



R&D Investor Briefing 2020

20th October 2020



Legal Notice

Forward looking statements

The information in this presentation is current as of the date of this presentation, and includes forward looking statements about CSL Limited and its related bodies corporate's (CSL) financial results and estimates, business prospects and product candidates in research, all of which involve substantial risks and uncertainties, many of which are outside the control of, and are unknown to, CSL. You can identify these forward looking statements by the fact that they use such as "anticipate," "estimate," "expect," "project," "intend," "plan," "believe," "target," "may," "assume," and other words and terms of similar meaning in connection with any discussion of future operating or financial performance. Factors that could cause actual results to differ materially include: the success of R&D activities, decisions by regulatory authorities regarding product registration and label claims; competitive developments; marketing challenges; difficulties or delays in manufacturing; trade buying patterns and fluctuations in interest and currency exchange rates; legislation or regulations that affect product production, distribution, pricing, reimbursement, access or tax; acquisitions or divestitures; research collaborations; litigation or government investigations, and CSL's ability to secure intellectual property protection. The statements made in this presentation should not be construed as an offer to sell, or solicitation of an offer to buy, any securities of CSL. No representation, warranty or assurance (express or implied) is given or made in relation to any forward looking statement by any person (including CSL), including in relation to any underlying assumption or that any forward looking statement will be achieved. Actual future events may vary materially from the forward looking statements and the assumptions on which such statements are based. Subject to any continuing obligations under applicable law or any relevant listing rules of the Australian Securities Exchange, CSL does not undertake to disseminate updates or revisions to any forward looking statements in these materials to reflect any change in expectations in relation to any forward looking statements or any change in events, conditions or circumstances on which any such statement is based. Nothing in these materials shall create an implication that there has been no change in the affairs of CSL since the date of these materials.

Trademarks

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

A man with dark hair and safety glasses, wearing a light blue lab coat and purple gloves, is working in a laboratory. He is focused on a task, possibly handling a sample or equipment. The background shows laboratory equipment, including a biosafety cabinet and various containers. A red vertical bar is visible on the left side of the image.

Introduction

William Mezzanotte MD

Executive Vice President,
Head of Research and Development
and CMO

CSL Behring

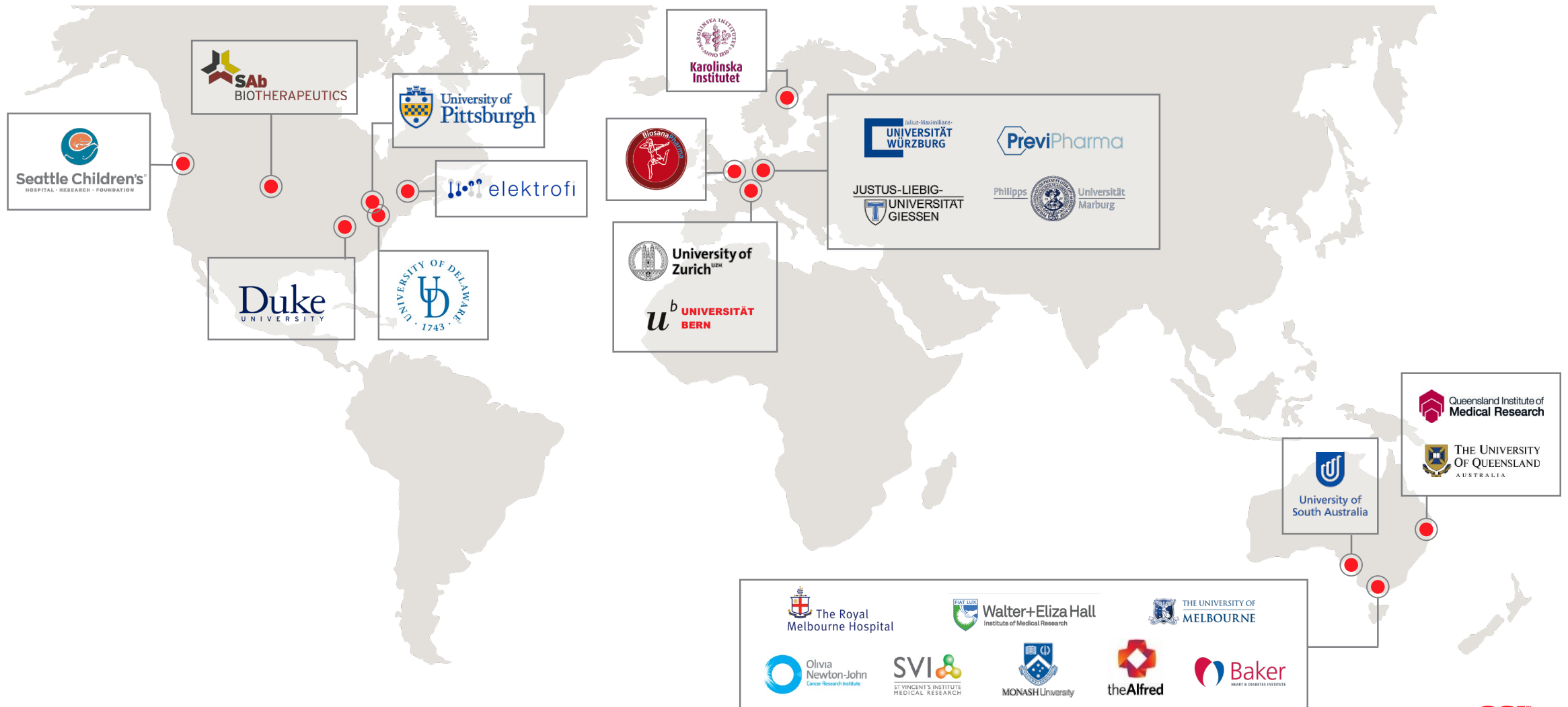
Agenda

Topic	Presenter
Welcome	Mark Dehring
Introduction and Highlights	Bill Mezzanotte
Research - Protein Therapies, Gene Therapies & Vaccines	Andrew Nash
Immunology Highlights & COVID-19 Response	Mittie Doyle
Commercial	Bill Campbell
Transplant Highlights	Laurie Lee
Summary	Bill Mezzanotte
Q&A	Panel
Close	

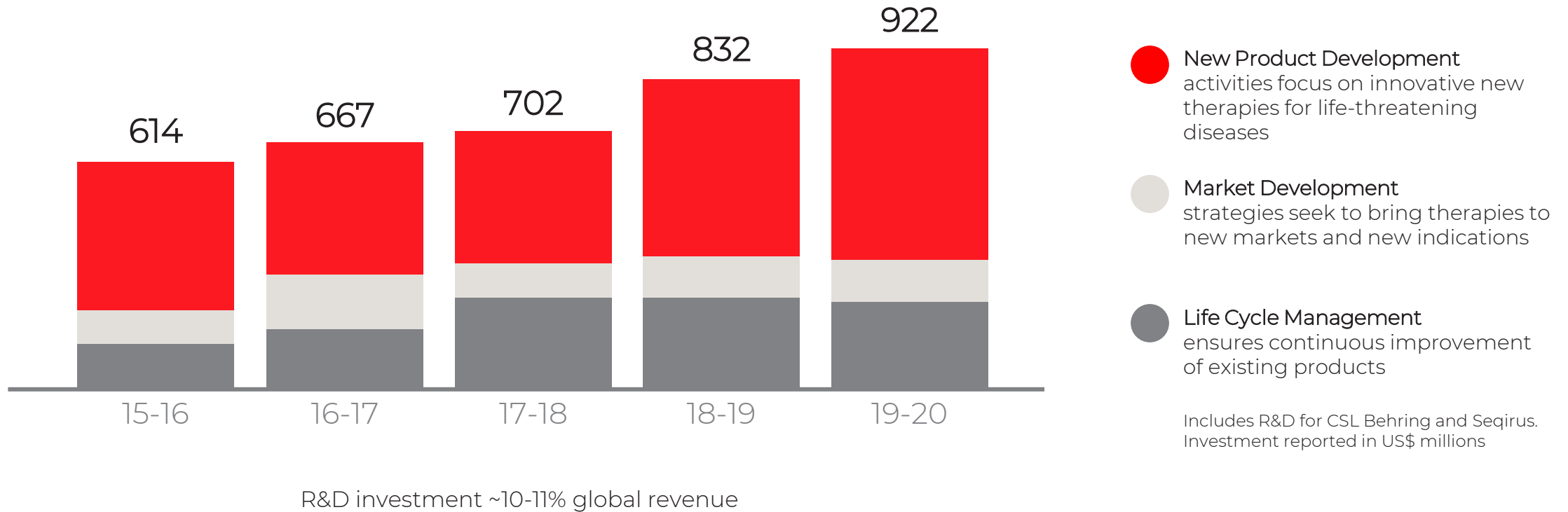
Global Research and Development Footprint



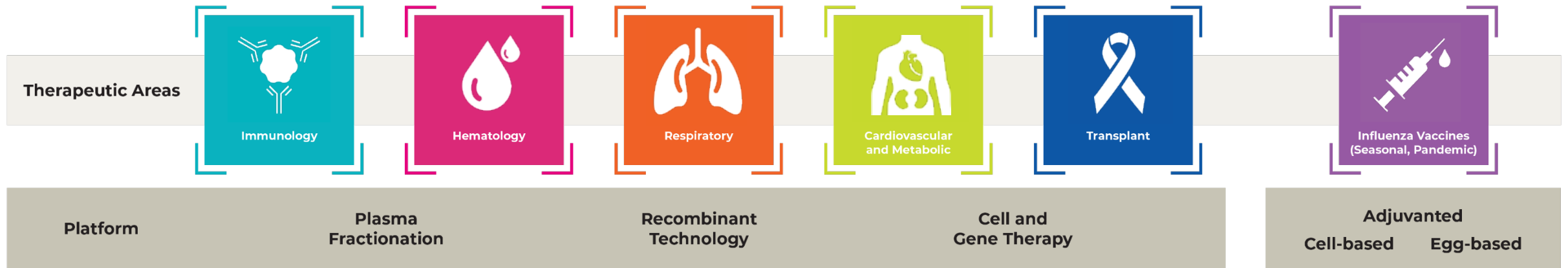
Key Global Research Partnerships for Early Innovation Access



Commitment to Research and Development



Focus Through Our Therapeutic Areas and Platforms



R&D Portfolio – December 2019



R&D Portfolio Highlights - FY20



Immunology

- HIZENTRA® Phase III DM study initiated
- HAEGARDA® Phase III HAE study in Japan initiated
- HAEGARDA® paediatric approval in US
- PRIVIGEN® approved for PID, SID & CIDP in Japan
- Garadacimab (Anti-FXIIa) Phase II HAE study results presented at EAACI Congress; FDA granted orphan drug designation (ODD)
- FDA granted HIZENTRA® ODD for CIDP



Haematology

- CSL200 (Gene Therapy) in SCD Phase I study initiated
- FDA granted CSL200 fast track designation
- CSL889 (Hemopexin) Phase I SCD study initiated
- CSL889 (Hemopexin) ODD approved in EU & US for SCD



Respiratory

- CSL311 (Anti-Beta Common) Phase I study in mild asthmatic patients initiated



Cardiovascular and Metabolic

- CSL112 (ApoA-1) Phase III study (AEGIS-II) >9500 patients recruited
- CSL112 (ApoA-1) AEGIS-II first futility analysis conducted; trial to continue as planned



Transplant

- AAT for prevention of GvHD Phase III study enrolment into Cohort 2 completed
- FDA granted AAT ODD for GvHD treatment & prevention
- Clazakizumab AMR study initiated
- FDA granted Clazakizumab ODD and fast track designation for CABMR



Acquisitions & Alliances

- Alliance with Seattle Children's Research Institute to develop WAS & XLA stem cell gene therapies for PID
- Agreed to acquire exclusive global license rights to AMT-061 (EtranaDez) for haemophilia B*
- Acquisition of Vitaeris Inc. and Clazakizumab

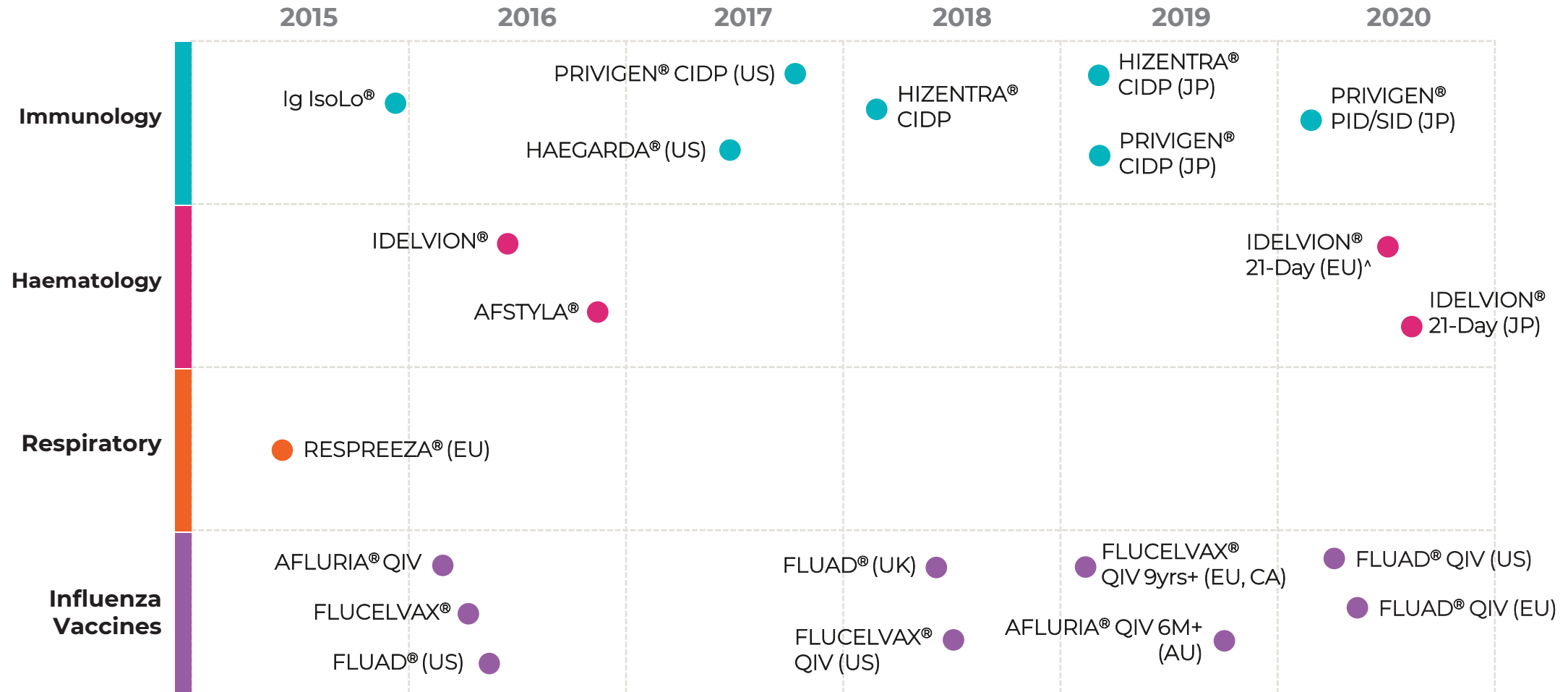
* Transaction with uniQure is subject to customary regulatory clearances before closing



Influenza Vaccines

- Adjuvanted quadrivalent influenza vaccine, FLUAD® TETRA, approval in EU and FLUAD® QUADRIVALENT in US
- US FDA approval of AUDENZ™ - adjuvanted, cell-based influenza A (H5N1) pandemic vaccine
- aQIVc (cell antigen + MF59®) new product development commenced

Key Past Launches from R&D Portfolio

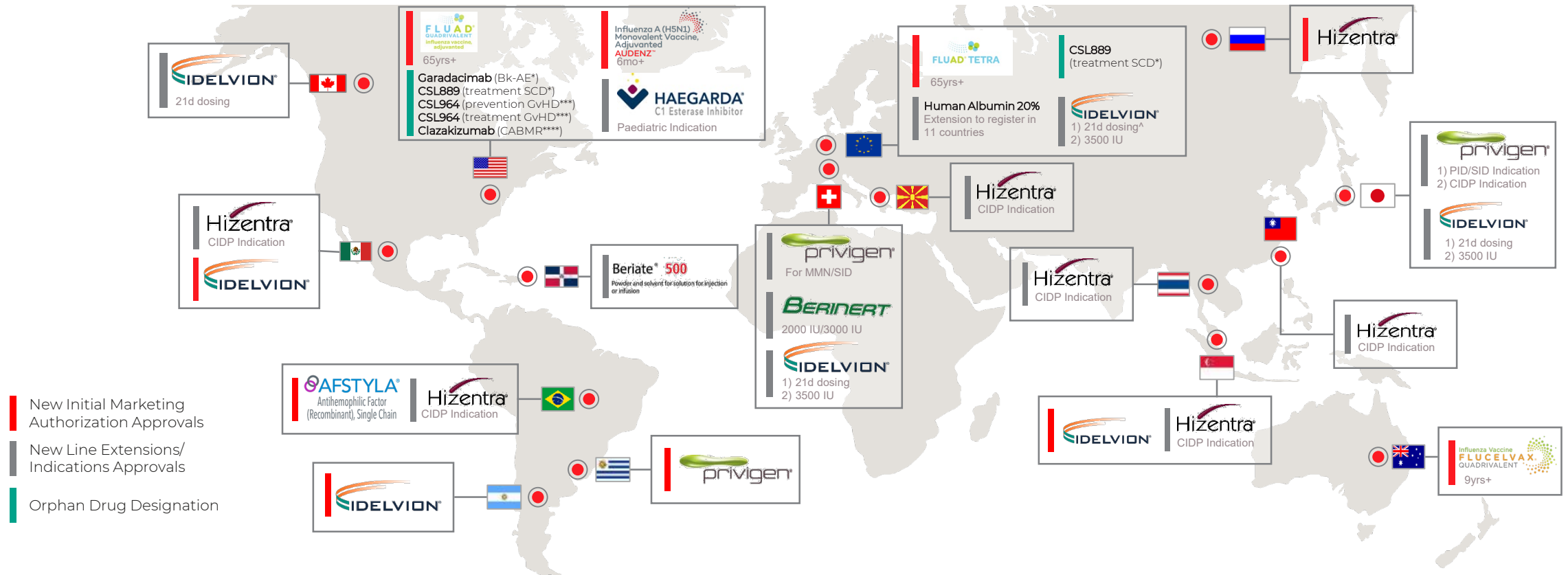


Timelines shown by calendar year

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

Notable Regional Regulatory Action

1 July 2019 – 1 October 2020



* Bk-AE: bradykinin-mediated angioedema

** SCD: Sickle Cell Disease

*** GvHD: Graft-versus-Host Disease

**** CABMR: Chronic Antibody-Mediated Rejection

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

12 Driven by Our Promise™

On-going Activities

Hizentra®

Expanded label for enhanced administration parameters

IDELVION®

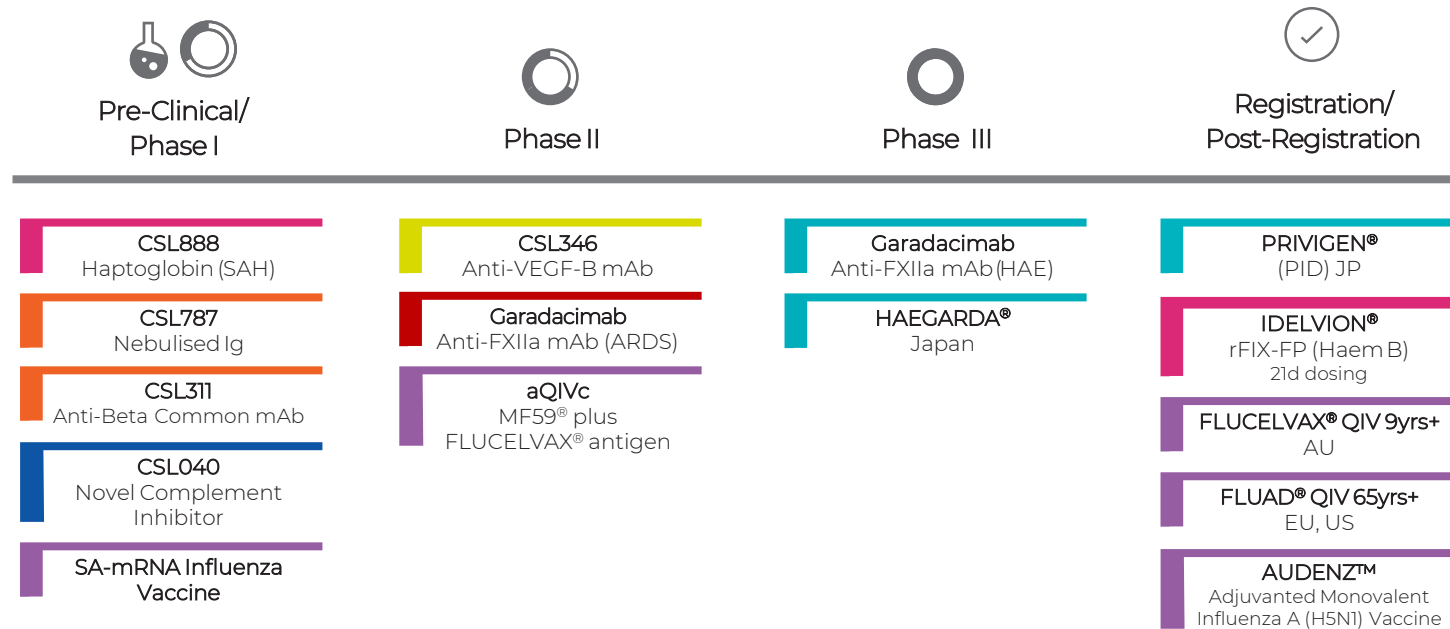
Expanded label for dosing every 21 days in patients ≥12 years of age

HAEGARDA® C1 Esterase Inhibitor

Labeling update for expanded populations

CSL

R&D Portfolio Progression in 2020

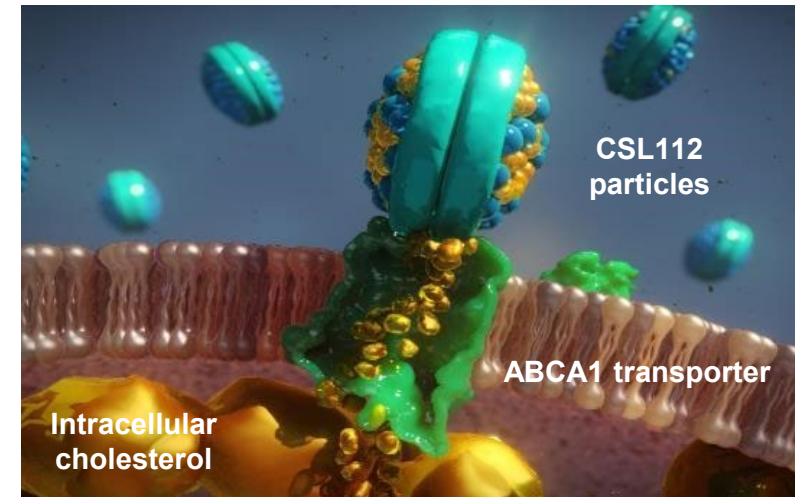


Calendar Year 2020

■ Immunology
 ■ Haematology
 ■ Respiratory
 ■ Cardiovascular & Metabolic
■ Transplant
 ■ Influenza Vaccines
 ■ COVID

CSL112 ApoA-1

- All countries and sites reactivated
- Japan now active and enrolling well
- 1st futility analysis in 2020 passed



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

Screening

Randomisation

1° Endpoint : MACE

D90

MACE Follow Up

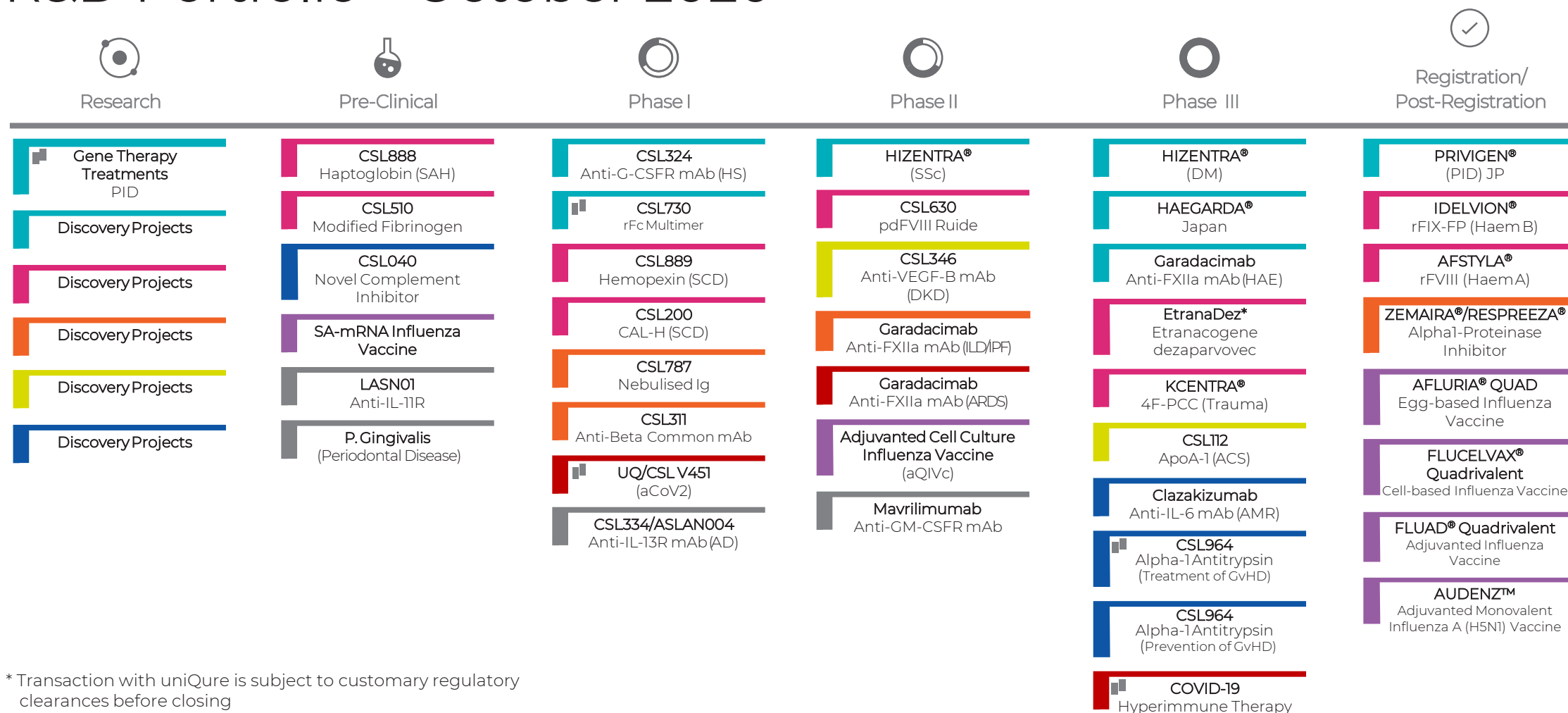
D180

D365

6g CSL112
Placebo

AMI – Acute Myocardial Infarction
MACE - major adverse cardiac events

R&D Portfolio – October 2020



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

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



Research

Protein Therapies
Gene Therapies
Vaccines

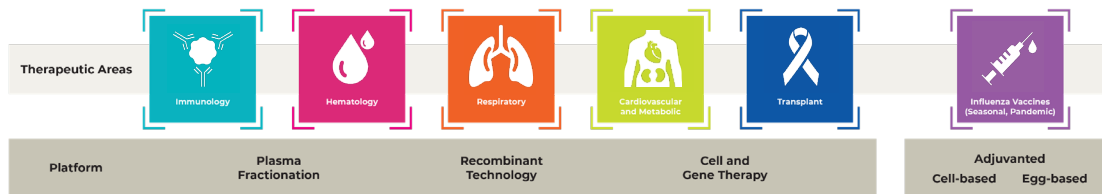
Andrew Nash PhD

Senior Vice President, Research and
CSO

CSL Behring

CSL Research

- Global team exploiting internal and external expertise and 4 drug discovery platforms to deliver innovative development opportunities across CSL therapeutic areas
- Expertise and track record in plasma and recombinant protein drug discovery, influenza vaccines and building capability in cell and gene therapy
- Expertise and depth of talent across 6 TAs



CSL Behring
Research
Melbourne

Bio21 Institute, University
of Melbourne



CSL Behring
Research Marburg



Seqirus Research Boston



CSL Behring
Research Bern

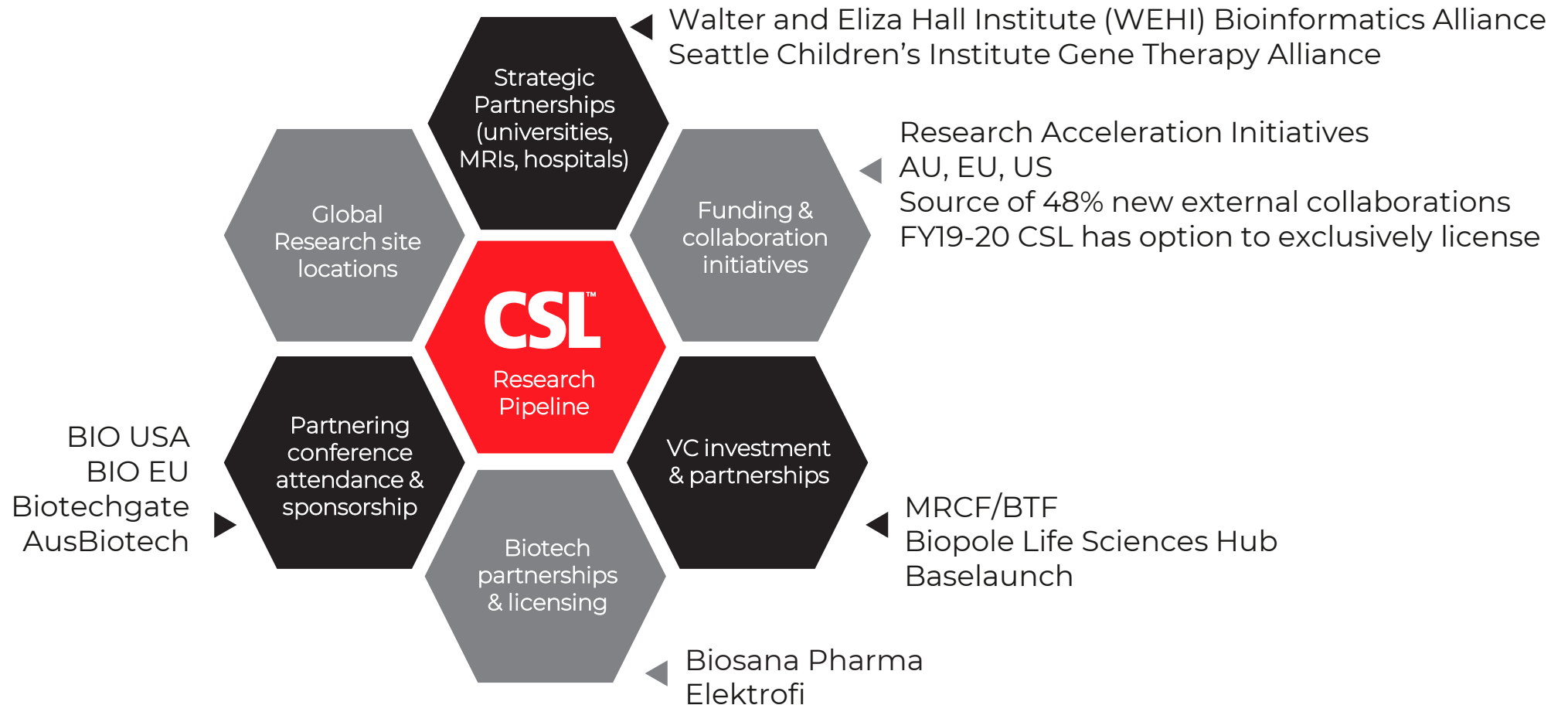
Swiss Inst. for Translational &
Entrepreneurial Medicine,
University of Bern



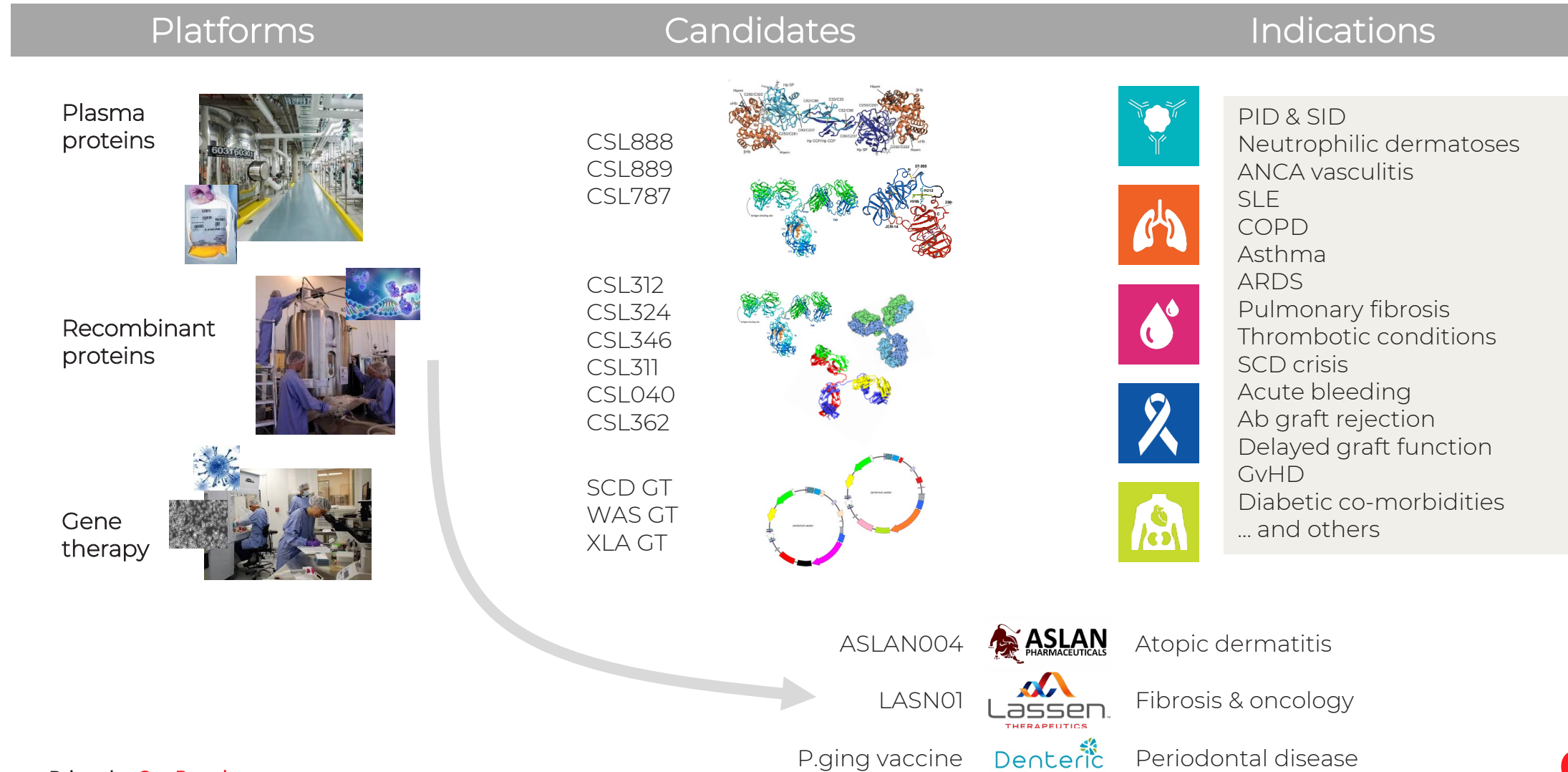
CSL Behring
Research US
Pasadena, KOP

CSL Behring Research – Sourcing Innovation

Research External Innovation Strategy
- the competition for innovation

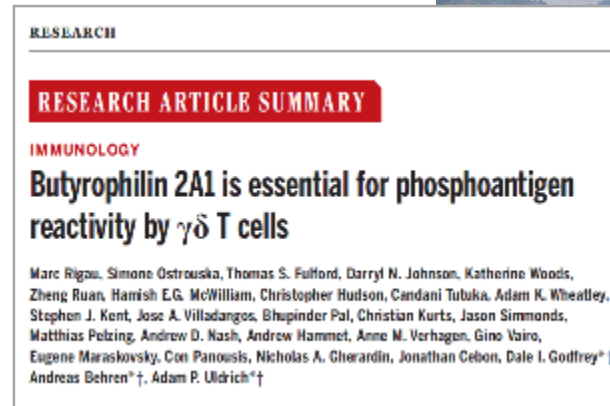


Growing the Development Portfolio

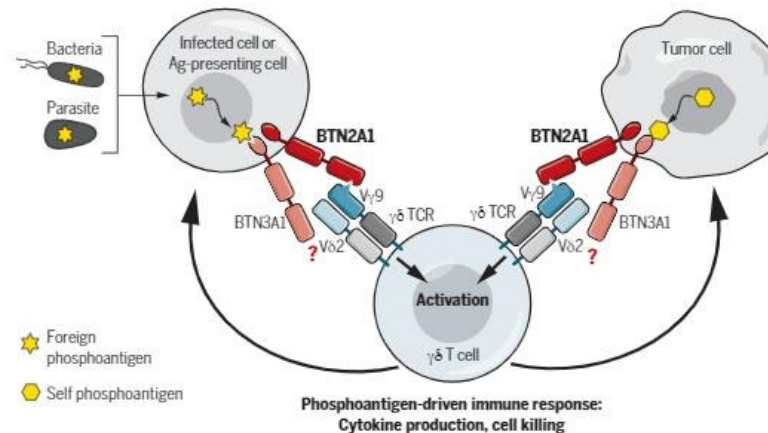
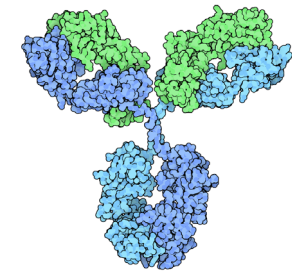


Collaboration Delivers Innovation

Collaboration leads to the discovery that BTN2A1 is required for the activation of $\gamma\delta$ T cells

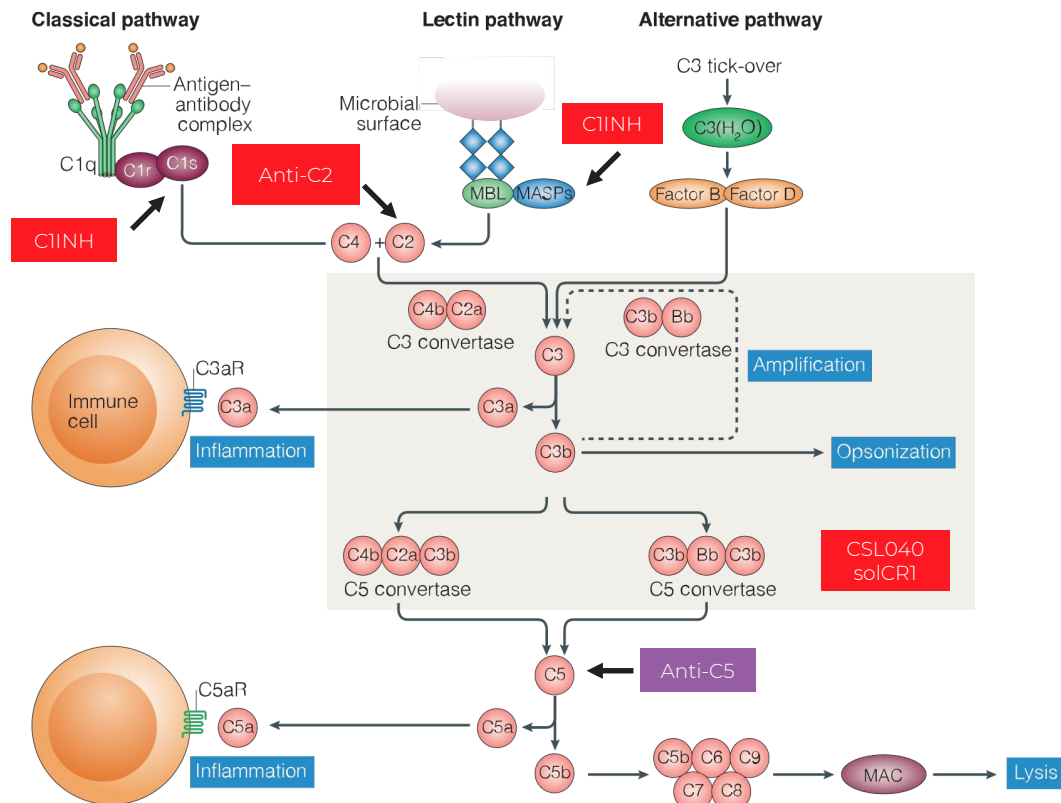


Antagonist and agonist monoclonal antibodies for use in autoimmune disease and immuno-oncology



Targeting Complement Regulation

Complement Pathways



Potential indications

Chronic Indications, Classical/Lectin Pathway (Anti-C2 mAb)



Acute Indications, Classical/Lectin Pathway (CSL040)



Cyclic Acute *ex vivo* Pathway (CSL040)



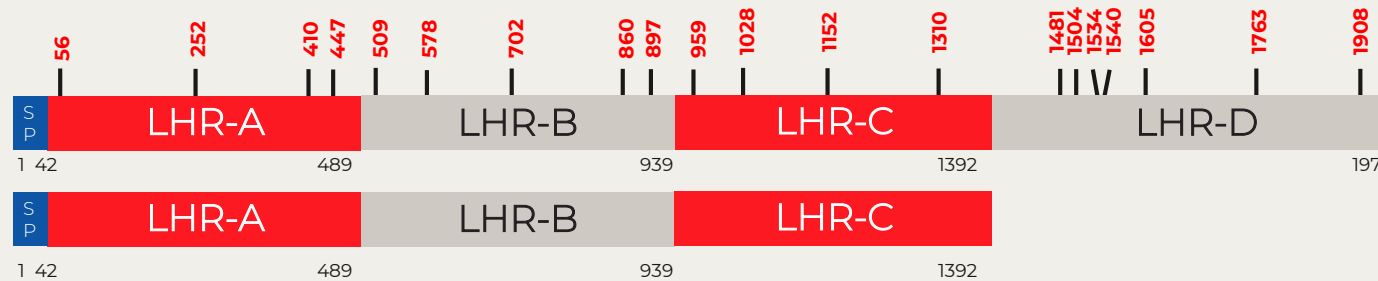
Alternative Pathway needing chronic inhibitor (CSL040)



Source: Trouw, L.A. et al., (2017) *Nat. Rev. Rheumatol.* 13(9);538-547

CSL040 Complement Receptor 1 Inhibitor

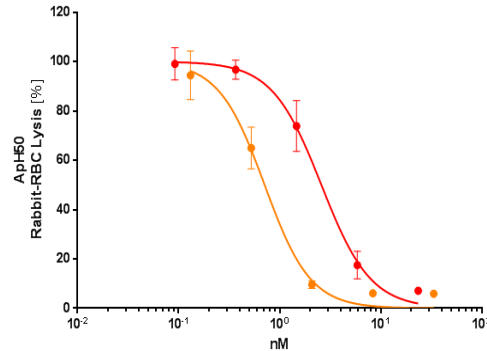
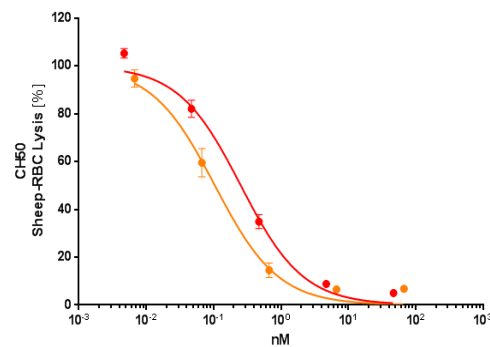
CR1 Truncation Mutant, rCR1(1392) / CSL040



rCR1(1971) / TP-10

rCR1(1392) = CSL040

Haemolytic complement inhibition assays (human serum)



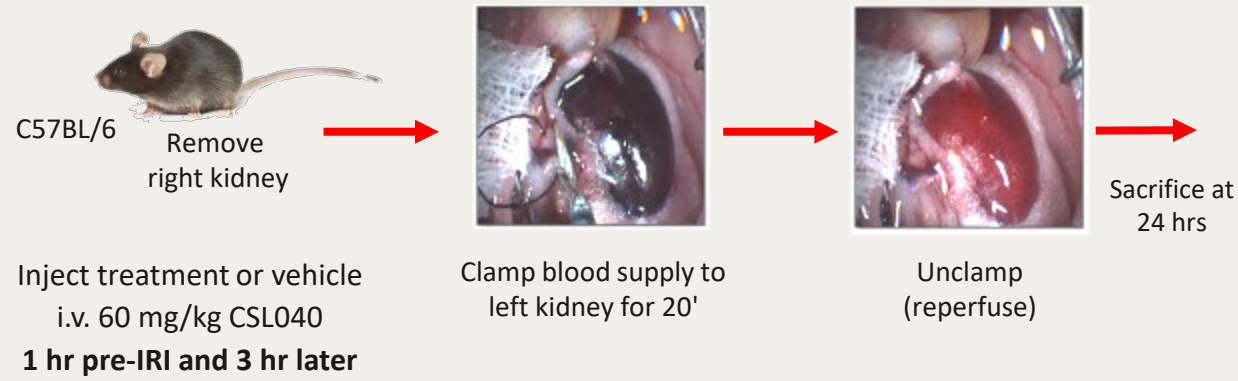
Inhibitor	IC ₅₀ Classical	IC ₅₀ Alternative
rCR1(1971)	253 pM	2587 pM
rCR1(1392)	104 pM	709 pM



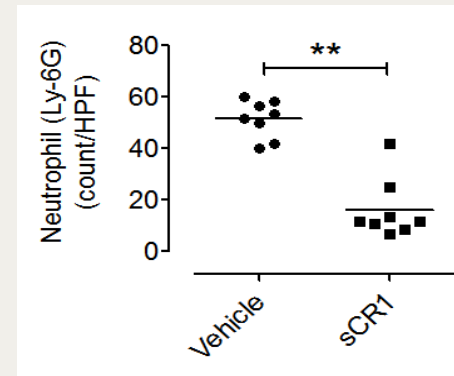
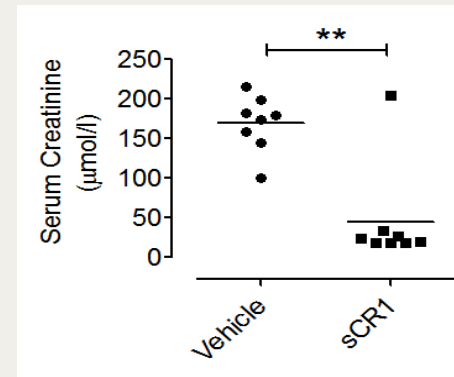
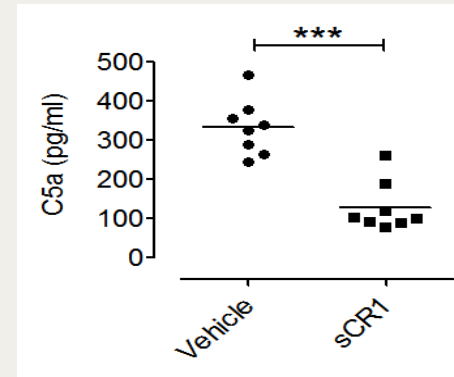
rCR1(1392) has 2-3 fold increased potency *in vitro* as compared to rCR1(1971) / TP-10

CSL040 Complement Receptor 1 Inhibitor

Renal Ischemia-reperfusion Injury (IRI) Mouse Model

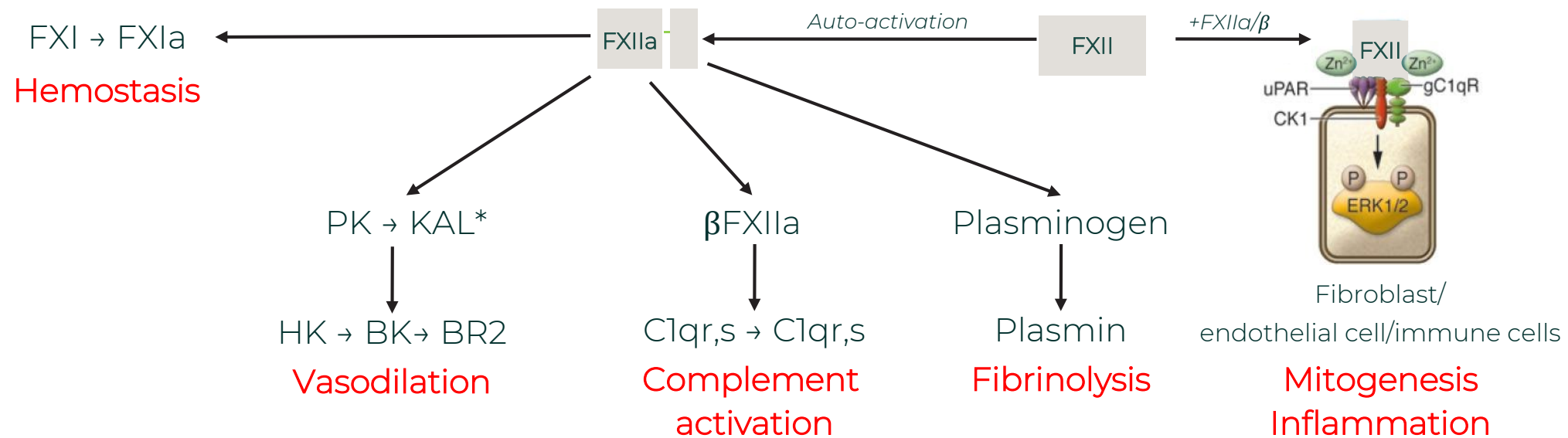


- CSL040 inhibits complement activity, leukocyte infiltration and renal damage in IRI model
- Pharm/Tox and product development to commence mid-2021



Garadacimab

Global leaders in FXII biology – new opportunities for Garadacimab



Beyond Hereditary Angioedema

- New opportunities in fibrotic disease, cardiovascular disease, inflammatory disease

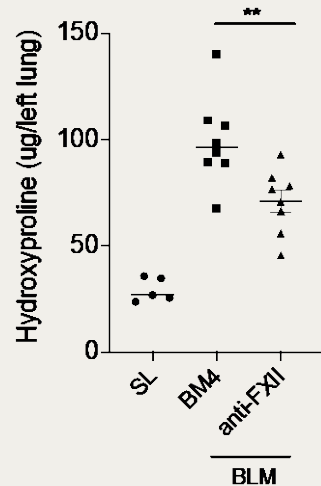
* Feedback loops removed for simplicity

Garadacimab

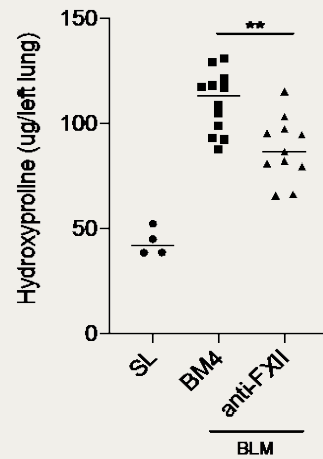
Pulmonary Fibrosis

Garadacimab reduces fibrosis in the mouse bleomycin model of IPF

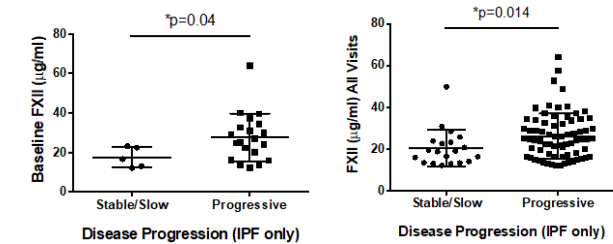
Garadacimab from D0



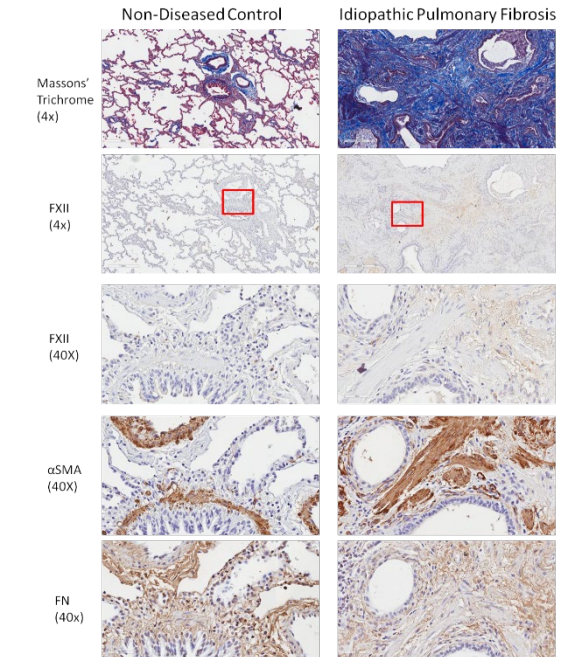
Garadacimab from D5



Plasma FXII levels are higher in IPF patients with progressive disease



FXII expression is higher in the IPF lung



Translation
to human disease



Phase II to commence H2 2021

IPF – Idiopathic Pulmonary Fibrosis

Gene Therapy

uniQure

AMT-061 (EtranaDez) gene therapy (GT) for the treatment of Haemophilia B

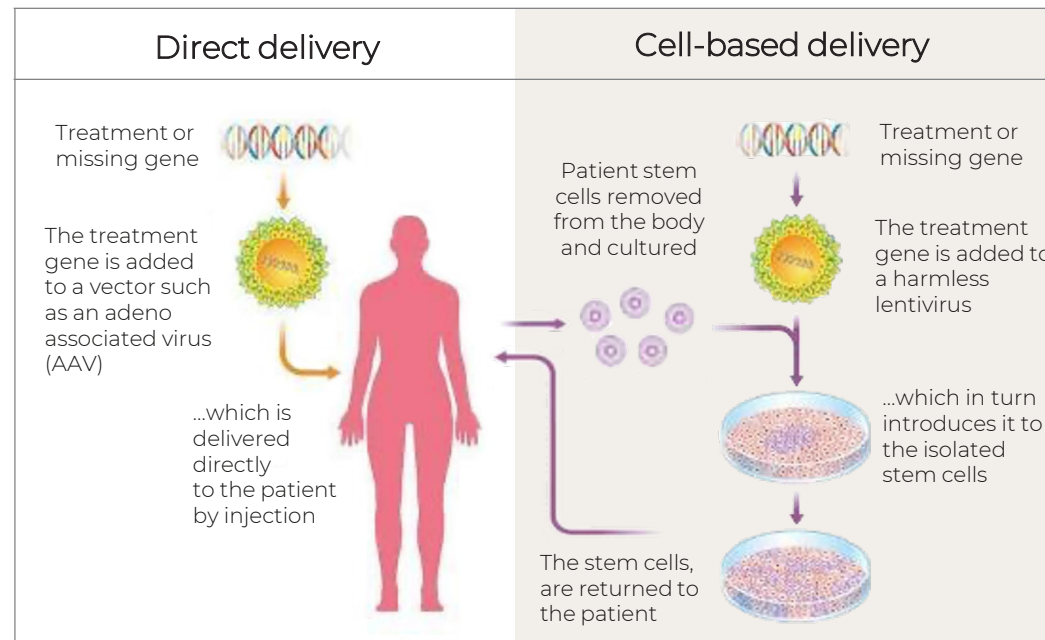
AAV5 vector encoding FIX Padua variant

May be clinically effective in patients with pre-existing Abs

Phase IIb mean FIX activity at 52 weeks 41%

Phase III study in progress

Upon deal completion, which is subject to customary regulatory clearances, CSL will have exclusive global rights to supply



Research Institute

Seattle Children's Research Institute (SCRI) – world leading preclinical & clinical experience with Lentivirus based GT

Alliance consolidates and extends CSL GT capability

Wiskott Aldrich Syndrome (WAS)

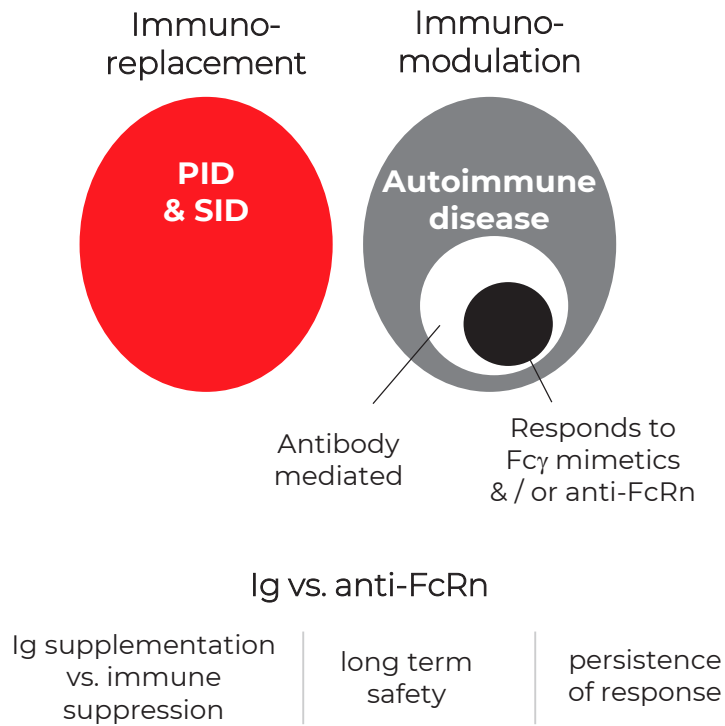
- CSL LVV and Select+ tech.
- Ph I/II expected to commence H2-2022

XLA

- SCRI LVV
- Ph I/II expected to commence H2-2022

Fc Mimetics and Anti-FcRn mAbs

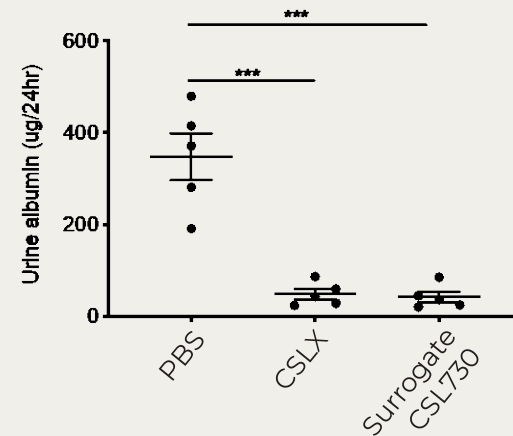
IVIg & SCIg Usage



IVIg – Intravenous Immunoglobulin
SCIg – Subcutaneous Immunoglobulin

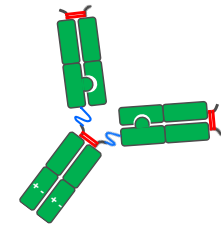
Novel Applications for IgFc Mimetics

Surrogate CSL730 is effective in a model of glomerulonephritis*



* Disease induced by administration and cross-linking of antibodies directed against the kidney glomerular basement membrane

CSL730 Clinical Development



CSL / Momena partnership



Phase I (moved to subcutaneous administration)

CSL – COVID-19 Vaccines

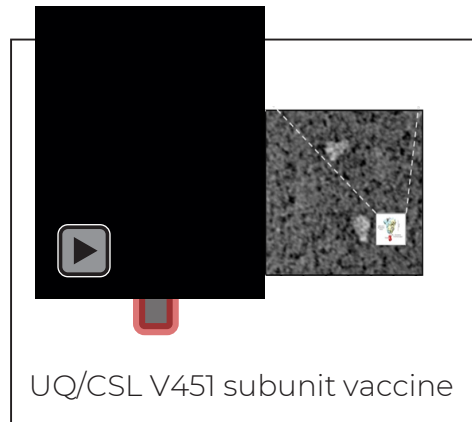
	UQ/CSL V451	AZD1222
Partners	University of Queensland, Coalition for Epidemic Preparedness Innovations (CEPI)	AstraZeneca
Vaccine Format	Recombinant virus spike protein (molecular clamp technology) formulated with MF59 [®] adjuvant	Adenovirus vector designed to express spike protein of COVID-19 virus <i>in situ</i>
CSL Responsibility	Vaccine manufacture, clinical trials, supply	Vaccine manufacture
Current Status	Ph I ongoing, FSI Ph II/III Dec 2020	Phase III ongoing

FSI – First subject in

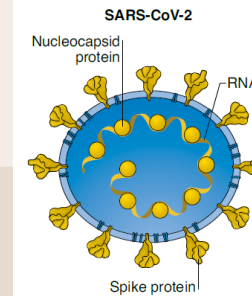
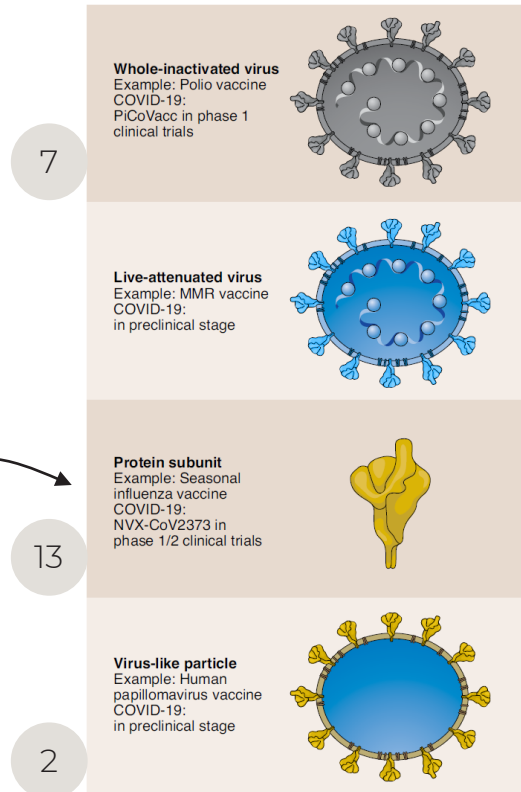
CSL – COVID-19 Vaccines

Candidates in clinical development - 42

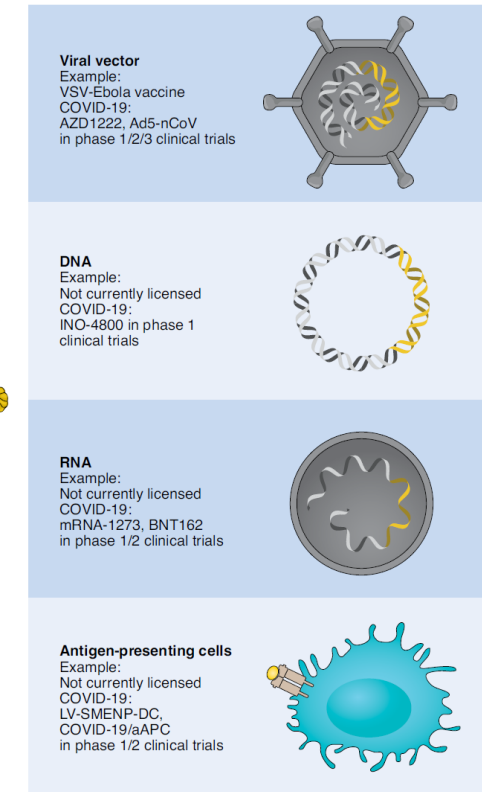
Candidates in pre-clinical development - 151



Classical Platforms



Next-Gen Platforms



AZD1222

plus 2 live replicating viral vectors

In Clinical Development

Source: van Riel, D & de Wit, E., (2020) *Nature Materials* 19; 810-812

CSL – Production of UQ/CSL V451

CSL Biotech. Manufacturing Facility, Broadmeadows



2000L Cell Culture



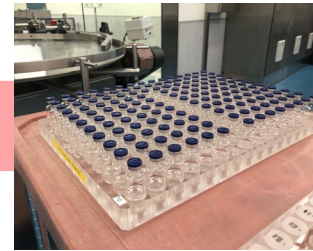
Harvest by Depth Filtration



Drug Substance



Drug Product Filling, to be Formulated with MF59®



Vaccination

- Process scaled up and industrialised from Ph I as required
- Production, Fill/Finish for Ph II/III underway
- Same manufacturing platform technology to be used for AZD1222



Immunology & COVID-19 Response

Mittie Doyle MD

Vice President, R&D Immunology

CSL Behring

Christal: a nurse living with chronic inflammatory demyelinating polyneuropathy (CIDP)



Working Together to Fight COVID-19 with Immunoglobulin (Ig) Therapy

1. FOUNDERS

The logo for CSL Behring, featuring the text "CSL Behring" in a bold, red, sans-serif font.



2. MEMBERS



The logo for octapharma, featuring the word "octapharma" in a blue, sans-serif font.

3. CONTRIBUTORS



4. SUPPORTERS



The logo for facebook, featuring the word "facebook" in a blue, sans-serif font.

The logo for Google, featuring the word "Google" in its multi-colored, sans-serif font.

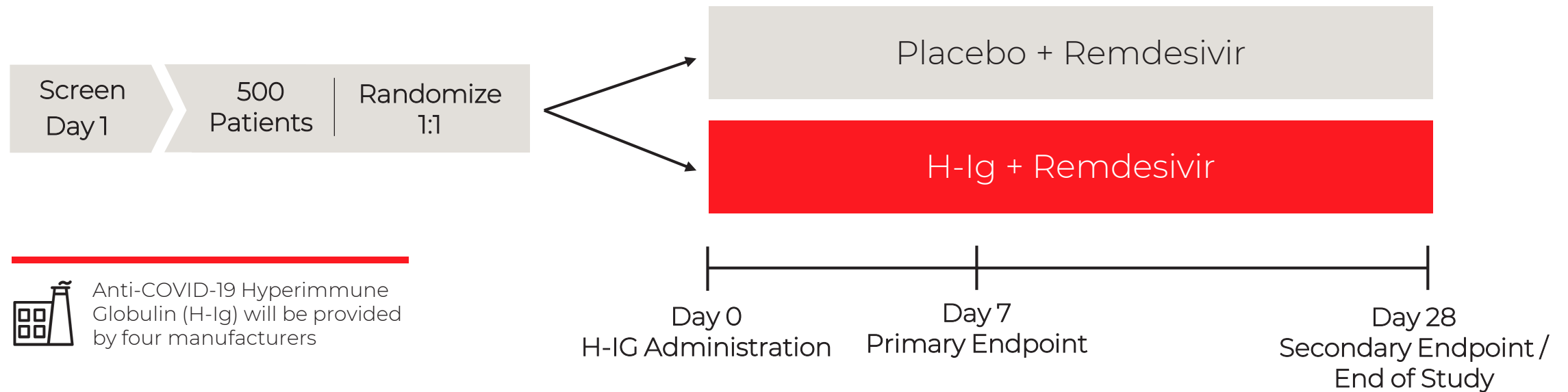


The logo for Uber Health, featuring the word "Uber Health" in a black, sans-serif font.



The logo for AsahiKASEI, featuring the text "AsahiKASEI" in a blue, sans-serif font.

Collaborative Hyperimmune Ig Trial in COVID- 19



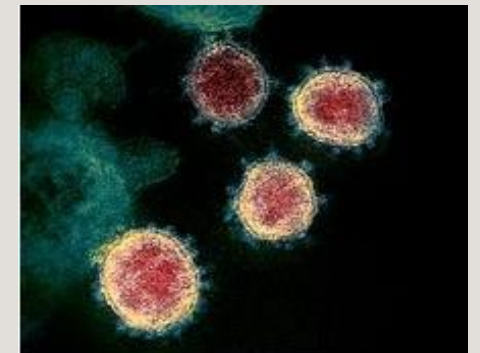
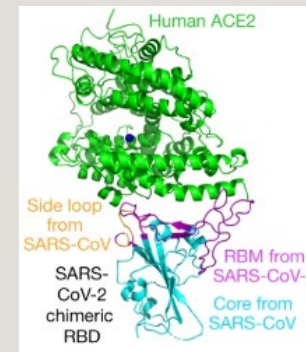
 Phase III enrolling

Hyperimmune Program for Australia

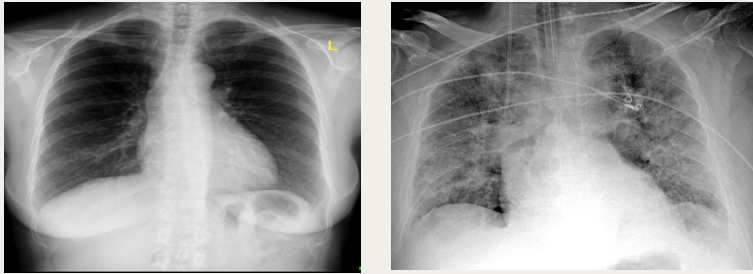
- Convalescent plasma collected by the Australian Red Cross Lifeblood
- CSLB has manufactured a clinical batch ready for clinical testing
- A single centre, Phase I, study of the Australian H-Ig product in 24 healthy volunteers
- Leverage global H-Ig data



Phase I to commence H2 2020

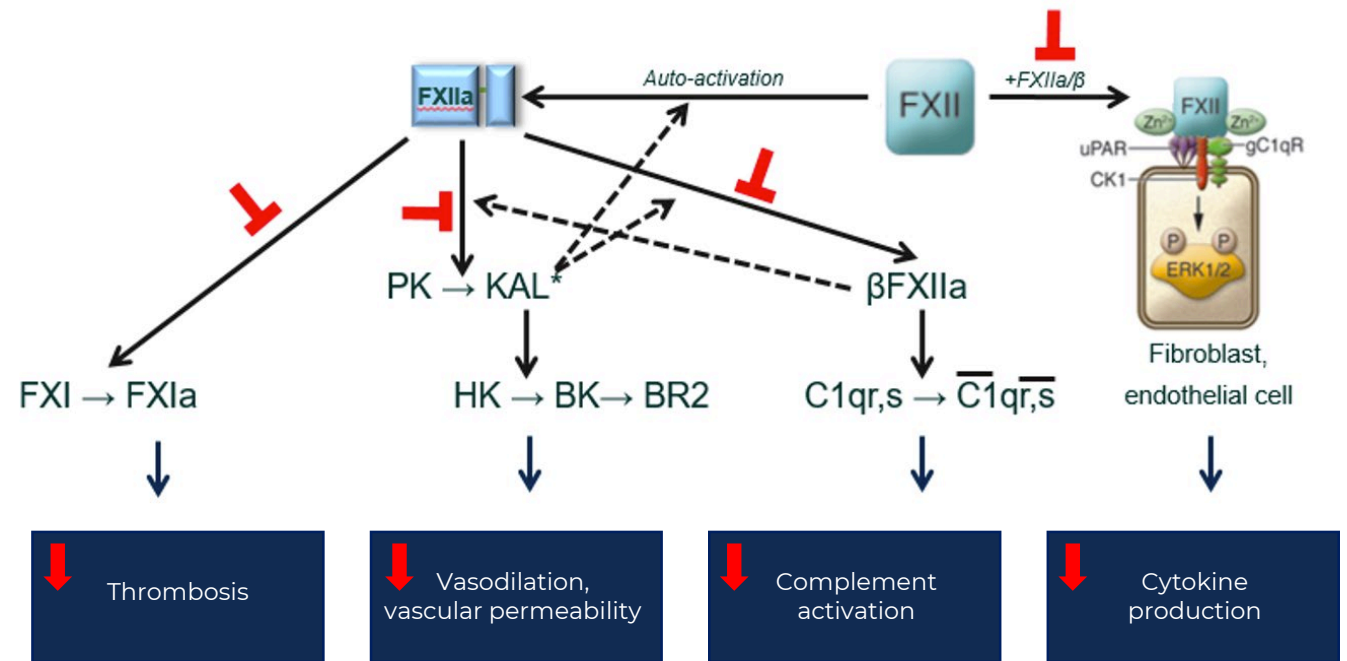


Potential Benefits of Blocking Factor XIIa in COVID-19



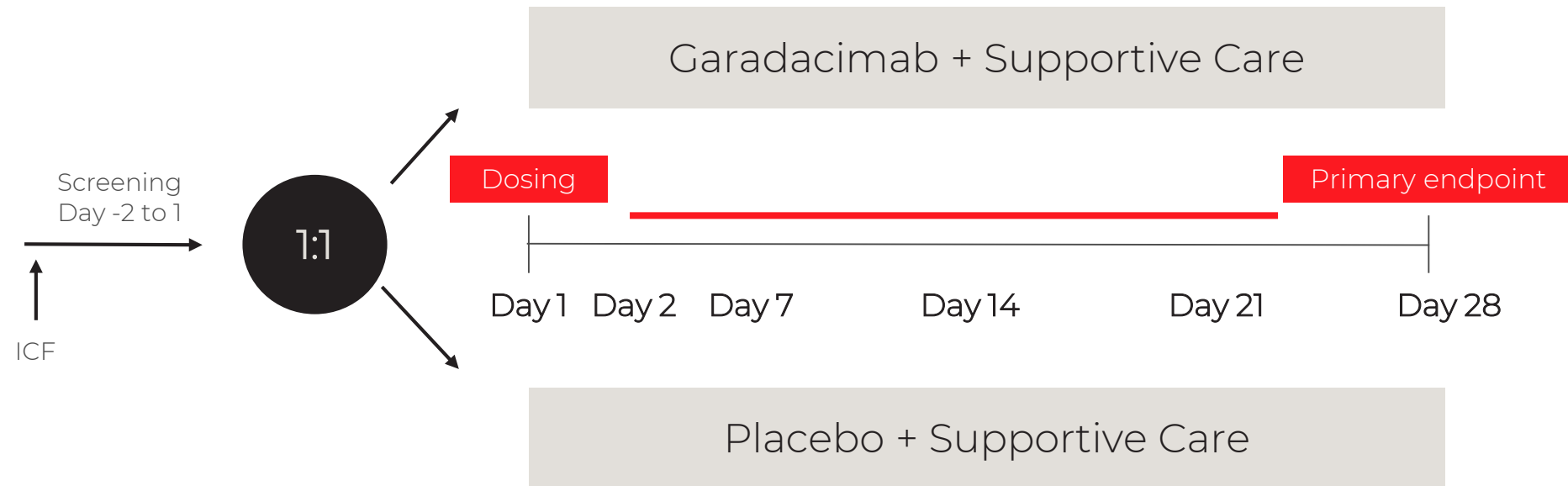
Primary Drivers of ARDS in COVID-19

- Inflammation
- Thrombosis
- Vascular Permeability



ARDS – Acute Respiratory Distress Syndrome

Garadacimab in COVID-19



- Population - 124 patients with severe COVID-19 complications
- Primary objective - prevent progression to intra-tracheal intubation or death



Phase II ongoing

Garadacimab in HAE: The Vanguard Program



Phase II Study
Phase III Study Design



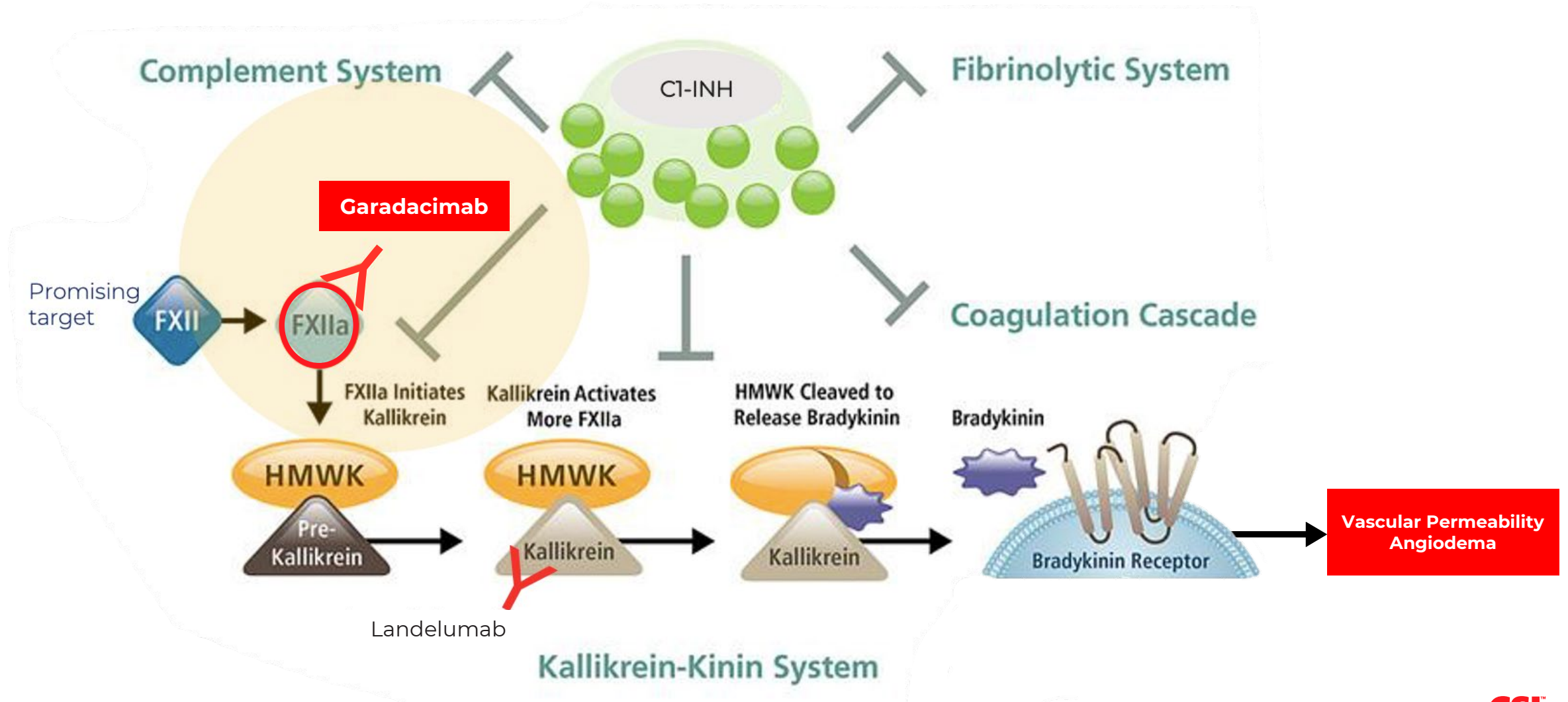
Autosomal dominant genetic condition
1 in 10,000 – 50,000 people

Unregulated protein cascade
→ elevated levels of bradykinin
→ fluid release into tissues
→ swelling in specific parts of body

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

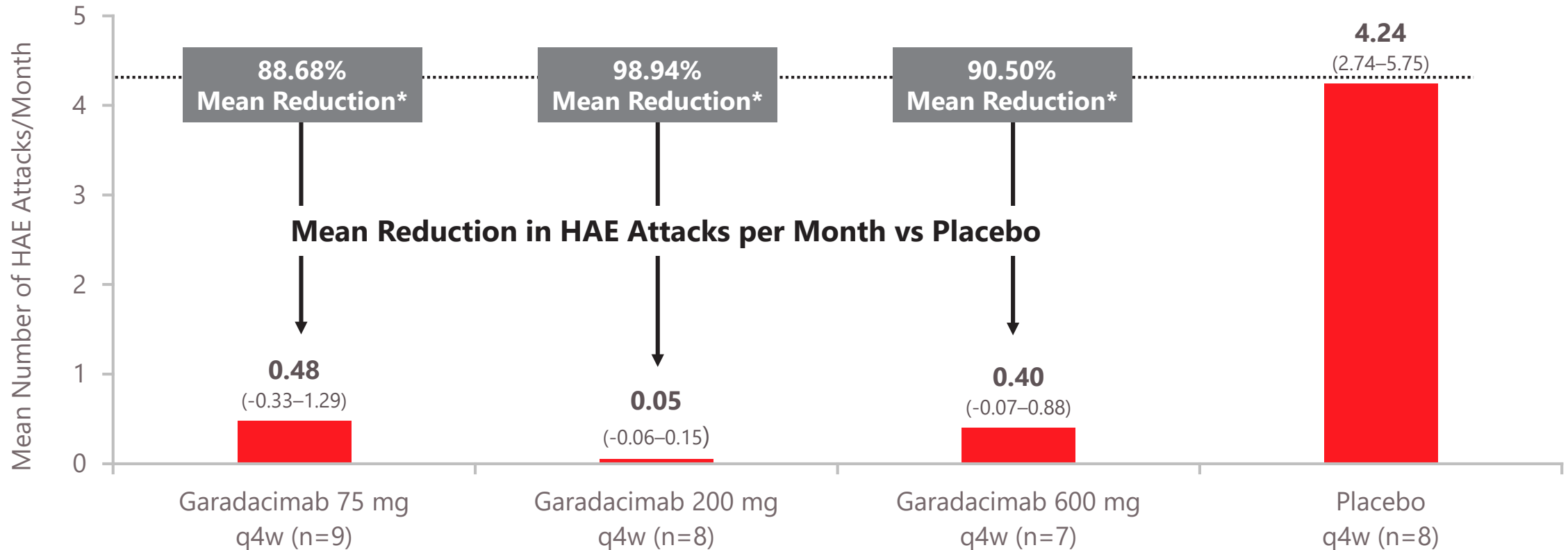
HAE – Hereditary Angioedema

Garadacimab and Factor XIIa in HAE



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

Primary Endpoint



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

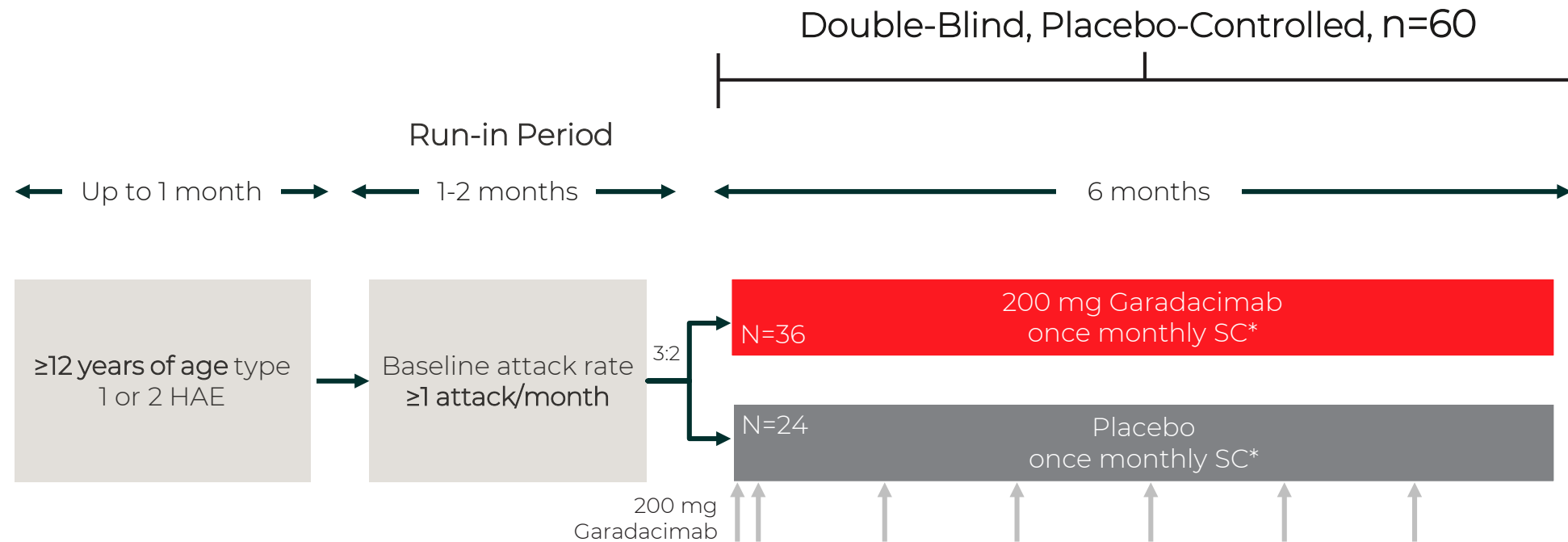
* Mean percentage reduction in HAE attacks vs Placebo

95% CI values are given in brackets

HAE - hereditary angioedema; q4w - every 4 weeks; TP1 - Treatment Period 1

VANGUARD

Garadacimab Pivotal Phase III Study



Randomization will be stratified by:

- Age (≤ 17 years and > 17 years)
- Disease severity

* Subjects will receive 400 mg loading dose as first dose (2×200 mg)



Phase III to commence H1 2021

HAE in Japan

Epidemiology

No ethnic differences worldwide*

Prevalence ~1/50,000, 2,400 estimated patients in Japan; HAE type 1 (85%), type 2 (15%)

Medical Practice

No drugs approved for long-term prophylaxis

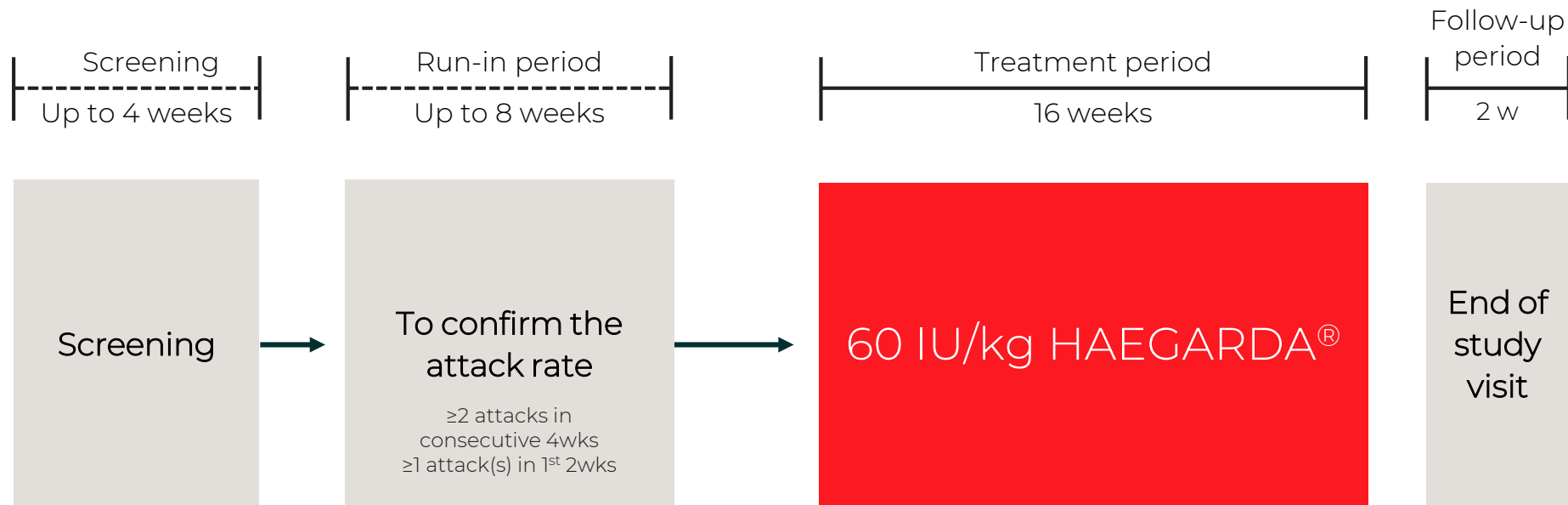
Investigating both Garadacimab and HAEGARDA® for long term prophylaxis

* Source: Zuraw, B. (2010) *World Allergy Organ J* 3(9 Suppl); S25-8

Investigating HAEGARDA® for HAE in Japan

Open-label, single-arm Phase III study in ≥ 8 patients with HAE₁₊₂

- Twice-weekly subcutaneous administration of 60 IU/kg HAEGARDA®
- Primary Endpoint: HAE attack rate during treatment vs during Run-in period



Phase III ongoing

Dermatomyositis – a Severe Autoimmune Disease

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

Presents with proximal weakness, characteristic rash and systemic manifestations

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

Current treatment: corticosteroids and azathioprine, other immunosuppressives: no approved disease-modifying anti-rheumatic drugs (DMARDs)

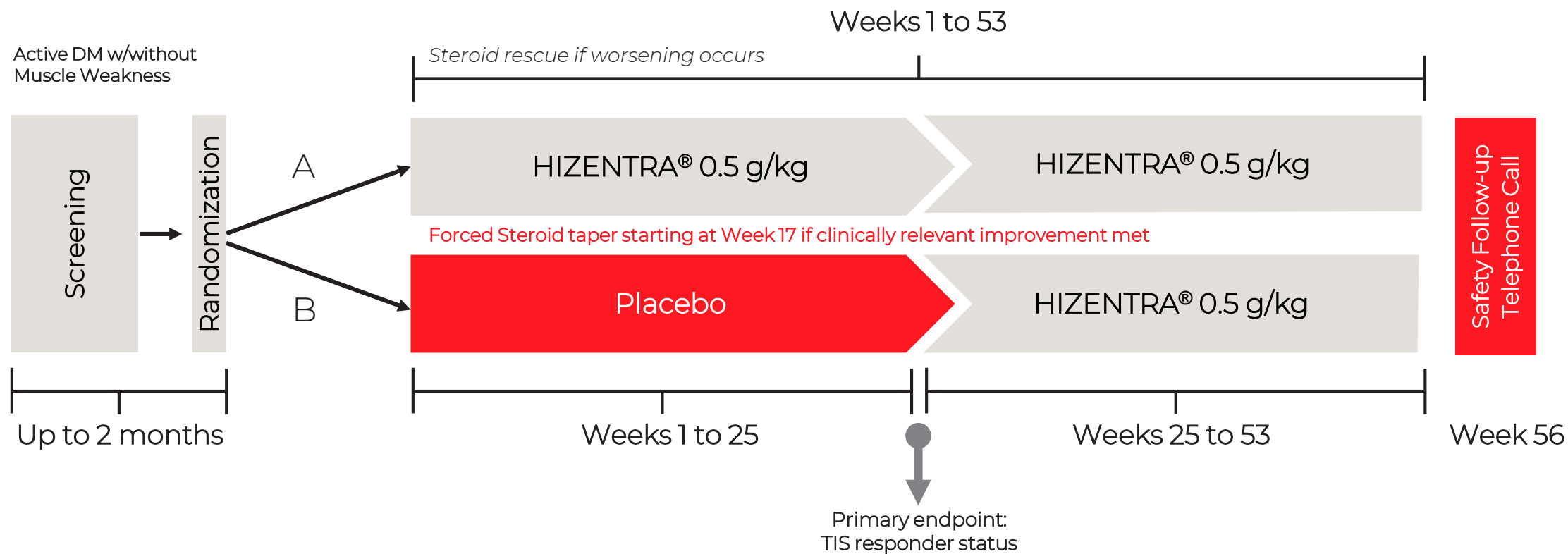
High unmet need for long-term treatments without systemic side effects

* Source: Svensson J, et al., (2017) *Clin Exp Rheumatol*. 35(3):512-515



RECLAIM

Phase III Study of HIZENTRA® in Adults with Dermatomyositis



Phase III ongoing



Commercial

Bill Campbell

Executive Vice President and Chief
Commercial Officer

CSL Behring

Zahra: living with Hereditary Angioedema (HAE).

FY20 Highlights



Sales of \$7.7Bn;
increased by 8%¹



Strong underlying demand across the portfolio



Balanced regional & key market growth



New products contributing significantly to growth



lg growth well above market



Continuing to invest in foundational tools for future growth



Successful transition of business model in China

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

FY20: Strong Performance Across the Portfolio



20% growth¹ in revenue YoY;
Continued growth² in PID, CIDP



New launches in EU, APAC and Canada;
12% growth¹ in revenue YoY



12% growth¹ in revenue YoY; **Further penetration²** in US



34% growth¹ in revenue YoY and clear **SCIg market leader²** globally



25% growth¹ in revenue YoY;
Market leadership² in several key markets, including US, Germany, Japan, Switzerland and Italy

21% growth¹ in revenue YoY;
Growth³ in nearly all launched markets



Transitioned to GSP in China;
11% growth¹ in revenue YoY ex-China



20% growth¹ in revenue YoY; approval of **4&5 gr vials**

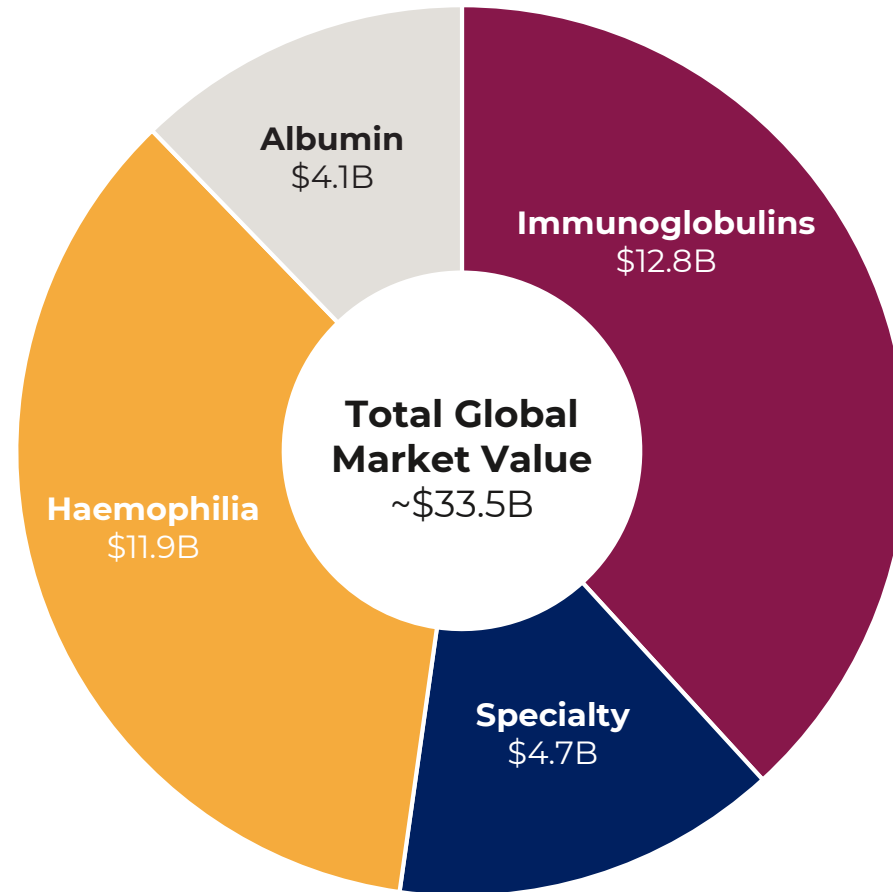


1. Growth percentages shown at constant currency to remove the impact of exchange rate movements, facilitating comparability of operational performance.

2. Data on file

3. CSL Internal Reports

Targeted Protein Therapeutic Market

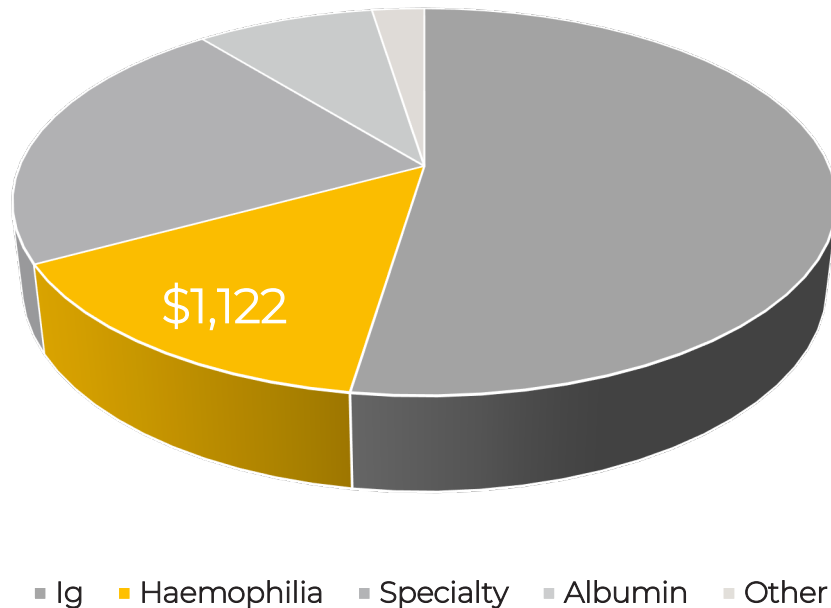


Source: Analyst Reports, Company Annual Reports, data on file;
Haemophilia mkt includes Inhibitor mkt

Haemophilia

Sales increased by 8%¹

FY20 Sales



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

2. Data on file

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



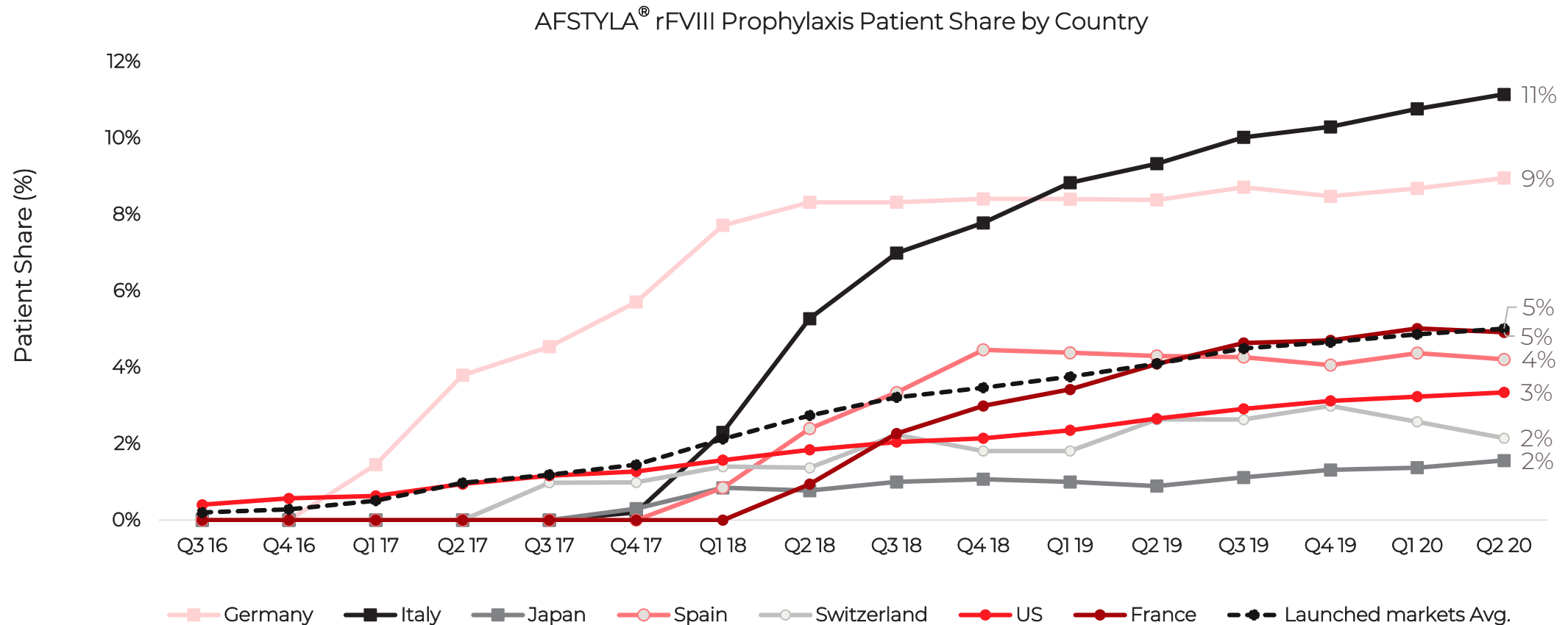
Plasma Coagulation Factors

- Transformational product
- Leadership position in several key markets²
- Approval of 21-day dosing in EU[^], CH, JP & CA
- Patient retention strategies and ongoing switches in competitive environment
- New market launches
- Modest growth in HUMATE[®] /HAEMATE[®] (vWF)
- pdVIII competitive pressures
- MONONINE[®] to IDELVION[®] switches

Recombinant Coags +18%¹

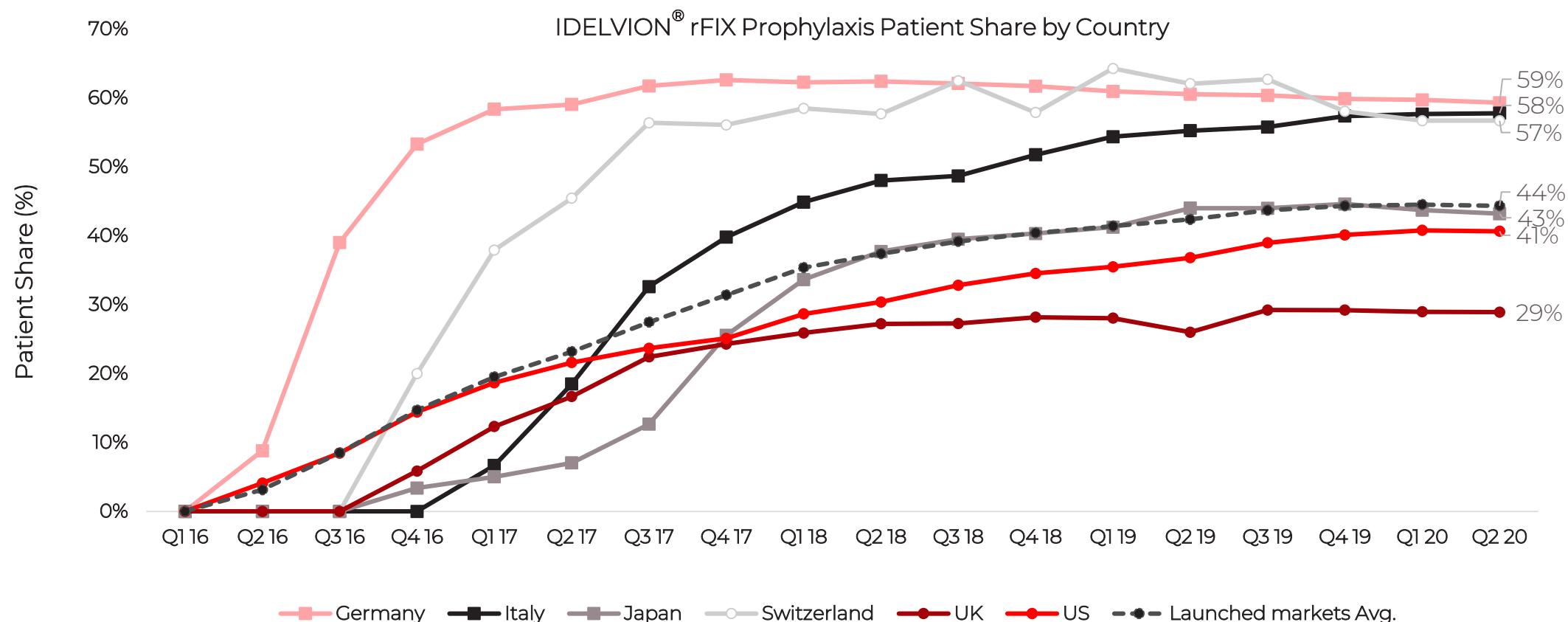
PD Coags (3%)¹

AFSTYLA® Share of rFVIII Prophylaxis – Growing Steadily



Source: Data on file. Data only available for 7MM, BR, CH and AR through Q2'20; Launched markets include DE, IT, JP, ES, CH, US, and FR
7MM refers to US, DE, FR, IT, UK, ES & JP

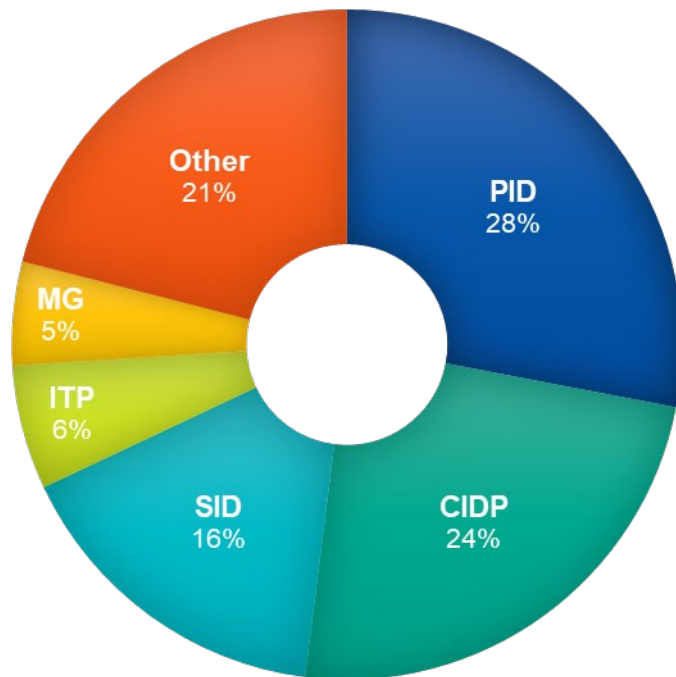
IDELVION® Share of rFIX Prophylaxis – Significant Shares



Source: Data on file. Only available for 7MM, BR, CH and AR through Q2'20; Launched markets include DE, IT, JP, CH, UK, and US
7MM refers to US, DE, FR, IT, UK, ES & JP

Immunoglobulin Market

Global Ig Volume by Indication



Source: Data on file

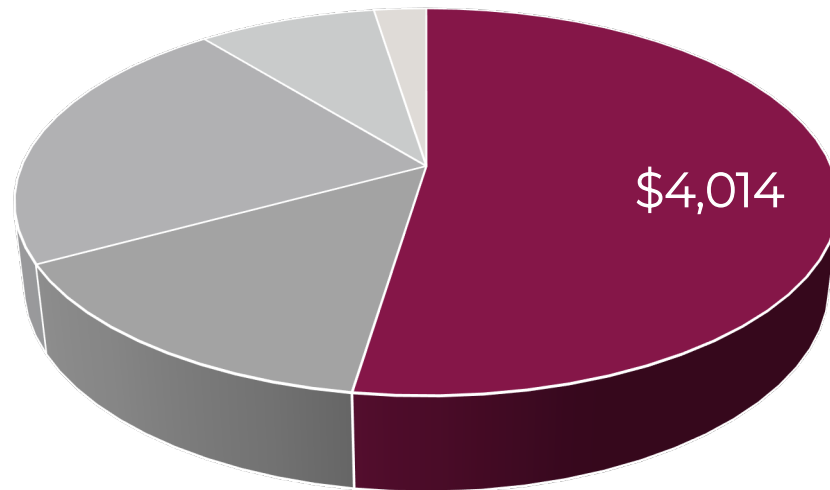
Market Dynamics

- Market growth above historical rates
- Growth in PID & CIDP
- Expanding usage for SID
- Market supply tightness pre-COVID-19
- COVID-19: Impact on plasma collection
- Shifting preference to SCIg and home administration

Immunoglobulins¹

Sales increased by 22%²

FY20 Sales



■ Ig ■ Haemophilia ■ Specialty ■ Albumin ■ Other



- Increased disease awareness & improved diagnosis in chronic therapies (PID & CIDP)
- Expansion of SID usage
- Launched PID/SID in Japan

- Market leader
- Increased preference for home administration
- Orphan exclusivity for CIDP in the US
- Continued CIDP launches

*IVIg +16%²

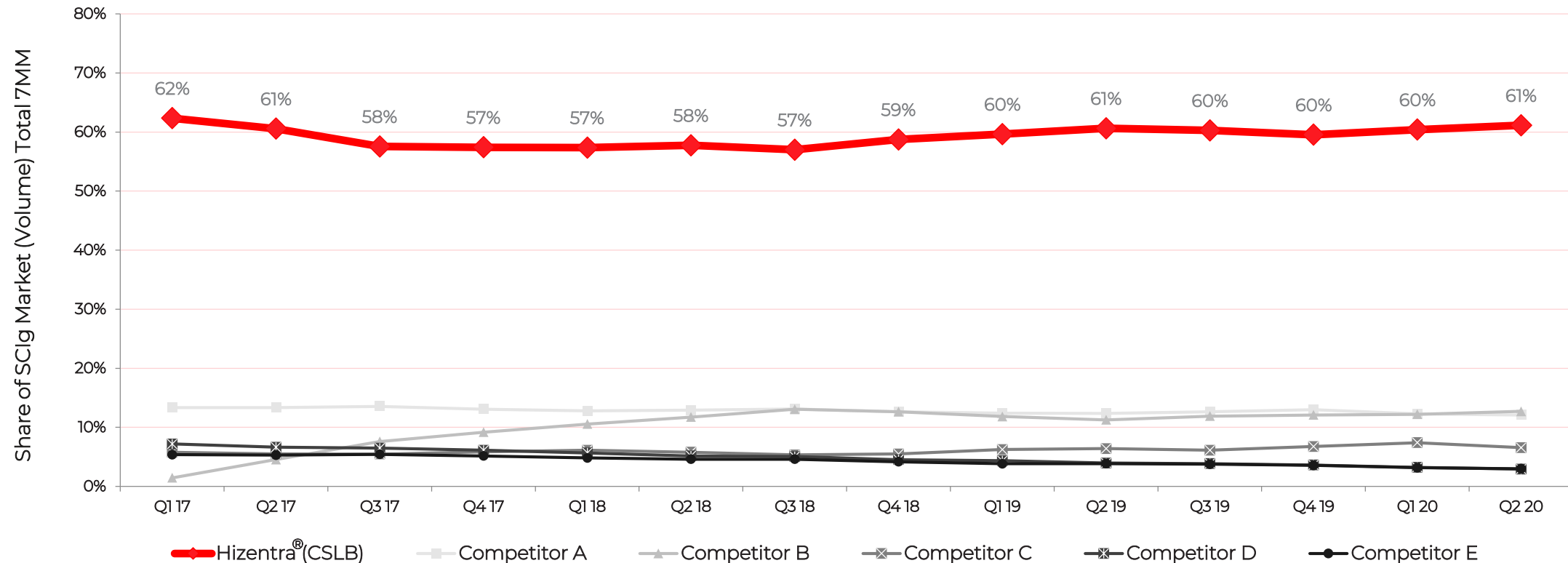
SCIg +34%²

1. Excludes Ig hyperimmunes

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

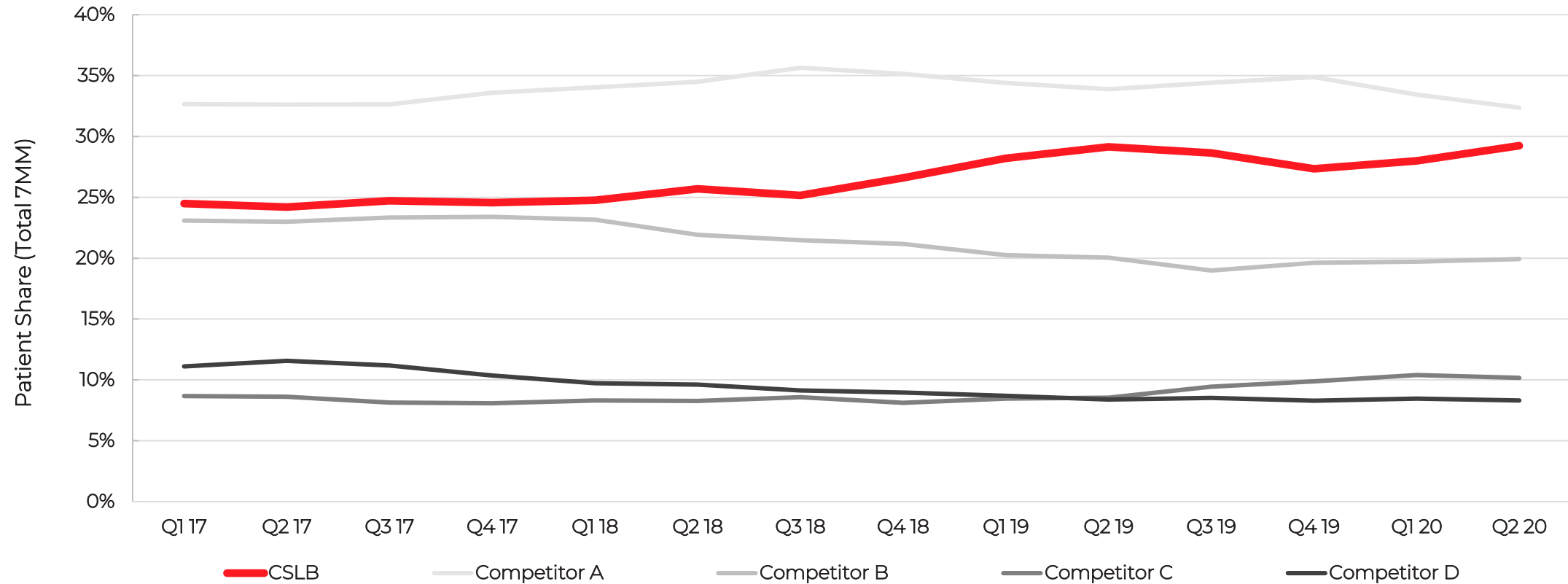
* Includes Privigen®, Sandoglobulin®/Carimune® and Intragam®

HIZENTRA®: Continued Strong Performance in SCIg Segment



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

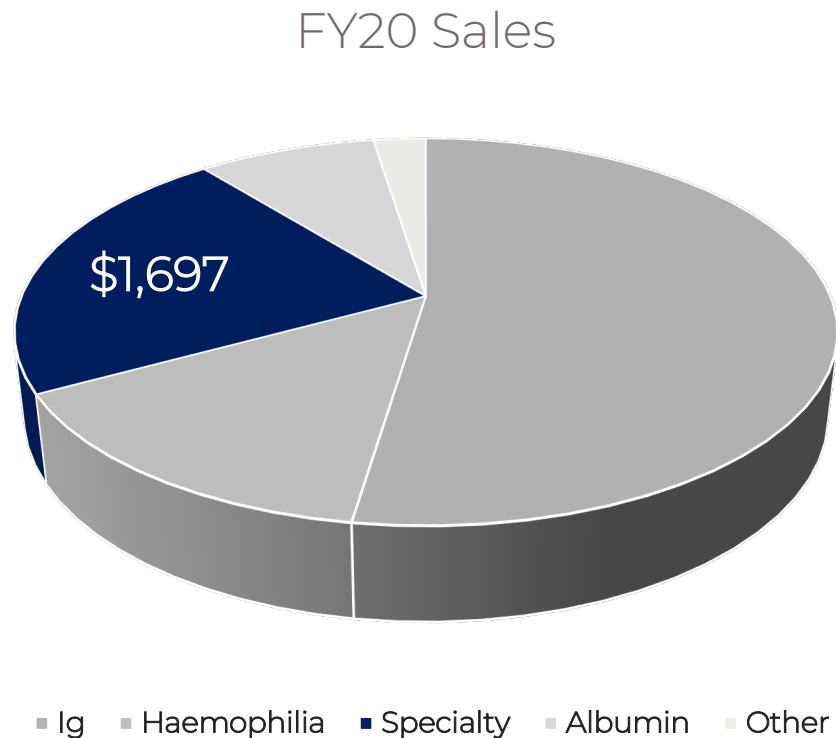
CSL Behring Well-Positioned in CIDP



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

Specialty Products

Sales increased by 10%¹



Kcentra[®]
Prothrombin Complex
Concentrate (Human)

RiaSTAP[®]
Fibrinogen Concentrate (Human)
Strengthens clots. Supports hemostasis.

HAEMOCOMPLETTAN P

HAEGARDA[®]
C1 Esterase Inhibitor
Subcutaneous (Human)

BERINERT[®]

Respreeza[®]
alpha₁-proteinase inhibitor (Human)

Zemaira[®]
alpha₁-proteinase inhibitor (Human)

**Peri-Operative
Bleeding +10%¹**

**Other
Specialty +9%¹**

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

HAEGARDA® Continues to Deliver in the US



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.

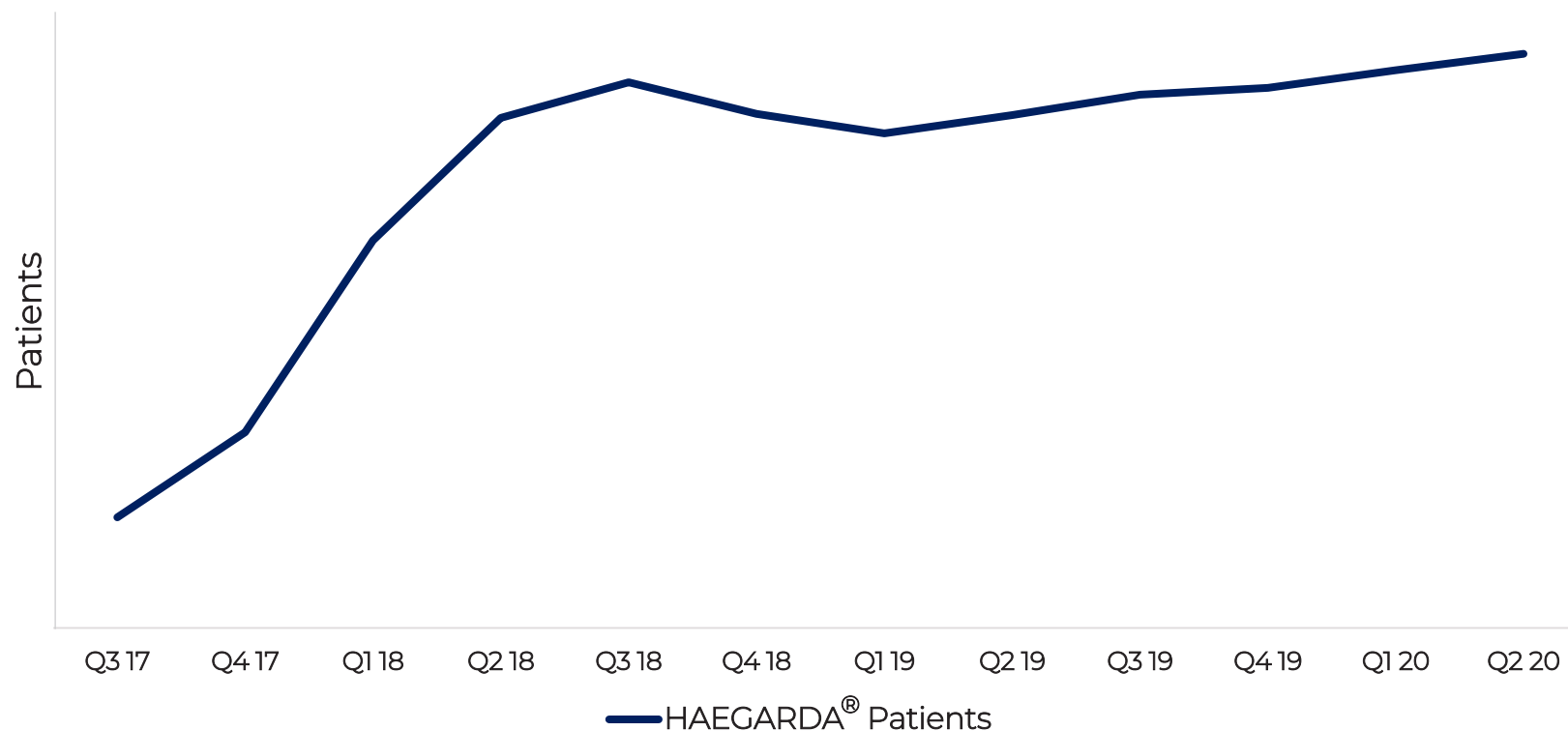
† Median reduction in rescue medication use in patients receiving 60 IU/kg of HAEGARDA® vs placebo.

‡ The World Allergy Organization (WAO) guidelines for the management of HAE state that patients should have HAE rescue medication available at all times.

** Prophylactic non-steroids patient market

¹. Data on file – represents US market only

Finished with Most Patients on HAEGARDA® Since Launch



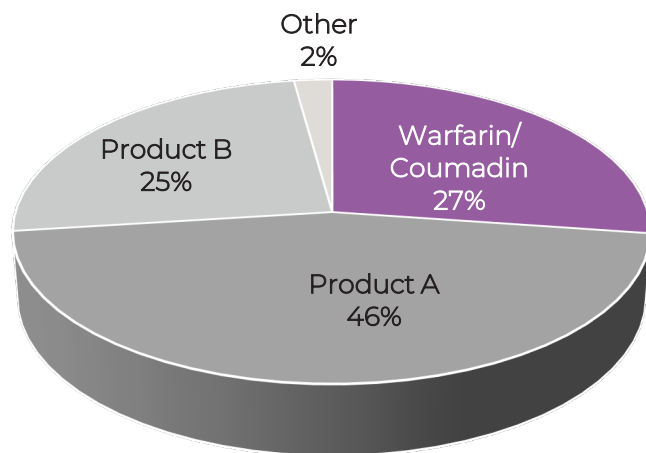
Source: Data on file – represents US market only

KCENTRA® : OAC Market & KCENTRA® Utilization

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

Oral Anticoagulant (OAC) Market FY 19/20

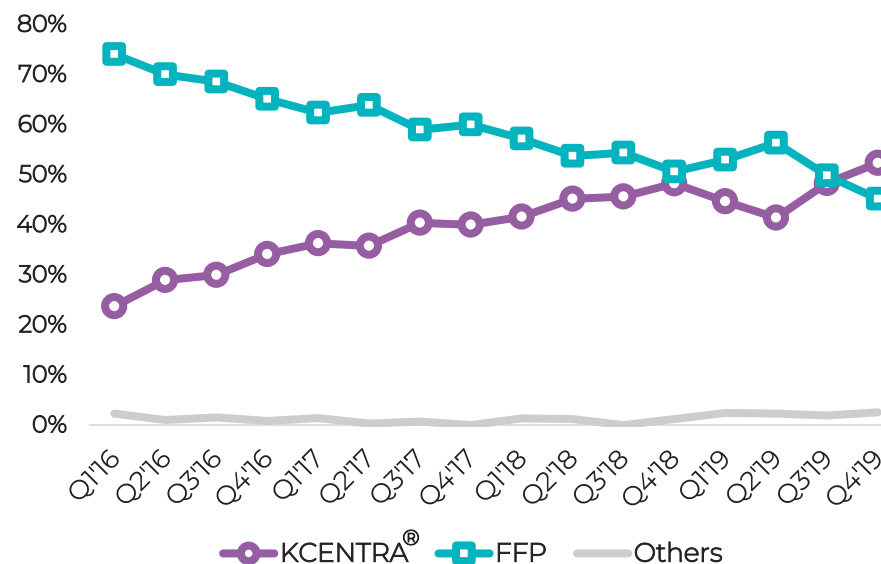
Total: 6.9M Patients



■ Warfarin/Coumadin ■ Product A ■ Product B ■ Other

Source: Data on file

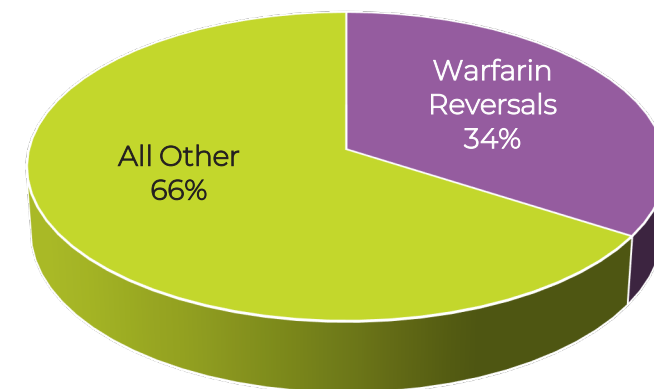
Warfarin Urgent/Major Bleed Reversal Shares



Source: Data on file + LRx Q4 2019

Kcentra® Utilization MAT CY Q4'19

Total: 246M IUs



■ Warfarin Reversals ■ All Other

Indicated for warfarin reversal. Not promoted in other areas

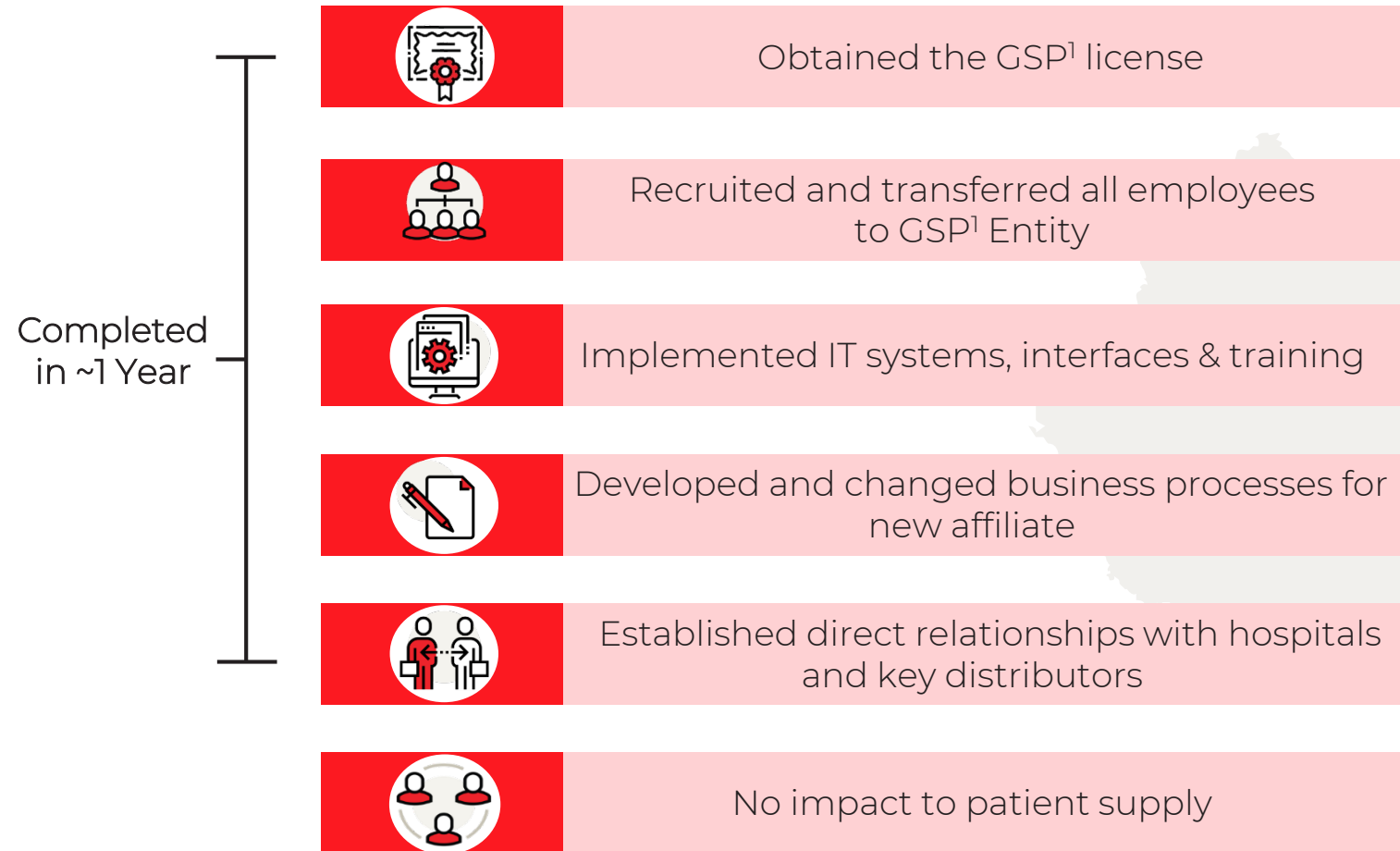
Source: CSL Internal data + Data on file+ LRx

All data represents US market only

* Neurocritical Care Society, Society of Critical Care Medicine, American College of Cardiology, American College of Chest Physicians, American Society of Gastrointestinal Endoscopy, American College of Surgeons

FFP – Fresh frozen plasma

Successful Transition of Business Model in China



1. Good Supply Practices (GSP)

Commercial Summary



Executing on strategies



Strong underlying demand
across the portfolio



Balanced regional & key
market growth



New products contributing
significantly to growth



Aligned therapeutic area
teams and strategy



Remain flexible and agile
managing through COVID-19

Transplant

Laurie Lee MD

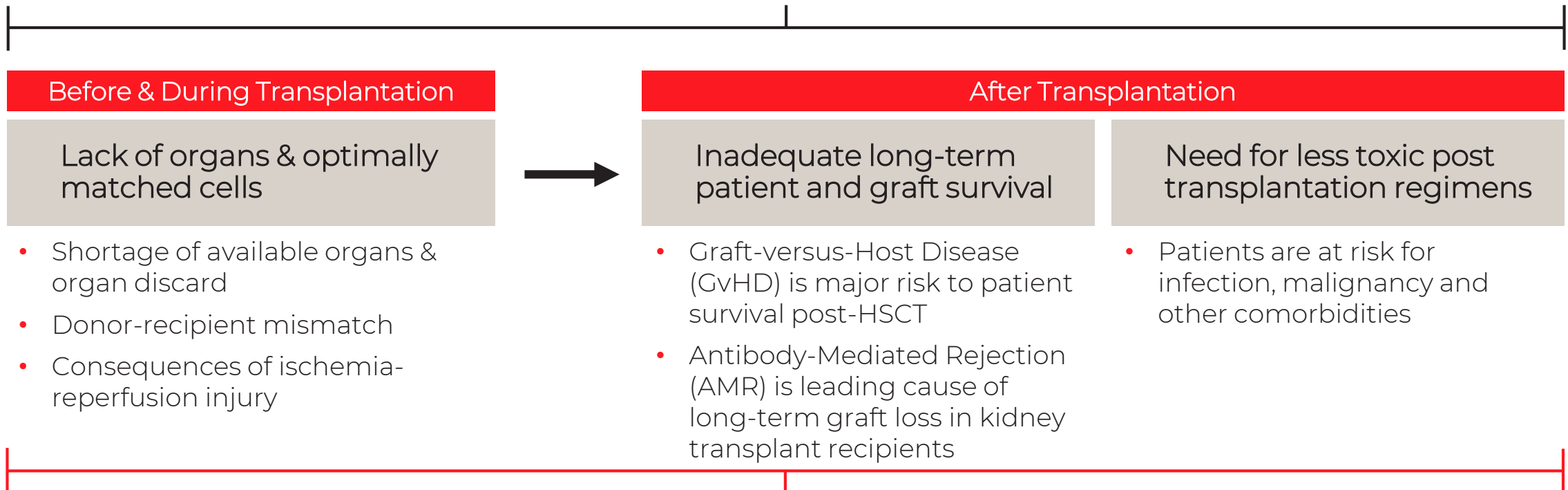
Vice President, R&D Transplant

CSL Behring



Improve Outcomes for Transplant Recipients

Unmet needs in hematopoietic stem cell (HSCT) & solid organ transplantation



Scientific focus:
Anti-inflammatory & immune modulation

Three Ongoing Late-Phase Transplant Programs

Inadequate long-term patient and graft survival

Graft-versus-Host Disease (GvHD)

Antibody-Mediated Rejection (AMR)



Phase III

AAT (CSL964)
treatment study in
collaboration with BMT
CTN (NHLBI/NCI)

1



Phase II/III

AAT (CSL964)
MODULAATE
prevention study

2



Phase III

Clazakizumab (CSL300)
IMAGINE trial

*Interleukin 6 Blockade Modifying Antibody-
Mediated Graft Injury and Estimated
Glomerular Filtration Rate (eGFR) Decline*

3

GvHD: Frequent Post-Transplantation Complication with High Morbidity and Mortality

Up to 50% of patients develop GvHD after allogeneic HSCT despite current prophylactic regimens

Of those who develop acute GvHD, only 50% respond to treatment* (termed “steroid-refractory”)

Severity of acute GvHD varies: grades III and IV are the most severe

Mortality associated with grade III and grade IV one year after transplant is 75% and 95%, respectively**

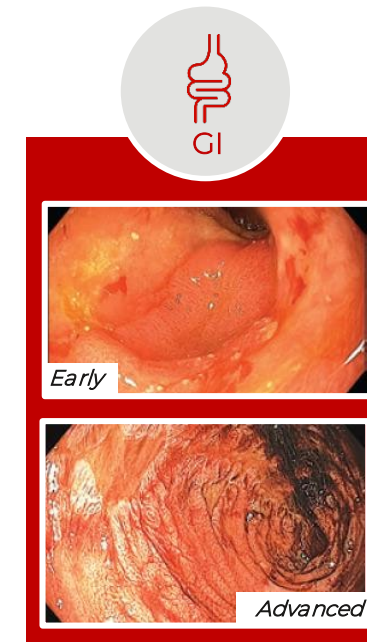
* Ferrara, J. & Chaudry, M. (2018) *Blood Adv.* 2(22):3411-3417

** Hill, L. et al., (2018) *Ther Adv Hematol.* 9(1):21-46

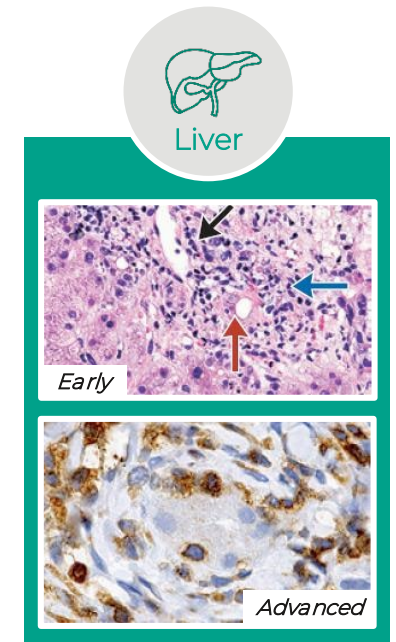
Clinical Manifestations



- Maculopapular rash

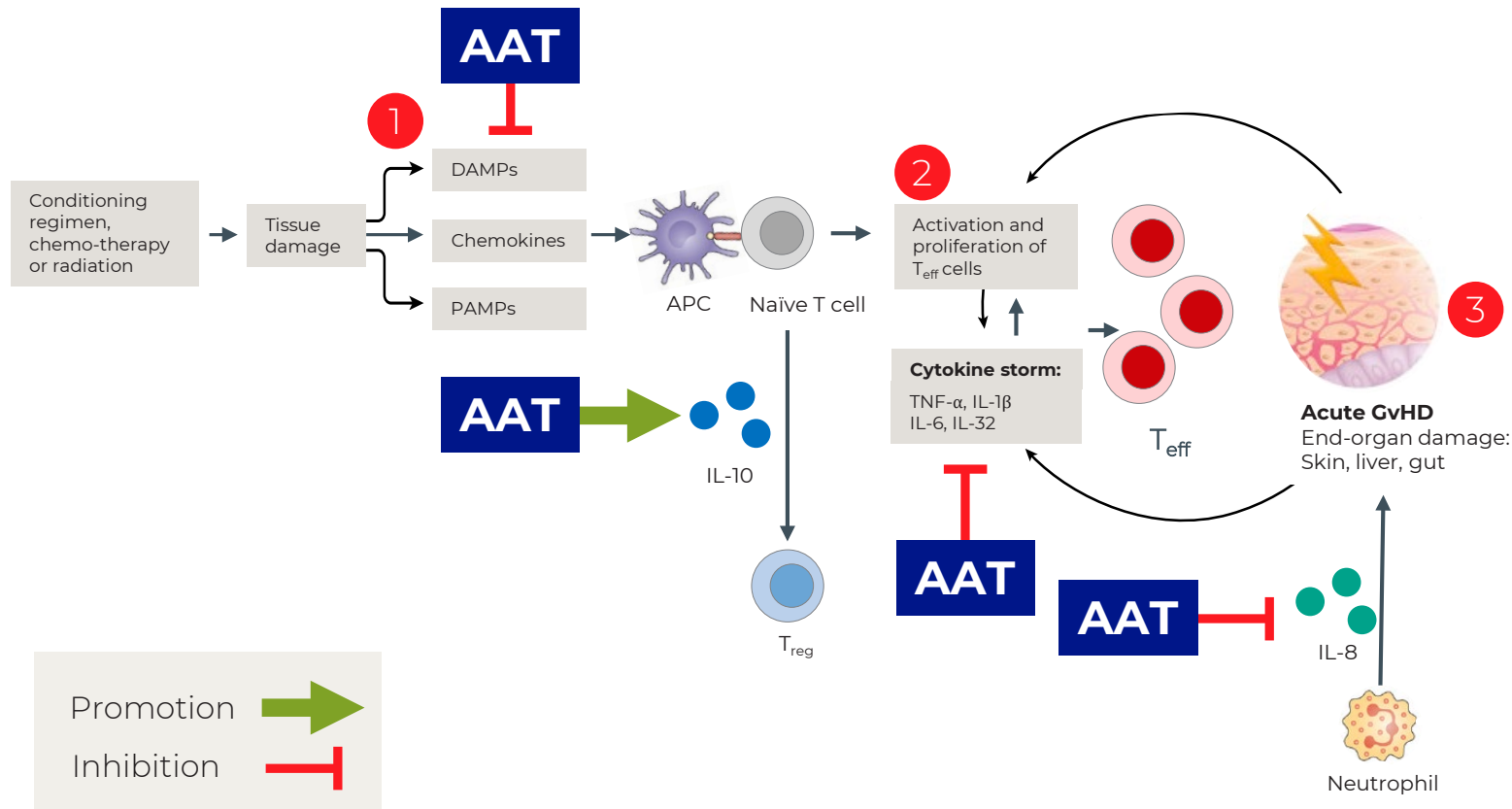


- Upper GI: nausea, vomiting
- Lower GI: profuse watery diarrhoea; bloody diarrhoea or ileus



- Cholestatic jaundice
- Hyperbilirubinemia

Potential Mechanisms of AAT in GvHD



Pre-Clinical Data

- Protease inhibition protects tissue
- Reduces pro-inflammatory cytokine secretion
- Decreases CD8+ effector memory cells
- Inhibits neutrophil migration to sites of inflammation
- Promotes release of anti-inflammatory cytokine IL-10

Source: Adapted from Blazar, B. R., et al., (2012). *Nat Rev Immunol* 12(6): 443-458

Clinical Response to AAT in Patients with Steroid-Refractory acute GvHD (SR-aGvHD)

Prospective, open label, Phase II study of i.v. AAT in SR-aGvHD*

- 40 subjects, steroid-refractory acute GvHD
- AAT twice weekly x 4 weeks at 60mg/kg
- Overall response rate (ORR) (CR + PR): at d28 = 65%; CR at d28=35%
- Sustained response at d60 of 73%

Second smaller study (n=12) had consistent findings**

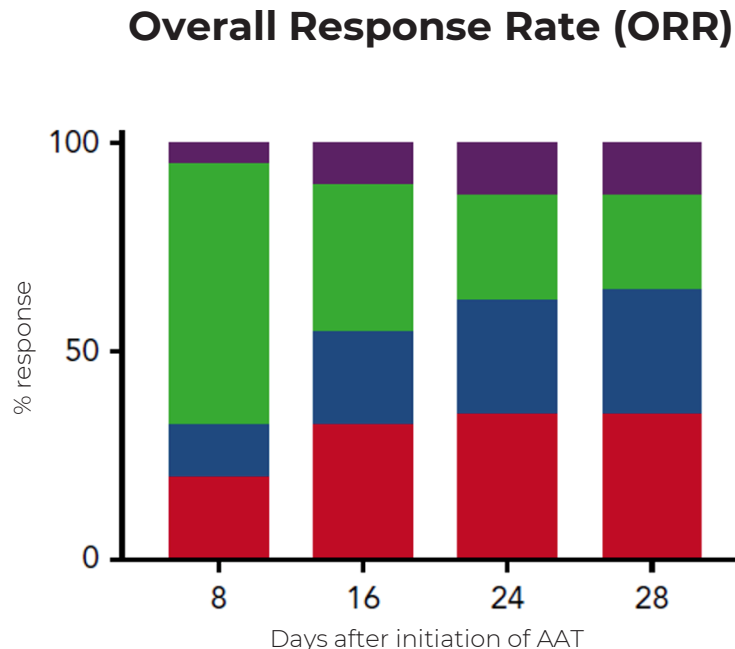
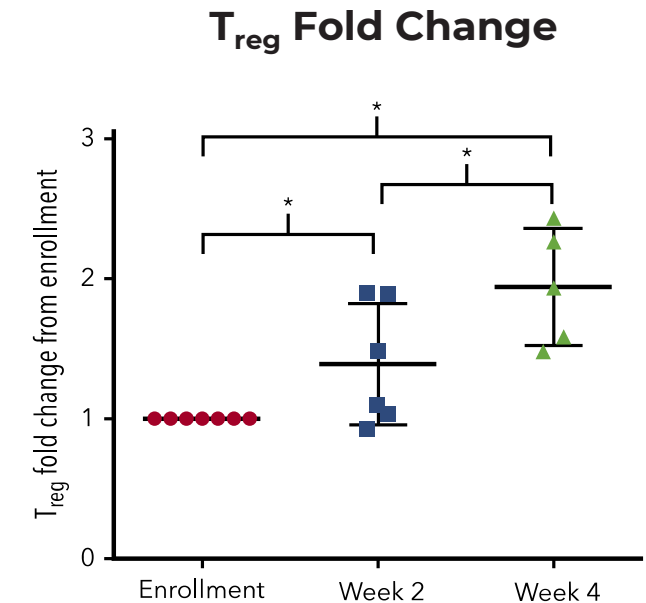


Figure 1. ORR. The percentage of patients who experienced an overall response (primary end point) as defined by the sum of patients with SR-aGvHD achieving complete response (CR) and partial response (PR) after initiation of AAT. NR, nonresponder; Prog, progression.

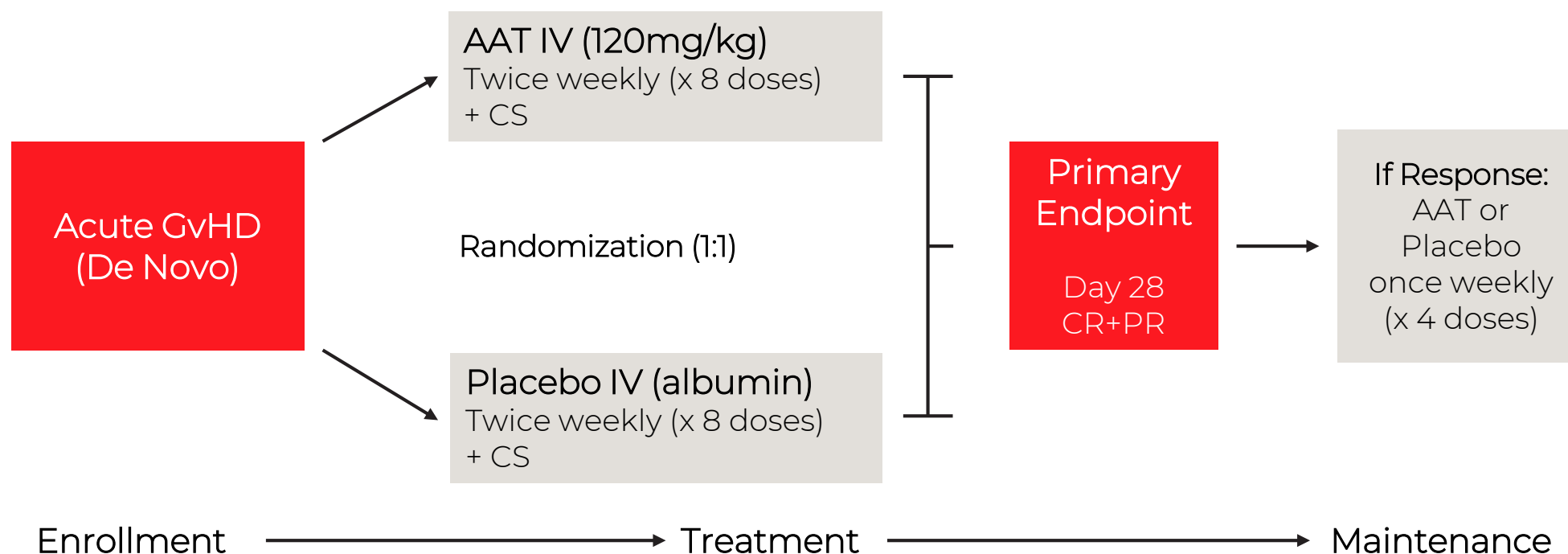


* Magenau, J.M. et al., (2018) *Blood*. 131(12):1372-1379

** Marcondes, A.M. et al., (2016) *BBMT* 22(9): 1596-1601

AAT for GvHD Treatment Study: BMT CTN 1705

Collaboration opportunity with Blood and Marrow Transplant Clinical Trials Network
BMT CTN (NHLBI/NCI)



Phase III ongoing

BMT CTN (NHLBI/NCI)

MODULAATE

MODULAATE
Immunomodulation by Alpha-1 Antitrypsin to Enable Prevention of GVHD

AAT GvHD Prevention Phase II/III Study

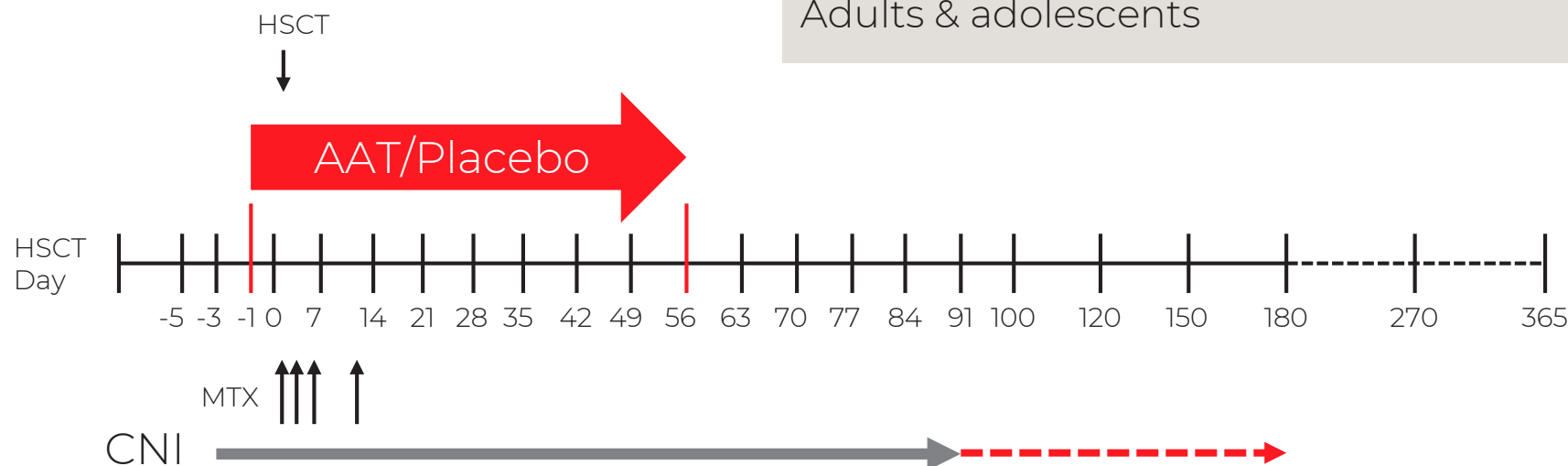
Part 1:
Dose Finding – Open Label

3 ascending cohorts
(n=15) for each cohort



Part 2:
Randomized Double Blind Placebo Controlled

Cohort 4
Selected dose from Part 1
(n=260, 1:1; AAT: Placebo)
Adults & adolescents



Phase II/III ongoing

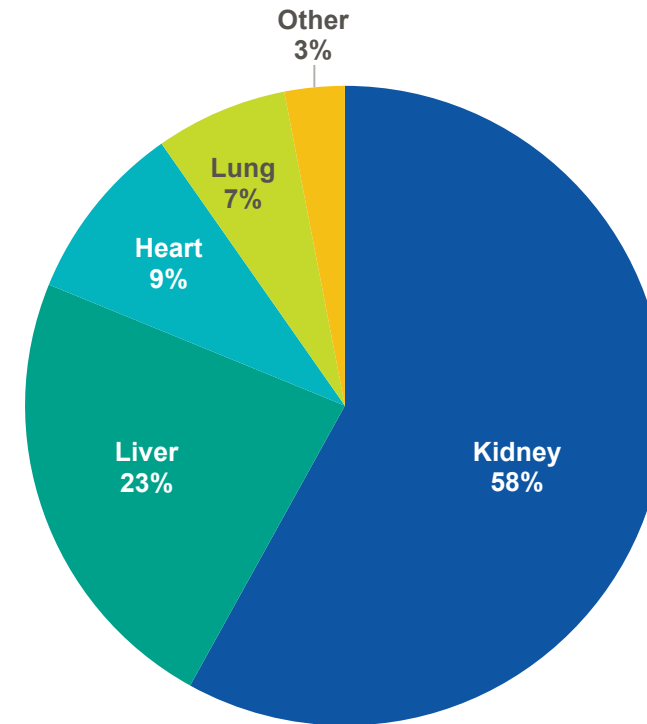
Primary Endpoint:
Proportion of acute Graft-versus-Host
Disease-free survival at 180 days post-HSCT

Solid Organ Transplantation



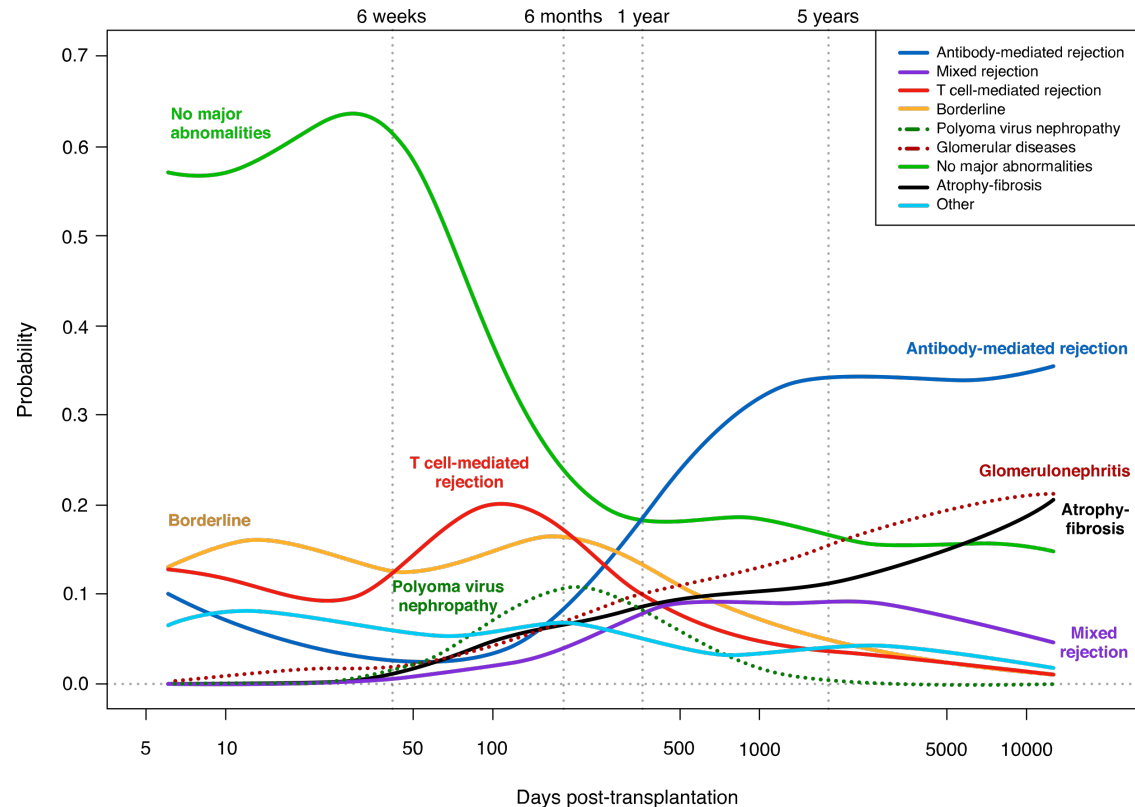
- >500,000 patients are living with a transplanted kidney*

**Transplants by Organ Type
(US - 2015)**

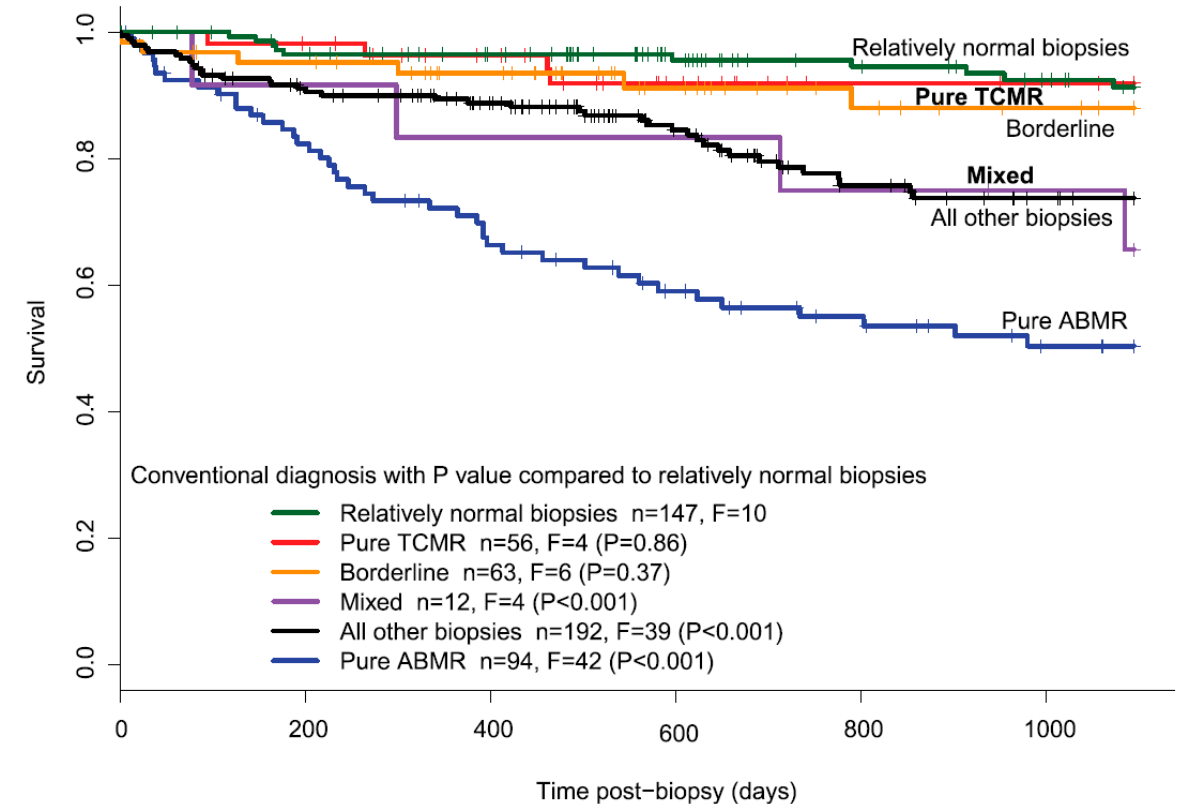


* Scientific Registry of Transplant Recipients (SRTR) and European Renal Association – European Dialysis and Transplant Association (ERA-EDTA)

Antibody-Mediated Rejection (AMR) is a Leading Cause of Long-Term Graft Loss

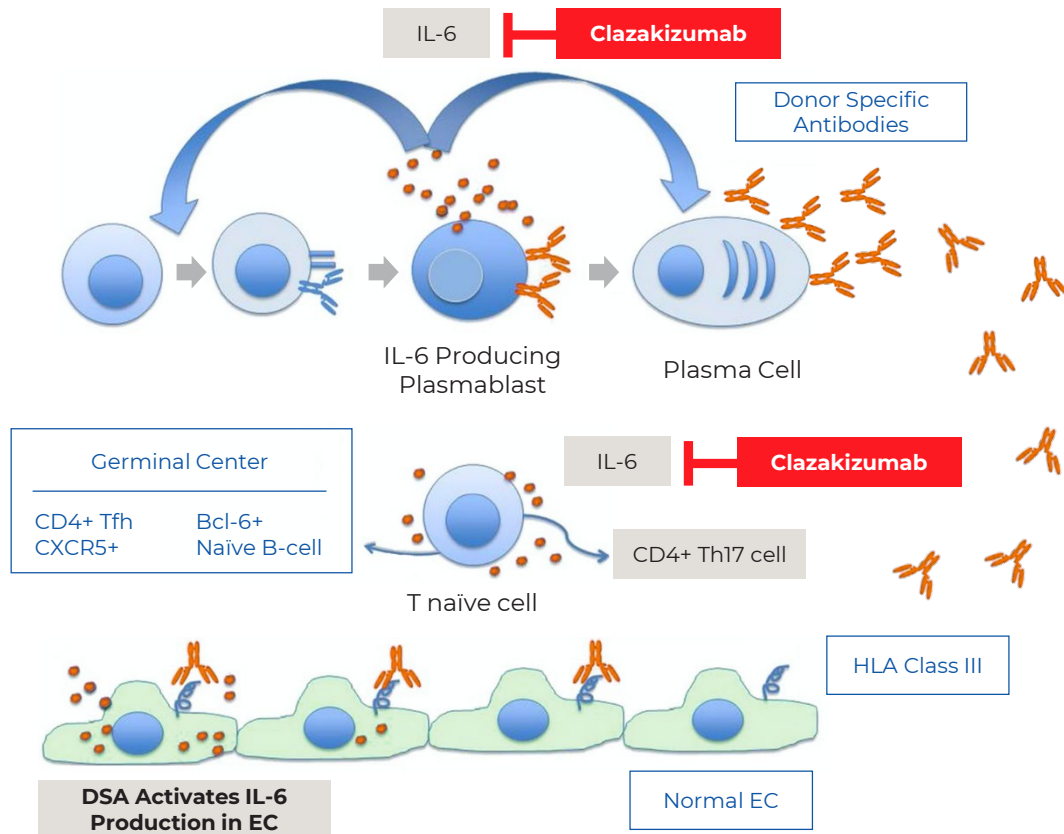


Source: Sellarés et al., (2012) *Am J Transplant*. 12:388-99



Source: Halloran et al., (2015) *J Am Soc Nephrol*. 26:1711-1720

IL-6 Plays a Key Role in the Development of AMR



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

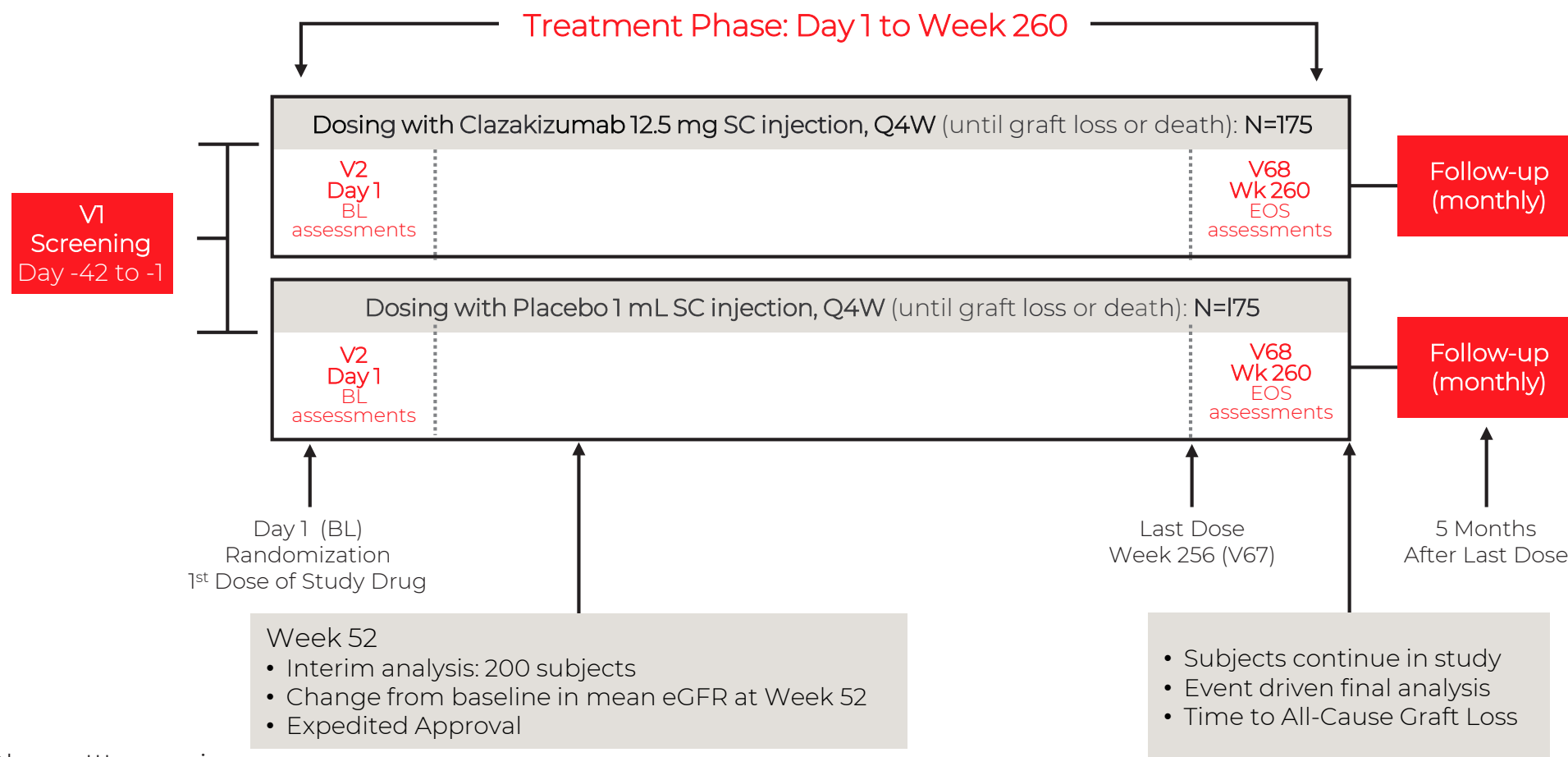
Anti-inflammatory and immune modulatory effects of IL-6 blockade:

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

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

IMAGINE

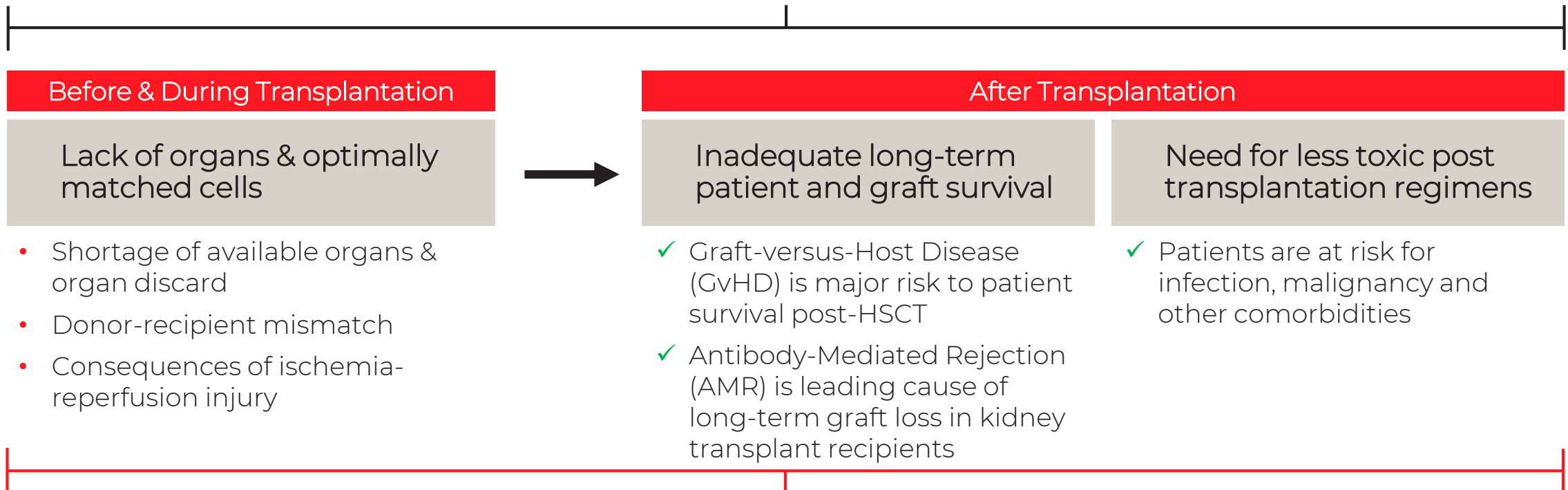
Clazakizumab for chronic AMR treatment study



Phase III ongoing

Improve Outcomes for Transplant Recipients

Unmet needs in hematopoietic stem cell (HSCT) & solid organ transplantation



Scientific focus:
Anti-inflammatory & immune modulation

A woman with dark hair in a ponytail, wearing a white lab coat and safety glasses, is working in a laboratory. She is holding a rack of test tubes with orange caps. In the background, other lab workers are visible at their stations. The image is partially overlaid with a white text box on the left and a red banner at the bottom.

Summary

William Mezzanotte MD

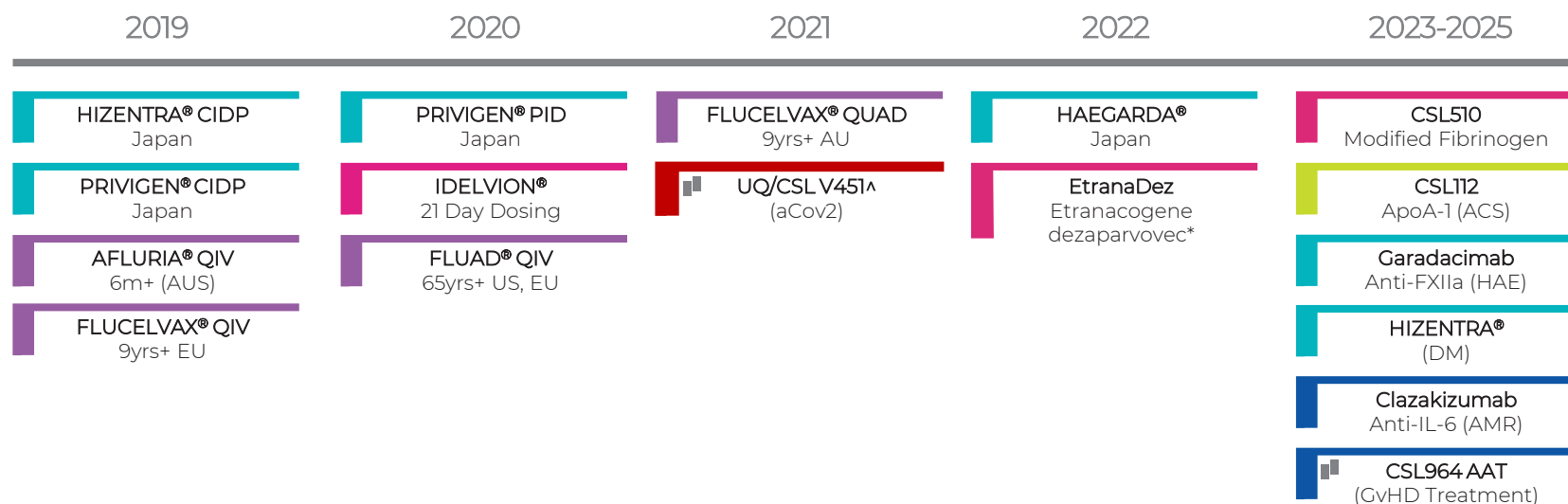
Executive Vice President,
Head of Research and Development
and CMO

CSL Behring

R&D Portfolio – October 2020



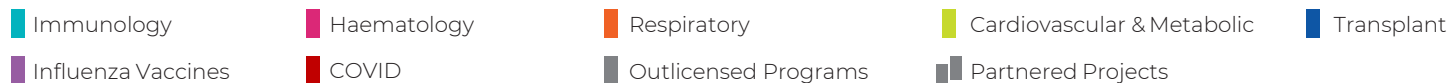
Significant Target Launch Dates



Timelines shown by calendar year

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

^ Provisional Approval



R&D Portfolio Highlights – FY21



Immunology

- **Garadacimab** (Anti-FXIIa) initiate Phase III study
- **HAEGARDA®** complete Phase III HAE study in Japan
- **CSL324** (Anti-G-CSFR) initiate PK/Ethnicity study for SC formulation and inclusion of Japan



Cardiovascular and Metabolic

- **CSL112** (ApoA-1) Phase III study (AEGIS-II) complete 2nd futility analysis (if applicable)
- **CSL346** (Anti-VEGF-B) initiate Phase II study for DKD



Respiratory

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



Haematology

- **KCENTRA®** initiate Phase III study for treatment of massive haemorrhage associated with severe traumatic injury
- **EtranaDez*** US Submission



Transplant

- **CSL964** (AAT) for prevention of GvHD - complete Part 1, adaptive phase of study, and advance to confirmatory Part 2



Influenza Vaccines

- **FLUCELVAX® Quadrivalent** EU & CA approvals in 2+yrs indication
- **FLUCELVAX® Quadrivalent** US & CA submissions 6mons+ indication
- **aQIVc** (cell antigen + MF59®) initiate Phase II safety & immunogenicity study in adults 50+yrs



COVID

- **COVID-19 Hyperimmune Therapy** Phase III First Patient In
- **Garadacimab** (Anti-FXIIa) complete Phase II study
- **UQ/CSL V451** Phase II/III First Patient In

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

The CSL logo is a red square with the letters "CSL" in white, bold, sans-serif font. A small trademark symbol (TM) is located to the upper right of the letters.

CSL™

A semi-transparent white rectangular box containing the text "Panel Q&A Session" in red, bold, sans-serif font. The box is positioned over a laboratory background.

**Panel Q&A
Session**