R&D Investor Briefing

December 4, 2019
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Introduction

William Mezzanotte, M.D.

Executive Vice President, Head of Research and Development
CSL Behring
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<td>Clinical Development Part 2 and Summary</td>
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<td>Panel Q&amp;A Session</td>
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Global Collaborations for Innovation Access

- Bern, Switzerland
- Marburg, Germany
- Amsterdam, Netherlands
- London, UK
- Liverpool, UK
- Siena, Italy
- Wuhan, China
- Tokyo, Japan
- Melbourne, Australia
- Sydney, Australia
- Pasadena, US
- Kankakee, US
- King of Prussia, US
- Summit, US
- Cambridge, US
- Holly Springs, US
- Dalhousie University
- Elektrofi
- CSL Behring
- Seqirus
- >1,700 scientists globally
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

* Includes R&D for CSL Behring and Seqirus. 
  m = US$ millions
Active R&D Support for Growth in Plasma Business

- Plasma Product Development
- Technical Operations
- Process Improvement
- New Formulations & Indications
- New Devices
- New Products
Focus Through Our Therapeutic Areas and Platforms

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

Platforms
- Plasma Fractionation
- Recombinant Technology
- Cell and Gene Therapy
- Adjuvanted Cell-based Egg-based
### R&D Portfolio – December 2018

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<tr>
<th>PRE-CLINICAL</th>
<th>PHASE I</th>
<th>PHASE II</th>
<th>PHASE III</th>
<th>REGISTRATION</th>
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<td>CSL200 (CAL-H)SCD</td>
<td>CSL730 rFc Multimer</td>
<td>CSL312 Anti-FXIIa HAE</td>
<td>PRIVIGEN® PID Japan</td>
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<td>CSL889 Hemopexin SCD</td>
<td>CSL324 Anti-G-CSFR</td>
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<td>CSL787 Nebulised Ig</td>
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<td>FLUCELVAX® QIV 9yrs+ EU</td>
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<td>CSL311 Anti-Beta Common</td>
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<td>HIZENTRA® CIDP</td>
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<td>P. gingivalis/POD</td>
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<td>ALSURIA® QIV 6M-4yrs AUS</td>
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### Partnered Projects

- Immunology and Neurology
- Haematology and Thrombosis
- Respiratory
- Cardiovascular and Metabolic
- Transplant
- Influenza Vaccines
### Key Past Launches from R&D Portfolio

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<td>AFLURIA® QIV</td>
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<td>AFLURIA® QIV 6M+ (AUS)</td>
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Notable Regional Regulatory Approvals
1 Dec 2018 – 20 Nov 2019

CSL842 (AMR*)
CSL964 (prevention GvHD**)
CSL964 (treatment GvHD**)

Beriate® 500

CSL842 (for treatment solid organ transplant)

Ongoing Activities
- Expanded Label for Enhanced Administration Parameters
- Expanded Label for Dosing Every 21 days in Patients ≥12yrs of Age
- Geographic Expansion
- Geographic Expansion
- Special Population Label Expansion
- aH5N1c New Registration in US

*AMR - Antibody-Mediated Rejection
**GvHD - Graft vs Host Disease
# Clinical Portfolio Progression in 2019

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<th>PRE-CLINICAL/PHASE I</th>
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<td>aQIVc (MF59 plus FLUCELVAX® antigen)</td>
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**Immunology and Neurology** | **Haematology and Thrombosis** | **Respiratory** | **Cardiovascular and Metabolic** | **Transplant** | **Influenza Vaccines**
### Key Partnerships and Collaborations

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<tr>
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<td><strong>Mavrilimumab GM-CSFR</strong></td>
<td><strong>Clazakizumab Anti-IL-6</strong></td>
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<td><strong>Denteric</strong></td>
<td><strong>CSL334 / ASLAN004 IL-13R</strong></td>
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<td><strong>ASLAN Pharmaceuticals</strong></td>
<td><strong>CSL964 GvHD Treatment</strong></td>
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### R&D Portfolio – December 2019

**Immunology and Neurology**
- CS730 rFc Multimer
- CSL324 Anti-G-CSFR
- CSL200 (CAL-H) SCD
- CSL312 Anti-FXIIa
- CSL311 Anti-Beta Common
- CSL346 Anti-VEGF-B
- CSL334 / ASLAN004 IL-13R

**Haematology and Thrombosis**
- Improved Fibrinogen
- CSL787 Nebulised Ig
- aQIVc (MF59 plus FLUCELVAX® antigen)
- P. gingivalis/POD
- CSL869 Hemopexin SCD
- CSL312 Anti-FXIIa Thrombosis
- CSL311 Anti-Beta Common
- CSL346 Anti-VEGF-B
- CSL334 / ASLAN004 IL-13R

**Respiratory**

**Cardiovascular and Metabolic**
- Mavrilimumab GM-CSFR

**Transplant**
- CSL964 GvHD Prevention

**Influenza Vaccines**
- FLUAD® QIV 6M+ KCENTRA® Japan
- AFLURIA® QIV 6M+ US, AUS

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<tr>
<th>RESEARCH</th>
<th>PRE-CLINICAL</th>
<th>PHASE I</th>
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<td>Pre-Pandemic aH5N1c</td>
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**Partnered Projects**

- Immunology and Neurology
- Haematology and Thrombosis
- Respiratory
- Cardiovascular and Metabolic
- Transplant
- Influenza Vaccines
Research, Gene and Cell Therapy

Dr. Andrew Nash
Senior Vice President, Research
CSL Behring
CSL Research

- **Capabilities and facilities**
  - [Image: Immunology and Neurology]
  - [Image: Haematology and Thrombosis]
  - [Image: Respiratory]
  - [Image: Cardiovascular and Metabolic]
  - [Image: Transplant]

- **New product opportunities**
  - **Plasma** – Haptoglobin for the treatment of Subarachnoid Haemorrhage (SAH)
    - Innosuisse grant awarded to the University Hospital Zürich and CSL Behring in 2017
  - **Recombinant** – CSL311 for the treatment of inflammatory disease
  - **Gene therapy** – Sickle Cell Disease (CSL200) and immune deficiencies
**CSL Research**

**New Facilities**

**Bio21 Institute, Melbourne**
- ~ 4100m² of lab and office space
- Parkville precinct
- Melbourne University, MRI’s
- 4 major teaching hospitals

**SITEM*, Bern**
- 2000m² of lab and office space
- Bern University and Hospital campus

*SITEM – Swiss Institute for Translational and Entrepreneurial Medicine

**Gene therapy, Pasadena**
- Expanding gene therapy expertise
  - Research, QA, cell processing and manufacture
  - Wet-lab space (non-GMP) tripled from 132 to 480 m²
  - GMP space (330 m²) to engineering qualification level
CSL Research
External Innovation Strategy

- Active partner in ~$700m of venture funding (Brandon Capital Partners)
- CSL – Walter and Eliza Hall Institute (WEHI)
  - Bioinformatics Alliance
  - CSL biologics discovery platform
- Research Acceleration Initiatives
  - AUS, EU and US
  - Innosuisse grant
  - University Hospital Zürich
- Strategic Partnerships
  - (universities, MRIs, hospitals)
- Funding & collaboration initiatives
- CSL R&D Pipeline
- Partnering conference attendance & sponsorship
- VC investment & partnerships
- Biotech partnerships
- Global Research site locations
- Momenta Aslan

m = AU$ millions
Haptoglobin for the Treatment of Subarachnoid Haemorrhage (SAH)

Pathophysiology of SAH

• Acute indication – rupture of an aneurysm in the brain, followed by bleeding and haemolyis within the subarachnoid space

• Survivors of initial bleeding are at risk for Delayed Ischemic Neurological Deficits (DIND)

• High mortality and morbidity
  – 5% of all strokes; high fatality rate
  – Very limited treatment options

• Haemoglobin (Hb) concentrations in cerebral spinal fluid (CSF) correlate with DIND in SAH patients

Source: www.strokecenter.org
Haptoglobin and SAH
Link Between CSF Hb Levels and DIND

39 year old, right-handed female with thunderclap headache, vomiting and loss of consciousness

Hb levels in CSF correlate with DIND

SAH patients (n=18) developing DIND have higher cumulative Hb exposure

Source: Hugelshofer et al. World Neurosurgery 2018
How the Body Deals with Toxic Free Haemoglobin (Hb) and Heme

Plasma proteins

- Opportunities to treat chronic and acute haemolytic disease
- Replacement and/or augmentation therapy
Haptoglobin for the Treatment of SAH
Haptoglobin Prevents Vasospasms Induced by Haemorrhagic CSF – ex vivo Functional Assay

Sheep Model of SAH

CSF From Sheep SAH Model

CSF Samples From SAH Patients

Source: J Clin Invest. 2019. https://doi.org/10.1172/JCI130630
Haptoglobin for the Treatment of SAH
Haptoglobin Prevents Penetration of Hb into Brain Tissue

Labeled Hb ± haptoglobin was injected into CSF 2 hours before analysis

Source: J Clin Invest. 2019. https://doi.org/10.1172/JCI130630
Haptoglobin for the Treatment of SAH

Summary

**Haemoglobin**
- Concentrations in CSF correlate with DIND in SAH patients
- Rapidly penetrates from CSF into the brain parenchyma
- Induces angiographic vasospasms in 100% of animals

**Haptoglobin**
- Blocks tissue penetration of cell-free Hb
- Prevents Hb induced vasospasms in ex vivo assay
- Prevents Hb induced segmental vasospasm in vivo

**Current Status - enter development H2 2020**

Source: www.strokecenter.org
Targeting multiple inflammatory mediators with a single therapeutic

Bone marrow → GM-CSF IL-3 & IL-5 → GM-CSF & IL-5 → Myeloid cell lineages → Airway Inflammation
CSL311 for the Treatment of Airways Inflammation

CSL311 Targets Multiple Cytokines via a Shared Receptor

CSL311

GM-CSF, IL-3 or IL-5 Rα-chain

GM-CSF
IL-3 & IL-5

Survival, Proliferation, Differentiation, Activation

Inflammation

Source: Panousis et al., Mabs 8:436, 20126
CSL311 for the Treatment of Airways Inflammation

*In Vivo* Efficacy in a Mouse Model of Human Airways Inflammation

Xenografting human nasal polyps into immunodeficient mice

- **GM-CSF**
- **IL-3**
- **IL-5**

**Source:** Yip et al., Allergy 2019 Sep 10. doi: 10.1111/all.14041
CSL311 for the Treatment of Airways Inflammation

In Vivo Efficacy – Mouse Model of Human Airways Inflammation

CSL311 restrains human nasal polyp xenograft progression *in vivo*

CSL311 treatment reduces mucous glad numbers and mucus production in nasal polyps *in vivo*

Source: Yip et al., Allergy 2019 Sep 10. doi: 10.1111/all.14041
CSL311 for the Treatment of Airways Inflammation

Summary

• CSL311 is a potent antagonist of IL-3, IL-5 and GM-CSF in vitro
• CSL311 inhibits the activity of multiple cell types involved in inflammation
• CSL311 demonstrates efficacy in an in vivo translational model of airways inflammation
• GLP Toxicology program successfully completed
**CSL Gene Therapy**

*In Vivo vs Ex Vivo Gene Therapy*

---

### Direct delivery

1. **Treatment or missing gene**
   - The treatment gene is added to a vector such as an adeno-associated virus (AAV).
   - ...which is delivered directly to the patient by injection.

### Cell-based delivery

1. **Treatment or missing gene**
   - The treatment gene is added to a harmless lentivirus.
   - ...which in turn introduces it to the isolated stem cells.

2. **The patients own stem cells are removed from the body and cultured**.

3. **The stem cells, now containing the treatment gene, are returned to the patient.**
Cell and Gene Therapy Research and Product Development

- 2+ years post-acquisition of Calimmune
- Integration into CSL R&D complete
- First clinical program recruiting patients
- Pipeline of early stage gene therapy projects

**Expertise/Know-how**
- Vector Design
  - Ability to design and make extremely efficient therapeutic vectors

**In Vivo Selection Tool**
- Select+™
  - Genetic cassette to render stem cells protected against well-known drug to drive *in vivo* selection

**Cell Processing**
- Proprietary Methods
  - Novel SOPs to achieve high cell yields and standardization of cell product

**Lenti Manufacturing**
- Cytegrity™
  - Only large-scale, stable vector production system used clinically
Sickle Cell Disease

- Group of disorders caused by abnormal beta-globin gene resulting in sickled red cells
- High unmet need

CSL200 for the Treatment of Sickle Cell Disease (SCD)

- CSL200 program aims to provide sufficient functional globin gene to prevent sickling
Gene Therapy for Wiskott-Aldrich Syndrome (WAS)

- WAS is a rare X-linked PID (~ 1:100,000 live births)
  - Mutations in the gene that encodes the WAS protein (WASp)
- WAS is exclusively expressed in blood cells and plays a key role in organizing the actin cytoskeleton, signal transduction and terminal differentiation
- WAS is characterised by:
  - Recurrent infections, microthrombocytopenia and eczema
  - An increased risk of autoimmune disorders and malignancy
  - Currently treated with IVIG
- Allogeneic Hematopoietic Stem Cell transplantation (HSCT) is the only available curative treatment

* Source: Icahn School of Medicine at Mt Sinai
Design and generation of lentiviral candidates based on our Cytegrity stable producer cell line backbone is in progress.
## Mechanism of Action Summary

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<th>Pathogen Neutralisation</th>
<th>Reduction of Pathologic Ig</th>
<th>Complement Scavenging</th>
<th>FcγR Expression Modulation</th>
<th>Immune Cells Modulation</th>
<th>Cytokine Modulation</th>
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- **No Activity**
- **Possible Activity**
- **Activity**
CSL Research

- Expanding capacity and capability across global research sites
- Continued investment in external innovation activities
- Leveraging our three strategic platforms across five therapeutic areas
- Continuing to innovate in areas of business strength
- Developing new opportunities in areas of unmet need
- Creating and progressing a sustainable portfolio of early stage opportunities
  - New gene therapy opportunities
Clinical Development – Part 1

Dr. Diana Lanchoney

Vice President, Clinical Pharmacology and Translational Development
CSL Behring
CSL Pipeline Progressing into Multiple New Disease Areas Using All Three Product Development Platforms

- **Sickle Cell Anemia** – CSL200 (lentiviral stem cell gene therapy), CSL889 (Hemopexin)
- **Contact Mediated Thrombosis** – Garadacimab (CSL312 Anti-Factor XIIa)
- **Respiratory Disease** – CSL311 (Anti-Beta Common)
- **Diabetic Nephropathy** – CSL346 (Anti-VEGF-B)
- **Neutrophilic Dermatoses** – CSL324 (Anti-GCSF)
- **Systemic Lupus Erythematosus** – CSL362 (Anti-IL-3Ra)
- **Scleroderma** – PRIVIGEN® and HIZENTRA®
- **Dermatomyositis** – HIZENTRA®
- **Hereditary Angioedema** – Garadacimab (Anti-Factor XIIa)
Overview of Sickle Cell Disease (SCD)

- Missense mutation of the β-globin gene
- Worldwide incidence ~300,000/year (US ~155,000)
- Sickle red blood cells are fragile, prone to endothelial adhesion
- Many downstream consequences
  - Avg. life expectancy 40 - 60yrs
- Vaso-occlusive crisis (VOC): commonly leads to hospitalization

Sickle Cell Anemia
CSL Programs Poised to Evolve the Paradigm

- Long Term Disease Management
  - Lentiviral stem cell gene therapy: CSL200
- Prophylaxis for VOC
- Treatment for VOC
  - Hemopexin: CSL889
- Supportive Care for VOC
CSL889 Hemopexin
Addresses the Toxic Effects of Free Heme

Chronic Intravascular Haemolysis

Vasculature
Haemolysis

Cell free haemoglobin → Plasma heme → Hemopexin (Hpx)

Hpx:heme

- Hemopexin, scavenger of heme with highest affinity
- Depleted in SCD

Hepatocytes

Clearance of free heme, and reduced inflammation
Garadacimab (CSL312 Anti-Factor XIIa)
Multiple Potential Indications

[Diagram showing the interactions between FXI, FXIIa, PK, C1 Inh, HK, BK, BR2, C1qr,s, and FXII in the context of haemostasis, vasodilation, vascular permeability, complement activation, and mitogenesis.]
Garadacimab (CSL312) Thrombosis Development Program Overview
Mechanism to Prevent Contact-Activated Thrombosis Without Bleeding Risk

Phase I (FIH study)
SAD in healthy subjects
- Safety
- Pharmacokinetics (PK)
- Biomarkers

Contact Activation Associated Thrombosis

Commercial Indications

Peripherally Inserted Central Catheter (PICC) Thrombosis
CSL311 Anti-Beta Common
A Broad Mechanism of Action With Potential to Address the Entire Spectrum of Severe Asthma

Asthma: ~300 million globally
Severe asthma: 2-10%

Source: https://www.atsjournals.org/doi/pdf/10.1513/AnnalsATS.201508-514MG
CSL311 Phase I Clinical Strategy Informs Early POC Expansion

2019-20
- Single Ascending Dose (SAD)
  - mild asthma
  - 1001a

2020-21
- Multiple Ascending Dose (MAD)
  - mild asthma
  - 1001b

2021+
- Proof of Concept (POC)
  - severe asthma exacerbation
  - endpoint dose range finding

Follow on indication
- chronic tox studies
- SC formulation

Follow on indication
CSL346 VEGF-B Antagonist

- CSL346 is a novel humanised monoclonal antibody (IgG4) that binds VEGF-B
- Strong renoprotective effects in diabetic kidney disease (DKD) animal models
- Phase II proof of concept study to start in early 2020

Source: http://dx.doi.org/10.1016/j.cmet.2017.01.004
Diabetes accounts for 30-50% of all chronic kidney disease

1 in 3 diabetics develop DKD over time

70% among them develop albuminuria (ACR ≥30 mg/g; i.e., incipient/overt nephropathy)

~300,000 People with DKD developed end stage renal disease (ESRD) in 2015

**CSL324 G-CSF Receptor Antagonist**

**G-CSF, neutrophils and inflammatory disease**

- Neutrophils are the most abundant white blood cells (WBC), $\sim 10^9$ cells / kg body weight leave the bone marrow daily.

- Excessive neutrophil production and persistence within tissues leads to chronic inflammation and tissue destruction.

- G-CSF plays a key role in neutrophil production, migration, lifespan and activation.

- No competitors known to pursue G-CSF inhibition: First-in-Class.
CSL324 G-CSF Receptor Antagonist Begins Phase Ib Study in Neutrophilic Dermatoses

- Hidradenitis Suppurativa (HS) and Other Neutrophilic Dermatoses (ND)
  - Hidradenitis Suppurativa – 1% prevalence
    - A disease of hair follicles, immune dysregulation
    - Chronic inflammation, discharge, scarring
    - Growing in prevalence, limited treatments
    - High impact on quality of life

- Phase I FIH trial complete
- Initiation of Phase Ib in HS / ND patients
- Safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and response

Systemic Lupus Erythematosus (SLE)

**Disease Features**
- Characterised by immunologic abnormalities, complex pathophysiology
- Heterogeneous disease

**Symptoms Diagnosis**
- Nearly every organ system may be affected
- Diagnosis based on clinical symptoms and laboratory testing

**Risk Factors**
- Women in childbearing years are most common
- Prevalence is higher in non-Caucasian populations

**Prognosis**
- Survival rate is ~90% at 10 years, driven by organ damage
- Quality of life may be significantly impacted
Strong Rationale for CSL362 Anti-IL-3Ra (CD123) in SLE

- Type 1 IFNs known to play a pivotal role in pathogenesis of SLE
- pDCs are the major producer of Type 1 IFNs
- CSL362 ex vivo
  - pDC depletion
  - Reduced interferon (IFN) gene signature
  - Basophil depletion
- Phase Ib in healthy volunteers and SLE patients to start in 1H2020

**Diagram:**
- Immune complex containing host-derived nucleic acid
- Stimulates TLR7 and 9
- pDC depletion
- Reduced interferon (IFN) gene signature
- Basophil depletion
- No production of IFN and other soluble factors
- Improvement of Symptoms
- Release of cytotoxic proteins → ADCC
Systemic Sclerosis (SSc)

- Most life-threatening rheumatic disease: 10-year cumulative survival is 62.5%
- Limited approved disease modifying agents
- Most treatments aimed at improving symptoms and managing complications
- Prevalence 7 - 43/100,000 (US/EU)

IMPRESS
PRIVIGEN® (IVIG) PhII, Efficacy and Safety Study

Screening
Up to 4 weeks

Double-Blind Treatment Period
48 Weeks

Week 48
End of DB Treatment

Open Label Treatment Period
24 Weeks

Week 72
End of OL Treatment

Subjects with dcSSc
2:1 Randomization

PRIVIGEN®
Placebo

PRIVIGEN®

End of Study (Safety F/U)
SURPASS
HIZENTRA® (SCIG) PhII, Safety and Bioavailability Study in Systemic Sclerosis

[Diagram showing study design]

- **Screening Patients with dcSSc**
- **Randomization**
  - Treatment Period A
    - Arm 1 (n=10)
      - HIZENTRA®
  - Treatment Period B
    - Arm 2 (n=10)
      - PRIVIGEN®

- 16 weeks
- Full PK Profile
Dermatomyositis (DM)

- Rare (2 - 9/100,000), serious, and life-threatening
  - 5-year mortality rate 10-30%
- Rash, muscle weakness, dysphagia, and systemic manifestations (heart, lung, gut, cancer) and specific autoantibodies
- Female predominant, typical onset in adults late 40’s – 60’s, in children 5 – 15yrs

HIZENTRA® DM Treatment Study Design

Weeks 1 to 53

Weeks 1 to 25

Weeks 25 to 53

Primary endpoint:
TIS responder status

126 patients,
1:1 randomisation

Driven by Our Promise™
Garadacimab Phase II Hereditary Angioedema (HAE) Study
Completed Double Blind Period

Run-in period
4–8 weeks
1:1:1:1
First 32 patients

Treatment Period 1
~13 weeks
Placebo q4W SC
Low dose Garadacimab q4W SC
Medium dose Garadacimab q4W SC
High dose Garadacimab q4W SC

Extension
≥44 weeks
Garadacimab SC

All subjects may use on-demand therapy to treat episodes of edema

Screened subjects with C1-INH HAE
CSL Pipeline Progressing into Multiple New Disease Areas Using All Three Product Development Platforms

- **Sickle Cell Anaemia** – CSL200 (lentiviral stem cell gene therapy), CSL889 (Hemopexin)
- **Contact-Mediated Thrombosis** – CSL312 Garadacimab (Anti-Factor XIIa)
- **Respiratory Disease** – CSL311 (Anti-Beta common)
- **Diabetic Nephropathy** – CSL346 (Anti-VEGF-B)
- **Neutrophilic Dermatoses** – CSL324 (Anti-GCSF)
- **Systemic Lupus Erythematosus** – CSL362 (Anti-IL-3Ra)
- **Scleroderma** – PRIVIGEN® and HIZENTRA®
- **Dermatomyositis** – HIZENTRA®
- **Hereditary Angioedema** – CSL312 Garadacimab (Anti-Factor XIIa)
Mr. Bill Campbell

Executive Vice President and Chief Commercial Officer
CSL Behring
Global Commercial Operations at a Glance

- **~1,800** Commercial employees
- **35** Affiliate Offices
- **US$7.2 Billion** in annual revenue
- Conducting business in **100+ Countries**
- **4 Commercial Regions**
- **5 Therapeutic Areas**
FY’19 Highlights

- Strong Business Performance
- Balanced Regional Growth: 9% – 17%
- Executing to Plan on New Launches
- Ig Growth well Above Market
- Expanding Market Presence through New Affiliates
- China GSP License Establishment
- Implemented TA Structure / Model
Strong Demand Across the Portfolio

**Ig**
- Strong underlying market growth
- Disciplined approach to market expansion
- Growth driven by volume and mix improvements

**Coagulation**
- Market leadership with IDELVION® in key markets
- Additional launch opportunities for AFSTYLA® / IDELVION®
- Life-cycle expansion (21-day dosing)

**Specialty**
- New launches with HAEGARDA®
- Continued growth of KCENTRA® in the US

**Albumin**
- Disciplined approach in China
- Volume growth in all regions
Immunoglobulin Market

Market Dynamics

- Increasing awareness and diagnosis
- Growth in PID and CIDP
- Expanding usage for SID
- Potential new indications
- Continued market supply tightness

Global IG Volume by Indication 8% Growth

- PID 28%
- CIDP 24%
- SID 16%
- Other 21%
- ITP 6%
- MG 5%

Source: Data on file
CSL Portfolio: Immunoglobulin

Positioned for Continued Growth

- Market Leading Products
- Substantial volume and share growth
- Balanced growth across all regions
- IV and SC for CIDP
- History of Innovation

Source: Data on file
M = US$ millions
#1 Prescribed IVIG Worldwide

Proven effective and well tolerated in **12+ years**

Used in **>100,000 patients** with chronic disease in the last year

Approved for use in multiple indications

**Indications:**
- **EU:** PID, SjD, ITP, GBS, KD, CIDP, MMN
- **US:** PID, ITP, CIDP
- **CA:** PID, SjD, ITP, CIDP
- **JP:** CIDP
- **AUS:** PID, SjD, ITP, GBS, CDP, MMN, MG, Lambert-Eaton Myasthenic Syndrome (LEMS), Stiff Person Syndrome (SPS)

Source: Data on file
PRIVIGEN® Performance Through Q2’19

Share of IVIG Market (Volume) Total 7MM

Q1’17 | Q2’17 | Q3’17 | Q4’17 | Q1’18 | Q2’18 | Q3’18 | Q4’18 | Q1’19 | Q2’19

Privigen | 23% | 23% | 24% | 24% | 23% | 24% | 24% | 26% | 27% | 28%
Competitor A | | | | | | | | | |
Competitor B | | | | | | | | | |
Competitor C | | | | | | | | | |
Competitor D | | | | | | | | | |

Source: Data on file
HIZENTRA®
Expanding Global Market Leadership: 57 Countries

Innovator, Market Leader,
Most Prescribed SCIG Worldwide

Proven efficacy and tolerability since 2010

100,000 patient-years of experience

More than 6,000,000 exposures worldwide*

Source: Data on file
*Hizentra® also has SID indication in most countries outside of the US.
HIZENTRA® Undisputed Market Leader in SCIG

Source: Data on file
HIZENTRA® Addresses Unmet Needs in CIDP

Approved March ‘18 US & EU
Approved March ‘19 Japan

Interest & Awareness
Remains High

Market Share Growth With
Both Privigen & Hizentra

Orphan Exclusivity Granted
for Hizentra CIDP

Source: Data represents patients reporting a preference between IVIG in the pre-randomised phase and HIZENTRA® in the randomised phase of the phase III study of subcutaneous immunoglobulin for the treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) – the PATH study.
CSL Behring on Track to Become Market Leader in CIDP

Source: Data on file
Market Leadership in Ig Therapy

Past
- **1979**: 1st IVIG, Sandoglobulin®
- **2006**: 1st SCIG, Vivaglobin®
- **2007**: Next generation IVIG, PRIVIGEN®
- **2010**: 1st 20% SCIG, HIZENTRA®
- **2013**: 1st SCIG in Japan, HIZENTRA®
- **2013**: CIDP in EU, PRIVIGEN®
- **2015**: 1st flexible dosing, HIZENTRA®

Present
- **2017**: CIDP in US, PRIVIGEN®
- **2018**: 1st SCIG in CIDP, HIZENTRA®
- **2018**: 1st SCIG in PFS, HIZENTRA® (Canada)
- **2019**: MMN EU, PRIVIGEN®

Future
- 1st SCIG up to 100 mL/hour, HIZENTRA®
- 1st SCIG with manual push, HIZENTRA®
- 1st SCIG in 5, 10 & 20 ml PFS, HIZENTRA®
- IsoLo label enhancement, PRIVIGEN®
- New indications: Dermatomyositis, Systemic Sclerosis
Panel Q&A Session
Break – 15 minutes
Commercial – Part 2

Mr. Bill Campbell
Executive Vice President and Chief Commercial Officer
CSL Behring
Haemophilia Market

Market Dynamics

- New therapies continue to increase competitiveness in Hem A segment
- Patient education about Prophylaxis in Hem B driving utilization of long acting products
- VWD is underserved due to lack of awareness/understanding of the disease

Source: Data on file
B = US$ billions
Haemophilia Portfolio

- 40% growth*
- Continued patient switching
- Additional countries to launch
- 21 day dosing
- Transformational product

- 85% growth*
- Long lasting and reliable bleed protection
- Successful product transition
  HELIXATE® phased out

- Leadership position in VWD: 59%^ market share globally

Recombinant Coags +7%*

vWD +7.5%*

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

^Source: Data on File
Based on 5 major markets (US, Japan, Germany, Italy and UK) where IDELVION® is reimbursed and commercially available.
Source: Data on File
### Positioning AFSTYLA® in a Competitive Market

<table>
<thead>
<tr>
<th>Feature</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higher binding affinity to vWF</td>
<td>• Unique single-chain molecular structure provides increased binding</td>
</tr>
<tr>
<td></td>
<td>• Enhanced binding affinity protects AFSTYLA® from degradation, extending time in circulation</td>
</tr>
<tr>
<td>2x weekly dosing</td>
<td>• FDA-approved for 2x or 3x weekly dosing</td>
</tr>
<tr>
<td></td>
<td>• Factor trough levels above 1.9% with 2x weekly dosing</td>
</tr>
<tr>
<td>Excellent bleed protection</td>
<td>• ZERO bleeds (median AsBR*) in all patients, regardless of age and dosing frequency</td>
</tr>
<tr>
<td>Low annual consumption</td>
<td>• AFSTYLA® delivers the benefits of an EHL† with the lowest annual consumption</td>
</tr>
</tbody>
</table>

* AsBR: Annualised spontaneous bleeding rate  
† EHL: Extended half life
CSL Portfolio: Specialty Products

M = US$ millions
Continued Growth Opportunity for KCENTRA®

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

Anticoagulation Market US¹

- Warfarin
- Product A
- Product B
- Other

Warfarin Market US (Patients)¹

0 200,000 400,000 600,000 800,000 1,000,000 1,200,000 1,400,000 1,600,000 1,800,000

Warfarin Reversal Market US²

- KCENTRA® 45%
- FFP & Others, 55%

¹Neurocritical 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
Sources: 1. Data on File. 2. (RWD) Charge Master Data & Medical History Data.
KCENTRA® Growth in US Since Launch

**KCENTRA®**

- KCENTRA® remains the first and only FDA approved 4F-PCC for reversing patients on warfarin
- KCENTRA® is supported by multiple clinical guidelines as the preferred reversal agent
- KCENTRA® growth driven by:
  - Penetration within existing large hospital systems
  - Expansion into new regional accounts

Source: Data on file
#1 prescribed therapy in the US for the prevention of HAE attacks

Address C1-INH deficiency with HAEGARDA®

C1-INH has been used in HAE > 35 years

HAEGARDA® reduced HAE attacks by 95%*

Rescue medication use was reduced by >99%†‡1

*Median reduction in number of attacks in patients receiving 60 IU/kg of HAEGARDA® vs placebo.
†Median reduction in rescue medication use in patients receiving 60 IU/kg of HAEGARDA® vs placebo.
‡The World Allergy Organization (WAO) guidelines for the management of HAE state that patients should have HAE rescue medication available at all times.

References: 1. Data on file
HAE Prophylaxis Market

- HAEGARDA® is the market leader in HAE prophylaxis in the US
- Rapid uptake at launch
- Significant brand loyalty
- Additional capacity to support new launches

Source: Data on file
Why HAEGARDA®?

HAEGARDA® Patients Rely On C1-INH For Efficacy And Safety

“I’ve been on HAEGARDA for one year, and I haven’t had an attack. It allows me to be more independent, confident, and free because I can take it with me wherever I go and don’t have to depend on anyone.” – Zahra

“Having a therapy that addresses the root cause of HAE is important to me. It’s like filling in the missing puzzle piece of C1-INH my body doesn’t make, versus putting a mystery compound in my body.” – Cheryl

“For me, I find it’s easier to give myself injections at night so it’s just part of my routine. And knowing how HAEGARDA works motivates me to take it on schedule.” – Cheryl B-J.

Physicians Highly Satisfied with HAEGARDA®, Delivering On its Promise of Efficacy With a Known MOA

“People ask about Takhzyro but they’re so well controlled on HAEGARDA® that they don’t want to take a chance on it”

– February 2019 KOL Advisory Board Participant

“HAEGARDA® represents a “natural approach, which some of my female patients prefer”

– February 2019 KOL Advisory Board Participant
Commercial Summary

- Strong Performance in FY19
- New Products Contributing significantly to Growth
- Balanced Regional Contribution
- Substantial Volume & Share Growth
- Market Leading Brands
Dr. Russell Basser
Senior Vice President, Research and Development
Seqirus
Milestones in 2019

**AFLURIA® QUADRIVALENT**
- AUS approval for 6M – 4yrs

**FLUCELVAX® QUADRIVALENT**
- European approval for 9yrs and older
- Paediatric efficacy study (2 - 17yrs) – met all clinical endpoints
- Canadian approval for 9yrs and older

**FLUAD® TRIVALENT**
- Strong effectiveness data in UK – again recommended by JCVI for people 65yrs and older

**FLUAD® QUADRIVALENT**
- AUS approval for 65yrs and older, with positive PBAC recommendation
- Submission of dossier EU

Pre-Pandemic vaccine (MF59-adjuvanted H5N1 cell = aH5N1c)
- US submission

*aQIVc* (MF59 plus FLUCELVAX® antigen) product development commenced

JCVI - Joint Committee on Vaccination and Immunisation
Influenza Vaccine Innovation Through Cell-based Manufacturing

**Eggs**
- Most influenza vaccines
- Egg supply – long lead times
- Low flexibility

**Cell Culture**
- Closed reactor
- High yield and volume
- Potential for rapid pandemic response

---

Egg-Derived Virus Seed

Cell-Derived Virus Seed
Science of Influenza Virus Mutation and the Rationale for Non-egg Vaccines

<table>
<thead>
<tr>
<th>Yearly seasonal vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 strains – currently</td>
</tr>
<tr>
<td>2 x “A” – H3N2, H1N1</td>
</tr>
<tr>
<td>2 x “B” – B/Victoria, B/Yamagata</td>
</tr>
</tbody>
</table>

**Circulating virus**

- **Manufacturing change**
  - altered strain
  - egg adaptation

- **Environmental drift**
  - altered strain
  - seasonal mismatch

- **Environmental shift**
  - new virus
  - pandemic

*Especially H3N2*
*Evidence emerging for other strains*

**HEMAGGLUTININ**

Density: 91 | Driven by Our Promise™
2018-19 was a Moderate Influenza Season in US (and elsewhere)

Estimated Cases of Influenza and Related Hospitalizations, U.S. 2010-19 Seasons

*2018-19 data are current estimates, https://www.cdc.gov/flu/about/burden/preliminary-in-season-estimates.htm
Influenza Vaccine Effectiveness Varies by Year and Age

2018-19 affected by strain mismatch due to “drift” in US

Vaccines least effective in older adults

Bringing the Benefits of MF59 Adjuvant and Cell-based Vaccine Together - aQIVc

Antigenic distance

- Cell Seed
- Circulating strain
- MF59 adjuvant

Increases "breadth" of immunity
Increases antibody response
Potential Benefits* of Cell-based Vaccine

- Evidence of egg adaptation strongly supported by non-clinical data#
- Studies of *Real World Evidence* from 2017-18 season show benefit of cell-based vs egg-based vaccine in a season dominated by H3N2 strain (~2 of every 4 years)
  - 36% reduction in outpatient Influenza-like Illness (electronic health record+)
  - 11% reduction in influenza-related hospital encounters (CMS/claims data**)
  - 43% reduction in H3N2-related influenza positive hospitalisation in people less than 65yrs old (Kaiser Permanente Southern California^)
- **Executive Order** from White House September 2019 called for modernisation of influenza vaccines and overhaul of seasonal flu vaccine production

---

* Superior efficacy has not been demonstrated in RCT
+ Boikos et al, US National Foundation for Infectious Disease 2018 Clinical Vaccinology Course, November 2018, (Poster), Bethesda MD.
Real World Evidence and the Important Impact of FLUAD®

- Recent data comparing FLUAD® to non-adjuvanted egg-based vaccines in people 65 years and above
  - US nursing home observational study* in 52,000 residents in 2016-17
    - 6% reduction in all-cause hospitalisation
  - Public Health England# analysis of first season of FLUAD® (2018-19) for older population
    - 30% reduction in influenza-related hospitalisation
  - 15 year experience in Italy^ in 43,000 people from 2002 - 2016
    - 39% reduction in hospitalisation due to pneumonia and cardiovascular events

- Ongoing recommendation for FLUAD® (TIV) by National Immunisation Advisory Groups in US, UK and Australia for people 65 years and older

- Rapid approval and reimbursement support for FLUAD® QIV in Australia – launch 2020

* Presented at National Foundation for Infectious Diseases, November 2019.
Strengthening the Power of RWE at Seqirus
From Electronic Medical Record to Integrated Understanding

- **Real world evidence** (RWE) is data regarding potential benefits or risks of a vaccine from sources other than traditional randomised clinical trials

- Influences decisions of policy makers, healthcare professionals, Regulatory Agencies (FDA Framework for RWE Program, December 2018)

---

*Refers to number of vaccinated people included in database for which healthcare outcomes can be assessed*
Focus on Influenza – Ongoing Process and Seed Innovation

**Process Improvement**

"Upstream" growth and isolation of virus

- Wave Bioreactors
- Infection Bioreactors
- Filtration

"Downstream" viral inactivation and purification of vaccine components

- Virus Concentration
- Inactivation
- Splitting
- Antigen Concentration
- Monobulk

**Seed Innovation**

- Viral Reassorting
  - Mixed Infection
  - Cell Reassorting

- Selection
  - Virus population
  - Selection of virus
  - Amplification of virus

- Synthetic Virus
  - Plasmid
  - Synthetic rescue
Shift to Differentiated Products is Expected to Drive Future Value Growth

- Global influenza vaccine market volumes between 500-600 million doses
  - 150 million doses distributed in US* in 2018-2019 season
  - Slow future growth, largely due to ageing population

- Seasonal global market value ~US$4B

- Differentiation a key driver of growth, especially in US – doses shifting to
  - Cell-based vaccines
  - Enhanced vaccines in 65 years and older segment (currently US, UK, AUS, Sth EU)
    - Potential for benefit in infants (6 months - 6 years)
  - Variable pace in geographical uptake

* Source: https://www.cdc.gov/flu/prevent/vaccine-supply-historical.htm
Anticipated Milestones in 2020

FLUCELVAX® QUADRIVALENT
- AUS approval 9yrs+
- Clinical study data for 6M - 4yrs

FLUAD® QUADRIVALENT
- US approval for 65yrs+
- EU approval for 65yrs+

Pre-Pandemic aH5N1c
- US approval

aQIVc
- Commence clinical program
Clinical Development – Part 2

William Mezzanotte, M.D.

Executive Vice President, Head of Research and Development
CSL Behring
Investigating the Benefit of Alpha-1 Antitrypsin in Graft vs Host Disease (GvHD)

**Alpha-1 Antitrypsin (CSL964) for GvHD Prevention**

- **Part 1**
  - Cohorts 1-3
  - Dose Levels 1-3
  - Open Label

- **Part 2**
  - Cohorts 4
  - Selected Dose
  - Placebo-controlled

**Bone Marrow Transplant Clinical Trial Network Collaborative Study CSL964 for GvHD Treatment**

- AAT 2x weekly
- Placebo
- Primary Endpoint at Day 28
- Follow up
- Study startup activities commenced

Cohort 1 completed

Driven by Our Promise™
Antibody-Mediated Rejection (AMR) in Renal Allografts

- Development of Donor Specific Antibodies (DSAs)
- Late in the post-transplant period
- Progressive decline in kidney function
- Loss of graft
- No approved therapies
  - Pilot data for C1 inhibitor and anti-IL-6

Source: Am J Transplant. 2018; 18:2849-2856
Donor-Specific Antibodies (DSA) & Antibody-Mediated Rejection (AMR)

- Complement-dependent antibody-mediated activity cytotoxicity
- Complement-independent antibody-mediated cellular toxicity
  - Direct endothelial activation & proliferation

C1 inhibitor – ARMOR study

Anti-IL-6 therapy – IMAGINE study

Both studies actively recruiting
CSL112 ApoA-1

- Study enrolment is active in >45 countries and progressing well
  - PMDA approval for Japan to join trial
- Independent Data Monitoring Committee – no safety concerns
- First futility analysis in 2020

>17,000 AMI subjects ≥18yrs of age with Acute Coronary Syndrome

Screening  Randomisation

1° Endpoint: MACE
D90

MACE Follow Up
D180
D365

6g CSL112
Placebo
Summary

William Mezzanotte, M.D.
Executive Vice President, Head of Research and Development
CSL Behring
# R&D Portfolio – December 2019

<table>
<thead>
<tr>
<th>RESEARCH</th>
<th>PRE-CLINICAL</th>
<th>PHASE I</th>
<th>PHASE II</th>
<th>PHASE III</th>
<th>REGISTRATION</th>
<th>POST-REGISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discovery Projects</td>
<td>Improved Fibrinogen</td>
<td>CSL730 rFc Multimer</td>
<td>CSL312 Anti-FXIIa HAE</td>
<td>HIZENTRA® DM</td>
<td>PRIVIGEN® PID Japan</td>
<td>CSL830 C1-INH Subcut EU</td>
</tr>
<tr>
<td>Discovery Projects</td>
<td>CSL787 Nebulised Ig</td>
<td>CSL324 Anti-G-CSFR</td>
<td>HIZENTRA® SSc</td>
<td>CSL112 ApoA-I</td>
<td>FLUAD® QIV 65yrs+ US/EU/Canada</td>
<td>PRIVIGEN® CIDP US, Japan</td>
</tr>
<tr>
<td>Discovery Projects</td>
<td>aQIVc (MF59 plus FLUCELVAX® antigen)</td>
<td>CSL200 (CAL-H) SCD</td>
<td>PRIVIGEN® SSc</td>
<td>Clazakizumab AMR</td>
<td>Pre-Pandemic aH5N1c</td>
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<td>CSL630 pdFVIII Ruide</td>
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<td>CSL964 GvHD Treatment</td>
<td>ZEMAIRA® / RESPREZA® AAT</td>
<td>AFLURIA® QIV 6M+ US, AUS</td>
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</table>

- **Immunology and Neurology**  | **Haematology and Thrombosis**  | **Respiratory**  | **Cardiovascular and Metabolic**  | **Transplant**  | **Influenza Vaccines**  

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**Partnered Projects**
## Expected Progress in Next 12 Months

<table>
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<tr>
<th>PRE-CLINICAL</th>
<th>PHASE I</th>
<th>PHASE II</th>
<th>PHASE III</th>
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<td>PRIVIGEN® PID PID</td>
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<td>aQIVc (MF59 plus FLUCELVAX® antigen)</td>
<td>Garadacimab (Anti-FXIIa) HAE</td>
<td>IDELVION® 21 Day Dosing</td>
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<td>Nebulised Ig</td>
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<td>Haptoglobin SAH</td>
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### Immunology and Neurology
- CSL787
- Nebulised Ig
- aQIVc (MF59 plus FLUCELVAX® antigen)
- Garadacimab (Anti-FXIIa) HAE
- IDELVION® 21 Day Dosing

### Haematology and Thrombosis
- FLUCELVAX® QIV 9yrs+
- AUS
- FLUAD® QIV 65yrs+
- US, EU, Canada
- Pre-Pandemic aH5N1c

### Respiratory

### Cardiovascular and Metabolic

### Transplant

### Influenza Vaccines
# Significant Target Launch Dates

<table>
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<tr>
<th>2019</th>
<th>2020</th>
<th>2021-2025</th>
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<td><strong>HIZENTRA® CIDP Japan</strong></td>
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<td><strong>PRIVIGEN® CIDP Japan</strong></td>
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<tr>
<td><strong>AFLURIA® QIV 6m+ (AUS)</strong></td>
<td>FLUAD® QIV 65yrs+ US, EU</td>
<td>HIZENTRA® DM</td>
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<td>Improved Fibrinogen</td>
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Partnered Projects

Immunology and Neurology | Haematology and Thrombosis | Respiratory | Cardiovascular & Metabolic | Transplant | Influenza Vaccines

Driven by Our Promise™
### 2019 Highlights

#### Immunology and Neurology
- HIZENTRA® and PRIVIGEN® approved for treatment of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) in Japan
- HIZENTRA® granted Orphan Drug Exclusivity for CIDP
- HIZENTRA® Dermatomyositis (DM) Phase III Study initiated
- Garadacimab (Anti-FXIIa) in Hereditary Angioedema (HAE) Phase II double blind period complete

#### Haematology and Thrombosis
- CSL200 (CAL-H) in Sickle Cell Disease (SCD) Phase I Study initiated
- CSL889 Hemopexin in SCD Phase I Study initiated

#### Respiratory
- CSL311 (Anti-Beta Common) Phase I study commenced
- Approval of convenient single-vial dosing for ZEMAIRA® (Alpha1-Proteinase Inhibitor) in the US

#### Cardiovascular and Metabolic
- CSL112 (ApoA-1) Phase III study (AEGIS-II) progressing well with >7000 patients recruited
- CSL346 (Anti-VEGF-B) Phase II Diabetic Nephropathy study initiation planned for 1H20

#### Transplant
- CSL964 Alpha-1 Antitrypsin (AAT) for prevention of Graft versus Host Disease (GvHD) after Transplantation of Allogenic Hematopoietic Cell Transplantation (HCT) Phase III study actively recruiting and on track

#### Influenza Vaccines
- First cell-based quadrivalent seasonal influenza vaccine, FLUCELVAX® TETRA, approved in Europe
- AFLURIA® QUAD (quadrivalent influenza vaccine) granted expanded indication for use in children 6M+ in Australia
- aQIVc (MF59 plus FLUCELVAX® antigen) new product development commenced
Panel Q&A Session