Important Notice and Disclaimer
This presentation contains summary information about CSL Limited (ACN 004 089 936) and its related bodies corporate (together, CSL) and CSL’s activities as at the date of this presentation. It is information given in summary form only and does not purport to be complete. It should be read in conjunction with CSL’s other periodic corporate reports and continuous disclosure announcements filed with the Australian Securities Exchange (ASX), available at www.asx.com.au. This presentation is for information purposes only and is not a prospectus or product disclosure statement, financial product or investment advice or a recommendation to acquire CSL shares or other securities.

No representation or warranty, express or implied, is made as to the fairness, accuracy, completeness or correctness of the information, opinions and conclusions contained in this presentation. To the maximum extent permitted by law, none of CSL or its directors, employees or agents, nor any other person, accepts liability for any loss arising from the use of this presentation or its contents or otherwise arising in connection with it, including, without limitation, any liability from fault or negligence on the part of CSL or its directors, employees, contractors or agents.

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

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

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

Trademarks
Except where otherwise noted, brand names designated by a ™ or ® throughout this presentation are trademarks either owned by and/or licensed to CSL.
Introduction

William Mezzanotte MD

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

CSL Behring
01 Welcome
Mark Dehring

02 Introduction – FY21 Retrospective & Highlights
Bill Mezzanotte

03 Research
Andrew Nash

04 Development
Deirdre BeVard

05 Commercial
Bill Campbell

06 Seqirus
Russell Basser & Ethan Settembre

07 Looking toward FY22 & Summary
Bill Mezzanotte

08 Q&A
Panel
Commitment to Research and Development

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

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

* Investment reported in US$ millions; includes R&D for CSL Behring and Seqirus
Key Past Launches from R&D Portfolio

**Influenza Vaccines**
- **FY17**: FLUAD® (UK)
- **FY18**: AFLURIA® QIV 6mo+ (AU)
- **FY19**: FLUCELVAX® QIV 9yrs+ (EU, CA)
- **FY20**: FLUCELVAX® QIV (US)
- **FY21**: FLUCELVAX® QUAD 9yrs+ (AU)

**Immunology**
- **FY17**: PRIVIGEN® CIDP (US)
- **FY18**: PRIVIGEN® CIDP (JP)
- **FY19**: PRIVIGEN® CIDP (JP)
- **FY20**: PRIVIGEN® PID/SID (JP)

**Haematology**
- **FY17**: HAEGARDA® (US)
- **FY18**: HIZENTRA® CIDP
- **FY19**: HIZENTRA® CIDP (JP)
- **FY20**: IDELVION® 21-Day (EU)*
- **FY21**: IDELVION® 21-Day (JP)*

* 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

* 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

**New Initial Marketing Authorization Approvals**
- Hizentra 5% (Pediatric Indication)
- CSL889 (Hemopexin) (treatment SCD)

**New Line Extensions/Indications Approvals**
- 2yr+ age extension approval
- CIDP optimized dosing
- 3500 IU 9yrs+

**Orphan Drug Designation**
- AlbuRx®
- Beriante®
- Rhophylac®
Focus Through Our Therapeutic Areas and Platforms

Therapeutic Areas
- Immunology
- Haematology
- Respiratory
- Cardiovascular and Metabolic
- Transplant
- Influenza Vaccines (Seasonal, Pandemic)

Platforms
- Plasma Fractionation
- Recombinant Technology
- Cell and Gene Therapy
- Adjuvanted Cell-based Egg-based sa-mRNA
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**

<table>
<thead>
<tr>
<th>Research</th>
<th>Pre-Clinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Registration/Post-Registration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gene Therapy Treatments PID</td>
<td>CSL888 Haptoglobin (SAH)</td>
<td>CSL324 Anti-G-CSFR mAb (HS)</td>
<td>HIZENTRA® (SSc)</td>
<td>HIZENTRA® (DM)</td>
<td>PRIVICEN® (PID) JP</td>
</tr>
<tr>
<td>Discovery Projects</td>
<td>CSL510 Modified Fibrinogen</td>
<td>CSL730 rFc Multimer</td>
<td>CSL630 pdFVIII Ruiude</td>
<td>HAEGARDA® Japan</td>
<td>IDELVION® rFIX rF (Haem B)</td>
</tr>
<tr>
<td>Discovery Projects</td>
<td>CSL40 Novel Complement Inhibitor</td>
<td>CSL899 Hemopexin (SCD)</td>
<td>CSL346 Anti-VEGF-B mAb (EKB)</td>
<td>Garadacimab Anti-FXIIa mAb (HAE)</td>
<td>AFSTYLA® rFVIII (Haem A)</td>
</tr>
<tr>
<td>Discovery Projects</td>
<td>sa-mRNA Influenza Vaccine</td>
<td>CSL200 CAL-H (SCD)</td>
<td>Garadacimab Anti-FXIIa mAb (LDIFP)</td>
<td>EtranaDex® Etranacogone dezaparvovec</td>
<td>ZEMAIRA®/RESPREEZA® Alphal-Proteinase Inhibitor</td>
</tr>
<tr>
<td>Discovery Projects</td>
<td>LASN01 Anti-IL-11R</td>
<td>CSL787 Nebulised Ig</td>
<td>Garadacimab Anti-FXIIa mAb (ARDS)</td>
<td>KCENTRA® 4F-PCC (Trauma)</td>
<td>AFLURIA® QUAD Egg-based Influenza Vaccine</td>
</tr>
<tr>
<td>Discovery Projects</td>
<td>P. Gingivitis (Periodontal Disease)</td>
<td>CSL11 Anti-Beta Common mAb</td>
<td>Adjuvanted Cell Culture Influenza Vaccine (aQIVC)</td>
<td>CSL12 ApoA-1 (ACS)</td>
<td>FLUCELVAX® Quadrivalent Cell-based Influenza Vaccine</td>
</tr>
<tr>
<td>Discovery Projects</td>
<td></td>
<td>UQ/CSL V451 [aC0V2]</td>
<td>Mavrilimumab Anti-IL-6R mAb (AD)</td>
<td>Clazakizumab Anti-IL-6 Med (AMR)</td>
<td>FLUAD® Quadrivalent Adjuvanted Influenza Vaccine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CSL334/ASLAN004 Anti-IL-15R mAb (IPD)</td>
<td></td>
<td>CSL964 Alpha-1-Antitrypsin (Treatment of CVD)</td>
<td>AUDENZ™ Adjuvanted Monovalent Influenza A (H5N1) Vaccine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CSL964 Alpha-1-Antitrypsin (Prevention of CVD)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>COVID-19 Hyperimmune Therapy</td>
<td></td>
</tr>
</tbody>
</table>

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

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

Driven by Our Promise™
R&D Product Progression in FY21

**Phase II**
- aQIVc
  - MF59® plus
  - FLUCELVAX® antigen
- CSL964
  - Alpha-1Antitrypsin
  - (Prevention of GvHD)

**Phase III**
- Caradacimab
  - Anti-FXIIa mAb (HAE)

**Registration/Post-Registration**
- HAEGARDA®
  - HAE
- HIZENTRA®
  - (SCIg) 20% Liquid
- PRIVIGEN®
  - (IVig) 10% Liquid
- AUDENZ™
  - Adjuvanted Monovalent
  - Influenza A (H5N1) Vaccine
- FOCLEVIA®FOCETRIA
  - Adjuvanted Egg-based
  - Influenza A (H5N1) Vaccine
- PANVAX®
  - Egg-based Influenza Vaccine

Legend:
- Immunology
- Transplant
- Influenza Vaccines
Kcentra® in Trauma

Trauma is the leading cause of morbidity and mortality in the US*
Haemorrhage is the most common, preventable cause of early death following Trauma

~880k
patients suffer traumatic injury annually in US

~85%
of haemorrhagic deaths occur within 6 hours

35-40%
of Trauma patients experience life threatening Acute Major Bleeding (AMB)

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

Data from preclinical and clinical 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
• Up to 8,000 patients

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

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
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
TA Research Strategy

- **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

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

**Individual Therapeutic Area (TA) Research Strategies**

- **Immunology**
- **Hematology**
- **Respiratory**
- **Cardiovascular & Metabolic**
- **Transplant**
Development of Garadacimab for Progressive Fibrosing Interstitial Lung Disease (PF-ILD)/ Idiopathic Pulmonary Fibrosis (IPF)

Role of FXII in Fibrogenesis

- **Hereditary Angioedema**
- **↑Vascular Permeability**
  - Bradykinin
- **↑Coagulation/wound clot formation and contact activation**

**FXIIa-β**

- **M0 Macrophage**
- **M1 Macrophage**
- **M2 Macrophage**
- **↑M2 hyper-polarization and pro-healing cytokines**
- **IL-6**

**Fibroblast**

**Fibrosis**

**↑ 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

Phase II – expected to commence H2 FY22

* Parental Monoclonal Antibody (mAb) of Garadacimab

Driven by Our Promise™
Research External Innovation & Collaboration Strategy

The Competition for Innovation

CSL
Research
Pipeline

Global Research site locations

Global funding & collaboration initiatives

Partnerships with universities, MRIs, hospitals, biotechs

Scouting & disruptive technology reviews

Partnering conference attendance & sponsorship

Partnerships with incubators, accelerators & venture funders

Abbreviations: MRI – Medical Research Institute

Driven by Our Promise™
Research External Innovation & Collaboration Strategy
Centre for Biologic Therapies

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


Driven by Our Promise™
**EtranaDez (Etranacogene dezaparvovec)**

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

- AMT-060 $5 \times 10^{12}$ Wild-Type FIX
- AMT-061 $5 \times 10^{12}$ Padua FIX

Gene Therapy for Immune Deficiencies

- 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

<table>
<thead>
<tr>
<th>Platform</th>
<th>Technologies</th>
<th>PIDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ex Vivo HSC Gene Therapy Platform</td>
<td>Lentiviral Gene Therapy Other Gene Editing Approaches</td>
<td>Wiskott-Aldrich Syndrome (WAS) X-linked Agammaglobulinemia (XLA) X-linked hyper IgM Syndrome (XHIM)</td>
</tr>
</tbody>
</table>

Abbreviations: PID – Primary Immune Deficiency, HSC – Hematopoietic Stem Cell
Gene Therapy for Immune Deficiencies

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

Phase I/II – expected to commence H1 FY23

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

Driven by Our Promise™
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%.

---

<table>
<thead>
<tr>
<th>Program &amp; Target</th>
<th>Discovery</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Anticipated Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASLAN004</td>
<td>Anti-IL-13Rα1</td>
<td>Atopic Dermatitis (AD)</td>
<td></td>
<td></td>
<td>Initiate Phase IIb - 4Q 2021</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Asthma*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*second indication to be confirmed

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)

<table>
<thead>
<tr>
<th>Endpoint (8 weeks)</th>
<th>RITT (n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>600mg (n=16)</td>
</tr>
<tr>
<td>Mean % change from baseline in EASI</td>
<td>-64.9</td>
</tr>
<tr>
<td>EASI-50 (%)</td>
<td>81.3</td>
</tr>
<tr>
<td>EASI-75 (%)</td>
<td>68.8</td>
</tr>
<tr>
<td>EASI-90 (%)</td>
<td>37.5</td>
</tr>
<tr>
<td>IGA 0/1 (%)</td>
<td>43.8</td>
</tr>
<tr>
<td>Mean % change from baseline in peak pruritus Numerical Rating Scale</td>
<td>-38.6</td>
</tr>
<tr>
<td>Mean change from baseline in POEM</td>
<td>-9.8</td>
</tr>
</tbody>
</table>

- 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

<sup>1</sup> 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

Phase II – initiating 4Q 2021
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.

---

Abbreviations: ARDS – Acute Respiratory Disease Syndrome.
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 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

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

>17,000 Acute Myocardial Infarction (AMI)

1\textsuperscript{st} Endpoint: MACE
- D90

MACE Follow Up
- D180
- D365

6g CSL112 Placebo

Screening Randomisation

Phase III – ongoing
EtranaDez
Gene Therapy (AAV5-Padua FIX) for Treatment of Haemophilia B

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

Abbreviations: AAV5 - Adeno-Associated Virus serotype 5;
BLA – Biologic Licence Application;
MAA – Market Authorisation Application
EtranaDez – HOPE-B Study 12 Month Data

- 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
- FIX activity similar (~44%) in participants with and without pre-existing nAbs to AAV5
- 96% of patients discontinued prophylaxis
- Mean FIX activity Ph IIb patients stable and durable at 2.5 years
- 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 Pipe, S.W. et al., (2021) ISTH, PB0653
2 Gomez, E. et al., (2021) ISTH, LPB0020

Abbreviations: AAV5 - Adeno-Associated Virus serotype 5
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

Hizentra® SSc - SURPASS

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

• Study fully enrolled ahead of schedule
• Anticipated study completion 2022
Hizentra® DM - RECLAIMM

Phase III Study of Hizentra® in Adults with Dermatomyositis

Active DM with/without Muscle Weakness

Screening → Randomisation

Weeks 1-53

Hizentra® 0.5g/kg → Hizentra® 0.5g/kg

Placebo → Hizentra® 0.5g/kg

Weeks 1-25

Weeks 25-53

Primary Endpoint:
Total Improvement Score
Responder Status

Long-term Follow-up

Phase III – ongoing

Driven by Our Promise™
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

Monthly SC Garadacimab Markedly Reduces Mean HAE Attack Rate
(Phase II Study Results)

<table>
<thead>
<tr>
<th>Dose</th>
<th>Mean Reduction*</th>
<th>Mean Reduction in HAE Attacks per Month vs Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garadacimab 75 mg q4w (n=9)</td>
<td>88.68%</td>
<td>0.48 (-0.33–1.29)</td>
</tr>
<tr>
<td>Garadacimab 200 mg q4w (n=8)</td>
<td>98.94%</td>
<td>0.05 (-0.06–0.15)</td>
</tr>
<tr>
<td>Garadacimab 600 mg q4w (n=7)</td>
<td>90.50%</td>
<td>0.40 (-0.07–0.88)</td>
</tr>
<tr>
<td>Placebo q4w (n=8)</td>
<td></td>
<td>4.24 (2.74–5.75)</td>
</tr>
</tbody>
</table>

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

Driven by Our Promise™
Garadacimab - CSL’s First mAb in Phase III

**Phase I**
- Safety, PK

**Phase II**
- Efficacy, Safety, PK/PD
- 3 doses & placebo tested

**Phase III**
- Efficacy, Safety, PK/PD
- Double-blind, Placebo-controlled
- Safety Extension
  - Including Phase II, Phase III & Naive Patients

**Completed**
- Healthy
  - Broad dose range
  - IV & SC
- ~40 HAE patients
  - POC
  - Dose selection, Safety, PK/PD

**Ongoing**
- ~60 HAE patients
  - Pivotal, Confirmatory
  - Efficacy, Safety, PK/PD, QoL
- ~150 HAE patients
  - Long term safety
  - Efficacy, PK/PD, QoL

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

Global submission targeted 2023
Comparable Efficacy of HAEGARDA® for HAE in Japanese Patients

**Global Phase III Pivotal Study**

- **Median Number of Attacks/month**
  - Placebo (n=42): 3.8
  - CSL830 (n=43): 0.3

- **Percentage of Patients with ≥50% Attack Reduction**
  - ≥ 50%: 90%
  - ≥ 70%: 82.5%
  - ≥ 90%: 57.5%
  - ≥ 100%: 40%

**Japan Phase III Study**

- **Median Number of Attacks/month**
  - Run-in (n=9): 3.6
  - CSL830 (n=9): 0

- **Percentage of Patients with ≥50% Attack Reduction**
  - ≥ 50%: 100%
  - ≥ 70%: 77.8%
  - ≥ 90%: 66.7%
  - ≥ 100%: 66.7%
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\(^\circledast\) revenue growth; continued success in CIDP

Immunology
- Strong growth from HAEGARDA\(^\circledast\) and KCENTRA\(^\circledast\)
- HAEGARDA\(^\circledast\) most patients since launch; 14% revenue growth
- KCENTRA\(^\circledast\) continued penetration vs FFP

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

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

2016

Total Global Market Value ~$27.0B

- Immunoglobulins $9.0B
- Haemophilia $10.8B
- Specialty $3.4B
- Albumin $3.8B

5-Year CAGR:
- Total Market: 6%
- Ig: 12%
- Specialty: 8%
- Haemophilia: 2%
- Albumin: 2%

2021

Total Global Market Value ~$36.8B

- Immunoglobulins $15.8B
- Haemophilia $11.7B
- Specialty $5.1B
- Albumin $4.2B

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

- PID 25%
- CIDP 22%
- SID 20%
- Other 23%
- MG 5%
- ITP 6%

$15.8B

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

Driven by Our Promise™
Immunoglobulins

FY21 Sales: $4,238M¹

Up 3%²

Christal: living with chronic inflammatory demyelinating polyneuropathy (CIDP)

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

US Ig Volume Mix Evolution³

<table>
<thead>
<tr>
<th>Year</th>
<th>Hizentra®</th>
<th>Privigen®</th>
<th>Carimune®</th>
</tr>
</thead>
<tbody>
<tr>
<td>FY17</td>
<td>61%</td>
<td>27%</td>
<td>13%</td>
</tr>
<tr>
<td>FY18</td>
<td>64%</td>
<td>27%</td>
<td>10%</td>
</tr>
<tr>
<td>FY19</td>
<td>68%</td>
<td>31%</td>
<td>1%</td>
</tr>
<tr>
<td>FY20</td>
<td>67%</td>
<td>33%</td>
<td>0%</td>
</tr>
<tr>
<td>FY21</td>
<td>63%</td>
<td>37%</td>
<td>0%</td>
</tr>
</tbody>
</table>

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

- Supply tightness intensified by COVID-19
- Privigen® volume impacted by shift to Hizentra®
- Global demand remains strong in core indications
Reasons for IVIg to Hizentra® Switch¹

- Need more flexibility/time: 39%
- Having problem finding a vein: 30%
- Impossibility of getting to the infusion center due to COVID-19: 26%
- Difficulty getting to IV infusion centers: 22%

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 PID¹ 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
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

Total Hizentra® CIDP Patients by Region\(^1\)\(^2\)

- **NA**
- **EU**
- **APAC**
- **ICO**

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

---

Driven by **Our Promise™**
**IDELVION®**
- Standard of care for Haemophilia B
- Maintained leadership 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

**HUMATE®**
- Strong revenue growth of 13% in the US

---

**Haemophilia**

FY21 Sales: $1,107M
Down 4%

Logan: living with Haemophilia B.

---

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

IDELVION® rFIX Prophylaxis Patient Share by Country

- Germany
- Italy
- Japan
- Spain
- Switzerland
- UK
- US
- Launched Markets Average

Market Share (Patient) %

Source: Data on file

Driven by Our Promise™
AFSTYLA® - Market Shares Within Key Markets

AFSTYLA® rFVIII Prophylaxis Patient Share by Country

Market Share (%)

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).

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.

KCENTRA®
- Remains the gold standard for warfarin reversal in the US
- Substantial growth opportunities, with FFP still used in ~40% of patients² in the US
- Demand rebounded to pre-COVID levels in the US

HAEGARDA®/Berinert SC®
- Offers best in class efficacy³
- 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
KCIENTRA® Growth in US

- KCIENTRA® remains first and only FDA approved 4F-PCC for reversing patients on warfarin
- KCIENTRA® is supported by multiple clinical guidelines as the preferred reversal agent
- ~1.7M patients on warfarin, with ~25k new patient starts per month
- KCIENTRA® 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
HAEGARDA®/Berinert® SC
Growth in the Face of Competition

- US: Most patients since launch
- EU/AU: New launches exceeding expectations
- Spain achieved 55% patient share 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

Driven by Our Promise™
HAEGARDA® /Berinert® SC Growth Potential

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

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

---

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

1 CSLB New Products include Hizentra® CIDP, Privigen® CIDP, HAEGARDA®/Berinert® SC, AFSTYLA® & IDELVION®

2 CAGR calculated off base of FY18 when launch occurred

Driven by Our Promise™
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)

**aQlVc**
- 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 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

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

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

### Flucelvax® - Benefit of Cell Culture

<table>
<thead>
<tr>
<th>Comparator</th>
<th>Study</th>
<th>Season</th>
<th>Age Group</th>
<th>Outcome*</th>
<th>% rVE (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>QIV</td>
<td>Boikos (2020)</td>
<td>2017/18</td>
<td>2-4</td>
<td>GP</td>
<td>36 (26, 45)</td>
</tr>
<tr>
<td>QIV</td>
<td>Divino (2020)</td>
<td>2017/18</td>
<td>4-64</td>
<td>Hospitalization</td>
<td>14 (9, 20)</td>
</tr>
<tr>
<td>QIV</td>
<td>Boikos (2021)</td>
<td>2018/19</td>
<td>2-4</td>
<td>Hospitalized or ED/GP</td>
<td>8 (7, 9)</td>
</tr>
<tr>
<td>QIV</td>
<td>Krishnarajah (2021)</td>
<td>2018/19</td>
<td>4-64</td>
<td>Hospitalization</td>
<td>7 (0.1, 13)</td>
</tr>
<tr>
<td>QIV</td>
<td>CORE (2021)</td>
<td>2019/20</td>
<td>2-4</td>
<td>Hospitalized or ED/GP</td>
<td>17 (16, 19)</td>
</tr>
<tr>
<td>QIV</td>
<td>HEOR (2021)</td>
<td>2019/20</td>
<td>4-64</td>
<td>Hospitalization</td>
<td>5 (1, 10)</td>
</tr>
</tbody>
</table>

*Outcomes due to influenza or pneumonia

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

---

Pelton, S.I. et al., (2020) Vaccines 8:446
CORE (2021): Presented at ECCMID 2021, manuscript pending
HEOR (2021): Manuscript pending

**Abbreviations:** CI - Confidence Interval; ED - Emergency Department; GP - General Practitioner; rVE - (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

4 Influenza Subtypes co-circulate

Frequent Antigenic Drift

Pre-existing Immunity

Waning - Developing Immune System

Protein + Adjuvant

Self-amplifying mRNA
Improving Influenza Vaccines by Combining Two Advanced Technologies

Cell-based Vaccine

Circulating Strains

Egg-based Vaccine

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

HF59® Adjuvant Drives Higher Immunogenicity

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

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

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

- **2008** Initiation of sa-mRNA research
- **2012** DARPA funds platform development
- **2015** SEQ continues Flu vaccine development
- **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

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

<table>
<thead>
<tr>
<th>Replicon Genes</th>
<th>Gene of Interest</th>
</tr>
</thead>
</table>

Bicistronic = 2 genes of interest encoded by mRNA

<table>
<thead>
<tr>
<th>Replicon Genes</th>
<th>Gene of Interest 1</th>
<th>Linker</th>
<th>Gene of Interest 2</th>
</tr>
</thead>
</table>

- 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

Key lipids

mRNA

100 nm

LNP

Driven by Our Promise™
sa-mRNA Platform Expresses More Protein than First Generation mRNA

In vivo Protein Expression

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

Unpublished data, Seqirus

Driven by Our Promise™
B-cell (Antibody) Response
- Serum antibodies (IgG): Protect lungs
- Mucosal antibodies (IgA): Prevent infection

T-cell Response
- CD4+ T cells (T helper): Increase B-cell response
- CD8+ T cells (CTLs): 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

COVID sa-mRNA Vaccination Cellular Responses

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

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

- 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

Influenza Hemagglutination Inhibition

- H1
- H3
- Bv
- By(c)

sa-mRNA Monovalent vaccine at 1 ug dose per target strain;
sa-mRNA Quadrivalent vaccine at 1 ug dose per strain
sa-mRNA SARS-CoV-2 Vaccines Protect Hamsters Against Viral Challenge
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

**Phase I**
- CSL324: Anti-G-CSFR mAb (HS)
- CSL730: rFc-Multimer
- CSL889: Hemopexin (SCD)
- CSL787: Nebulised Ig
- CSL311: Anti-Beta Common mAb
- ASLAN004: Anti-IL-13R mAb (AD)

**Phase II**
- HIZENTRA®: Anti-FXIIa mAb (HAE)
- Garadacimab: Anti-FXIIa mAb (LD/PP)
- CSL346: Anti-VEGF-B mAb (DKD)
- CSL112: apoA-I (AMI)
- Clazakizumab: Anti-IL-6 mAb (AMR)
- CSL964: Alpha 1 Antitrypsin (Treatment of GvHD)
- CSL964: Alpha 1 Antitrypsin (Prevention of GvHD)

**Phase III**
- Garadacimab: Anti-FXIIa mAb (HAE)
- HIZENTRA®: Anti-FXIIa mAb (LD/PP)
- EtranaDez: Etranacogene dezaparvovec (Haem B)
- KCENTRA®: 4F-PCC (Trauma)
- HIZENTRA®: Anti-FXIIa mAb (LD/PP)
- PRIGEN®: Anti-FVIII (IVIg) 10% Liquid
- ASLAN004: Anti-GM-CSFR mAb (GCA, COVID)
- ZEMAIRA®/RESPREEZA®: Alpha-1 Antitrypsin
- FOCLIVIA®/FOCETRIA: Adjuvanted Egg-based Influenza A (H5N1) Vaccine

**Registration/Post-Registration**
- FLUAD®: Adjuvanted Monovalent Influenza A (H5N1) Vaccine
- AUDENZ™: Adjuvanted Monovalent Influenza A (H5N1) Vaccine
- FLUAD® QUAD: Egg-based Influenza Vaccine
- AFLURIA® QUAD: Cell-based Influenza Vaccine
- FLUAD® Quadivalent: Adjuvanted Influenza Vaccine
- FLUCELVAX® Quadivalent: Egg-based Influenza Vaccine
- PANVAX®: Egg-based Influenza Vaccine
Significant Target Launch Dates

FY22

- **HAEGARDA®**
  - Japan (HAE)

FY23-FY26

- **Garadacimab**
  - Anti-FXIIa (HAE)
- **HIZENTRA®**
  - (DM)
- **IDELVION®**
  - China (Haem B)
- **Etranacogene dezaparvovec**
  - (Haem B)
- **CSL112**
  - ApoA-1 (AMI)
- **Clazakizumab**
  - Anti-IL-6 (AMR)
- **CSL964 AAT**
  - (GvHD Treatment)
- **Adjuvanted Cell Culture Influenza Vaccine (aQIVc)**
- **sa-mRNA Influenza Vaccine (sa-mRNA)**

**Categories:**
- 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