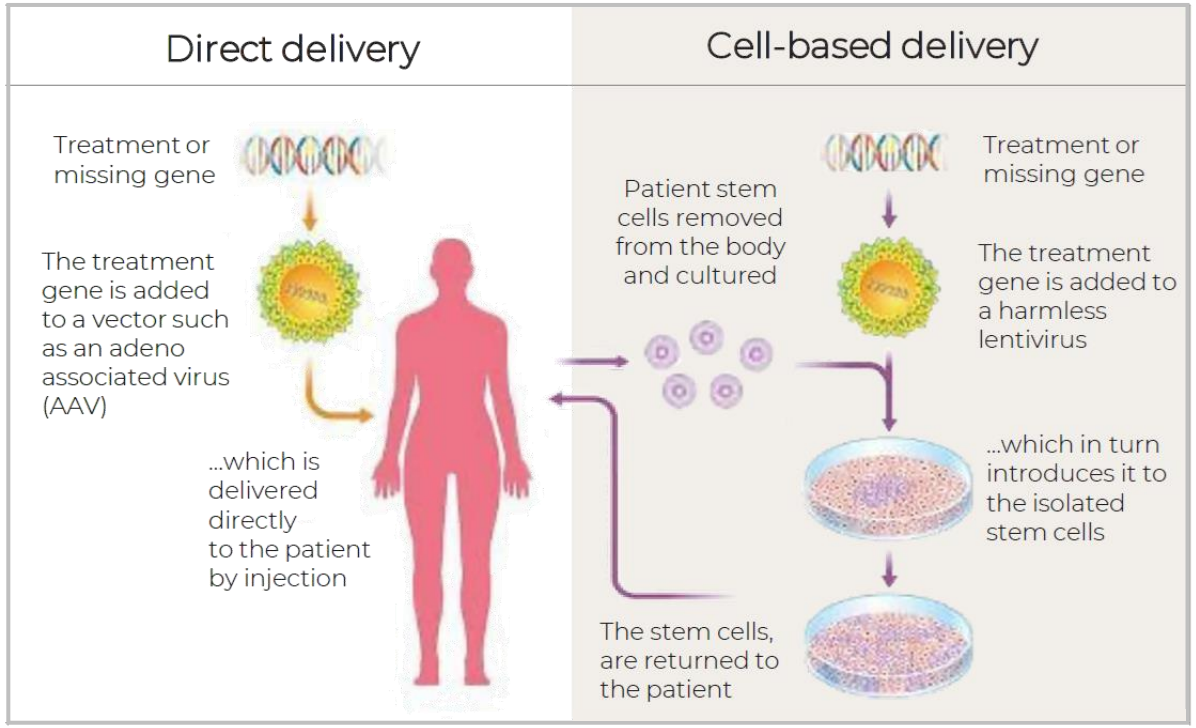
Seattle Children's®
HOSPITAL • RESEARCH • FOUNDATION
Research Institute

## EtranaDez (Etranacogene dezaparvovec)

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




## Gene Therapies for Immune Deficiencies




Source: Spronck, E.A. *et al.*, (2019) *Mol. Ther. Meth. Clin. Dev.* 13; P334-343.



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# Gene Therapy for Immune Deficiencies

Seattle Children's®
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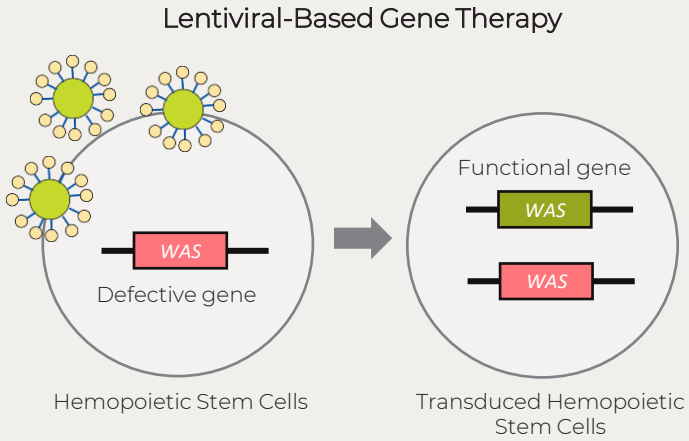
Research Institute

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




| Platform | Technologies | PIDs |
|---|---|---|
| *Ex Vivo* HSC Gene Therapy Platform | Lentiviral Gene Therapy<br>Other Gene Editing Approaches | Wiskott- Aldrich Syndrome (WAS)<br>X-linked Agammaglobulinemia (XLA)<br>X-linked hyper IgM Syndrome (XHIM) |

**Abbreviations:** PID – Primary Immune Deficiency; HSC – Hematopoietic Stem Cell



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# Gene Therapy for Immune Deficiencies

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Research Institute

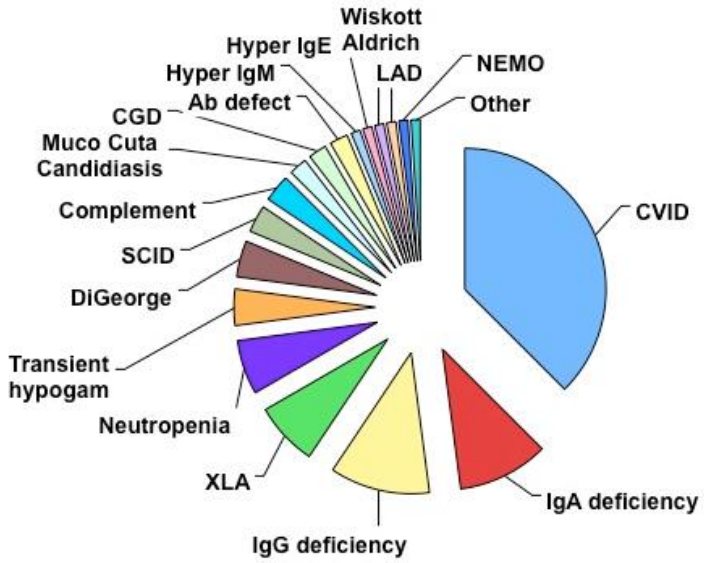
## WAS Gene Therapy Program

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


1-2-3

Phase I/II – expected to commence H1 FY23

## Primary Immune Deficiencies*




**Source:** Icahn School of Medicine at Mt Sinai
**Abbreviations:** WAS – Wiskott- Aldrich Syndrome



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# Biotech Out-Licensing & Partnering

# ASLAN Pharmaceuticals - Atopic Dermatitis

- In May 2019, CSL granted ASLAN full global rights to develop, manufacture and commercialise ASLAN004 (formerly CSL334) in all indications. CSL receives milestones and royalties
- ASLAN004 is a novel, first-in-class monoclonal antibody that targets the IL-13 receptor α1 subunit (IL-13Rα1), one of the components of Type 2 IL-4 / IL-13 receptor
- By blocking Type 2 receptors, ASLAN004 prevents signalling of both IL-4 and IL-13, key drivers of inflammation and central to triggering symptoms of allergy in atopic dermatitis
- Dupilumab / Dupixent targets Type I and Type II receptors to block both IL-4 and IL-13 activity
  - rate of dupilumab-associated ocular surface disease was 32%[1]

| Program & Target | Discovery | Preclinical | Phase I | Phase II | Anticipated Milestones |
|---|---|---|---|---|---|
| ASLAN004<br>Anti-IL-13Rα1 | Atopic Dermatitis (AD)<br>Asthma* | | | | Initiate Phase IIb - 4Q 2021 |

*second indication to be confirmed

[1] Popiela, M.Z. *et al.,* (2021) *Eye;* https://doi.org/10.1038/s41433-020-01379-9

# ASLAN Pharmaceuticals - Atopic Dermatitis

## Phase I MAD Study (ASLAN004)

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


Phase II – initiating 4Q 2021

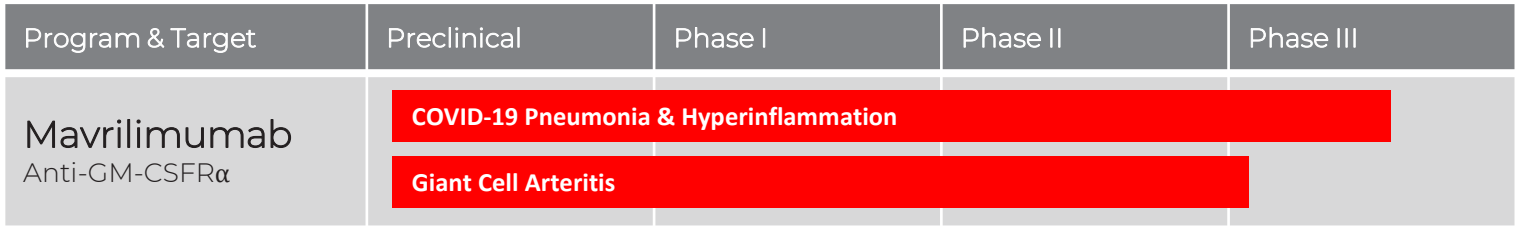
| Endpoint (8 weeks) | RITT (n=29) | | |
|---|---|---|---|
| | 600mg (n=16) | Placebo (n=13) | p-value[1] |
| Mean % change from baseline in EASI | -64.9 | -27.2 | 0.021 |
| EASI-50 (%) | 81.3 | 30.8 | 0.008 |
| EASI-75 (%) | 68.8 | 15.4 | 0.005 |
| EASI-90 (%) | 37.5 | 15.4 | 0.183 |
| IGA 0/1 (%) |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

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

[1] One-sided p-value. Study powered to assess statistical significance in primary efficacy endpoint at one-sided 5% level.
**Abbreviations:** MAD – Multiple Ascending Dose; IGA – Investigator's Global Assessment; POEM – Patient-Oriented Eczema Measure; RITT – Revised Intent to Treat

# Kiniksa - Giant Cell Arteritis (GCA) and COVID

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



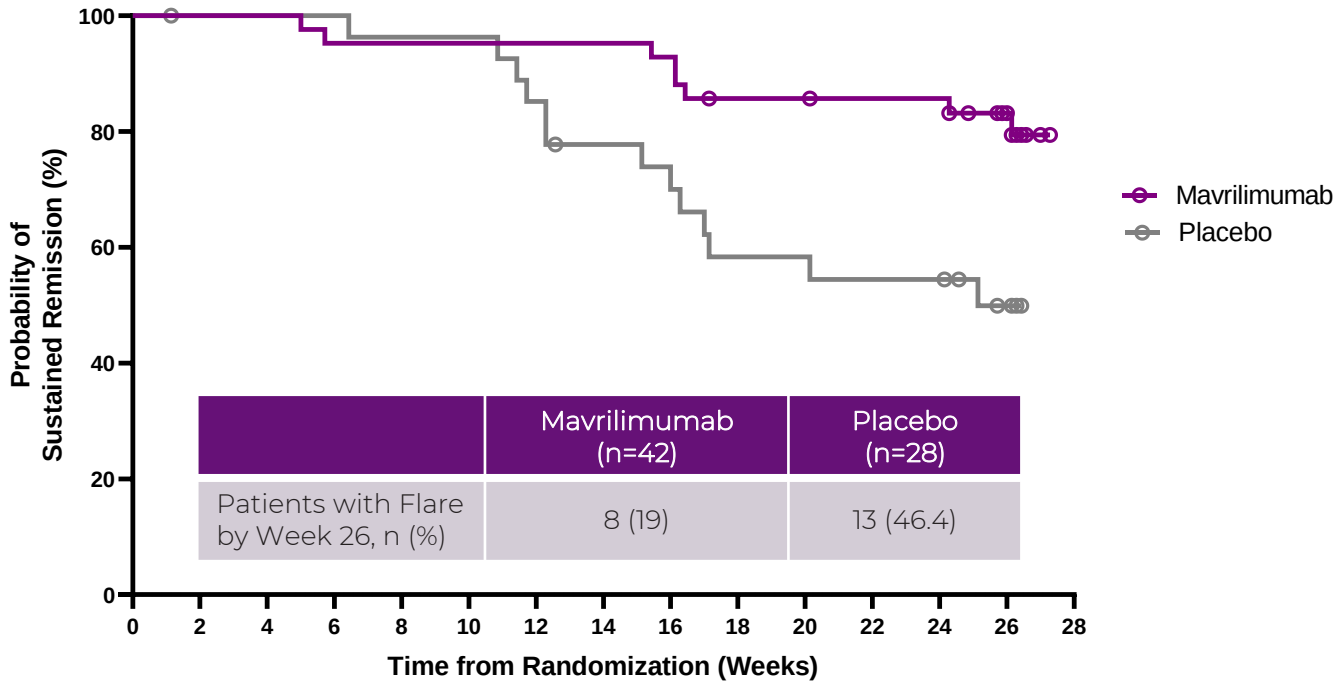

[1] Pupim, L. *et al.,* (2021) *Ann. Rheum Dis* 80(1); 198-199.
**Abbreviations:** ARDS – Acute Respiratory Disease Syndrome

# Kiniksa - Giant Cell Arteritis (GCA) and COVID

## Phase II Study - GCA

- Active biopsy- or imaging-proven new onset or relapsed refractory GCA
- n=70; 35 NO and 35 R/R
- 150mg q2wk for 26 wks, Mavri:placebo 3:2
- 26 week steroid taper
- Primary endpoint – time to first adjudicated flare
- Secondary endpoint – sustained remission through week 26

Mavrilimumab reduces risk of flare and increases sustained remission in patients with GCA[1]




| | Mavrilimumab (n=42) | Placebo (n=28) |
|---|---|---|
| Patients with Flare by Week 26, n (%) | 8 (19) | 13 (46.4) |

Phase III – ongoing

[1] Cid, M.C. *et al.,* (2021) *Ann. Rheum Dis* 80(1); 31-32
**Abbreviations:** NO – New Onset; R/R – Relapsing/ Refractory; q2wk – every 2 weeks

# CSL Behring Research

Creating and progressing a sustainable portfolio of early stage opportunities

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

Three drug discovery platforms applied across five TAs

- Leveraging in-house technologies to support external innovation

Expanding capacity and capability across global Research sites

Continued investment in external innovation

- From venture capital investment to long term strategic collaborations

# Development

## Deirdre BeVard

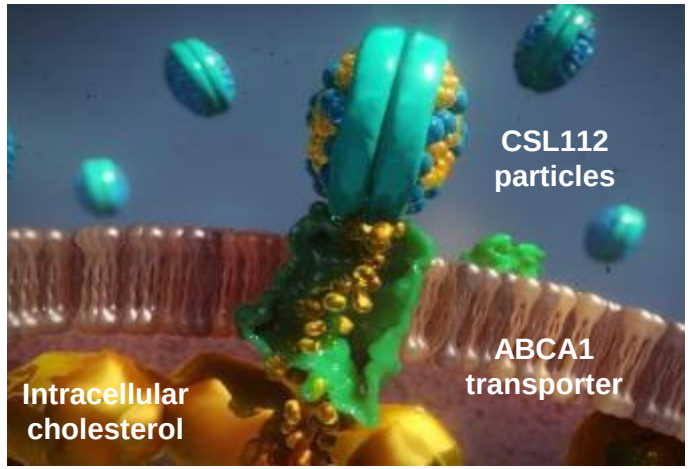
Senior Vice President,
R&D Strategic Operations

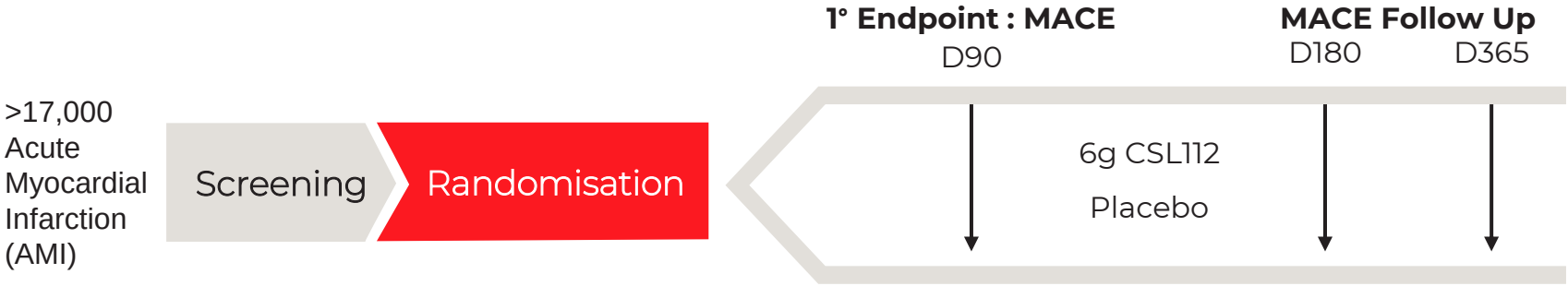
CSL Behring

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

Cardiovascular and Metabolic

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




1-2-3 Phase III – ongoing



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# EtranaDez

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

Haematology

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

**Abbreviations:** AAV5 - Adeno-Associated Virus serotype 5;
BLA – Biologic Licence Application;
MAA – Market Authorisation Application



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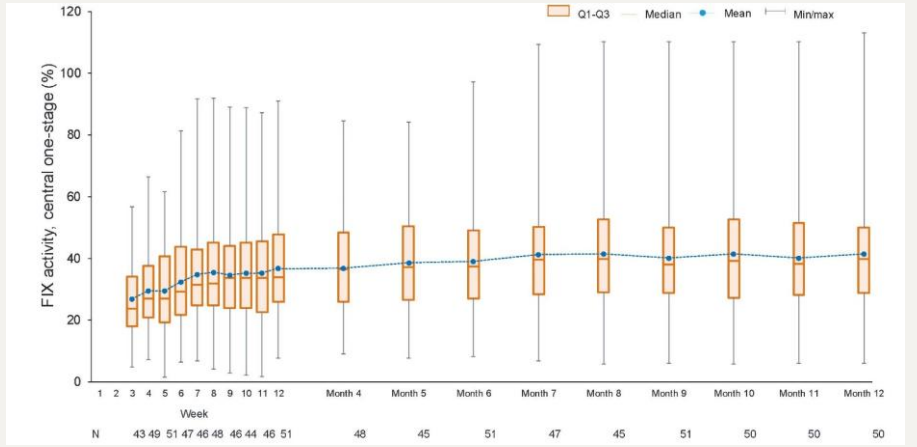
# EtranaDez – HOPE-B Study 12 Month Data

Haematology

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

Endogenous FIX Activity over 52 weeks[1]




Adjusted Annualized Bleeding Rates (ABR) in the First 12 months Post-treatment[1]

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

[1] Pipe. S.W. *et al*., (2021) ISTH, PB0653
[2] Gomez, E. *et al*., (2021) ISTH, LPB0020
**Abbreviations:** AAV5 - Adeno-Associated Virus serotype 5

# Ongoing New Investigations with Hizentra®

Immunology

## Systemic Sclerosis (SSc)

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

- Incidence: 0.8 – 5.6 per 100,000[1]
- Prevalence rate: 3.8 – 34.1 per 100,000[1]
- 3-4 times more common in females than males[2]

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

Highest mortality among systemic autoimmune diseases

No treatment currently addresses all of the multi-system impact

## Dermatomyositis (DM)

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

- Incidence 11 per 1,000,000
- Prevalence rate 14 per 100,000
- Increases with age (peak ages 70-79)[3]

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

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

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

[1] Varga, J. (2020) In J.S. Axford (Ed.), *UptoDate,* Accessed June 1, 2021.
[2] National Organization for Rare Diseases. Scleroderma. Accessed June 4, 2021.
[3] Svensson J. (2017) *Clin Exp Rheumatol*. 35(3):512-515



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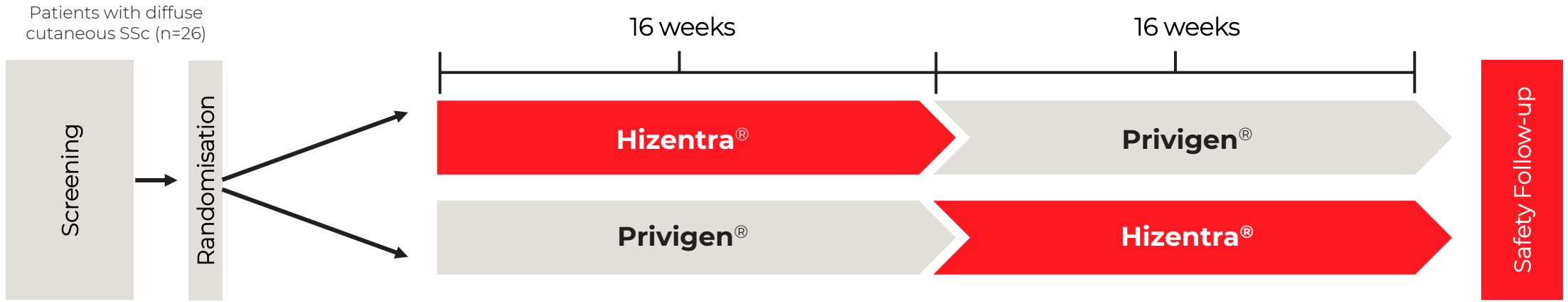
# Hizentra® SSc - SURPASS

Immunology

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

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

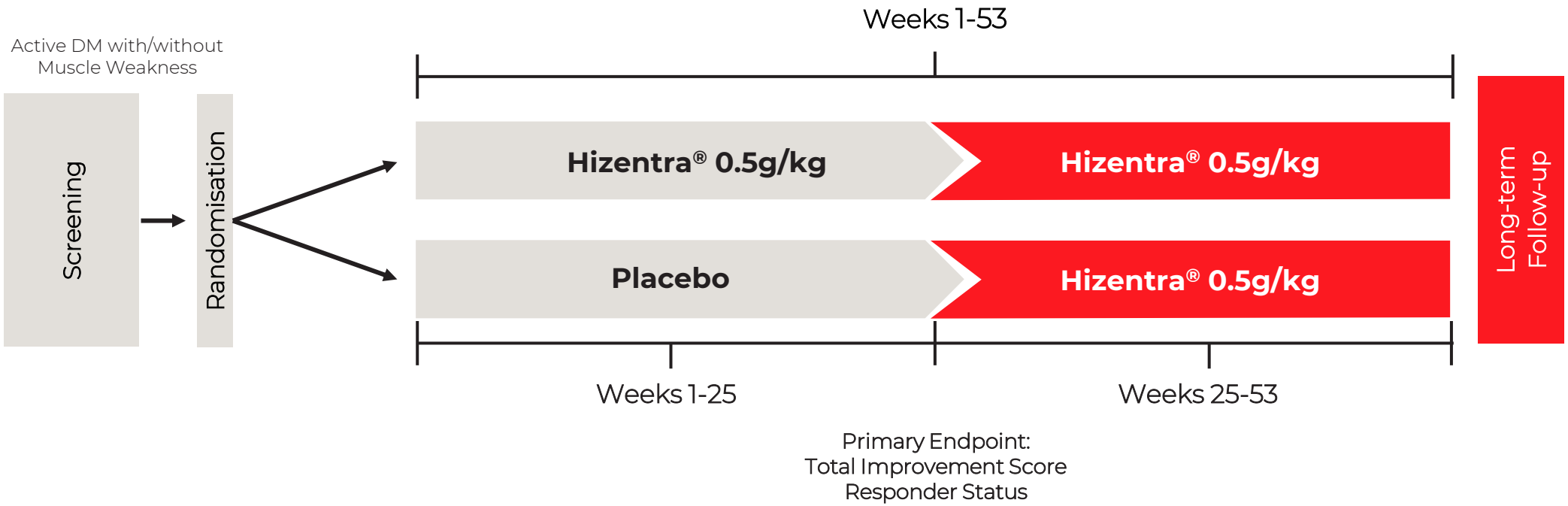



Phase II – ongoing

# Hizentra® DM - RECLAIIM

## Phase III Study of Hizentra® in Adults with Dermatomyositis

Immunology




Phase III – ongoing

# Hereditary Angioedema (HAE)

Autosomal dominant genetic condition

1 in 10,000 – 50,000 people

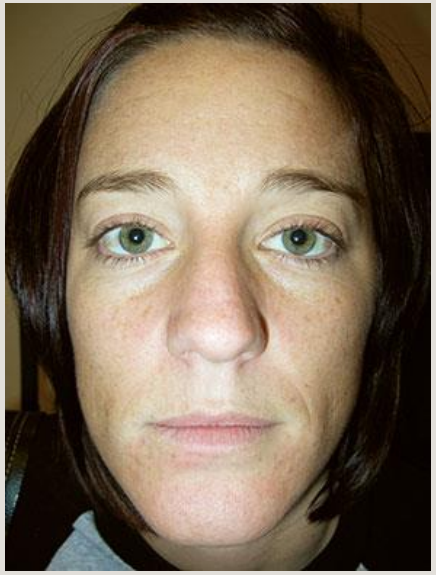
Unregulated protein cascade

→ elevated levels of bradykinin

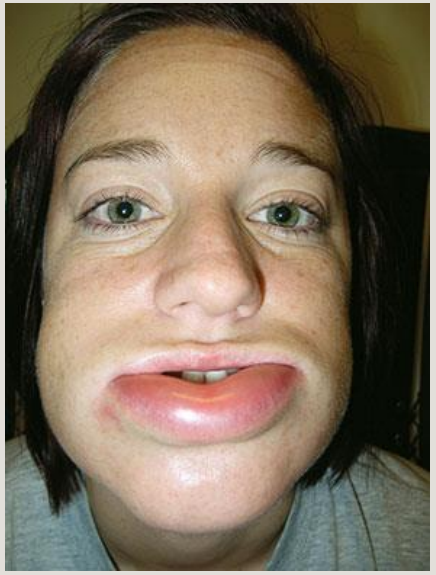
→ fluid release into tissues

→ swelling in specific parts of body

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



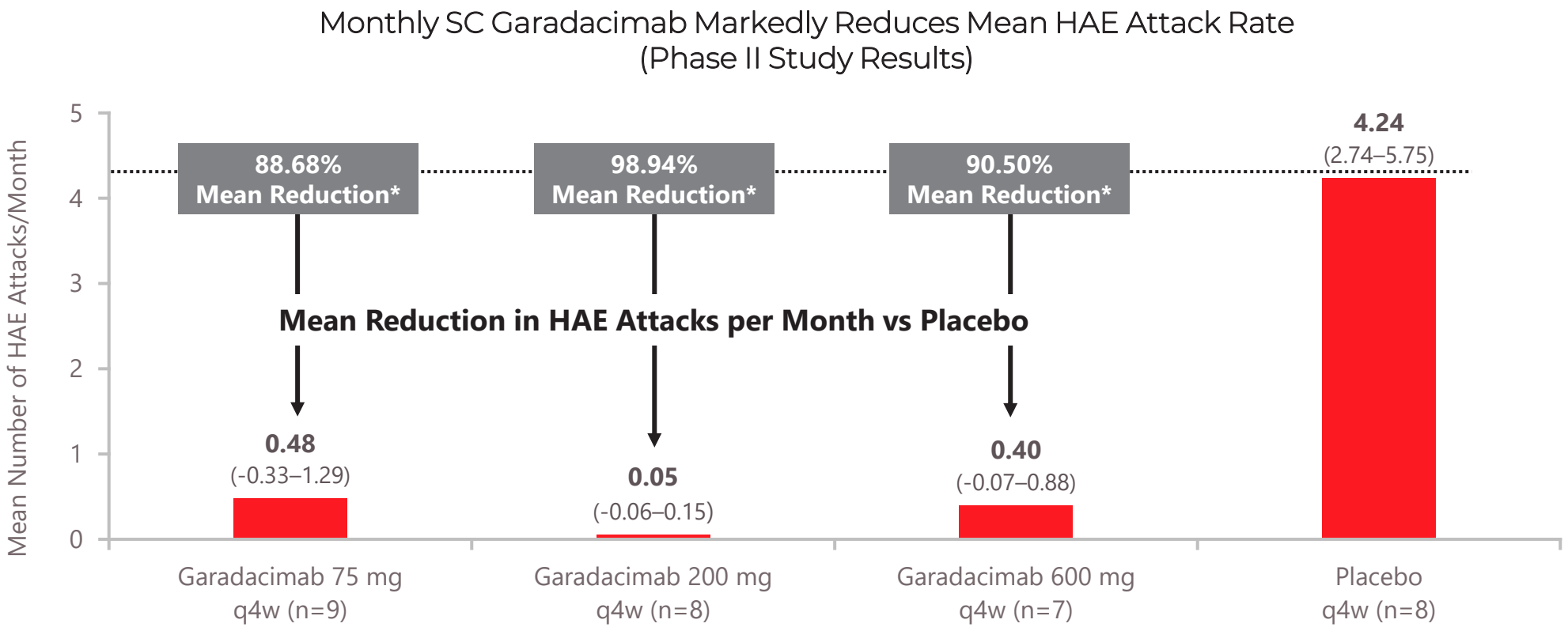
Normal appearance



During cutaneous attack

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

Immunology




**Source:** Craig, T., (2020) *European Academy of Allergy and Clinical Immunology Congress*



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# Garadacimab - CSL's First mAb in Phase III

Immunology

VANGUARD
Prove CSL312 Efficacy and Safety to Guard Against HAE Attacks


| Completed | Completed | Ongoing | Ongoing |
|---|---|---|---|
| Healthy | ~40 HAE patients | ~60 HAE patients | ~150 HAE patients |
| Broad dose range<br>IV & SC | POC<br>Dose selection,<br>Safety, PK/PD | Pivotal, Confirmatory<br>Efficacy, Safety,<br>PK/PD, QoL | Long term safety<br>Efficacy, PK/PD, QoL |

Abbreviations: PK - Pharmacokinetic; PD – Pharmacodynamic; POC – Proof of Concept; QoL – Quality of Life

1-2-3

Global submission targeted 2023



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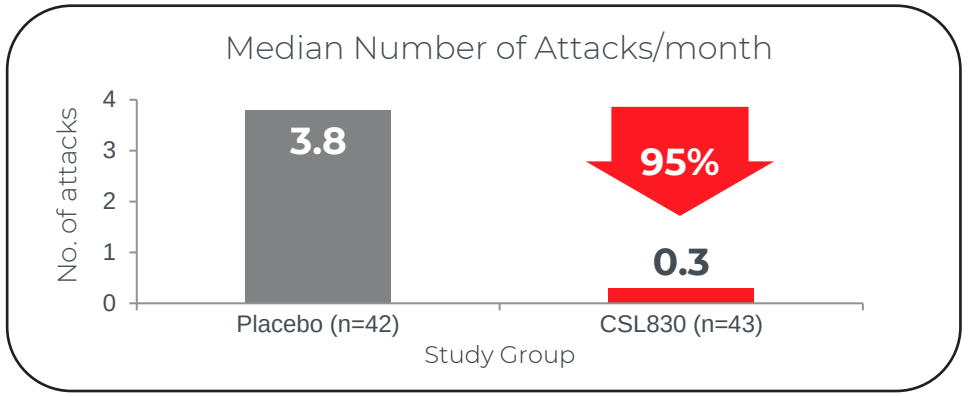
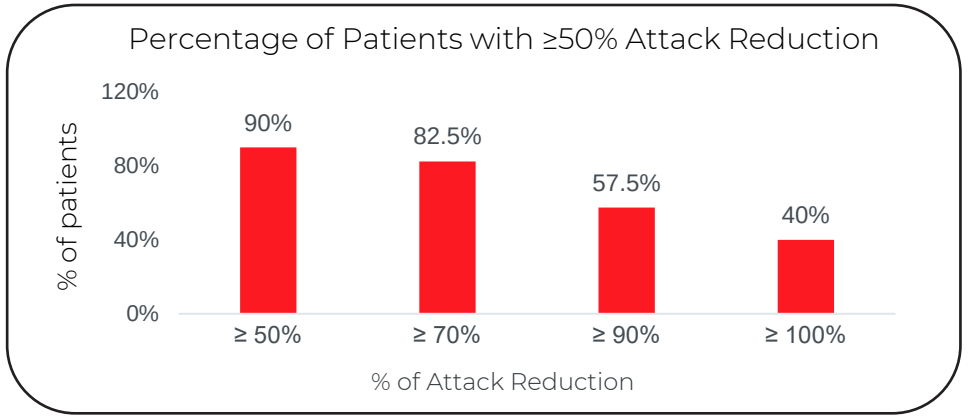
# Comparable Efficacy of HAEGARDA® for HAE in Japanese Patients

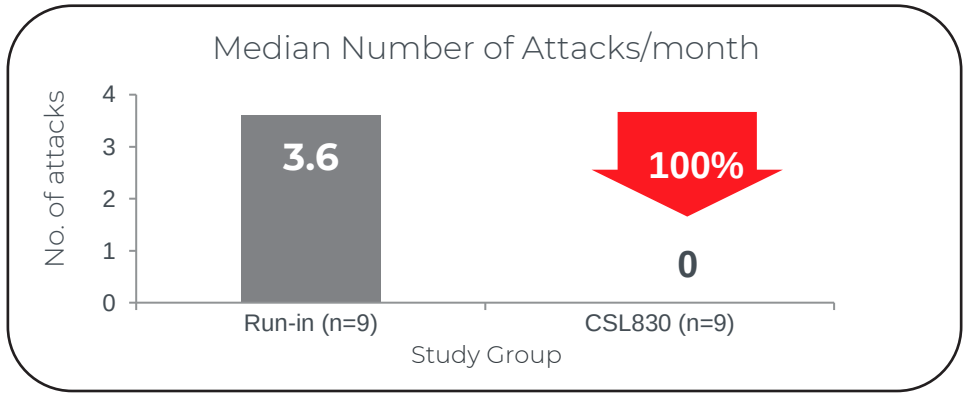
Immunology

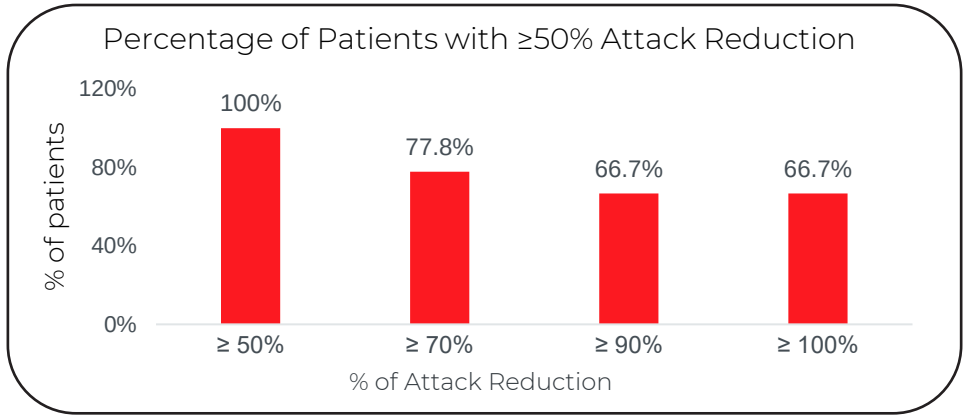
## Global Phase III Pivotal Study



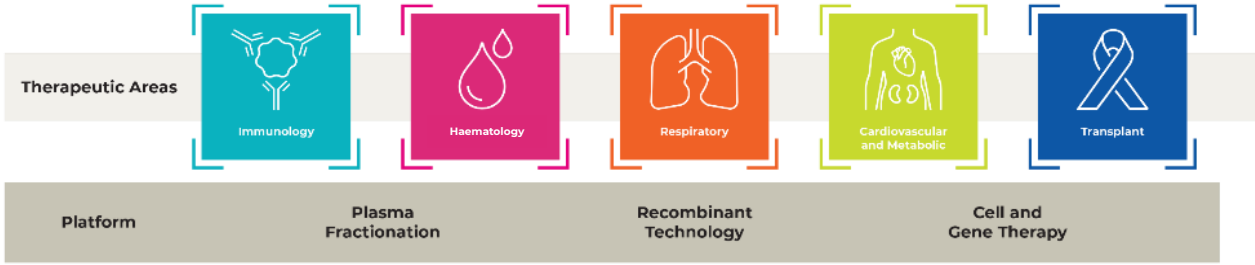

## Japan Phase III Study



# Progress Across All of our TAs and Scientific Platforms

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



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

# Commercial

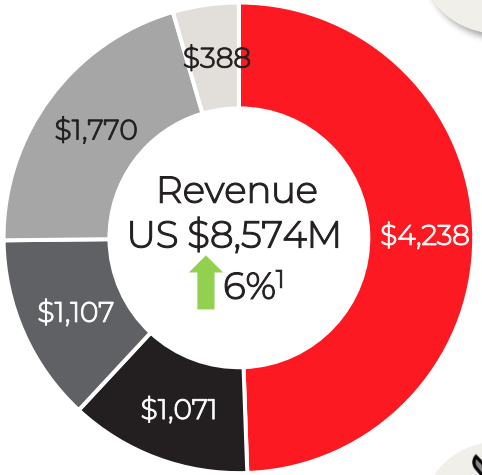
## Bill Campbell

Executive Vice President and Chief Commercial Officer

CSL Behring

Zahra: living with Hereditary Angioedema (HAE).

# CSL Behring FY21 Commercial Highlights




## Performance

- Global revenue of $8,574M/+6%[1]

## Immunology

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

## Albumin

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

## Haemophilia

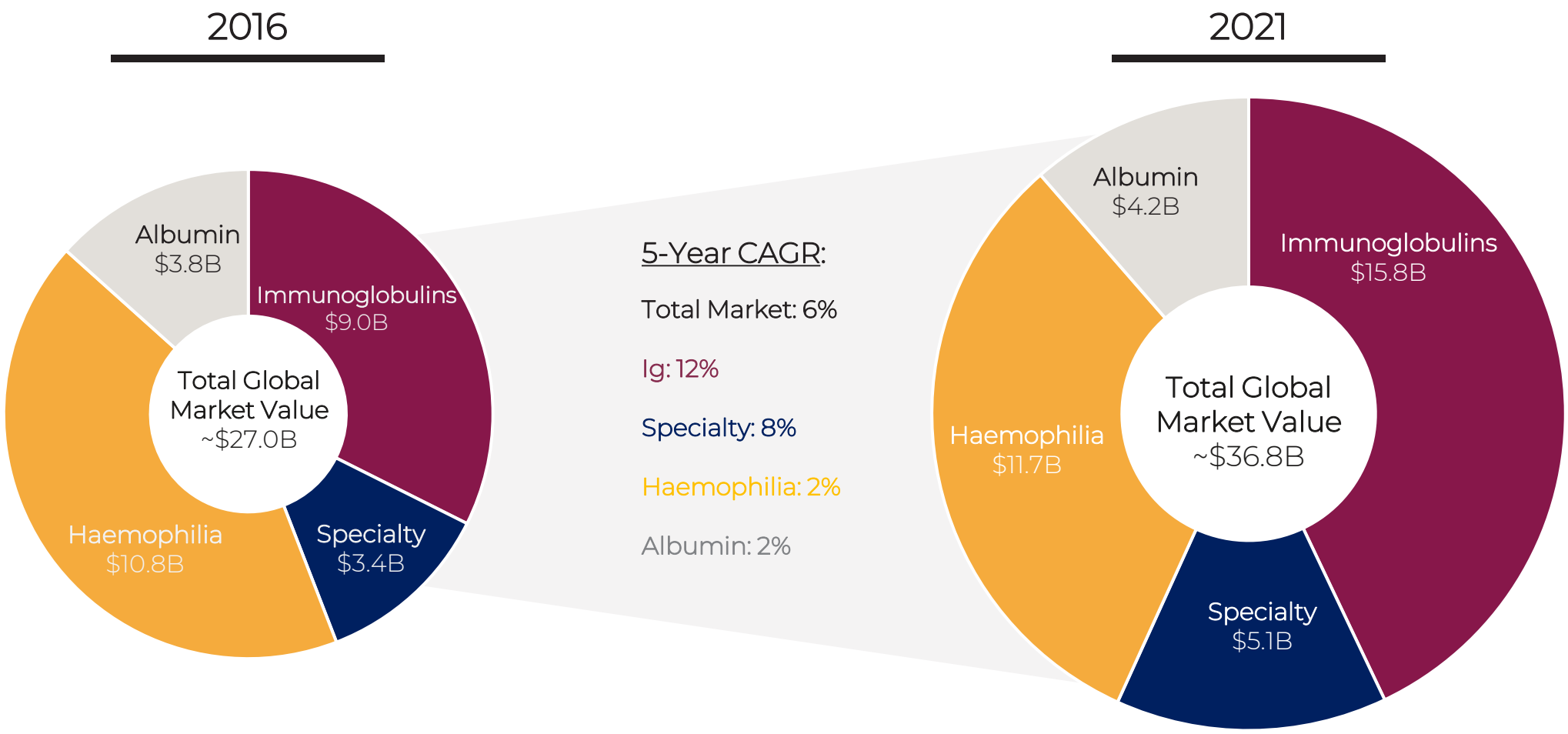
- Maintained IDELVION® leadership in key markets[3]

## Specialty

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

Source:
[1] Growth percentages shown at constant currency to remove the impact of exchange rate movements, facilitating comparability of operational performance.
[2] Includes HPV royalties & Ig Hyperimmunes
[3] Data on file
Abbreviations: CIDP - Chronic inflammatory demyelinating polyneuropathy; FFP - Fresh Frozen Plasma; GSP – Good Supply Practices; YoY – Year on Year

# Targeted Protein Therapeutic Market Continues to Grow




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

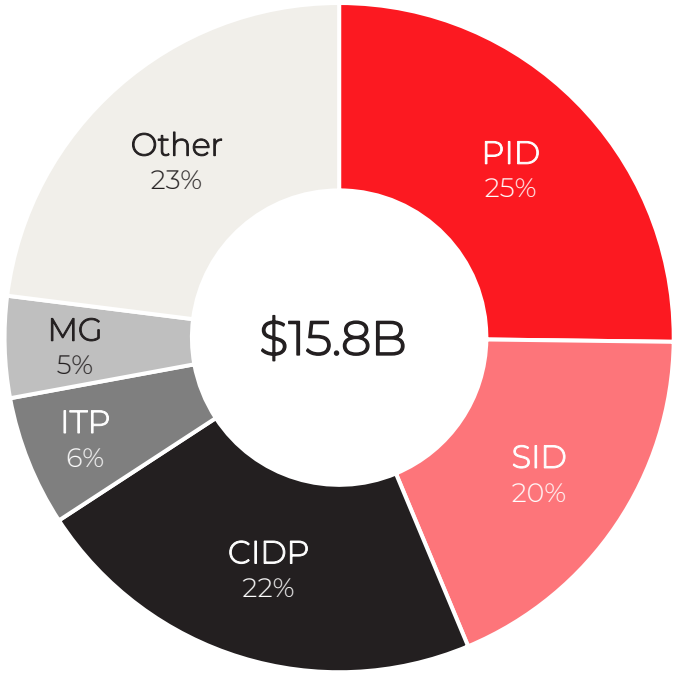
**Source:** Analyst Reports; Company Annual Reports; Data on file; CSL Actuals FY21; Immunoglobulins market include Hyperimmunes; Haemophilia market include Factor XIII and non-factor; Specialty includes AAT, HAE, Fibrinogen, PCC, ATT markets

# Immunoglobulin Market

## Market Dynamics

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

## Global Ig Volume by Indication




**Source:** Data on file for 2020

Abbreviations: CIDP - Chronic inflammatory demyelinating polyneuropathy; ITP - Idiopathic thrombocytopenic purpura; MG – Myasthenia Gravis; PID – Primary Immune Deficiency; SID –Secondary Immune Deficiency

# Immunoglobulins

FY21 Sales: $4,238M[1]

Up 3%[2]

Christal: living with chronic inflammatory demyelinating polyneuropathy (CIDP)

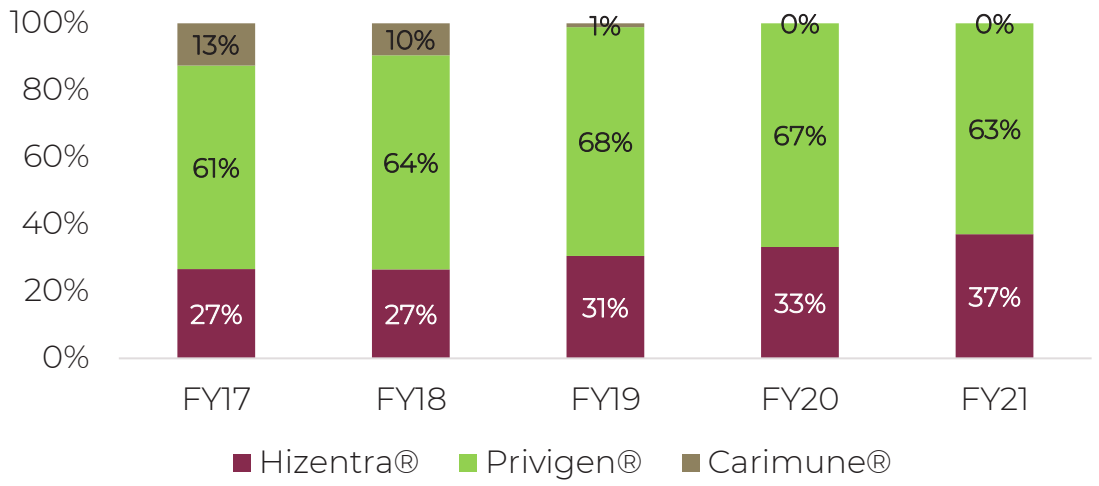
Hizentra® Immune Globulin Subcutaneous (Human) 20% Liquid

- Hizentra® +15% revenue growth[2]; remains the clear SCIg market leader
- Increased preference for at-home treatment
- Continued uptake in CIDP
- Recent Medicare Part B reimbursement approval

privigen® Immune Globulin Intravenous (Human), 10% Liquid
IVIg therapy made simple

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

## US Ig Volume Mix Evolution[3]




[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] CSL Internal Data



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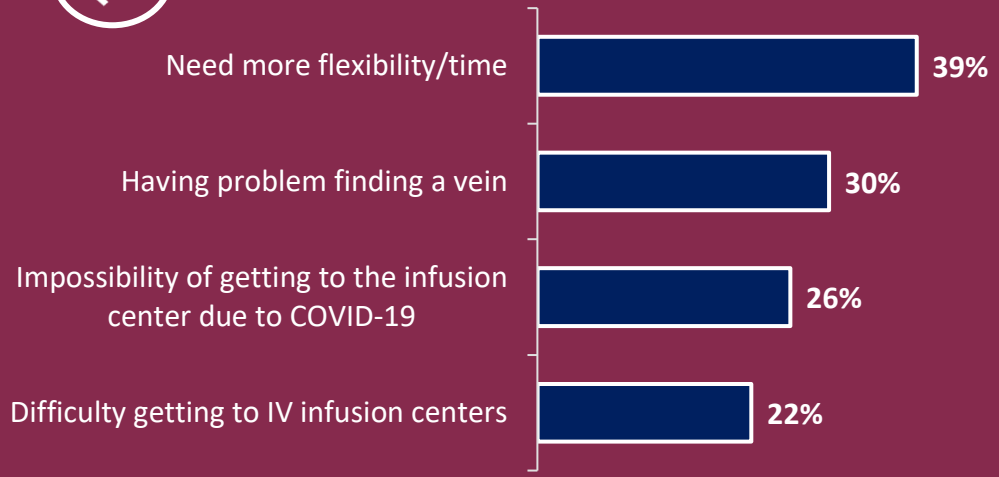
Hizentra®
Immune Globulin Subcutaneous (Human) 20% Liquid

## Reasons for IVIg to Hizentra® Switch[1]




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

# Hizentra®

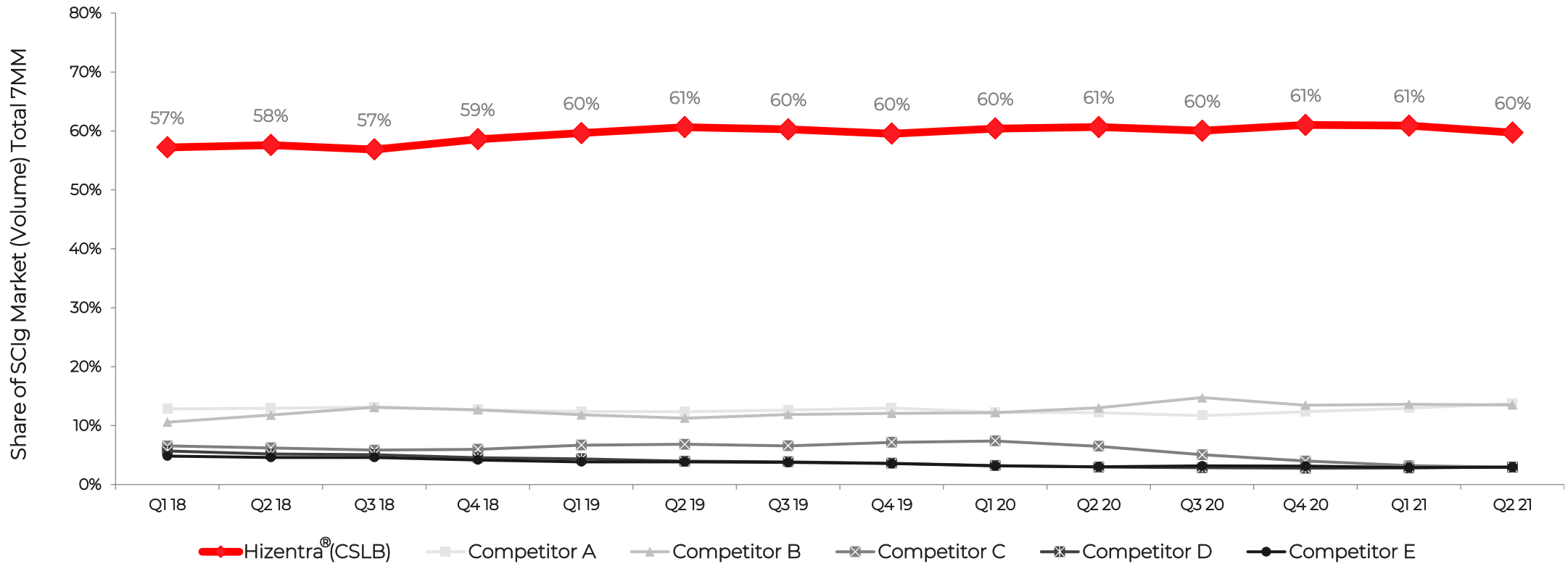
- #1 Ig used worldwide for PID[1] and the only SCIg approved for use in CIDP
- Proven long-term protection with over 3.5 years of clinical evidence and 10+ years of real-world experience
- Continue to lead within SCIg as we bring more innovative and personalized treatment options to patients

[1] Data on file

CSL

# Hizentra® - Continued Strong Performance

## Robust SCIg Market Growth of 13.1% During Same Period

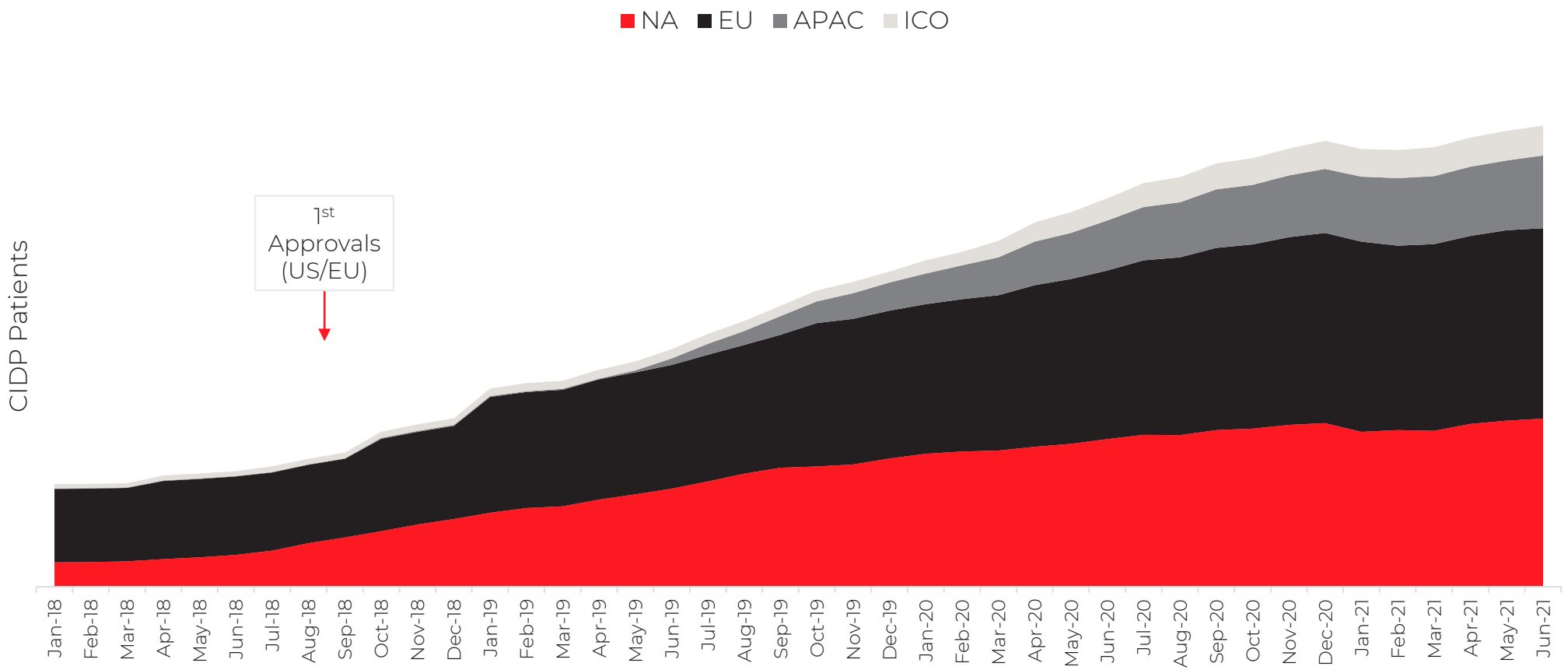



**Source:** Data on file
7MM refers to US, DE, FR, IT, UK, ES & JP

# CIDP Patients Benefitting From Hizentra® Across the Globe

Hizentra® Immune Globulin Subcutaneous (Human) 20% Liquid

## Total Hizentra® CIDP Patients by Region[1,2]




[1] Countries Included – JP, AT, IT, NL, SK, UK, IS, CH, US, GER, GR, DE.
[2] Data on file



CSL™

# Haemophilia

FY21 Sales: $1,107M

Down 4%[1]

Logan: living with Haemophilia B.

IDELVION®

- Standard of care for Haemophilia B
- Maintained leadership[2] in several key markets, including US, Germany, Italy, Switzerland & Japan
- Recent strong launches in France, Spain and Taiwan

AFSTYLA®

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

pdFVIII

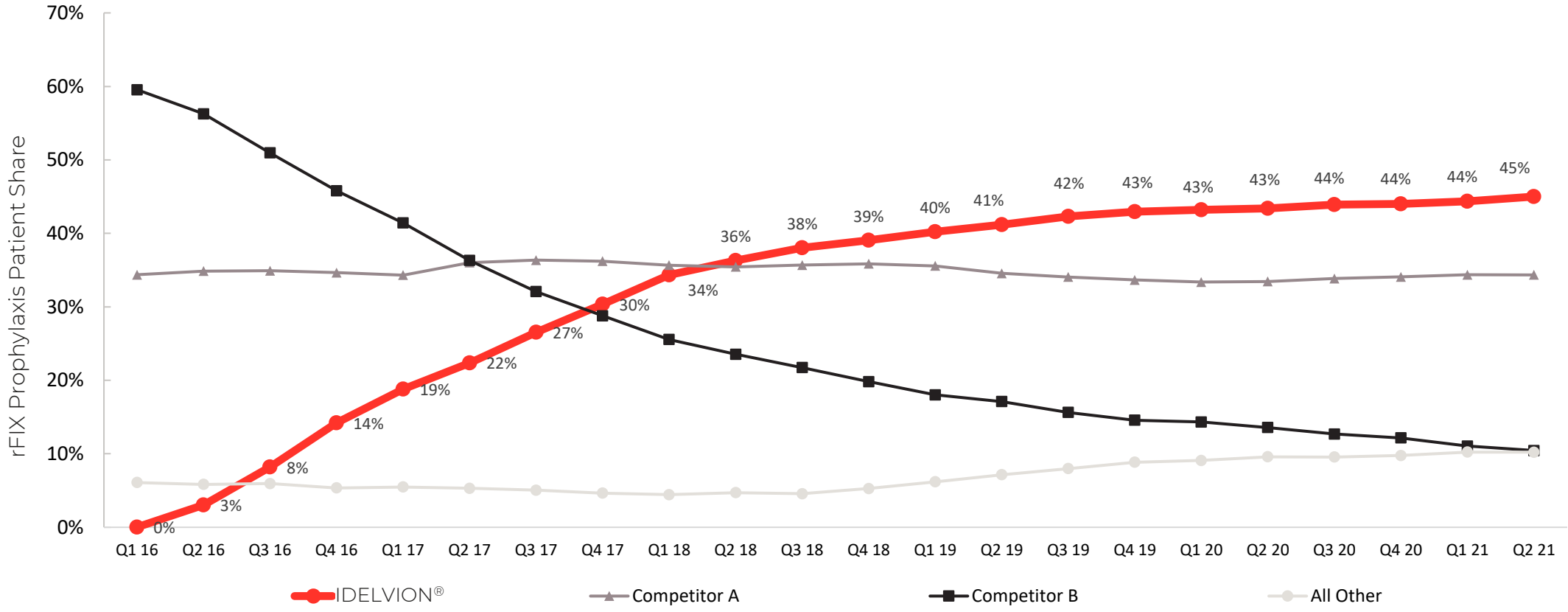
- Maintained market leadership globally in vWD with 56% patient share[2,3]

HUMATE®

- Strong revenue growth of 13%[1] in the US

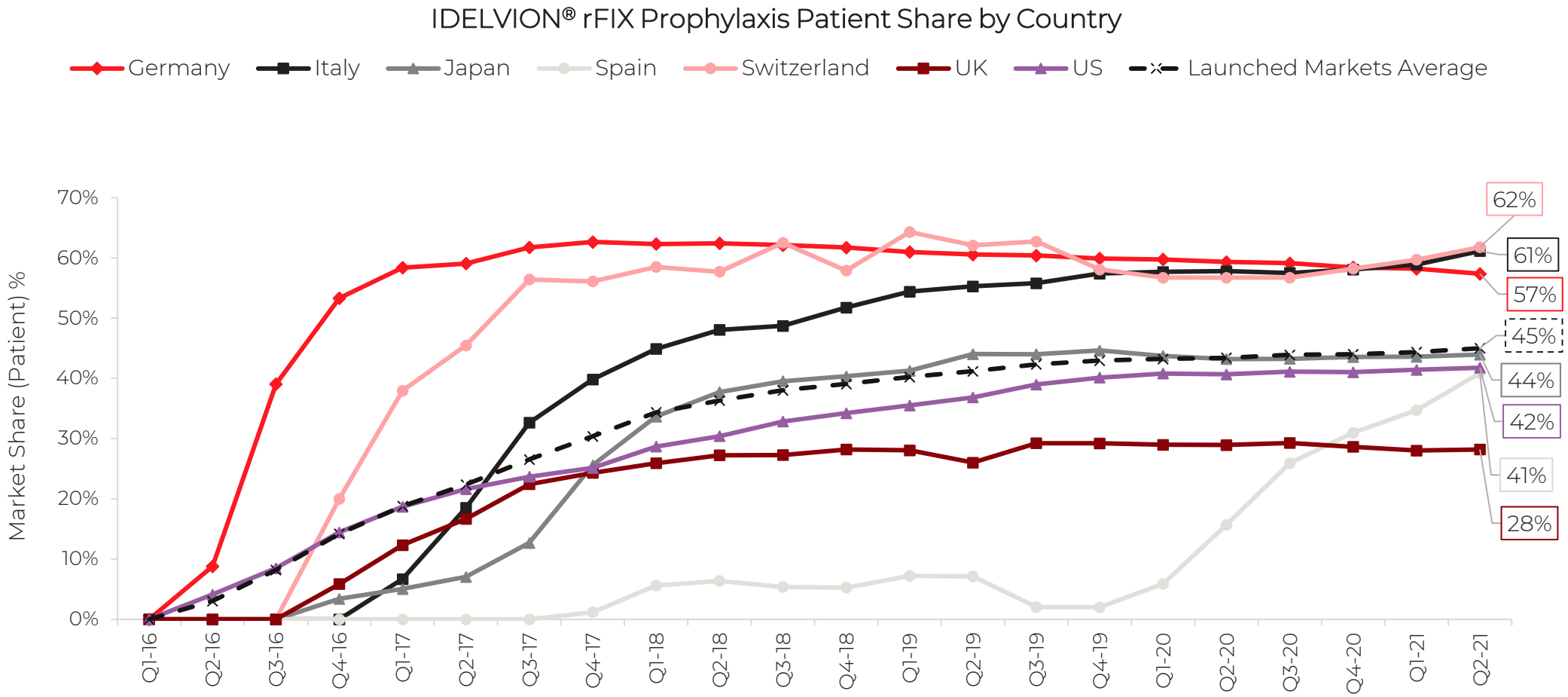
[1] Growth percentages shown at constant currency to remove the impact of exchange rate movements, facilitating comparability of operational performance.
[2] Data on file
[3] Includes HUMATE®/HAEMATE® and VONCENTO®
**Abbreviations:** vWD – von Willebrand Disease

# IDELVION® - Maintaining Market Leadership



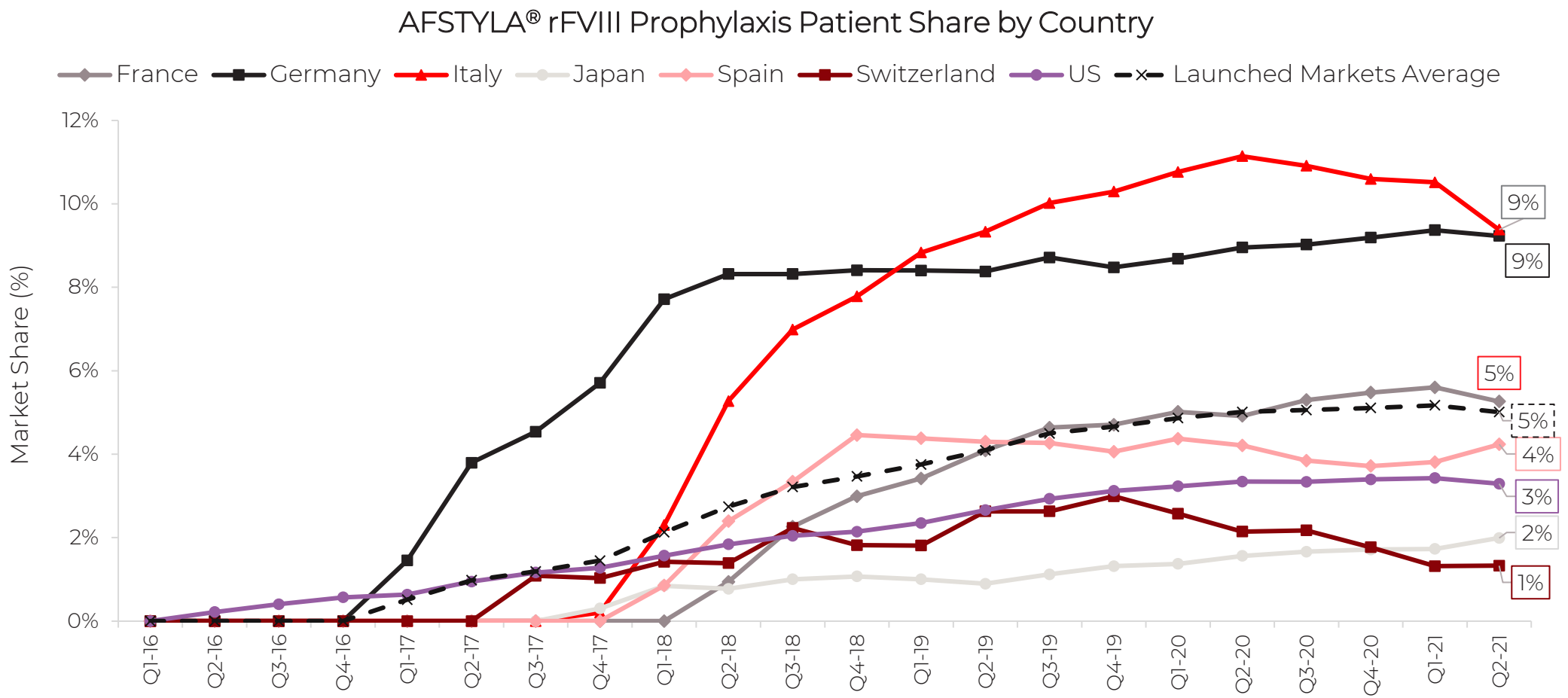

Based on data from US, JP, DE, IT, ES, CH and UK where IDELVION® is reimbursed and commercially available.
**Source:** Data on file

# IDELVION® - Market Shares Within Key Markets




**Source:** Data on file

# AFSTYLA® - Market Shares Within Key Markets




**Source:** Data on file


# EVERY STEP HAS BEEN LEADING TO THE NEXT BREAKTHROUGH FOR HEMOPHILIA B

# Specialty Products

FY21 Sales: $1,770M

Up 2%[1]

Cheryl: living with Hereditary Angioedema (HAE).

Kcentra® Prothrombin Complex Concentrate (Human)

## KCENTRA®

- Remains the gold standard for warfarin reversal in the US
- Substantial growth opportunities, with FFP still used in ~40% of patients[2] in the US
- Demand rebounded to pre-COVID levels in the US

HAEGARDA® C1 Esterase Inhibitor Subcutaneous (Human)

Respreeza® alpha$_1$-proteinase inhibitor (Human)

Zemaira® alpha$_1$-proteinase inhibitor (Human)

## HAEGARDA® / Berinert SC®

- Offers best in class efficacy[3]
- US: Most patients since launch
- Treatment paradigm further shifts from on-demand to long-term prophylaxis

## Respreeza® / Zemaira®

- Investing to enhance supply chain & ensure future supply

[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] 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.

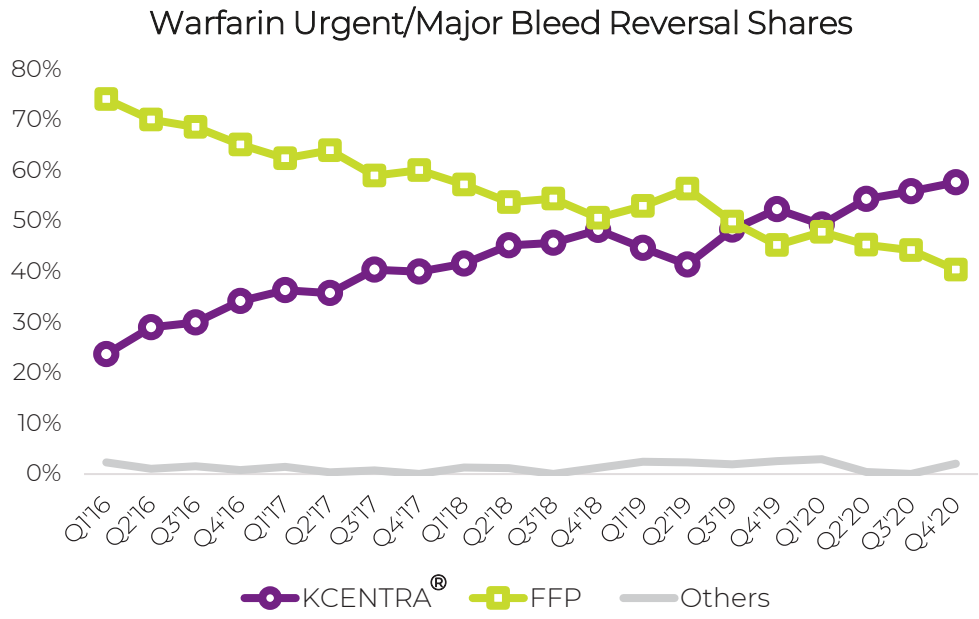


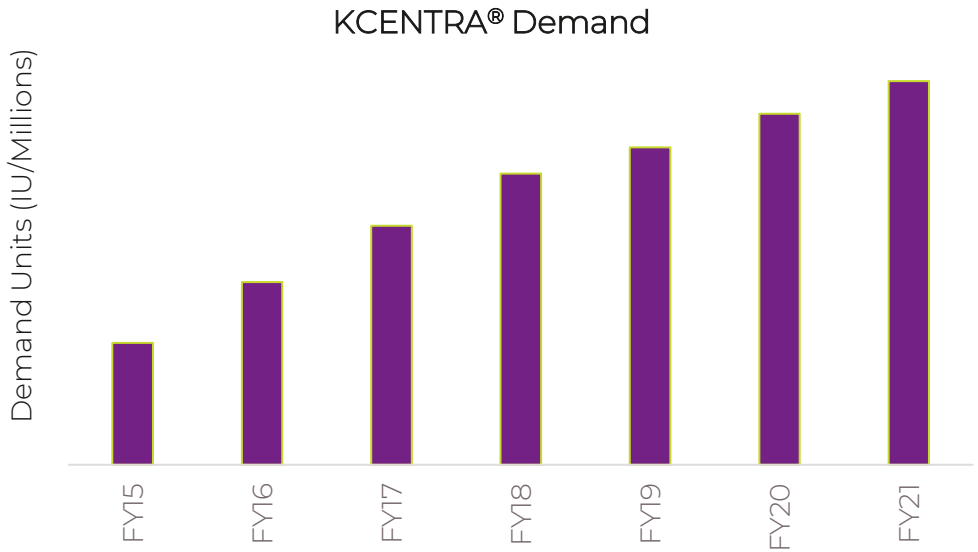
CSL™

Kcentra®
Prothrombin Complex Concentrate (Human)

# KCENTRA® Growth in US

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



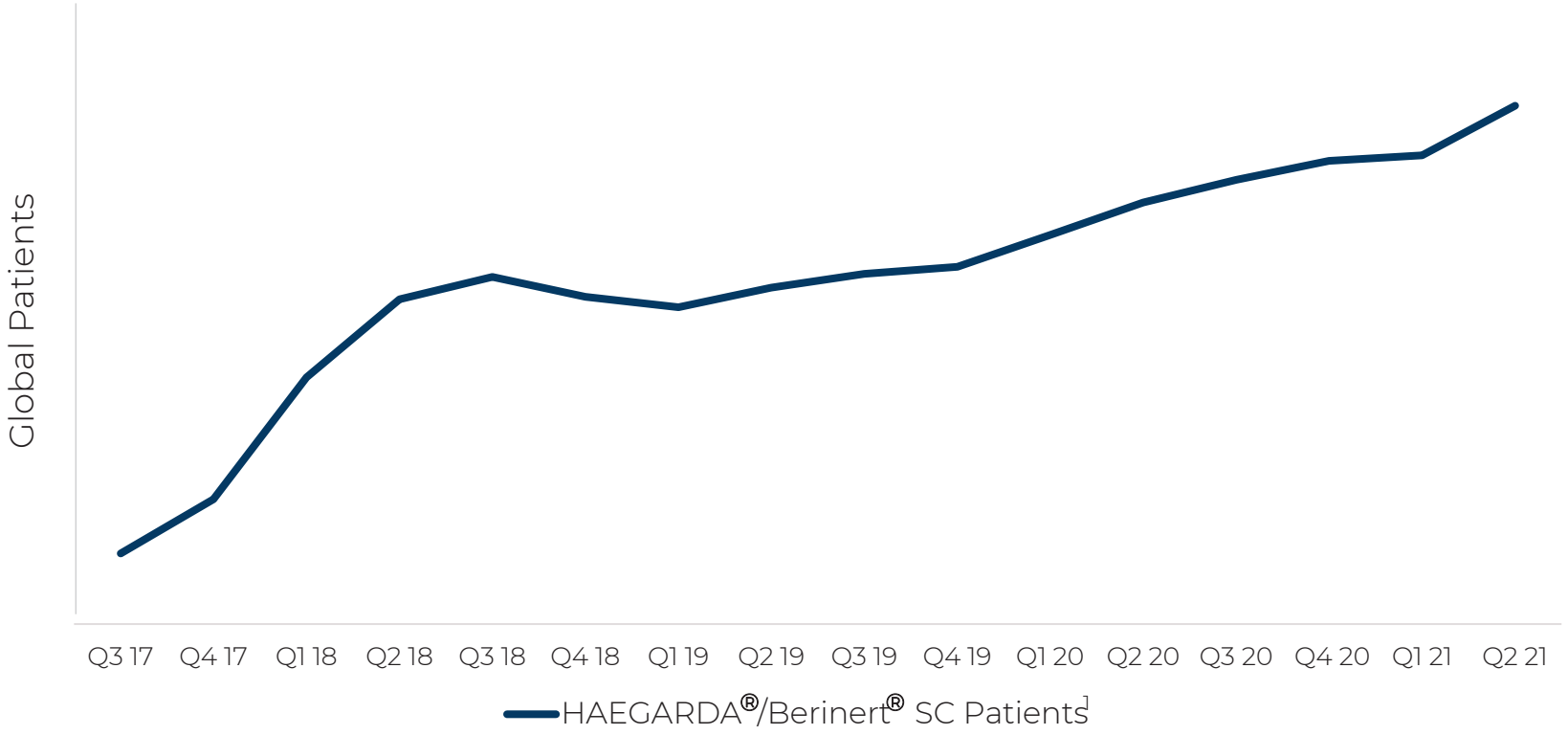

[1] Neurocritical Care Society; Society of Critical Care Medicine; American College of Cardiology; American College of Chest Physicians; American Society of Gastrointestinal Endoscopy; American College of Surgeons
[2] Data on file – represents US market only



CSL

# HAEGARDA® /Berinert® SC

## Growth in the Face of Competition




### Regional Progress

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

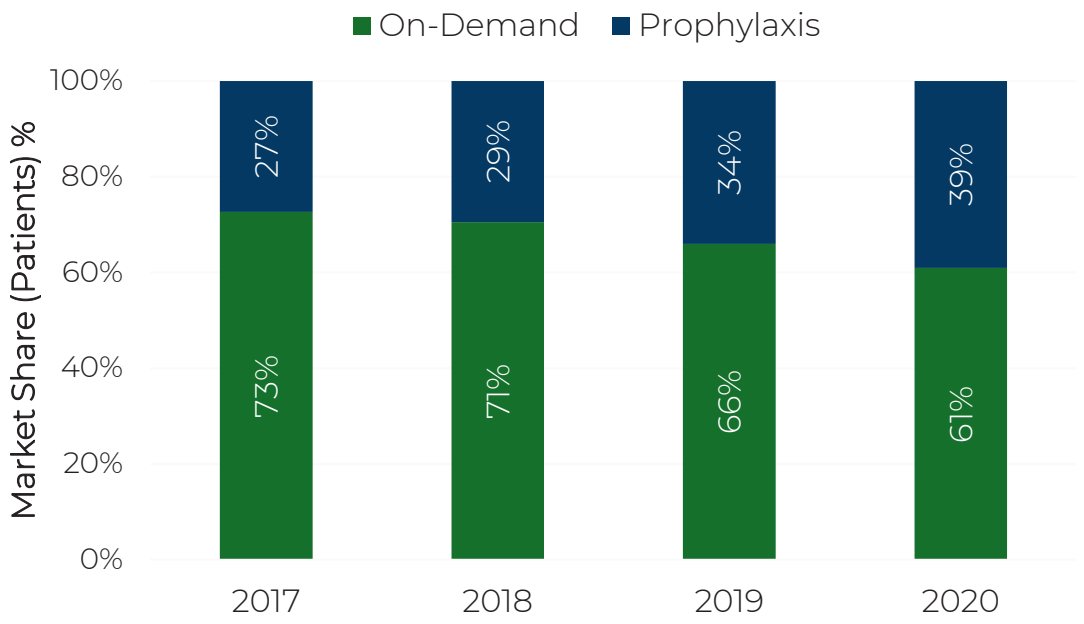
[1] Data on file
[2] Patient share in the non-steroidal prophylaxis segment

# HAEGARDA® /Berinert® SC Growth Potential

HAEGARDA® C1 Esterase Inhibitor Subcutaneous (Human)

BERINERT® C1 Esterase Inhibitor, Human

## HAE Market Share (Patients) by Regimen[1]




- Prophylaxis segment continues to grow but ~60% of patients still on acute therapy
- HAEGARDA® /Berinert® SC has proven record of high efficacy and safety[2]
- Continue to see patients switch back from competing products to the benefits of HAEGARDA® /Berinert® SC[1]

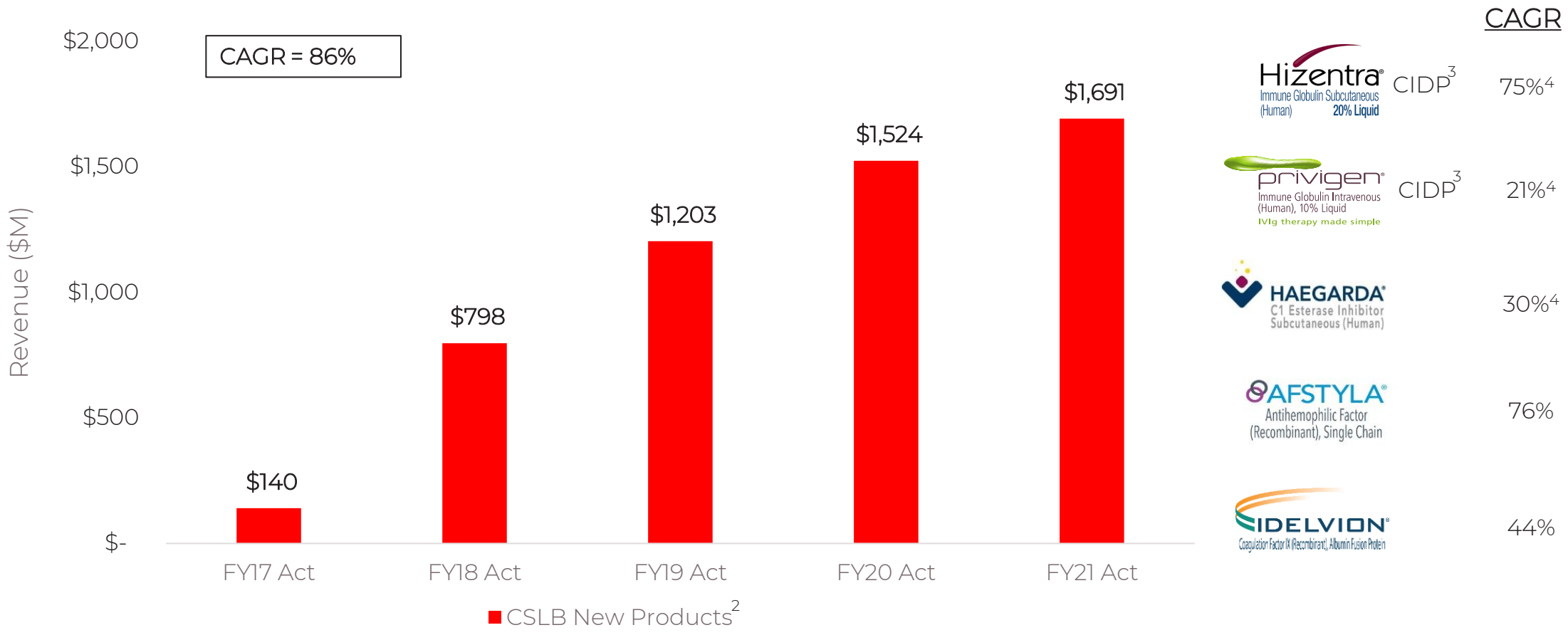
***Efficacy ultimately drives patient preference**. Patients define convenience as being free from attacks, not just frequency and ease of administration[3]. Prophylaxis treatment with **HAEGARDA® /Berinert® SC** addresses this need.*

[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.
[3] Per 2020 Harris Poll



CSL

# New Products Contributing Significantly to Growth[1]




[1] Revenues shown at constant currency to remove the impact of exchange rate movements, facilitating comparability of operational performance.
[2] CSLB New Products include Hizentra® CIDP, Privigen® CIDP, HAEGARDA®/Berinert® SC, AFSTYLA® & IDELVION®
[3] CIDP revenue represents markets where the indication was recently acquired
[4] CAGR calculated off base of FY18 when launch occurred

Peter, who lives with Haemophilia B, enjoying reading with his kids

# Commercial Summary

Executing on strategies

Strong underlying demand across the portfolio

COVID restrained commercial activity

Balanced regional & key market growth

New products contributing significantly to growth

Robust new product pipeline to fuel growth

# SEQIRUS

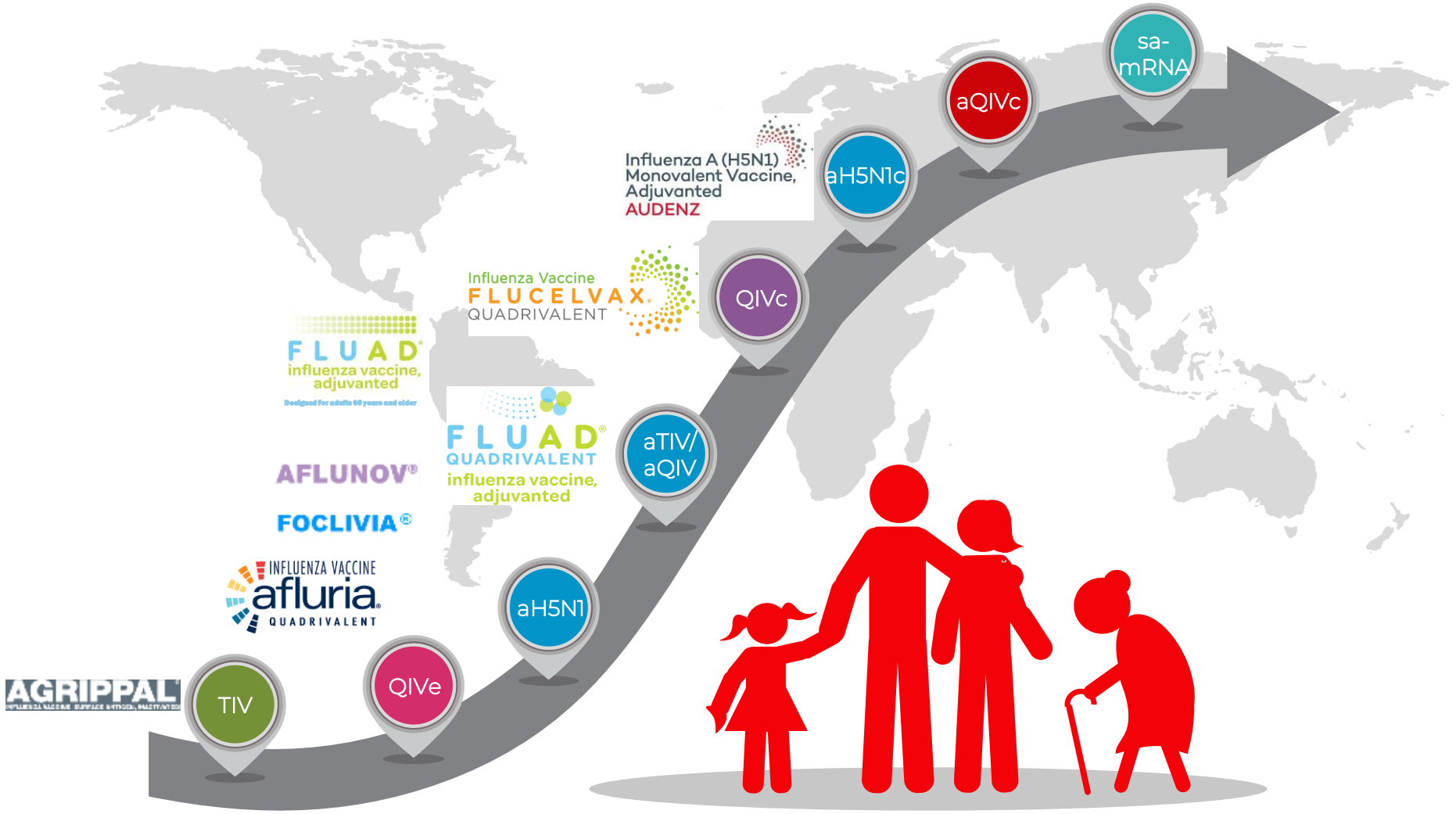
## Russell Basser MD

Senior Vice President, R&D

## Ethan Settembre PhD

Vice President, Research

# Population Protection Through Innovation



# Seqirus Milestones in FY21 & FY22 (to date)

## FLUCELVAX® QUAD

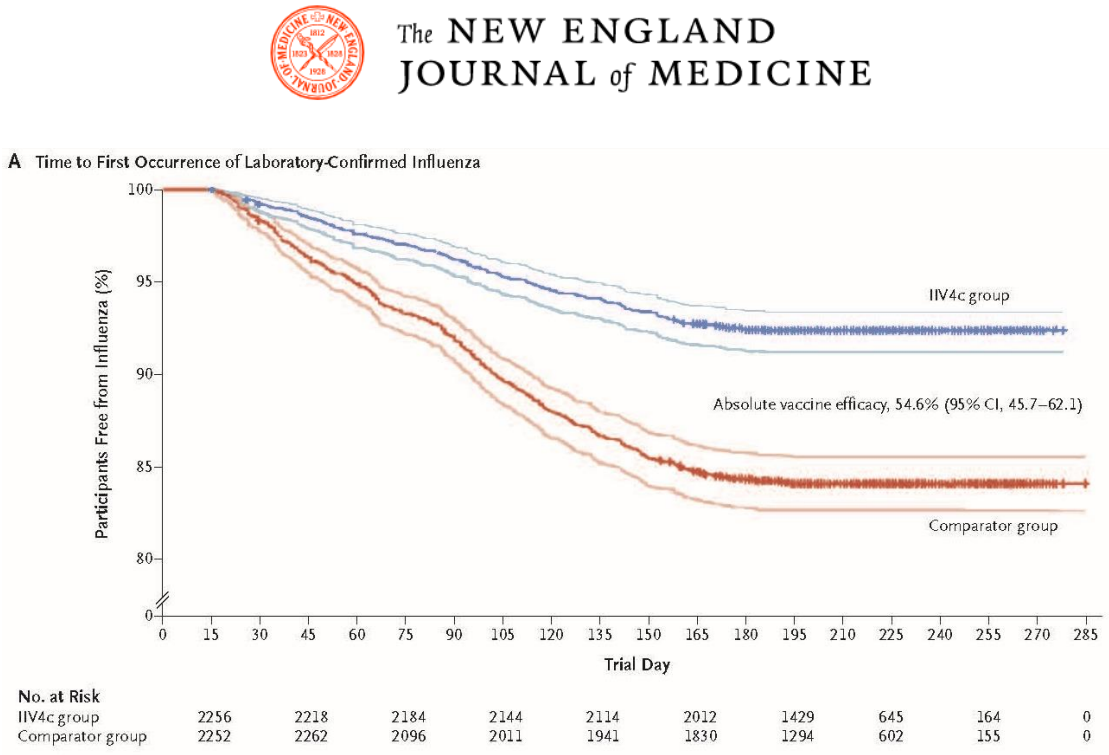
- Paediatric efficacy study (2-17yrs) – published in New England Journal of Medicine - 14 Oct 2021
- US 6mo+ age extension approval
- Regulatory approvals – 2yr+ in US/EU/UK/CA, 9yr+ in AU (5 further regulatory approval submissions)
- Paediatric immunogenicity (6mo-4yr) – met all endpoints

## FLUAD® QUAD

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

## aQIVc

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



# New Cell Culture Facility in Australia

## Tullamarine, Victoria

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

# Collaboration with BARDA

## Biomedical Advanced Research and Development Authority

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

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

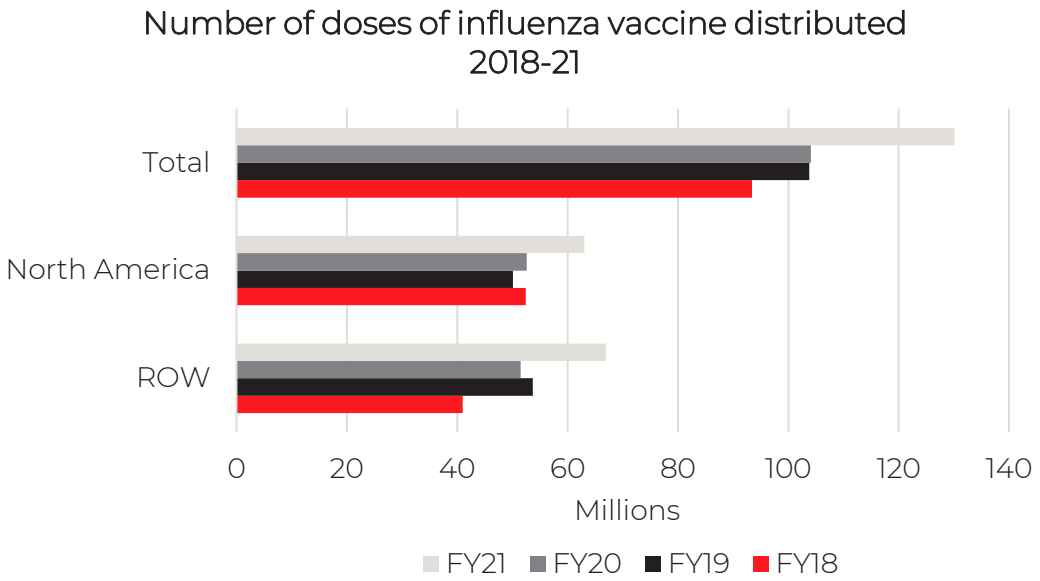
US$35M multi-year contract extends to clinical proof of concept early trials

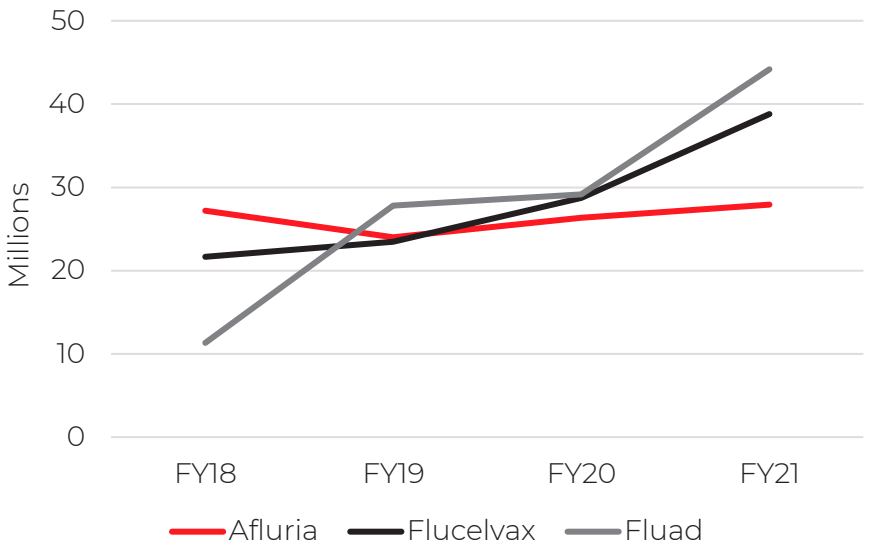
# Impact of COVID-19 on Influenza and Vaccination

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

- low level circulation
- bird and animal reservoirs remain

Strong demand for influenza vaccine – increased doses and differentiated products

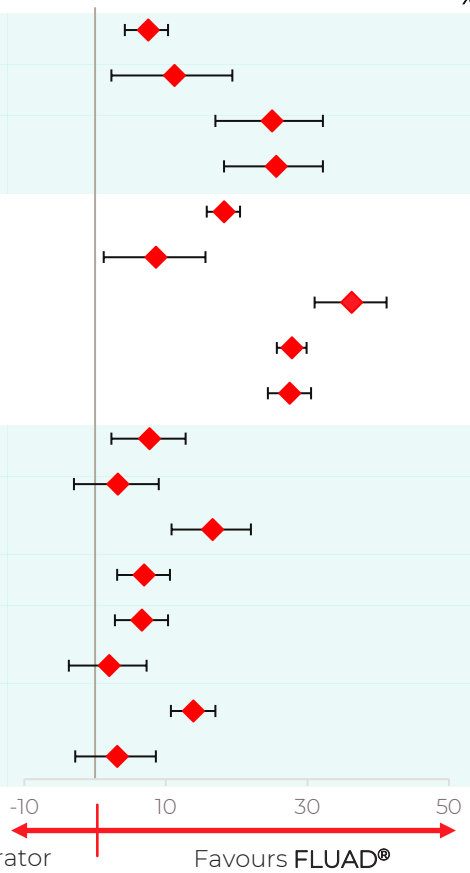


# Real World Evidence – Consistent Benefit of MF59® Adjuvant and Cell Technology over Multiple Seasons

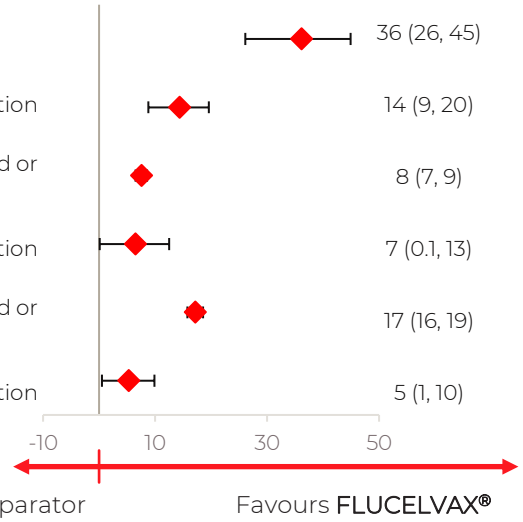
## Fluad® (3 strain) – Benefit of MF59®

| Comparator | Study | Season | Outcome* | % rVE (95%CI) |
|---|---|---|---|---|
| TIV | Boikos (2020) | 2017/18 | Hospitalized or ED/GP | 8 (4, 10) |
| TIV | Pelton (2020) | 2017/18 | Hospitalized or ED | 11 (2, 19) |
| TIV | Pelton (2020) | 2017/18 | GP | 25 (17, 32) |
| TIV | Boikos (2020) | 2018/19 | Hospitalized or ED/GP | 26 (18, 32) |
| QIV | Boikos (2020) | 2017/18 | Hospitalized or ED/GP | 18 (16, 21) |
| QIV | Pelton (2020) | 2017/18 | Hospitalized or ED | 9 (1, 16) |
| QIV | Pelton (2020) | 2017/18 | GP | 36 (31, 41) |
| QIV | Boikos (2020) | 2018/19 | Hospitalized or ED/GP | 28 (26, 30) |
| QIV | CORE 2021 | 2019/20 | Hospitalized or ED/GP | 28 (24, 31) |
| HD-TIV | Boikos (2020) | 2017/18 | Hospitalized or ED/GP | 8 (2, 13) |
| HD-TIV | Pelton (2020) | 2017/18 | Hospitalized or ED | 3 (-3, 9) |
| HD-TIV | Pelton (2020) | 2017/18 | GP | 17 (11, 22) |
| HD-TIV | Boikos (2020) | 2018/19 | Hospitalized or ED/GP | 7 (3, 11) |
| HD-TIV | Pelton (2021) | 2018/19 | Hospitalized or ED | 7 (3, 10) |
| HD-TIV | Pelton (2021) | 2018/19 | GP | 2 (-4, 7) |
| HD-TIV | CORE 2021 | 2019/20 | Hospitalized or ED/GP | 14 (11, 17) |
| HD-TIV | HEOR 2021 | 2019/20 | Hospitalized or ED | 3 (-3, 9) |




## Flucelvax® - Benefit of Cell Culture

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



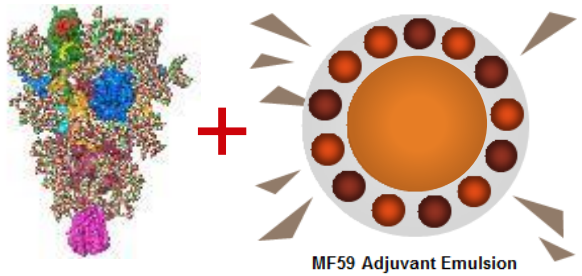

*Outcomes due to influenza or pneumonia

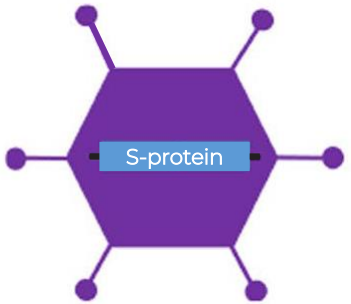
2017/18 was the first season a cell-based seed (H3N2) was included in FLUCELVAX®


Boikos, C. *et al.*, (2020) *CID* 73:816-823
Pelton, S.I. *et al.*, (2020) *Vaccines* 8:446
Pelton, S.I. *et al.*, (2021) *Vaccine* 39:2396-2407
CORE (2021): Presented at ECCMID 2021, manuscript pending
HEOR (2021): Manuscript pending


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

# CSL Strengths Applied to COVID-19




## University of Queensland

(V451)

*Recombinant S-clamp protein*
*MF59® adjuvant*

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

## AstraZeneca

(AZD1222)

*Recombinant replication competent vector that expresses S-protein*

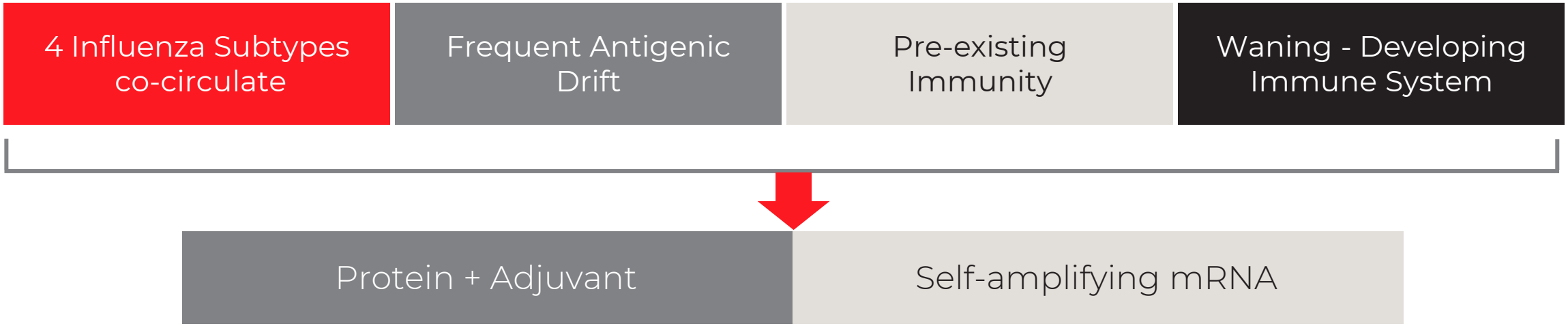
*Manufacturing under contract to supply to AZ for AU*

# What to Expect from Next-Generation Influenza Vaccines

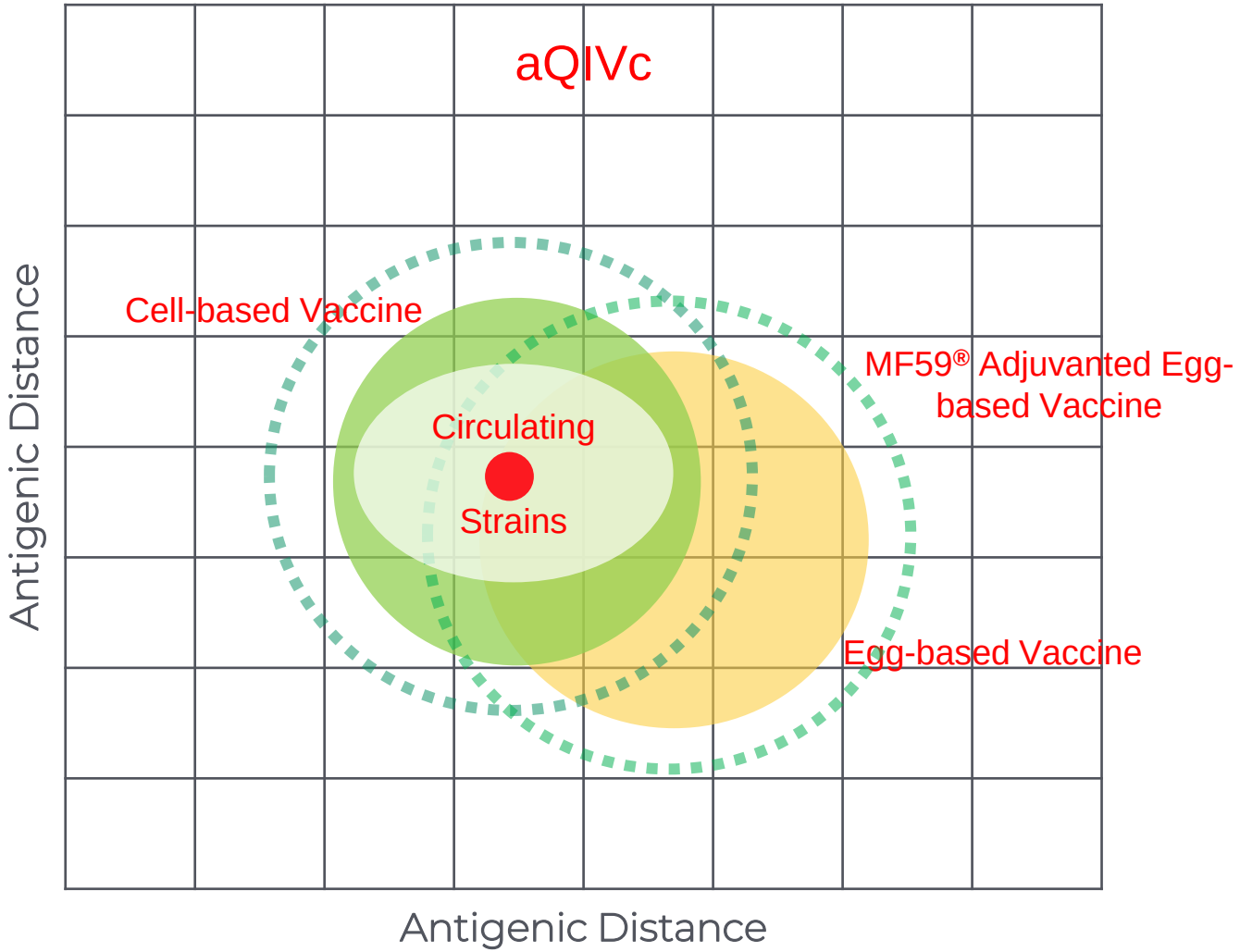
aQIVc

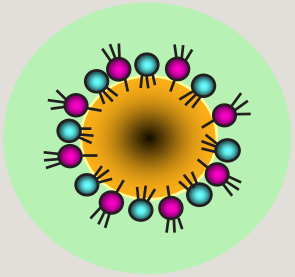
Self-amplifying mRNA

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



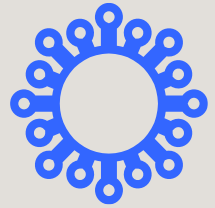
# Improving Influenza Vaccines by Combining Two Advanced Technologies



## MF59® Adjuvant

Increases “breadth”
Increases antibody response
Dose-sparing potential (pandemic)



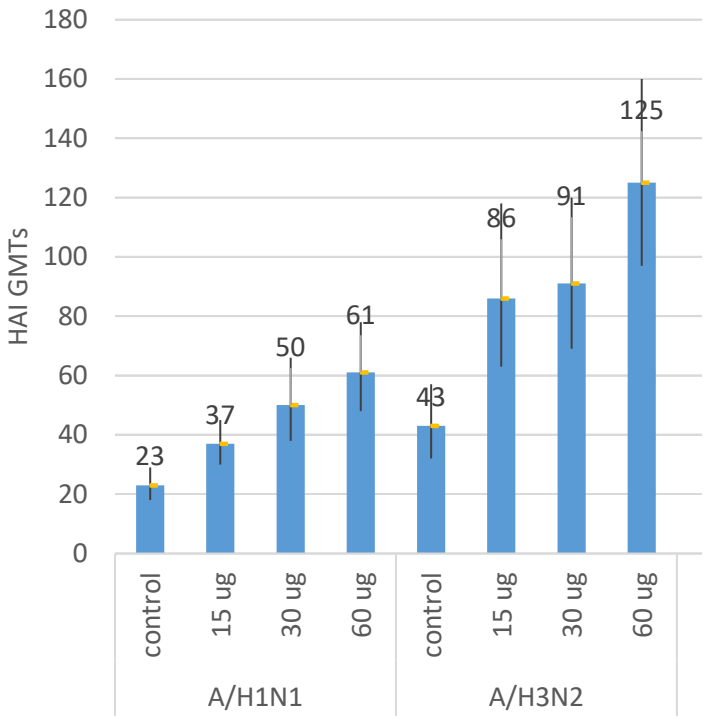
## Cell Culture

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

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

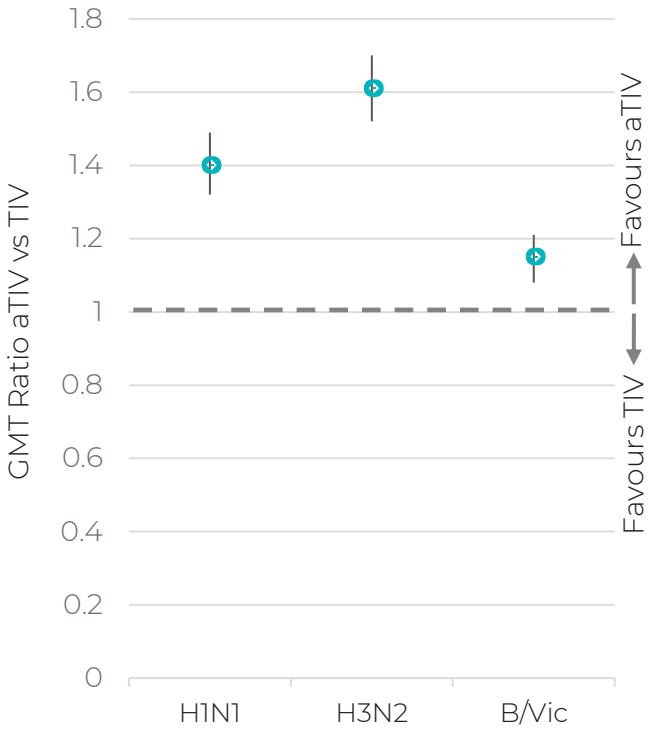
## Higher Antigen Dose Drives Higher Immunogenicity

Hemagglutination Inhibition Titers




## MF59® Adjuvant Drives Higher Immunogenicity

GMT Ratio aTIV vs TIV




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

**Source:** Keitel, W. *et al*, (2006) *Arch Intern Med* 166: 1121-1127

Unpublished data, Seqirus

**Abbreviations:** GMT - Geometric Mean Titer; HAI - Hemagglutination Inhibition

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


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

The Journal of Clinical Investigation 2021;131(19):e153721. https://doi.org/10.1172/JCI153721.

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

By Maggie Fox, CNN

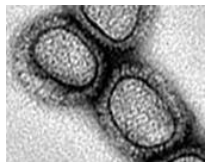
Updated 3:41 PM ET, Tue June 1, 2021

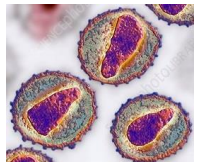
**HOW COVID UNLOCKED THE POWER OF RNA**

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

Nature | Vol 589 | 14 January 2021 |

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





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

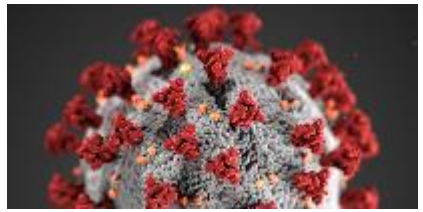
**2008** Initiation of sa-mRNA research

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

**2012** DARPA funds platform development

H5N1 vaccine candidate generated

**2015** SEQ continues Flu vaccine development



COVID vaccine candidate generated

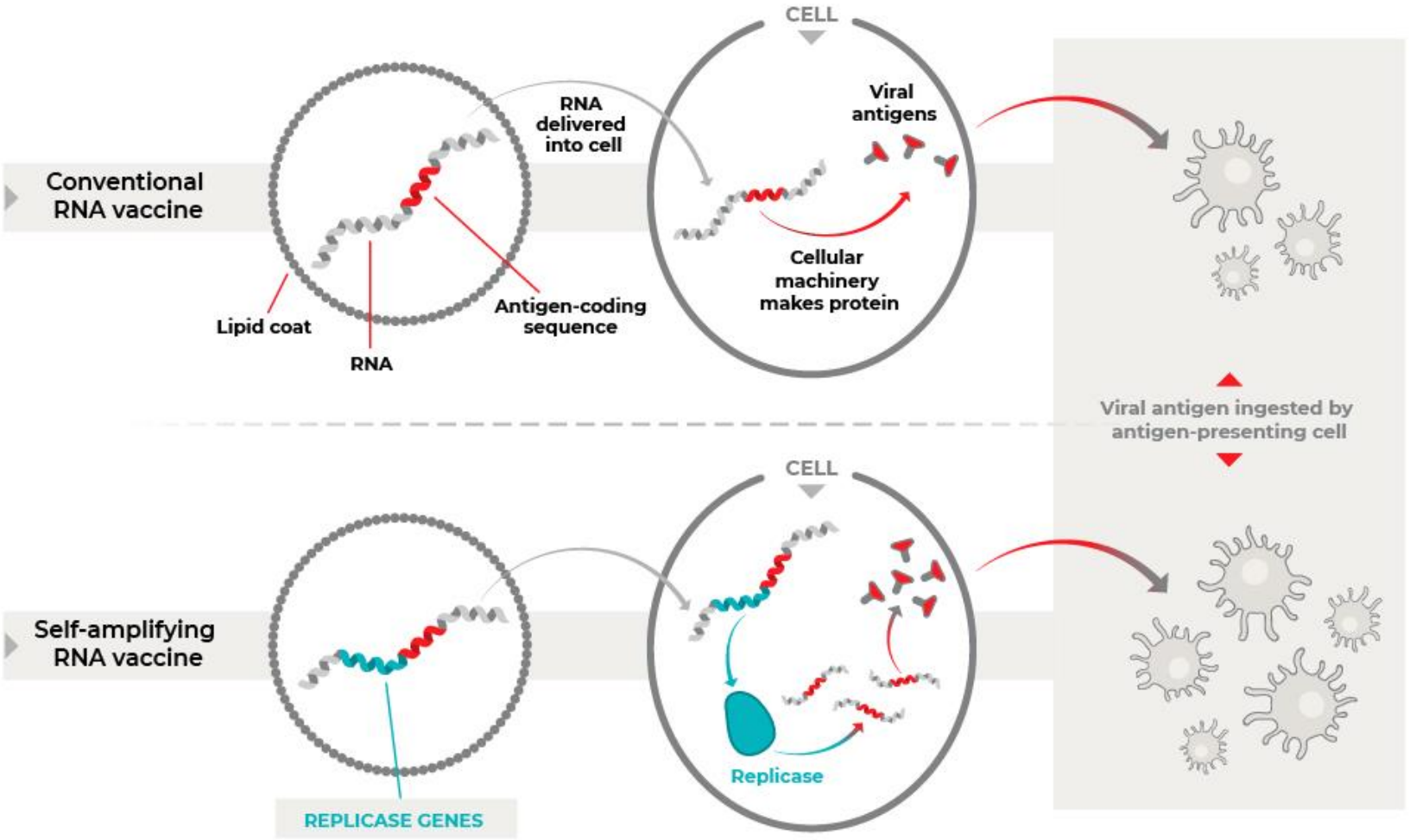
**2019** seasonal Flu into Development

***2021*** *Pre-pandemic (H2) collaboration for sa-mRNA and cell culture platforms*



Abbreviations: CMV – Cytomegalovirus; HIV - Human Immunodeficiency Virus; RSV - Respiratory Syncytial Virus

# mRNA Technology – Two Main Approaches Have Important Differences




**Source:** Adapted from Dolgin E. (2021) *Nature* 589(7841):189-191

# Seasonal Influenza Challenges Differ from SARS-CoV-2

| | | | | |
|---|---|---|---|---|
| COVID | 1 Circulating Virus | Unknown Antigenic Drift | No Pre-existing Immunity | Waning - Developing Immune System |
| Flu | 4 Influenza Subtypes co-circulate | Frequent Antigenic Drift | Pre-existing Immunity | |

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

# sa-mRNA – Two Key Elements Drive Immune Responses

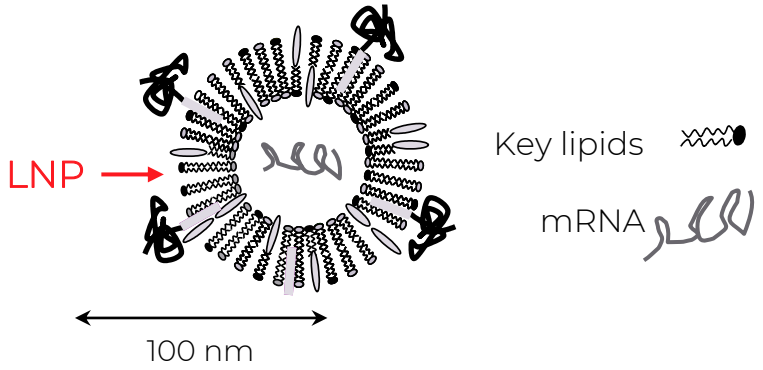
## Self-amplifying mRNA payload

Monocistronic = 1 gene of interest encoded by mRNA


Bicistronic = 2 genes of interest encoded by mRNA

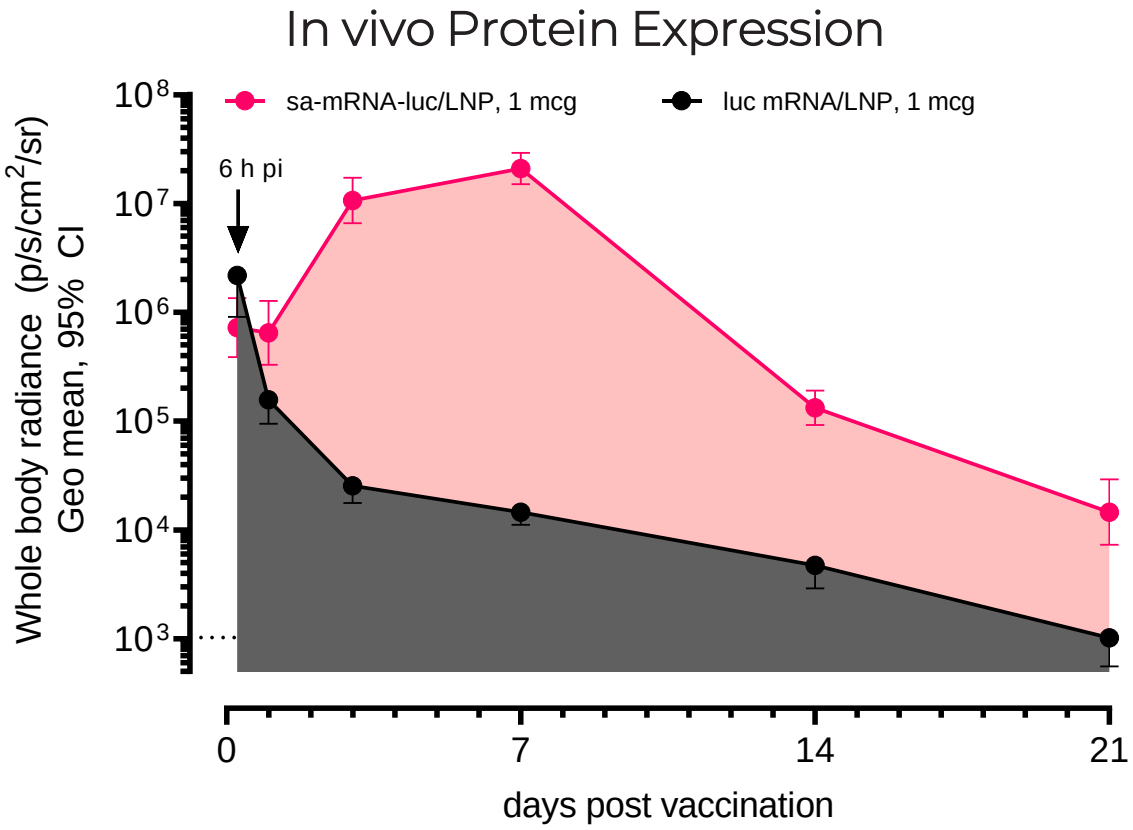

- Ability to include multiple antigens means vaccine can have greater control of gene expression with increased safety
- With lower dose it is easier to include additional antigens on the same sa-mRNA

## Lipid Nanoparticle (LNP)




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

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

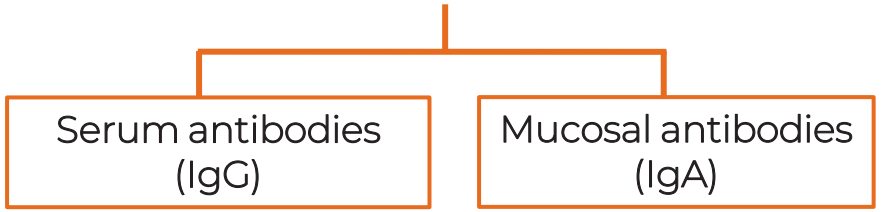



- sa-mRNA expresses 100+ fold more protein than mRNA
- sa-mRNA expression prolonged compared to mRNA
- Lower potential dose is benefit for influenza vaccines that require multiple strains

Unpublished data, Seqirus

# More Engaged Immune System = More Protective Response

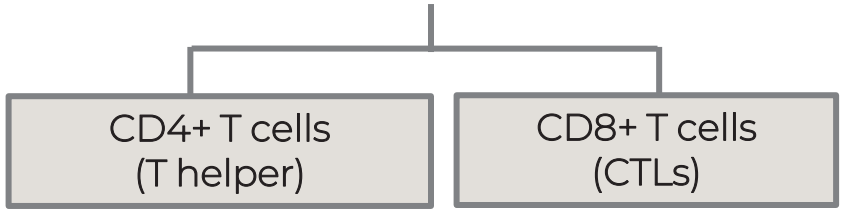
## B-cell (Antibody) Response




Protect lungs

Prevent infection

## T-cell Response




Increase B-cell response

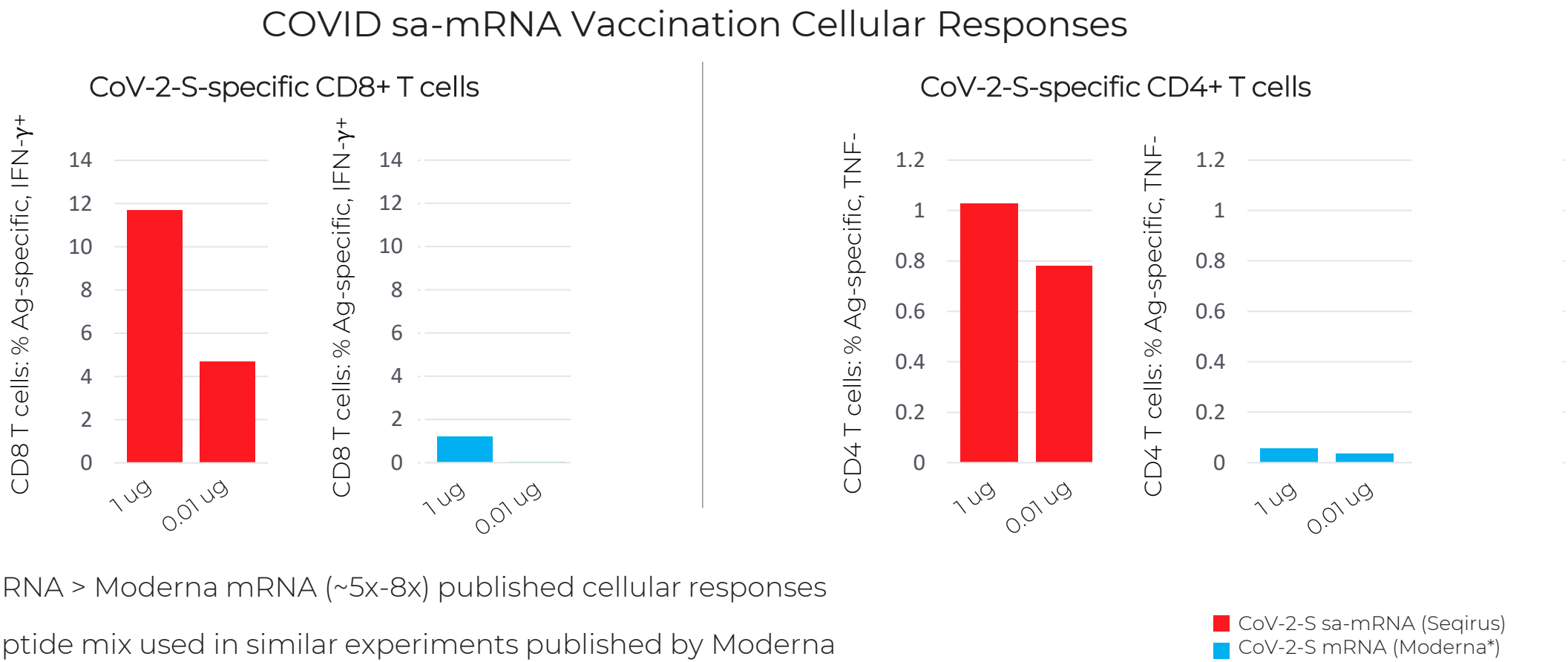
Lyse virus-infected cells

Protect against infection
Wane with age

Reduce severity of infection
Cross strain reactivity

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

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

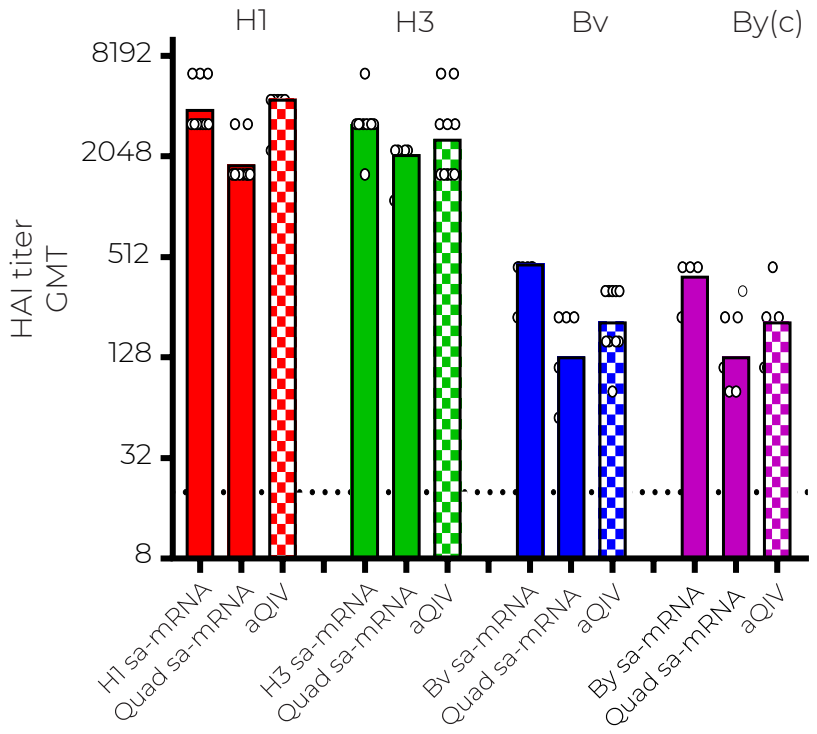



- sa-mRNA > Moderna mRNA (~5x-8x) published cellular responses
- S1 peptide mix used in similar experiments published by Moderna

*Moderna data; Corbett, K.S. *et al.,* (2020) BioRxiv. Unpublished data, Seqirus

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

## Influenza Hemagglutination Inhibition



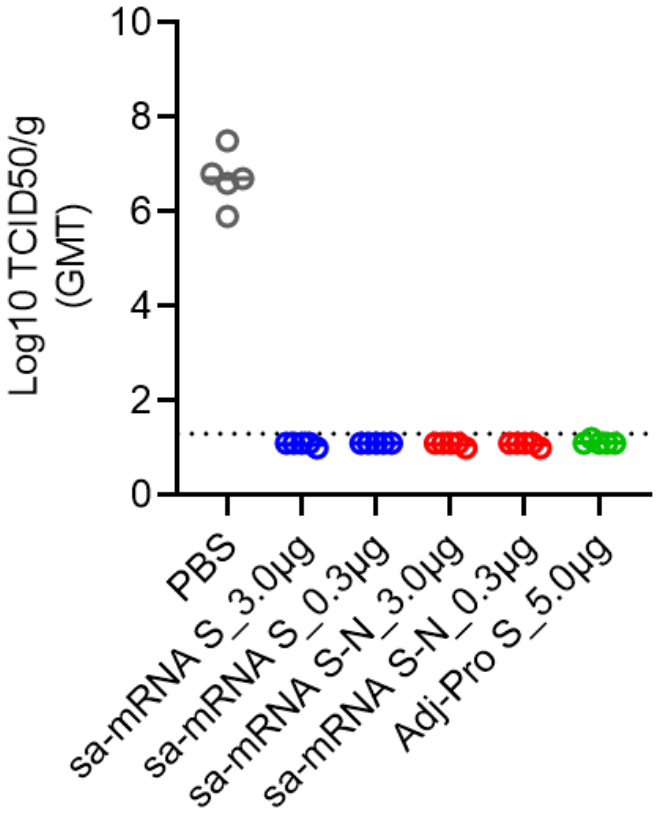

sa-mRNA Monovalent vaccine at 1 ug dose per target strain;
sa-mRNA Quadrivalent vaccine at 1 ug dose per strain

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

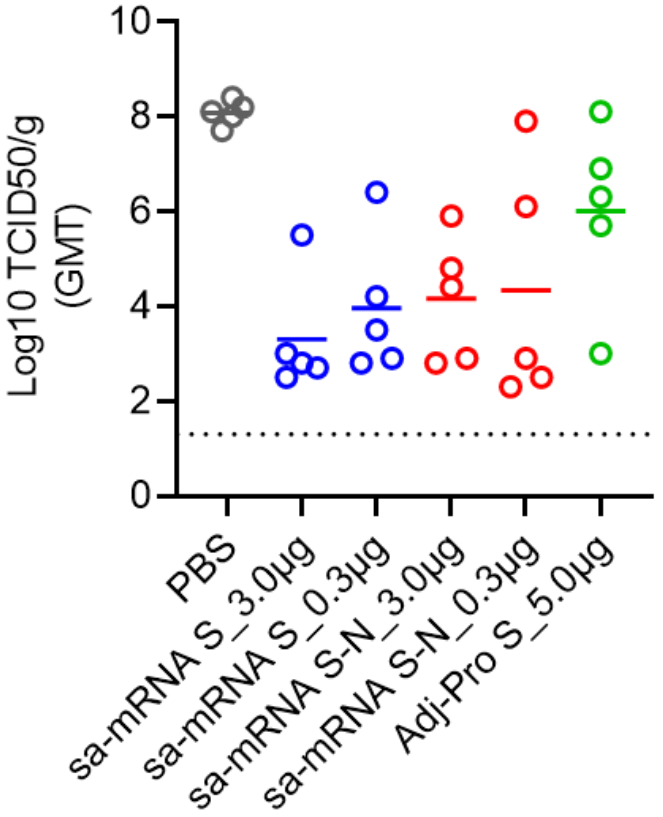
 Unpublished data, Seqirus

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

Lung virus titers (Day 4)




Nasal turbinate titers (Day 4)




Unpublished data, Seqirus

# Seqirus and Future Influenza Vaccine Portfolio

# FY22 Seqirus Milestones

## FLUCELVAX® QUAD

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

## FLUAD® QUAD

- Adult 50-64yr immunogenicity study start

## aQIVc

- Phase II Older Adult study results

## Self-amplifying mRNA

- Completion of GLP Tox study

Abbreviations: GLP – Good Laboratory Practice

# The Promise and Challenges of New Influenza Vaccines

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

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

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

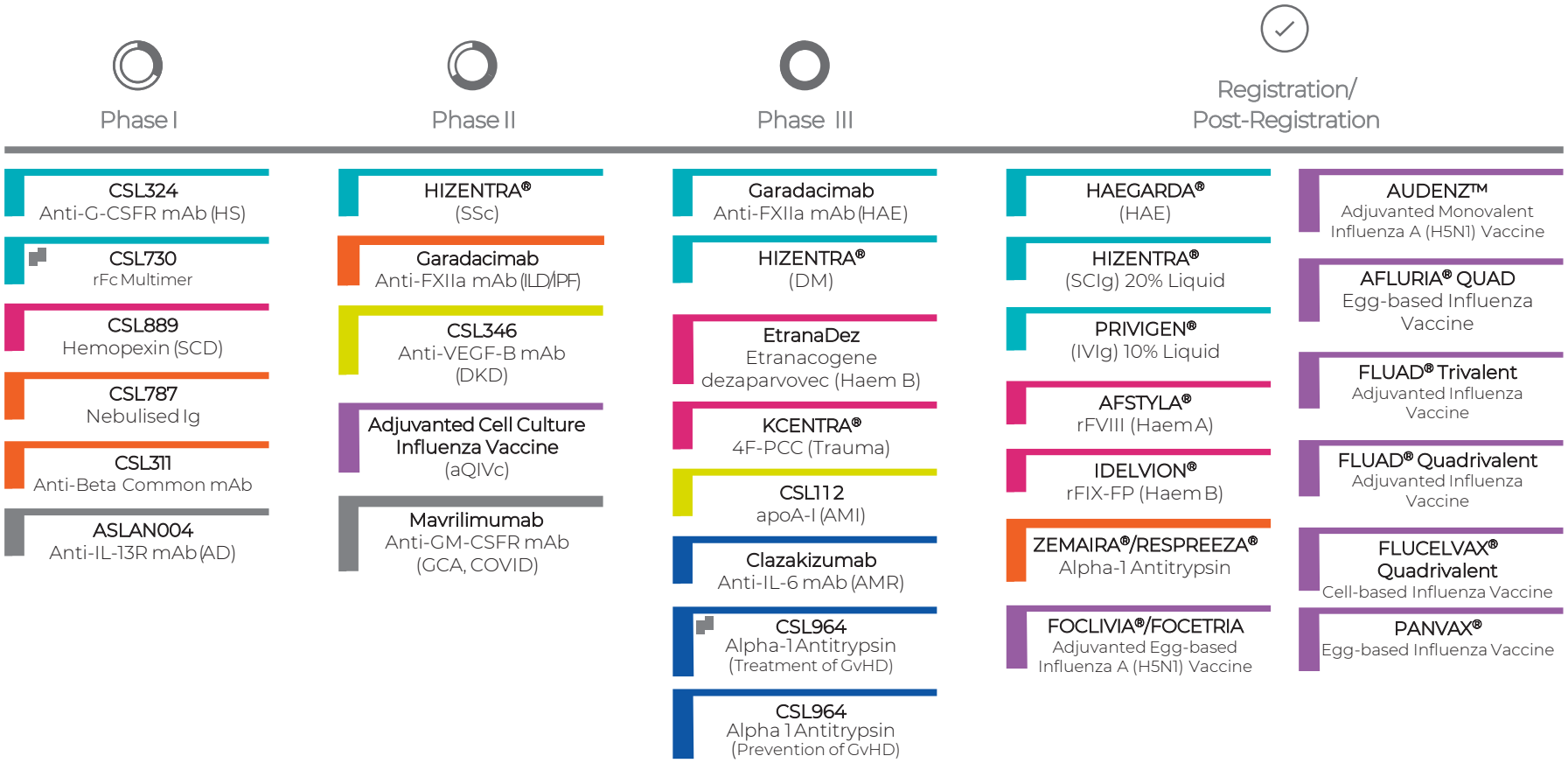
# Summary

## William Mezzanotte MD

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

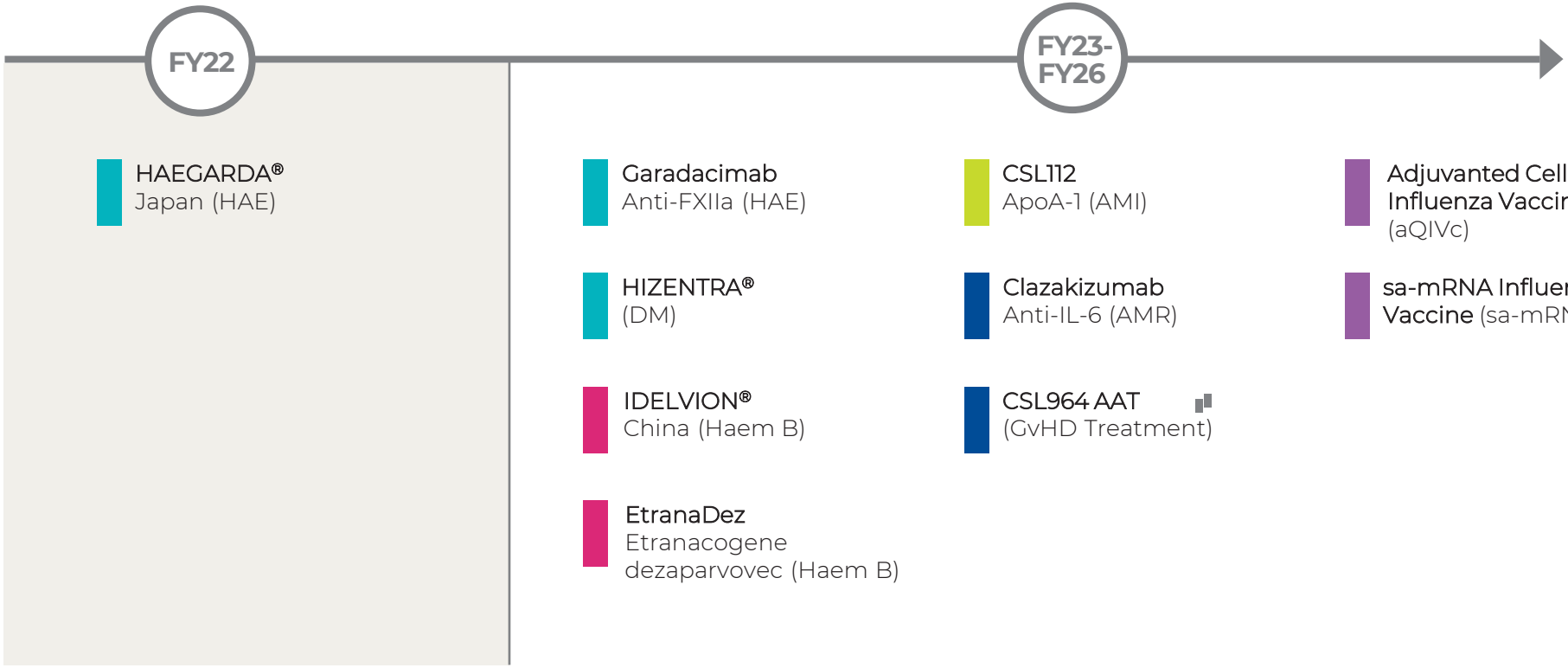
CSL Behring

# R&D Portfolio – FY22




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

# Significant Target Launch Dates




Immunology
Haematology
Cardiovascular & Metabolic
Transplant
Influenza Vaccines
Partnered Projects

# R&D Portfolio Highlights – FY22

## Immunology

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

## Respiratory

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

## Haematology

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

## Cardiovascular and Metabolic

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

## Transplant

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

## Influenza Vaccines

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

# Panel Q&A Session