A NEW DEDICATED FOCUS ON INNOVATIVE, SUSTAINABLE SOLUTIONS FOR PLASMA-DERIVED THERAPIES

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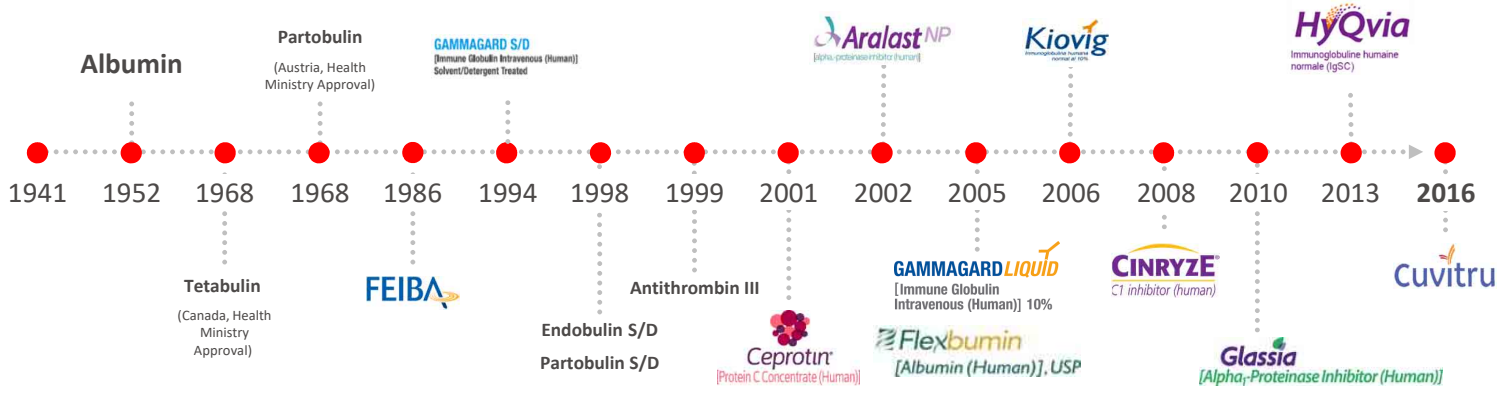
Head of R&D, Plasma-Derived Therapies

Better Health, Brighter Future

PDT R&D'S CREDENTIALS AND INFRASTRUCTURE ARE WELL-ESTABLISHED

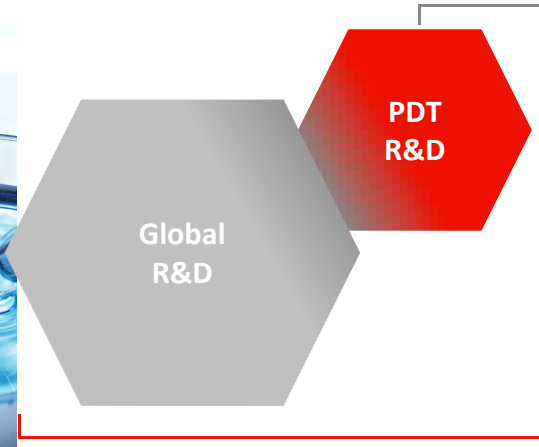


Pathogen Safety
Global Center of Excellence for Pathogen Safety

Pharmaceutical Science
Strong team connected across the value chain

Pilot Labs
Within Vienna, Los Angeles, Georgia and Lessines sites

OUR INDEPENDENCE BRINGS FOCUS ON PLASMA AND IS BOLSTERED BY ACCESS TO BROADER R&D CAPABILITIES AND RESOURCES



- Focused entirely on plasma-derived therapies
- Lean and agile team
- Based in Cambridge, MA and Vienna, Austria
- Separate R&D prioritization
- Dedicated budget

- Common Takeda values, patient-focused vision
- Common governance
- Shared resources (e.g. Medical Affairs, Safety, Quality)

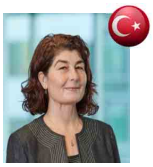
These links strengthen Takeda R&D's modality mix, now the broadest among the Top 10 global biopharmaceutical companies

THE PDT R&D LEADERSHIP TEAM IS WELL-INTEGRATED AND BRINGS DEEP AND DIVERSE FUNCTIONAL EXPERTISE

Christopher Morabito MD
R&D Head
Boston, MA

Catherine Parham MD
Program Leadership
Boston, MA

Rory Bukofzer
Program Leadership
Boston, MA



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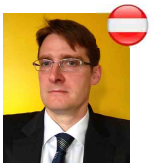

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Regulatory Affairs & Development Operations
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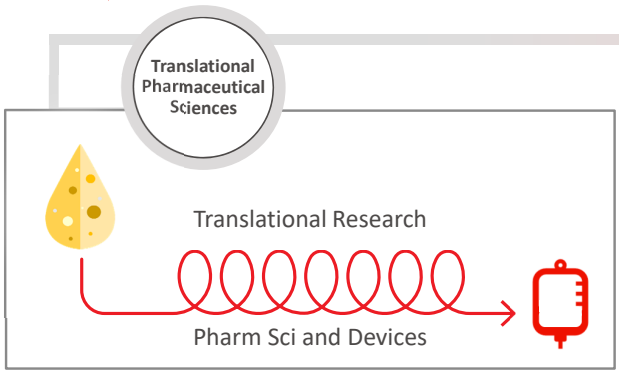
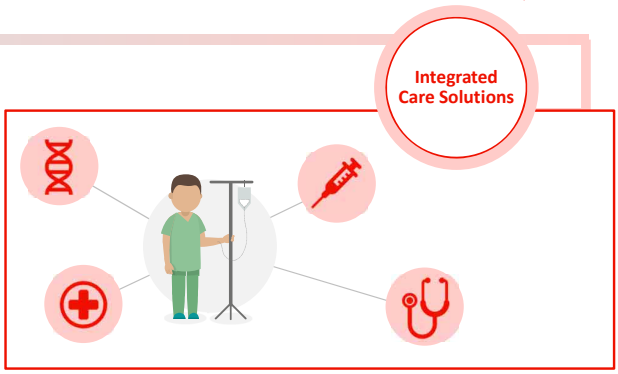
WE ARE DRIVING A CULTURE OF INNOVATION THROUGH TWO R&D ENGINES

Research/Early Development → **Late Development**



Early Development Innovation Engine



Late Development Innovation Engine

Generate new and improved therapeutics by:

- Investigational new drug candidates
- Mechanisms of action
- Responder populations
- New process development

Improve health outcomes by:

- Diagnostic efficiencies
- Expanded data and devices to support effectiveness
- Point of Care services and drug delivery services
- Data-driven guidelines for acute and chronic management

PDT R&D Strategy

Maximize the therapeutic value of plasma-derived therapies for patients with rare and complex diseases through innovation across the product life cycle

Realize full potential of in-line First and Last Liter products

- Expanded indications and benefit-risk datasets
- Device-driven solutions for diagnosis, management, and long-term follow-up
- Global expansion
- New formulations

Optimize efficiencies of plasma-derived therapy production

- Pharmaceutical science support for manufacturing

Identify and develop new plasma-derived therapies

- New targeted therapies for diverse therapeutic areas

WE ARE PRIORITIZING NEAR-TERM LATE DEVELOPMENT…

	RESEARCH / NON-CLINICAL DEVELOPMENT	LATE DEVELOPMENT	
IMMUNOLOGY	**CUVITRU** Wearable Device	**HYQVIA** ***Halozyme*** US - Pediatric PID	**HYQVIA** ***Halozyme*** EU - Pediatric PID
		HYQVIA ***Halozyme*** Chronic inflammatory demyelinating polyneuropathy (CIDP)	**HYQVIA - HyHub** ***Flextronics*** Delivery Device
		HYQVIA Geographic expansion	**CINRYZE** Geographic expansion
		CUVITRU Geographic expansion	**GLASSIA** ***Kamada*** Immunogenicity/ bronchioalveolar lavage
HEMATOLOGY			**FEIBA** Volume reduction

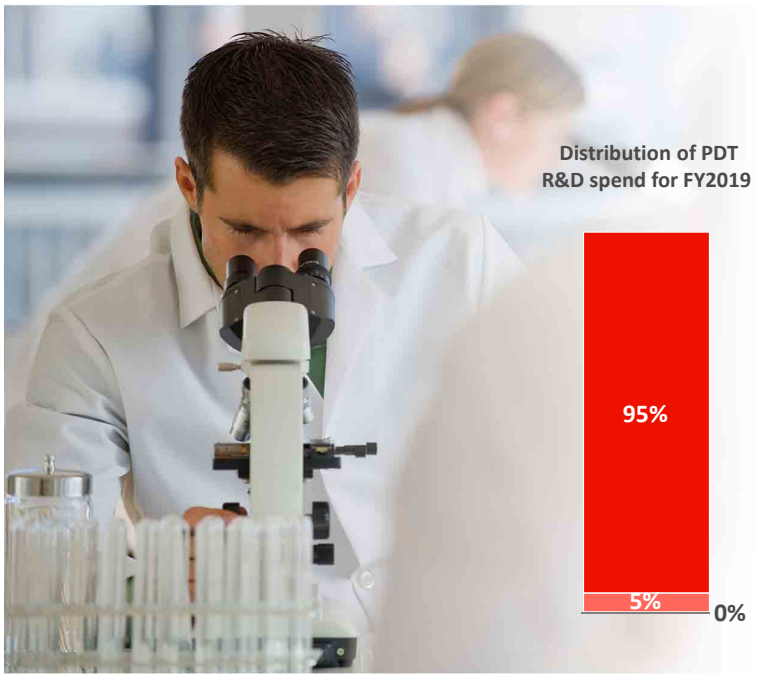
… WHILE ENABLING DISCOVERY OF NEXT GENERATION THERAPEUTICS

	RESEARCH / NON-CLINICAL DEVELOPMENT		LATE DEVELOPMENT	
IMMUNOLOGY	**CUVITRU** Wearable Device	**TAK 881** **Facilitated 20% SC IgG** ***Halozyme*** Primary Immunodeficiency (PID)	**HYQVIA** ***Halozyme*** US - Pediatric PID	**HYQVIA** ***Halozyme*** EU - Pediatric PID
	TAK 880 **Low IgA-IgG (IV)** Primary Immunodeficiency	**Alpha-1 Antitrypsin (A1AT)** Next generation formulations	**HYQVIA** ***Halozyme*** Chronic inflammatory demyelinating polyneuropathy (CIDP)	**HYQVIA - HyHub** ***Flextronics*** Delivery Device
	Hyper-Immune IG Infectious disease		**HYQVIA** Geographic expansion	**CINRYZE** Geographic expansion
	CINRYZE Ex-HAE indications TBD		**CUVITRU** Geographic expansion	**GLASSIA** ***Kamada*** Immunogenicity/ bronchioalveolar lavage
			GLASSIA ***Kamada*** A1ATD-emphysema*	**CUVITRU** Japan - PID (FPI Q4 2019)
HEMATOLOGY	**PROTHROMPLEX TOTAL** Device and formulation	**Butyryl Cholinesterase** Organophosphate poisoning	**PROTHROMPLEX TOTAL** US - Drug-induced bleeding**	**FEIBA** Volume reduction
			CEPROTIN Geographic expansion	

*Subject to regulatory approval
**Pending FDA Pre-IND consultation and future acceptance of an IND

Programs and projects added since Day 1

OVER THE NEXT 3 YEARS, WE PLAN TO ALLOCATE RESOURCES TO RESEARCH AND EARLY DEVELOPMENT



Distribution of PDT R&D spend for FY2019

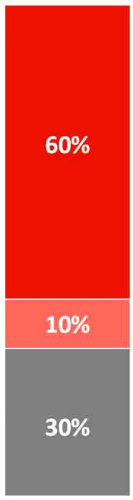
Estimated % of PDT R&D spend for FY2023

~70% of resources will be allocated to improving in-line products and production efficiencies

- Optimizing value of in-line products
- Plasma production efficiencies
- New plasma-derived therapies

OUR GOAL IS TO REALIZE THE FULL POTENTIAL OF IN-LINE FIRST AND LAST LITER PRODUCTS

Estimated % of PDT R&D spend for FY2023



- Expanded indications and benefit-risk datasets
- Device-driven solutions for diagnosis, management, and long-term follow-up
- Global expansion
- New formulations

- Optimizing value of in-line products
- Plasma production efficiencies
- New plasma-derived therapies

IMMUNOGLOBULINS PROVIDE THE SCAFFOLD FOR PDT INNOVATION

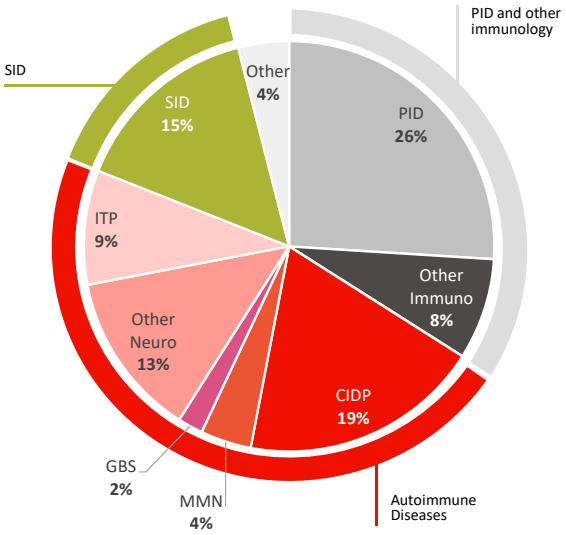
Current State

- Exploring efficacy and safety of HYQVIA in patients with neuro-immune diseases (e.g. CIDP)
- Ongoing delivery device development

Opportunities

- Indications: New neuro-immunology and secondary immunodeficiencies (SID) programs**
- Geographic expansion: CUVITRU-Japan first patient to be enrolled in Q4 FY 2019
- Integrated care solutions:
  - Advance point of care diagnosis of primary immunodeficiency (PID)
  - New delivery and eHealth devices
- Develop f-20% SCIG

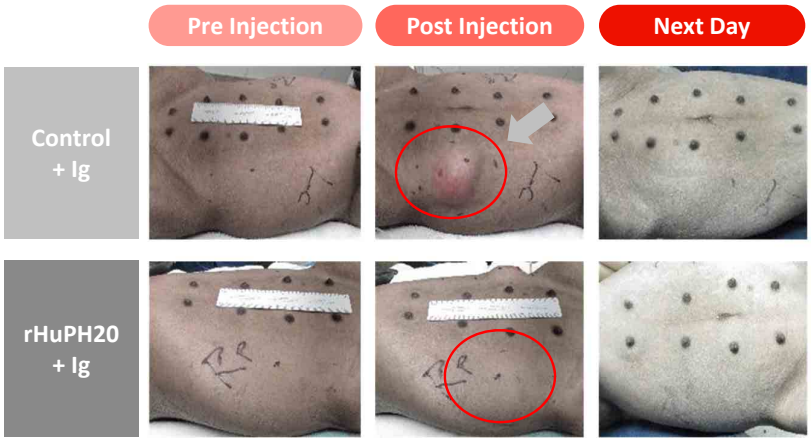
US & EU IgG use by indication*

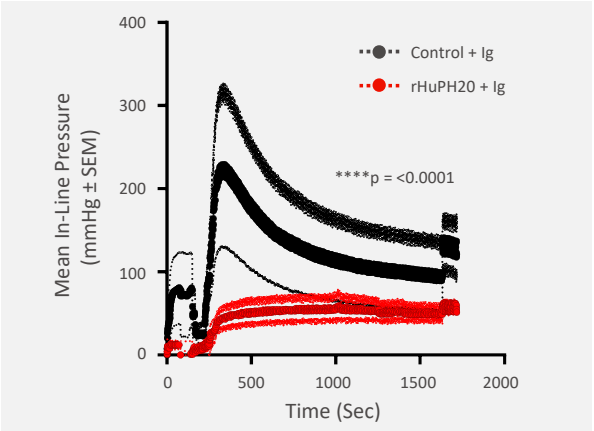


Source: Bain Study (US&EU), Volumes, Estimates based on internal calculations on EU Country Data
*Not all indications are approved for a Takeda product
**Subject to regulatory approval

FACILITATED 20% SCIG HAS THE POTENTIAL TO PROVIDE FURTHER VALUE TO PATIENTS WHO REQUIRE HIGHER VOLUME ADMINISTRATIONS

Pig model, sequentially administered recombinant human hyaluronidase (rHuPH20) and 20% IgG (CUVITRU)*





Significantly decreased induration and infusion pressure, with improved cutaneous blood flow

* In collaboration with Halozyme
Sequentially administered rHuPH20 and CUVITRU is for investigational use only

PROTHROMPLEX TOTAL CAN BE DEVELOPED TO TREAT A VARIETY OF BLEEDING DISORDERS

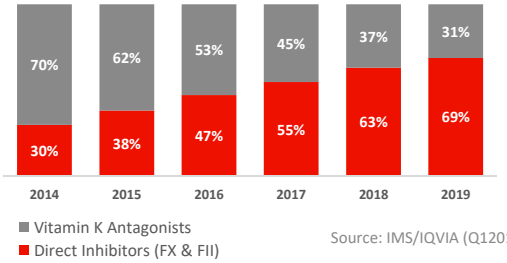
Current State

- Many different mechanisms used for prophylactic and surgical anti-coagulant therapy
- PROTHROMPLEX TOTAL use is limited to Vitamin K antagonists associated bleeding ex-US

Opportunities

- Geographic expansion into the US*
- Broaden indication to include treatment of multiple types of drug-induced bleeding
- Improved use via new formulations and device

Changing Treatment Paradigm
(EU Total Prescriptions)



Source: IMS/IQVIA (Q12019)

 *Pending FDA Pre-IND consultation and future acceptance of an IND; Investigational use, subject to regulatory approval

ARALAST & GLASSIA PROVIDE OPPORTUNITIES TO IMPROVE OUTCOMES IN PATIENTS WITH ALPHA-1 ANTITRYPSIN DEFICIENCY (A1ATD)

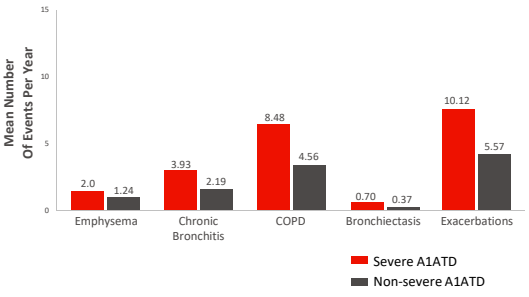
Current State

- Current standard of care does not adequately treat A1ATD

Opportunities

- New clinical study to assess the efficacy of a higher dose of GLASSIA in patient with emphysema related to A1ATD
- Next generation A1AT*: formulation, delivery and management devices
- Explore A1AT as acute phase reactant

Healthcare Resource Utilization in A1ATD-Emphysema



Source: Herrera et al (2019) Chest annual meeting

 *Investigational use, subject to regulatory approval

INVESTIGATIONAL A1AT-REPLACEMENT FORMULATIONS MAY OFFER ADDITIONAL VALUE TO PATIENTS

Short term

Highly purified post-fractionations pdA1AT-precursor

→

Concentration
of A1AT by ultra filtration potentially leading to an **extended $t_{1/2}$**

Mid term

Protein Modification
site-specific modification leading to an **extended $t_{1/2}$**

→

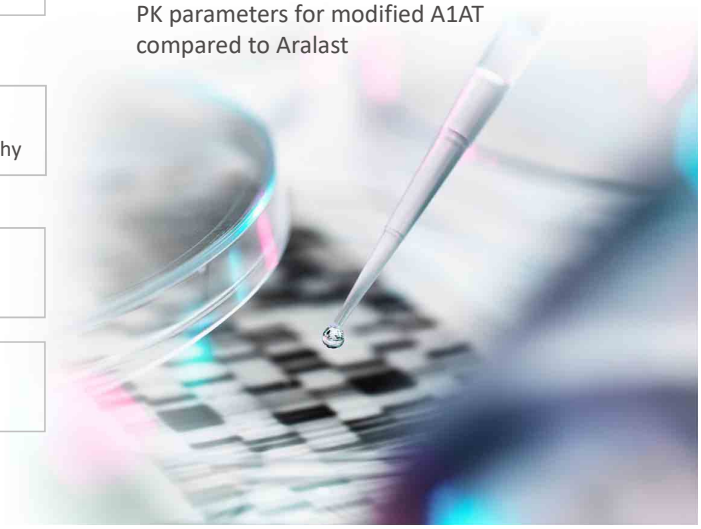
Purification
by ion-exchange chromatography

Formulation Development
Evaluate SC administration

Device Development
Potential to add incremental value for patients

In Vivo Model

- PK parameters for a modified A1AT have been assessed in vivo
- Statistically significant improvement of PK parameters for modified A1AT compared to Aralast



40 Subject to regulatory approval

WE ARE OPTIMIZING EFFICIENCIES OF PLASMA-DERIVED THERAPY PRODUCTION

Estimated % of PDT R&D spend for FY2023

- Optimizing value of in-line products
- Plasma production efficiencies
- New plasma-derived therapies

→ Pharmaceutical science support for manufacturing

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WE ARE FURTHER IMPROVING MANUFACTURING EFFICIENCIES TO INCREASE YIELD

High yield high throughput initiatives will improve delivery of last liter products to patients globally

A new high yield & high throughput process:

- Process development to shorten IgG upstream and total albumin cycle times
- Capture of purification waste to isolate proteins for possible new development

Potential benefit of higher yield and increased capacity

Significantly reduced COGS with positive ROI

WE ARE IDENTIFYING AND DEVELOPING NEW PLASMA-DERIVED THERAPIES

Estimated % of PDT R&D spend for FY2023

- Optimizing value of in-line products
- Plasma production efficiencies
- New plasma-derived therapies

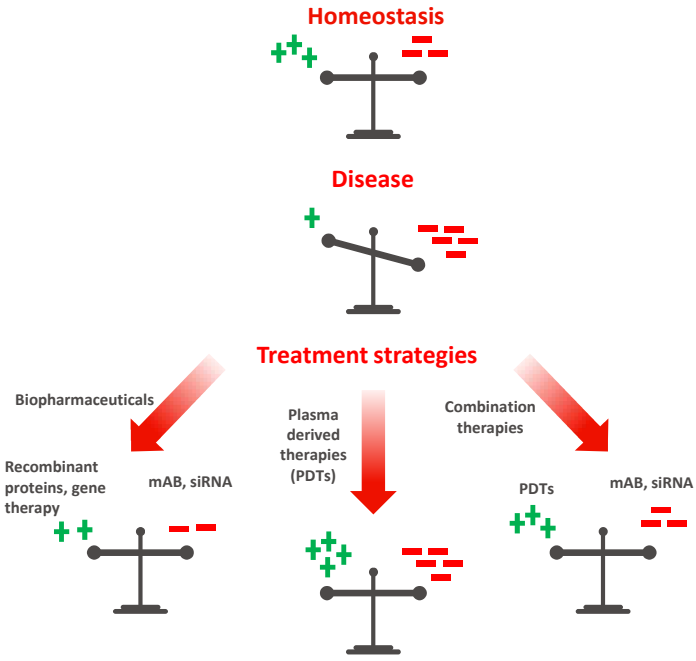
→ New targeted therapies for diverse therapeutic areas

WE BELIEVE THERE IS A TREMENDOUS AMOUNT OF UNTAPPED POTENTIAL IN PLASMA PROTEINS

>3000 plasma proteins control balance, some with health promoting + effects and other with disease associated − effects

Generally, PDTs have been developed to **replace functional deficiencies** in health promoting proteins

We believe PDTs, alone or in combination, **can be developed to address acute and chronic diseases**



We are well-positioned to create near-term and sustainable growth

TARGET APPROVAL FY	NEAR TERM CATALYSTS		SUSTAINED GROWTH	
	FY19 – FY22	FY23 – FY24	FY25 AND BEYOND	
IMMUNOLOGY	**HYQVIA** *Halozyme* Chronic inflammatory demyelinating polyneuropahty (CIDP)	**CUVITRU** Japan PID (FPI Q4 2019)	**GLASSIA** *Kamada* A1ATD-emphysema*	HYPERIMMUNE IGx GENERATION
	GLASSIA *Kamada* Immunogenicity/bronchioalveolar lavage	**HYQVIA** *Halozyme* EU Pediatric PID	**CINRYZE** Ex-HAE indications TBD	ACUTE PHASE REACTANTS
	HYQVIA - HyHub *Flextronics* Delivery Device	**TAK 880** **Low IgA-IgG (IV)** Primary Immunodeficiency	**CINRYZE** Geographic expansion	NEUROIMMUNOLOGY/OTHER AUTOIMMUNE
	HYQVIA Geographic expansion	**HYQVIA** *Halozyme* US Pediatric PID	**Hyper-Immune IG** Infectious disease	PLASMA-DRUG COMBINATIONS
	CUVITRU Geographic expansion	**CUVITRU** Wearable Device	**Alpha-1 Antitrypsin (A1AT)** Next generation formulations	INTEGRATED CARE: DEVICES AND DIAGNOSTICS
		TAK 881 Facilitated 20% SC IgG *Halozyme* Primary Immunodeficiency (PID)		PLASMA PROTEOMICS for BIOMARKERS and NEW DRUG DISCOVERY
HEMATOLOGY	**CEPROTIN** Geographic expansion	**PROTHROMPLEX TOTAL** Device and formulation	**PROTHROMPLEX TOTAL** US - Drug-induced bleeding **	
	FEIBA Volume reduction	**Butyryl Cholinesterase** Organophosphate poisoning		

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Clinical-stage assets | Platforms

TREATMENT PARADIGMS OF RARE AND COMPLEX DISEASES ARE DYNAMIC AND WE ARE INNOVATING CONTINUOUSLY

	Uncertainties	PDT Innovation
	→ Deepening understanding of underlying mechanisms of diseases and co-morbidities	→ Directed most appropriate uses of PDTs → With Takeda Global R&D, investigate plasma-drug combinations
	→ Evolution of Fc- and Fc-Receptor approaches (including anti-FcRn) → Gene therapies and RNAi for specific diseases	→ Focus on primary and secondary immunodeficiencies → Identify IG responders in specific auto-immune diseases → Develop PDTs in conjunction with gene therapies and RNAi (e.g. A1ATD-liver disease)
	→ Perception of lack of plasma product differentiation	→ Integrated care solutions will help to expand therapeutic values and differentiate Takeda products → New formulations may offer new approaches for patients

KEY TAKEAWAYS FOR PLASMA-DERIVED THERAPIES R&D

1

Dedicated PDT R&D organization focused on – and investing in – reimagining plasma, while leveraging Takeda's broader R&D resources and capabilities

2

Poised to deliver near-term value by optimizing our in-line portfolio and improving efficiencies throughout the value chain

3

Committed to creating long-term value by unlocking the full potential of plasma to develop innovative, integrated solutions that meaningfully benefit patients globally

REALIZING THE POTENTIAL OF PLASMA-DERIVED THERAPIES

21st November 2019

Julie Kim
President, Plasma-Derived Therapies Business Unit