ANNUAL RESEARCH AND DEVELOPMENT INVESTOR BRIEFING

Melbourne, Australia – CSL (ASX:CSL; USOTC:CSLLY)

Please find attached the presentation and an accompanying media release ahead of CSL’s Annual Research and Development Investor Briefing being held today at 9am ADST.

The briefing will be webcast and can be accessed in the “Investor” section of CSL’s website (www.CSL.com).

Fiona Mead
Company Secretary

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Introduction

William Mezzanotte, M.D.
Executive Vice President, Head of Research and Development
CSL Behring
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Global Research and Development Footprint

- Bern, Switzerland
- Marburg, Germany
- Amsterdam, Netherlands
- London, UK
- Liverpool, UK
- Wuhan, China
- Tokyo, Japan
- Melbourne, Australia
- Sydney, Australia
- Pasadena, US
- Kankakee, US
- King of Prussia, US
- Summit, US
- Cambridge, US
- Holly Springs, US

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- CSL Behring
- Seqirus
- >1,700 scientists globally
Global Collaborations for Innovation Access

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- King of Prussia, US
- Summit, US
- Cambridge, US
- Holly Springs, US
- Dalhousie University
- UBC
- Università Cattolica del Sacro Cuore
- Univ. of Queensland
- RMIT University
- Walter & Eliza Hall Institute
- Medical University of Graz
- UCSF
- Washington University in St. Louis
- The Royal Melbourne Hospital
- Walter Eliza Hall Institute
- RMIT University
- Universitätsklinikum Essen
- Medizinische Hochschule Hannover
- Uni Bern

>1,700 scientists globally

Driven by Our Promise™
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

* Includes R&D for CSL Behring and Seqirus.
  m = US$ millions

R&D investment ~10-11% global revenue
Active R&D Support for Growth in Plasma Business
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
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<td>CSL312 Anti-FXIIa HAE</td>
<td>PRIVIGEN® PID Japan</td>
<td>PRIVIGEN® CIDP Japan</td>
<td>CSL830 C1-INH Subcut EU</td>
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<td>Mavrilimumab GM-CSFR</td>
<td>HIZENTRA® IIM</td>
<td>HIZENTRA® CIDP Japan</td>
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<td>Pre-Pandemic Vaccine (aH5N1c)</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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Notable Regional Regulatory Approvals
1 Dec 2018 – 20 Nov 2019

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

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

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<th>Phase II</th>
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<th>Registration</th>
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<tr>
<td>CSL200 (CAL-H) SCD</td>
<td>PRIVIGEN® SSc</td>
<td>HIZENTRA® DM</td>
<td>PRIVIGEN® PID Japan</td>
<td>PRIVIGEN® CIDP Japan</td>
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<td>CSL312 Anti-FXIIa Thrombosis</td>
<td>HIZENTRA® SSc</td>
<td>CSL964 GvHD Treatment</td>
<td>AFLURIA® QIV 6M-4yrs AUS</td>
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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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<td>CSL730 rFc Multimer</td>
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<td>Clazakizumab Anti-IL-6</td>
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<td>MOMENTA</td>
<td>KINIKSA</td>
<td>Vitaeris</td>
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<td>CSL334 / ASLAN004 IL-13R</td>
<td>ASLAN PHARMACEUTICALS</td>
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<td>CSL964 GvHD Treatment</td>
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### RESEARCH

- **Discovery Projects**
  - Improved Fibrinogen
  - CSL730 rFc Multimer
  - CSL324 Anti-G-CSFR
  - aQIVc (MF59 plus FLUCELVAX® antigen)
  - P. gingivalis/POD
  - CSL312 Anti-FXIIa Thrombosis
  - CSL311 Anti-Beta Common
  - CSL346 Anti-VEGF-B
  - CSL347 / ASLAN004 IL-13R

### PRE-CLINICAL

- **Discovery Projects**
  - CSL787 Nebulised Ig
  - CSL200 (CAL-H) SCD
  - CSL630 pdFVIII Ruide
  - CSL347 / ASLAN004 IL-13R

### PHASE I

- **Discovery Projects**
  - CSL703 HAE
  - CSL324 Anti-G-CSFR
  - CSL200 (CAL-H) SCD
  - CSL312 Anti-FXIIa Thrombosis
  - CSL346 Anti-VEGF-B
  - CSL347 / ASLAN004 IL-13R

### PHASE II

- **Discovery Projects**
  - CSL730 HAE
  - CSL324 Anti-G-CSFR
  - CSL200 (CAL-H) SCD
  - CSL312 Anti-FXIIa Thrombosis
  - CSL346 Anti-VEGF-B
  - CSL347 / ASLAN004 IL-13R

### PHASE III

- **Discovery Projects**
  - CSL312 Anti-FXIIa HAE
  - CSL324 Anti-G-CSFR
  - CSL200 (CAL-H) SCD
  - CSL312 Anti-FXIIa Thrombosis
  - CSL346 Anti-VEGF-B
  - CSL347 / ASLAN004 IL-13R

### REGISTRATION

- **Discovery Projects**
  - CSL312 Anti-FXIIa HAE
  - CSL324 Anti-G-CSFR
  - CSL200 (CAL-H) SCD
  - CSL312 Anti-FXIIa Thrombosis
  - CSL346 Anti-VEGF-B
  - CSL347 / ASLAN004 IL-13R

### POST-REGISTRATION

- **Discovery Projects**
  - CSL312 Anti-FXIIa HAE
  - CSL324 Anti-G-CSFR
  - CSL200 (CAL-H) SCD
  - CSL312 Anti-FXIIa Thrombosis
  - CSL346 Anti-VEGF-B
  - CSL347 / ASLAN004 IL-13R

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**Partnered Projects**

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

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15 | Driven by Our Promise™
Research, Gene and Cell Therapy

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

- **Capabilities and facilities**

- **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
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

*SITE - 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

- CSL – Walter and Eliza Hall Institute (WEHI)
- Bioinformatics Alliance
- CSL biologics discovery platform

- Global Research site locations
- Strategic Partnerships (universities, MRIs, hospitals)

- Funding & collaboration initiatives
- Research Acceleration Initiatives
  - AUS, EU and US
  - Innosuisse grant
  - University Hospital Zürich

- Partnering conference attendance & sponsorship

- Biotech partnerships
- VC investment & partnerships

- Active partner in ~$700m of venture funding (Brandon Capital Partners)

- 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

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

Haemolysis
- haemoglobin
- heme
- iron

Damage
- Nitric Oxide (NO) scavenging
- Tissue damage

Protection
- haptoglobin (Hp)
- hemopexin (Hx)
- transferrin

Treatment
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

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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
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

Shared βc receptor

Survival, Proliferation, Differentiation, Activation

Inflammation

Source: Panousis et al., Mabs 8:436, 2012
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

**Myeloid cell lineages**

GM-CSF
IL-3
or
IL-5

**Polyp**

**Inflammation**

**Mucus**

**Nasal Polyp**

**Xenograft**

CSL311 1 x / week for 4 weeks, 5 mg/kg

Graft size, cellular composition, mucus production, transcriptomics

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 \textit{in vitro}
• CSL311 inhibits the activity of multiple cell types involved in inflammation
• CSL311 demonstrates efficacy in an \textit{in vivo} translational model of airways inflammation
• GLP Toxicology program successfully completed
CSL Gene Therapy

In Vivo vs Ex Vivo Gene Therapy

**Direct delivery**

- 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**

- Treatment or missing gene
- The treatment gene is added to a harmless lentivirus
- ...which in turn introduces it to the isolated stem cells
- The patients own stem cells are removed from the body and cultured
- 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

- CSL200 program aims to provide sufficient functional globin gene to prevent sickling

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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.
# Immunoglobulin Therapy

## Mechanism of Action Summary

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<th>Reduction of Pathologic Ig</th>
<th>Complement Scavenging</th>
<th>FcyR Expression Modulation</th>
<th>Immune Cells Modulation</th>
<th>Cytokine Modulation</th>
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<td><strong>FcRn Binding Agents</strong></td>
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</tbody>
</table>

- ![No Activity](no_activity.png)
- ![Possible Activity](possible_activity.png)
- ![Activity](activity.png)

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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
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**

- **Haemolysis**
  - Cell-free haemoglobin
  - Plasma heme

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

- **Hpx:heme**
  - Clearance of free heme, and reduced inflammation

**Endothelial Cells**
- Heme intercalation into lipid membrane → peroxidation
- Toll-like receptor 4
- P-selectin
- vWF

**Hepatocytes**
- Internalization of Hpx:heme
- HO-1
- HO-2
- Biliverdin
- Ferritin
- CO
- Fe

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Garadacimab (CSL312 Anti-Factor XIIa)  
Multiple Potential Indications

Adapted from: Schmaier, AH., J Clin Invest. 2008 Sep 2; 118(9): 3006–3009.
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

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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; ie, incipient/overt nephropathy)

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

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

### Symptoms
- **Skin**
  - Skin butterfly rash and red patches
- **Lungs**
  - Pleuritis
  - Pneumonitis
  - Pulmonary emboli
  - Pulmonary hemorrhage
- **Kidneys**
  - Blood in the urine
- **Heart**
  - Endocarditis
  - Atherosclerosis
  - Inflammation of the fibrous sac
- **Blood**
  - Anemia
  - High blood pressure
- **Muscle and Joints**
  - Pain
  - Arthritis
  - Swollen joints

### 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

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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
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 | Double-Blind Treatment Period | Open Label Treatment Period
---|---|---
Up to 4 weeks | 48 Weeks | 24 Weeks

Week 48
End of DB Treatment

Week 72
End of OL Treatment

End of Study
(Safety F/U)

Subjects with dcSSc

2:1 Randomization

PRIVIGEN®

Placebo

PRIVIGEN®
SURPASS
HIZENTRA® (SCIG) PhII, Safety and Bioavailability Study in Systemic Sclerosis

<table>
<thead>
<tr>
<th>Treatment Period A</th>
<th>Treatment Period B</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIZENTRA®</td>
<td>PRIVIGEN®</td>
</tr>
<tr>
<td>PRIVIGEN®</td>
<td>HIZENTRA®</td>
</tr>
</tbody>
</table>

Arm 1 (n=10)
Arm 2 (n=10)

Screening Patients with dcSSc
Randomization

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

Sources:

Heliotrope Rash  Gottron’s Papules  Skin Signs of DM

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Driven by Our Promise™
RECLAIM
HIZENTRA® DM Treatment Study Design

Weeks 1 to 53

Screening → Randomization

Up to 2 months

126 patients, 1:1 randomisation

Primary endpoint: TIS responder status

Weeks 1 to 25

HIZENTRA® → Placebo → HIZENTRA®

Weeks 25 to 53

HIZENTRA® → HIZENTRA®
Garadacimab Phase II Hereditary Angioedema (HAE) Study
Completed Double Blind Period

Run-in period
4–8 weeks

1:1:1:1
First 32 patients

Screened subjects with C1-INH HAE

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
CSL Pipeline Progressing into Multiple New Disease Areas Using All Three Product Development Platforms

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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

Conducting business in 100+ Countries

US$7.2 Billion in annual revenue

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

<table>
<thead>
<tr>
<th>Segment</th>
<th>Products</th>
<th>Overview</th>
</tr>
</thead>
</table>
| Ig      | privigen | - Strong underlying market growth  
          - Disciplined approach to market expansion  
          - Growth driven by volume and mix improvements |
| Coagulation | IDELVION® | - Market leadership with IDELVION® in key markets  
              - Additional launch opportunities for AFSTYLA® / IDELVION®  
              - Life-cycle expansion (21-day dosing) |
| Specialty | HAEGARDA® | - New launches with HAEGARDA®  
            - Continued growth of KCENTRA® in the US |
| Albumin | AlbuRx® | - 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%
- Other 21%

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, SID, ITP, GBS, KD, CIDP, MMN
- **US:** PID, ITP, CIDP
- **CA:** PID, SID, ITP, CIDP
- **JP:** CIDP
- **AUS:** PID, SID, 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%  24%  27%  28%
Competitor A  20%  20%  21%  21%  20%  21%  21%  21%  24%  24%
Competitor B  15%  15%  15%  15%  15%  15%  15%  15%  16%  16%
Competitor C  10%  10%  10%  10%  10%  10%  10%  10%  10%  10%
Competitor D  5%   5%   5%   5%   5%   5%   5%   5%   5%   5%

Source: Data on file

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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

HIZENTRA® does not require venous access

Market Share Growth With Both Privigen & Hizentra

Have venous access issues

Orphan Exclusivity Granted for Hizentra CIDP

Require more frequent infusions to manage their disease

HIZENTRA® provides steady state Ig levels for continuous control

Experience IV-related systemic adverse reactions

5x as many patients said they felt fewer side effects with HIZENTRA®

Seek the flexibility, freedom, and control of self-infusing

8x as many patients said HIZENTRA® offers more freedom than IVIG

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<sup>®</sup>
- **2006**: 1st SCIG Vivaglobin<sup>®</sup>
- **2007**: Next generation IVIG PRIVIGEN<sup>®</sup>
- **2010**: 1st 20% SCIG HIZENTRA<sup>®</sup>
- **2013**: 1st SCIG in Japan HIZENTRA<sup>®</sup>
- **2013**: CIDP in EU PRIVIGEN<sup>®</sup>
- **2015**: 1st flexible dosing HIZENTRA<sup>®</sup>

### Present
- **2017**: CIDP in US PRIVIGEN<sup>®</sup>
- **2018**: 1st SCIG in CIDP HIZENTRA<sup>®</sup>
- **2018**: 1st SCIG in PFS HIZENTRA<sup>®</sup> (Canada)
- **2019**: MMN EU PRIVIGEN<sup>®</sup>

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

Total value
$11.7B

Hem A 66%
Hem B 14%
vWD 4%
Inhibitor 16%
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
IDELVION® Prophylaxis Market Leadership

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

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

- **Berinert**: C₁ Esterase Inhibitor, Human
  - On-Demand Treatment

- **HAEGARDA**: C₁ Esterase Inhibitor Subcutaneous (Human)

- **Kcentra**: Prothrombin Complex Concentrate (Human)

- **Zemaira**: α₁-proteinase inhibitor (Human)
  - Strengthens clots. Supports hemostasis.

- **Respreeza**: α₁-proteinase inhibitor (Human)

- **RiaSTAP**: Fibrinogen Concentrate (Human)

- **HAEMOCOMPLETTAN P**: Hemostatic Agent

The pie chart shows:
- **Immunoglobulin**: $1,572M (+6%)
- **Albumin**:
- **Haemophilia**:
- **Specialty**:

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

*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

Sources: 1. Data on File. 2. (RWD) Charge Master Data & Medical History Data.
**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%**†‡†

*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
- Market Leading Brands
- Balanced Regional Contribution
- Substantial Volume & Share Growth
- New Products Contributing significantly to Growth
Dr. Russell Basser
Senior Vice President, Research and Development
Seqirus
Seqirus Influenza Vaccines

- **Standard risk populations**
  - Seasonal TIV / QIV
- **High-risk populations**
  - Adjuvanted seasonal TIV / QIV
- **Pandemic**
- **Influenza Science**
  - Egg Based
  - Cell Based

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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

Diagram:
- Eggs → Egg-Derived Virus Seed
- Circulating Virus
- Cell Culture → Cell-Derived Virus Seed
- Injection
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

- Environmental drift
  - altered strain
  - seasonal mismatch

- Environmental shift
  - new virus
  - pandemic

Manufacturing change
- altered strain
- egg adaptation

Especially H3N2
Evidence emerging for other strains

Receptor binding site
Hemagglutinin
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

- Egg Seed
- Cell Seed
- Circulating strain

Antigenic distance

- 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.

*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

- **Cohort 1 completed**

**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**

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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
AMR: Complement Dependent and Independent Pathways

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

1° Endpoint: MACE
- D90

MACE Follow Up
- D180
- D365

6g CSL112
Placebo

Screening → Randomisation
Summary

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

### RESEARCH
- **Discovery Projects**
  - Improved Fibrinogen (CSL730)
  - rFc Multimer (CSL324)
  - Anti-G-CSFR (aQIVc, FLUCELVAX®)
- **Discovery Projects**
  - Nebulised Ig (CSL87, Nebulised Ig)
  - (CAL-H) SCD (CSL200)
  - (MF59 plus FLUCELVAX®) (CSL200)
- **Discovery Projects**
  - P. gingivalis/POD (CSL364, Anti-VEGF-B)

### PRE-CLINICAL
- **Partnered Projects**
  - HAE (HIZENTRA®)
  - HIZENTRA® DM (HIZENTRA®)
  - ApoA-I (CSL112)
  - C1-INH Subcut EU (CSL830)

### PHASE I
- **Phase I Projects**
  - Improved Fibrinogen (CSL730)
  - rFc Multimer (CSL324)
  - Anti-G-CSFR (aQIVc, FLUCELVAX®)
- **Phase I Projects**
  - Nebulised Ig (CSL87, Nebulised Ig)
  - (CAL-H) SCD (CSL200)
  - (MF59 plus FLUCELVAX®) (CSL200)
- **Phase I Projects**
  - P. gingivalis/POD (CSL364, Anti-VEGF-B)

### PHASE II
- **Phase II Projects**
  - Anti-FXIIa (CSL312, Anti-FXIIa)
  - HAE (HIZENTRA®)
  - ApoA-I (CSL112)
- **Phase II Projects**
  - Nebulised Ig (CSL87, Nebulised Ig)
  - (CAL-H) SCD (CSL200)
  - (MF59 plus FLUCELVAX®) (CSL200)
- **Phase II Projects**
  - P. gingivalis/POD (CSL364, Anti-VEGF-B)

### PHASE III
- **Phase III Projects**
  - Improved Fibrinogen (CSL730)
  - rFc Multimer (CSL324)
  - Anti-G-CSFR (aQIVc, FLUCELVAX®)
- **Phase III Projects**
  - Nebulised Ig (CSL87, Nebulised Ig)
  - (CAL-H) SCD (CSL200)
  - (MF59 plus FLUCELVAX®) (CSL200)
- **Phase III Projects**
  - P. gingivalis/POD (CSL364, Anti-VEGF-B)

### REGISTRATION
- **Registration Projects**
  - HIZENTRA® DM (HIZENTRA®)
  - ApoA-I (CSL112)
  - C1-INH Subcut EU (CSL830)
- **Registration Projects**
  - HAE (HIZENTRA®)
  - Hizentra® (HIZENTRA®)
  - ApoA-I (CSL112)
- **Registration Projects**
  - P. gingivalis/POD (CSL364, Anti-VEGF-B)

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**Immunology and Neurology | Haematology and Thrombosis | Respiratory | Cardiovascular and Metabolic | Transplant | Influenza Vaccines**
# Expected Progress in Next 12 Months

<table>
<thead>
<tr>
<th>PRE-CLINICAL</th>
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<th>PHASE II</th>
<th>PHASE III</th>
<th>POST-REGISTRATION</th>
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<td>recC1-INH</td>
<td>CSL362</td>
<td>CSL346</td>
<td>HAEGARDA®</td>
<td>PRIVIGEN® PID PID</td>
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<td></td>
<td>Anti-IL-3Ra</td>
<td>Anti-VEGF-B</td>
<td>Japan</td>
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<td>Novel Complement Inhibitor</td>
<td>CSL787</td>
<td>aQIVc (MF59 plus FLUCELVAX® antigen)</td>
<td>Garadacimab (Anti-FXIIa) HAE</td>
<td>IDELVION® 21 Day Dosing</td>
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<tr>
<td>Haptoglobin SAH</td>
<td>Nebulised Ig</td>
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**Immunology and Neurology** | **Haematology and Thrombosis** | **Respiratory** | **Cardiovascular and Metabolic** | **Transplant** | **Influenza Vaccines**
## Significant Target Launch Dates

<table>
<thead>
<tr>
<th>2019</th>
<th>2020</th>
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<tr>
<td><strong>HIZENTRA® CIDP Japan</strong></td>
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<td><strong>Garadacimab (Anti-FXIIa) HAE</strong></td>
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<td><strong>PRIVIGEN® CIDP Japan</strong></td>
<td><strong>IDELVION® 21 Day Dosing</strong></td>
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<td><strong>AFLURIA® QIV 6m+ (AUS)</strong></td>
<td><strong>FLUAD® QIV 65yrs+ US, EU</strong></td>
<td><strong>HIZENTRA® DM</strong></td>
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<td><strong>FLUCELVAX® QIV 9yrs+ EU</strong></td>
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<td><strong>IVIG Kidney AMR</strong></td>
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<td><strong>HAEGARDA® Japan</strong></td>
<td><strong>CSL842 C1-INH rAMR</strong></td>
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<td><strong>Improved Fibrinogen</strong></td>
<td><strong>CSL964 GvHD</strong></td>
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<tr>
<td></td>
<td><strong>FLUCELVAX® 6m+ US, EU, AUS</strong></td>
<td><strong>CSL112 ApoA-I</strong></td>
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<td><strong>aQIVc 50yrs+</strong></td>
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**Partnered Projects**

Immunology and Neurology | Haematology and Thrombosis | Respiratory | Cardiovascular & Metabolic | Transplant | Influenza Vaccines
### 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
CSL Continues to Advance R&D Capabilities

Unique portfolio mix of plasma, cell and gene therapy, recombinant proteins and antibody assets highlighted at Research & Development Briefing

Sydney, Australia, 4 December 2019 – CSL Limited (ASX:CSL; USOTC:CSLLY) is steadily advancing its Research & Development (R&D) pipeline and capabilities to deliver a highly differentiated product portfolio mix, addressing a broader range of patients’ unmet needs,” said Head of Research & Development Dr. William Mezzanotte today.

At CSL’s annual R&D briefing to investors, Dr. Mezzanotte noted the company is building on its leadership in plasma therapies through the identification of emerging new medicines from both within its existing portfolio of plasma-derived products, and through newer platforms such as gene and cell therapies and recombinant proteins.

To support this approach, CSL has forged targeted innovation partnerships in close proximity to its R&D locations, including at the Bio21 Institute in Melbourne, Australia, the Swiss Center for Translational Medicine in Bern, Switzerland and the University Science Center in Philadelphia, US.

“Our Phase 3 clinical program targeting the reduction of early recurrent cardiovascular events in heart attack survivors, CSL112, continues to track well.

“We continue our focus on developing new medical indications for immunoglobulins while improving manufacturing efficiencies across our plasma product portfolio,” Dr Mezzanotte said.

In FY19, CSL invested US$832 million into its R&D portfolio, representing 9.7% of total revenues.

R&D Pipeline Highlights

A novel treatment for asthma which has this month advanced to Phase 1, first-inhuman trials for patients with mild to moderate asthma. Asthma is a common chronic respiratory disease that is estimated to affect as many as 235 million1 people worldwide and is the most common chronic disease among children. Despite advances in the treatment of asthma, it is estimated that every year, more than 1,0002 people around the world die each day from this disease.

CSL’s trial will test for the safety of a therapy delivered by subcutaneous injection that asthma sufferers could self-administer at home once every two to four weeks, acting prophylactically to prevent asthma attacks.

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1 World Health Organisation: https://who.int/respiratory/asthma/en/
The potential therapy, which currently holds the working title “CSL311,” is a monoclonal antibody that targets multiple inflammatory agents involved in various diseases.

CSL311 is the first monoclonal antibody to simultaneously target three cell-signaling cytokines, or molecules, that are responsible for the immune response that causes asthma and in doing so, suppresses inflammation of airways.

Commenting on the potential of the research, University of Melbourne Professor Jo Douglass, Head of the Immunology and Allergy Department at the Royal Melbourne Hospital and a research collaborator on the project, said, “Asthma is a serious disease that in extreme cases can be fatal. Currently, our treatment options for severe asthma are limited. We are excited by the potential of CSL311 to address a problem that affects the lives of so many.”

**Addressing Severe Muscle Disease**

Another pipeline project featured today is a Phase 3 clinical trial for novel use of CSL Behring’s existing subcutaneous Immunoglobulin (Ig) product in patients with a severe condition called Dermatomyositis. The Ig product is currently indicated for use in a rare neurological disorder, Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) as well as primary and secondary immunodeficiencies.

Dermatomyositis is one of a group of acquired muscle diseases called inflammatory myopathies which are characterized by chronic muscle inflammation accompanied by muscle weakness. If the disease goes untreated it can lead to difficulty in walking or the need for a wheelchair or even becoming bedridden.

“Our pipeline is as robust and promising as ever,” Dr. Mezzanotte said. “Our R&D portfolio holds the potential to unlock a broad range of new therapies for people with challenging medical conditions. That promise is what drives our 1,700-plus scientists to work every day as if someone’s life depends on it – because it really does.”

**About CSL:** CSL (ASX:CSL) is a leading global biotechnology company with a dynamic portfolio of life-saving medicines, including those that treat haemophilia and immune deficiencies, as well as vaccines to prevent influenza. Since our start in 1916, we have been driven by our promise to save lives using the latest technologies. Today, CSL — including our two businesses, CSL Behring and Seqirus - provides life-saving products to more than 70 countries and employs more than 25,000 people. Our unique combination of commercial strength, R&D focus and operational excellence enables us to identify, develop and deliver innovations so our patients can live life to the fullest.

For more information about CSL Limited, visit [www.csl.com](http://www.csl.com)

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