

# Our strategy and targeted investments extend across the entire value chain



PLASMA SOURCING



MANUFACTURING



COMMERCIALIZATION



RESEARCH & DEVELOPMENT

# BioLife, part of Takeda's Plasma-Derived Therapies Business Unit, is an industry leader in the sourcing of high-quality plasma



## Broad global footprint

- 140+ collection centers across four countries
- Plasma sourced externally from eight countries
- Three dedicated screening labs



## Recognized expertise

- Trained medical staff at each center
- Dedicated quality, regulatory and medical employees
- Recognized safety and quality expertise, industry-leading standards

Fully compliant with requirements from:



# Our BioLife centers offer an exceptional donor experience



**Efficiency & convenience** central to our approach

- Repeat donors spend just ~1 hour at the center
- Appointment-based process with digital scheduling



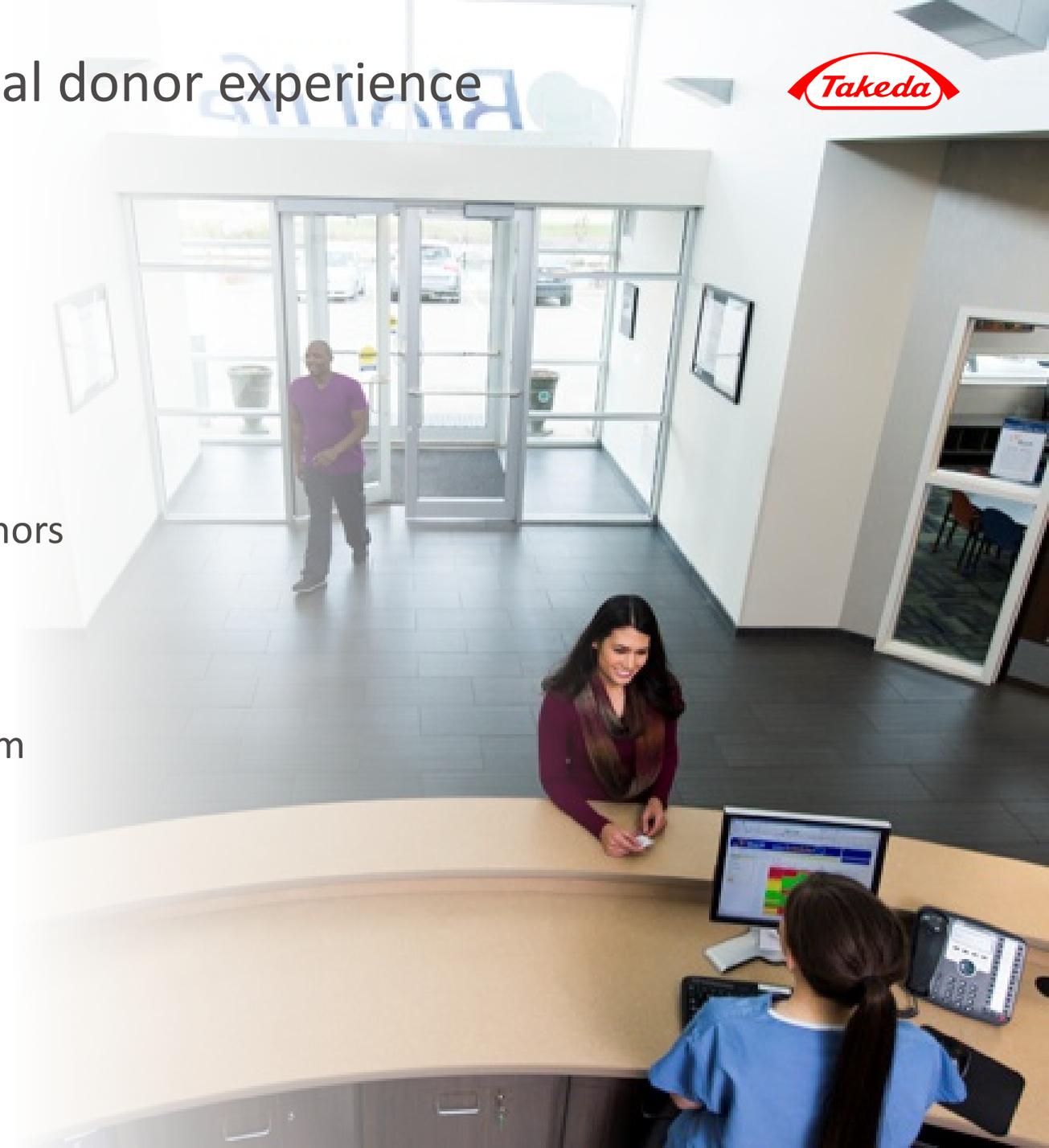
Staff committed to the **well-being** of our donors



**Modern, high quality facilities**, with free Wi-Fi and supervised children's playroom in certain centers



Facilities designed for **donor comfort** and **regulatory compliance**



# We are accelerating the rate of plasma collection and incrementally increasing overall volume through third parties and acquisition



## We are building momentum....



- Increased plasma volumes by approximately 20% in 2018
- Expanded European presence from 7 to 30 collection centers within past 12 months
- Completed 5 acquisitions in the past 12 months in US, Austria, Hungary and Czechia
- Plan on opening a total of 19 additional new collection centers in fiscal year 2019
- Leveraging third party supply through long-term contracts
- Participating in contract agreements with governments

## We will continue to focus on operational excellence



- Open collection sites faster
- Increase speed to peak collection volumes
- Create efficiency via new models and approaches

We are accelerating growth with the goal of increasing plasma supply by

**>65%**

over the next 5 years

# We are further enhancing and digitalizing facilities and services to meet growing needs for the future



## Attracting new donors in the community

- Reaching new donors
- Increasing community engagement

Improving the donor experience and improving cost-per-liter through omnichannel engagement



Mobile App



Website



Scheduling



Payment



Information

Donor

PLASMA SOURCING



MANUFACTURING

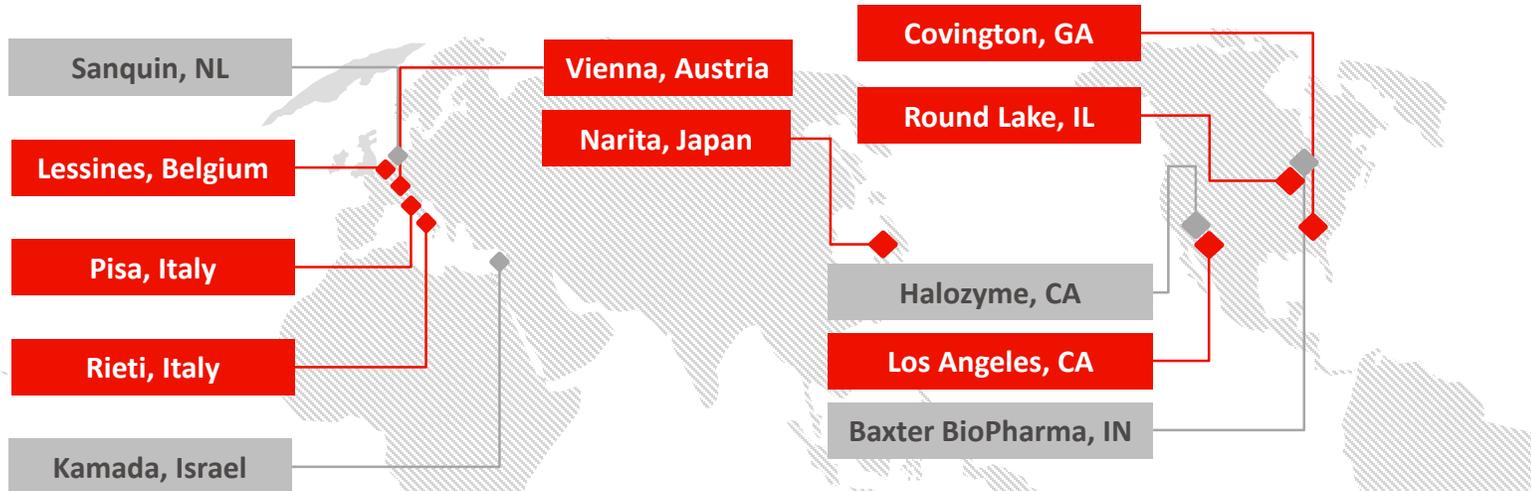


COMMERCIALIZATION



RESEARCH & DEVELOPMENT

We have a world-leading plasma-derived therapies manufacturing network in which we continue to significantly invest



## 8 STRATEGIC LOCATIONS

plus four strategic partners, allowing independent yet inter-related manufacturing operations

## INNOVATION MINDSET

digitalization and constant drive for excellence to accelerate supply to patients

## CONTINUED CAPACITY EXPANSION

to increase production of our portfolio to meet market growth while driving efficiencies

## CONTINUALLY INVESTING

in state-of-the-art facilities that meet the highest quality standards



Takeda Mfg.

External Mfg.

The global network builds on the strengths of each location while leveraging operational excellence across the sites



## Mass Capture, Fractionation



Los Angeles, USA



Rieti, Italy



Vienna, Austria



Sanquin, NL



Covington, USA



## Downstream Processing



Lessines, Belgium



Covington, USA



Round Lake, USA



Pisa, Italy



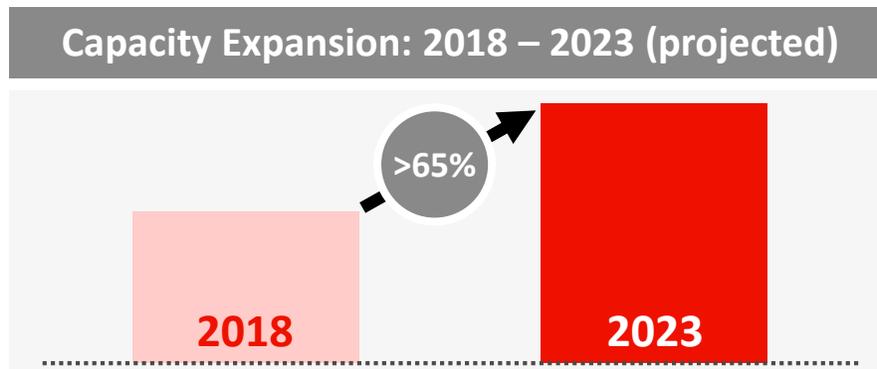
Vienna, Austria

We're increasing production capacity by accelerating investment, while further enhancing our quality standards



## Investing in manufacturing capacity

- Continually investing in technologies and processes to **maximize yield**
  - Higher yield, lower cost fractionation techniques
  - Analytics, automation and digitization to optimize network
- **Optimizing plasma efficiency** through the value chain
- **Downstream optimization** within broader Takeda manufacturing network



We plan to increase our manufacturing capacity within our existing network by

**>65%**

over the next 5 years

# Takeda has world-class safety capabilities and an unsurpassed reputation in both plasma donation and pathogen safety



## Donation safety standards

Strict donation criteria and screening at each visit

Donation frequency management system

Strong inspection record

Plasma screening, inventory hold and look back procedure

Every plasma donation screened for HIV, hepatitis A, B & C, parvo B19

## Pathogen safety standards

**BioSafety Level 3+ Lab**  
Purpose-built, state-of-the-art biocontainment laboratory

**Process sciences**  
Qualified models of all bioprocessing steps

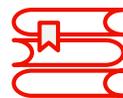
**Virology**  
Classical & molecular virology expertise and capability

**Publication / presentation**  
Strong track record

## Dedicated virology expertise and capabilities



**40+** highly trained staff



**>50%** with specialized education



**>200** years post-graduate experience



PLASMA SOURCING



MANUFACTURING



COMMERCIALIZATION



RESEARCH & DEVELOPMENT

# Our broad and differentiated portfolio of plasma-derived therapies treats rare and complex diseases worldwide



A world map with various plasma-derived therapy logos overlaid on different geographical regions. The logos include:

- HyQvia** (North America)
- Kiovig** (Europe)
- CINRYZE™** C1 inhibitor (human) (Europe)
- Factor IX Complex BEBULIN** (North America)
- HUMAN ALBUMIN** SOLUTION FOR INFUSION (North America)
- FEIBA** (North America)
- Ceprotrin** (Protein C Concentrate (Human)) (Africa)
- Flexbumin 5%** [Albumin (Human)] (Europe)
- IMMUNINE** (Human coagulation factor IX) (North America)
- IMMUSEVEN** (Human Coagulation Factor VII) (North America)
- ATIII** (Africa)
- Glassia** (Asia)
- KENKETU ALBUMINATE™** (North America)
- GAMMAGARD LIQUID** (Africa)
- IMMUNATE** (North America)
- HEMOFIL M** (North America)
- kenketu glovenin®-I** (Africa)
- Prothromplex NF 600** (Asia)
- PROTHROMPLEX PARTIELL** (North America)
- Aralast NP** (Africa)
- Cuvitru** (North America)
- GAMMAGARD S/D** [Immune Globulin Intravenous (Human)] Solvent/Detergent Treated (Africa)
- KENKETU ALBUMIN** (Africa)
- KENKETU NONTHRON®** (North America)

# Our two SCIG brands complement each other and address different patient needs



**Cuvitru**  
 [Human Normal Immunoglobulin, 20%  
 for subcutaneous administration]

**HyQvia**  
 Human Normal Immunoglobulin (10%)  
 Recombinant Human Hyaluronidase



## Key Features

- Well tolerated
- Limited volumes (up to 60ml per site) through frequent infusions
- Ease of use/preparation
- 2 or 4 infusion sites/needles

- Similar efficacy to IVIG and IV-like administration features
- High volumes (up to 600ml per site) and monthly infusions (every 3-4 weeks)
- Improved Bioavailability vs cSCIG
- 1 or 2 infusion sites/needles



## Indications

- PID and SID\*

- PID, SID\*
- CIDP (regulatory approval decision expected in 2023)



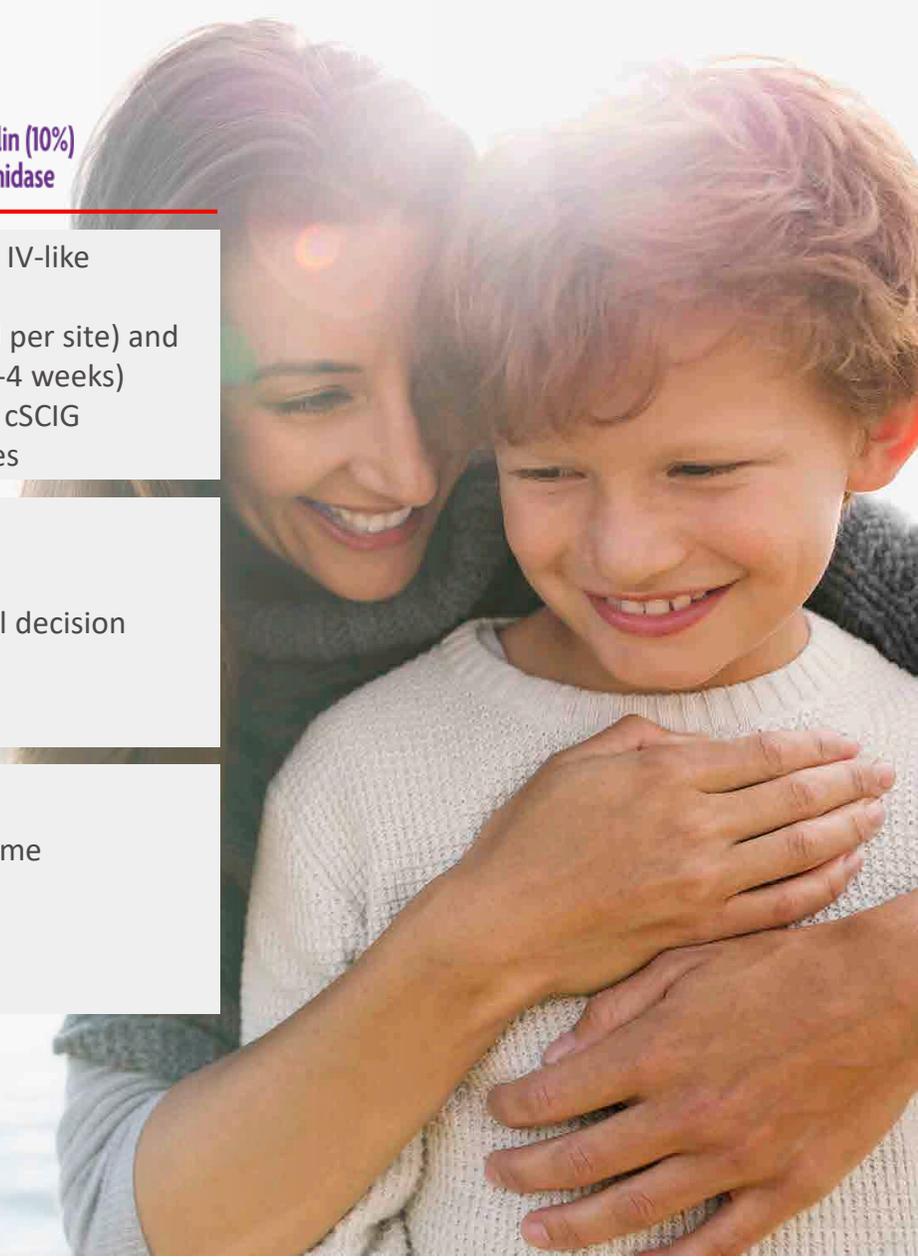
## For patients who prefer

- Fast, regular infusions
- Daily to biweekly
- Home setting

- Less frequency, high volume
- Monthly to biweekly
- Home or hospital setting

Source: Borte, et al., Clin Exp Immunol. 2017 Jan;187(1):146-159. (doi: 10.1111/cei.12866) / Suez, et al., J Clin Immunol. 2016 Oct;36(7):700-12. (doi: 10.1007/s10875-016-0327-9) / CUVITRU SmPC. / Wasserman RL, et al, J Allergy Clin Immunol. 2012 Oct;130(4):951-7. (doi: 10.1016/j.jaci.2012.06.021) / HyQvia SmPC. / Wasserman RL, et al., J Clin Immunol. 2016 Aug;36(6):571-582. (doi: 10.1007/s10875-016-0298-x) / Clinical trials.gov with published study completion Dec 31 2021

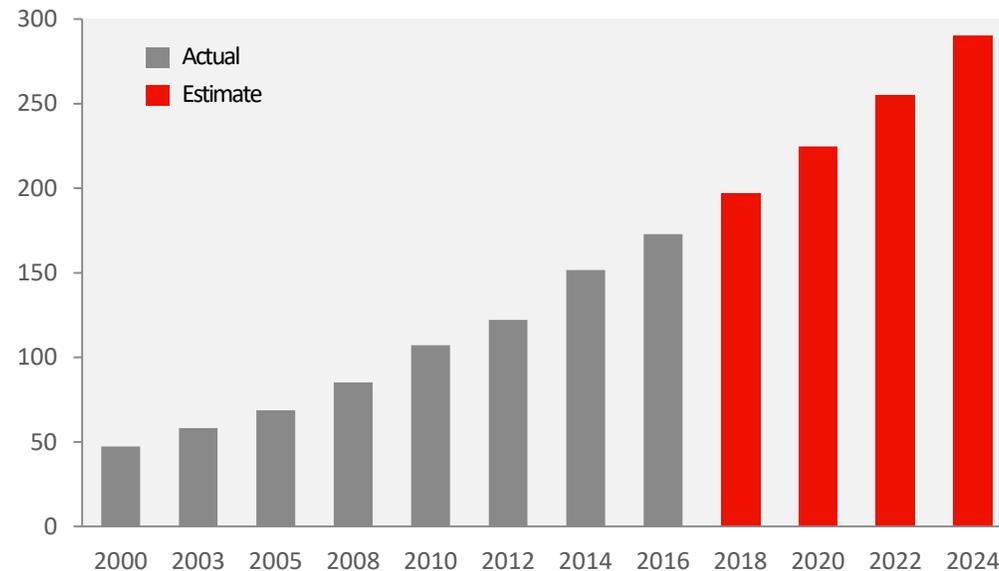
\*SID not approved in the US. Only select SIDs are approved for the above-mentioned products: chronic lymphocytic leukemia, multiple myeloma and hematopoietic stem cell



# Currently, global supply is not keeping up with demand for IG therapies



**The Global Polyvalent IG Market (IVIg/SCIG)  
from 2000 to 2016, with Projected Global Demand Through 2024**  
Millions of grams



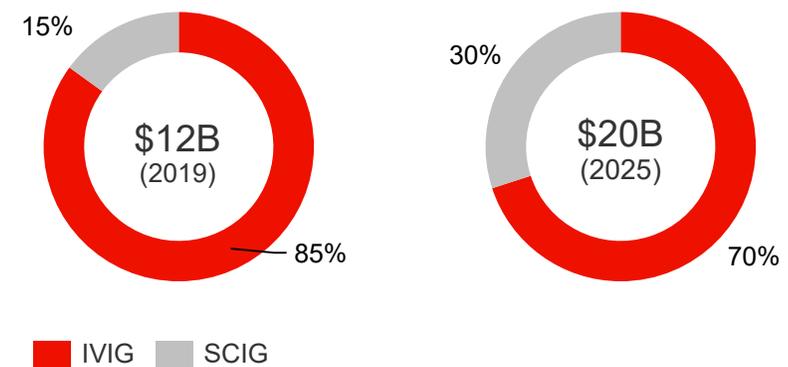
Source: The Marketing Research Bureau, Inc. (Orange, CT)

## STRONG & CONTINUED IG DEMAND

IG is increasingly recognized for its diverse therapeutic value, and is expected to grow in approved indications for a range of diseases

## MARKED BY SCIG GROWTH RATE

SCIG market continues to drive IG growth at CAGR of 20%



# Takeda's commitment during times of supply-demand imbalance is to focus on sustainable patient care



**Consider the global community**



**Support for those with highest need to gain treatment**



**Focus on existing patients first and responsibly pursue new opportunities**



**Partner to explore and implement policies and practices that enable sustainable supply**

Our goal is to continue to bring personalized, innovative, lifelong care to as many people as possible throughout the patient journey



## Diagnosis

---

- Partnership with large hospital systems in the US to leverage electronic medical records
- Co-chairing the Global Commission to End the Diagnostic Odyssey for Children with Rare Disease
- Awareness campaigns
- Diagnostic test kits



## Access

---

- Sustainable pricing
- Dedicated access support
- Patient assistance programs
- Broad portfolio of products

## Personalized Care & Support

---

- Enhanced patient services
- Nurse training to support new patients
- Devices and delivery systems

# We anticipate significant growth opportunities across our portfolio



		Example Takeda products	Takeda revenue (OY, 2018)	Global plasma market size (OY, 2018)
Last Liter	Immunoglobulin	GAMMAGARD LIQUID / Kiovig, Cuvitru, HyQvia, kenketu glovenin-I	~2,870	~12,500
	Albumin	Flexbumin, HUMAN ALBUMIN, KENKETU ALBUMIN, KENKETU ALBUMINATE	~580	~5,000
First Liter	Hemophilia products	HEMOFIL M, FEIBA, IMMUNINE, IMMUNATE	~890	~2,800
	Other products	Aralast NP, Glassia [Alpha <sub>1</sub> -Proteinase Inhibitor (Human)], CINRYZE, Ceprotin, Prothromplex NF 600, KENKETU NONTHRON, Antithrombin III	~660	~3,700
<b>Total</b>			<b>~5,000*</b>	<b>~24,000</b>

\*2018 revenue is a pro-forma which adds Legacy Shire's 9 month (April – December 2018) revenue previously reported under US GAAP and conformed to IFRS without material differences and converted to JPY using FY2018 actual rate for the period. 2018 revenue also includes product sales of Nihon Pharmaceutical products, Takeda's consolidated subsidiary.

# And we are embarking on a trajectory to improve overall Plasma-Derived Therapies business performance



## Key Growth & Margin Drivers for PDT

- Focused **sustainable, value-based commercial strategies**, including tenders
- **Process efficiencies** across the network
- **Capacity increase** across collections and manufacturing
- **R&D investments** across portfolio

## Key Financial Aspiration for PDT\*

Annual revenues  
(CAGR)

Mid to high  
single digit

CAPEX  
(% of Revenue)

Mid single digit

## 1

At Takeda, plasma is a **long-term strategic focus**, led by a **dedicated business unit investing to grow** across the value chain and leveraging Takeda capabilities

## 2

Our goal is to **accelerate growth in capacity by >65%** over the next 5 years to bring additional and improved therapies to more people around the world

## 3

Our **broad and differentiated portfolio** brings **personalized, innovative, lifelong care** and underlines our credentials for **reimagining the industry**



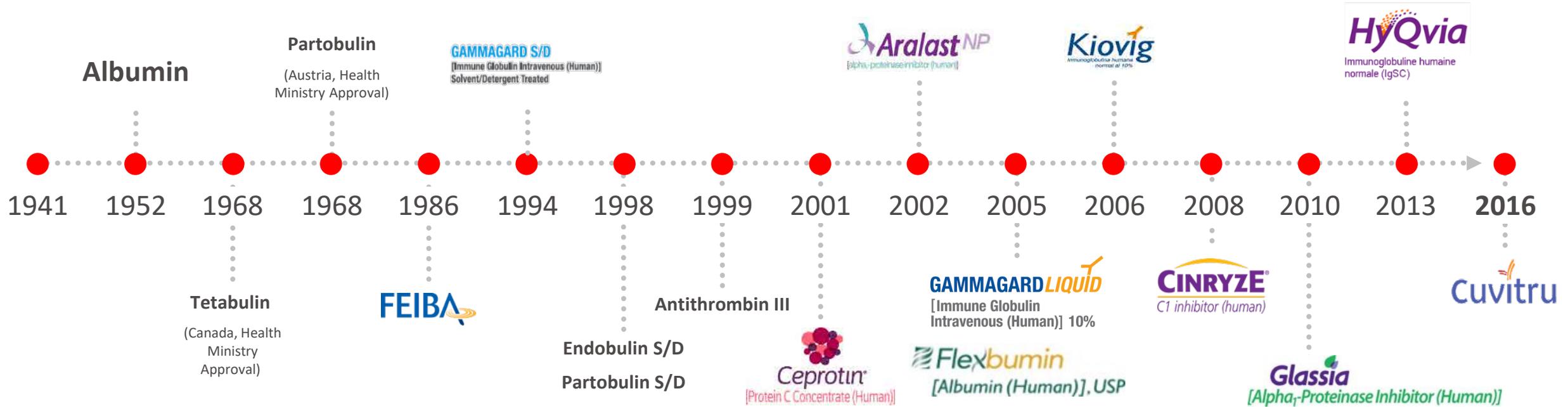
# A New Dedicated Focus on Innovative, Sustainable Solutions for Plasma-Derived Therapies

Christopher Morabito, M.D.  
Head of R&D, Plasma-Derived Therapies



Better Health, Brighter Future

# PDT R&D's credentials and infrastructure are well-established

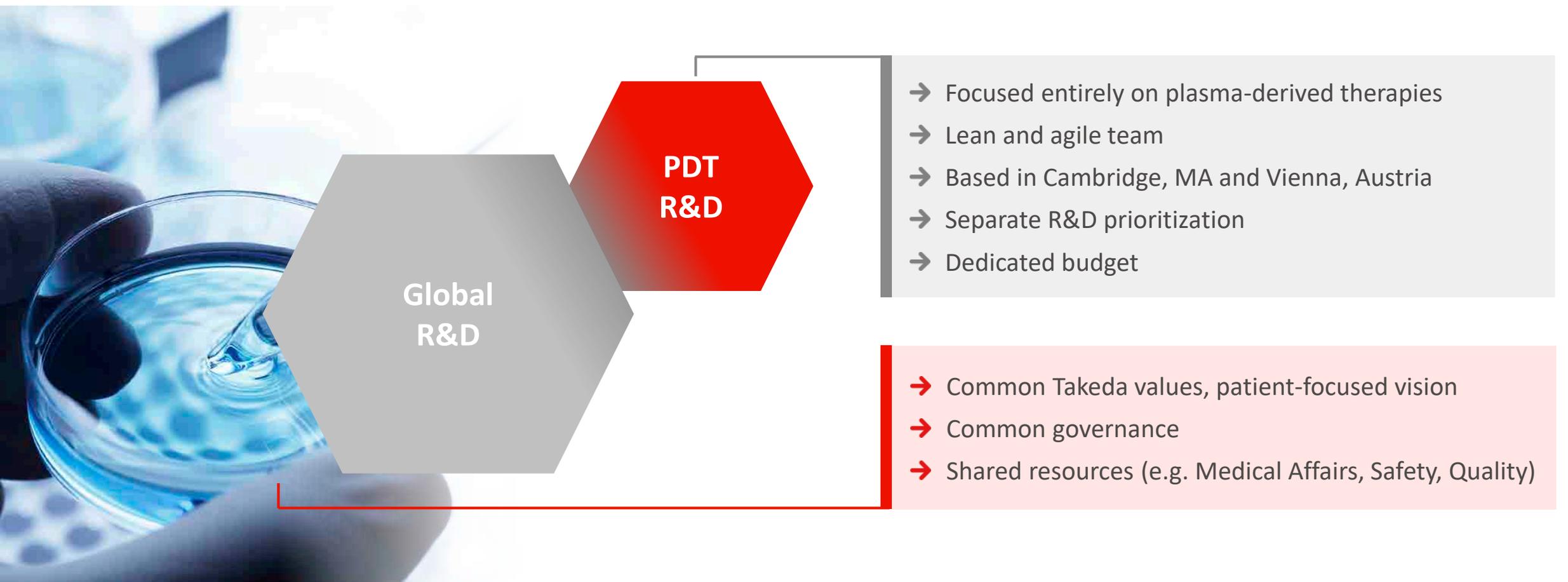


**Pathogen Safety**  
Global Center of Excellence for Pathogen Safety

**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



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



**Leman Yel MD**  
Clinical Medicine  
Boston, MA



**Chris Tremblay**  
R&D Operations  
Boston, MA



**Bagirath Gangadharan PhD**  
Translational Research  
Vienna, Austria



**Andreas Liebming PhD**  
Pharmaceutical Sciences  
& Devices  
Vienna, Austria/Boston, MA



**Sascha Haverfield DPhil**  
Regulatory Affairs &  
Development Operations  
Boston, MA



**Geoffrey Pot PhD**  
Global Manufacturing  
External Supply & Plasma  
Innovation  
Lessines, Belgium



**Gabriele Ricci**  
Digital Technologies  
Boston, MA



**William Standaert**  
Legal  
Zurich, Switzerland



**Cara Laurello**  
Ethics and Compliance  
Boston, MA



**Ambreen Landa**  
Human Resources  
Boston, MA

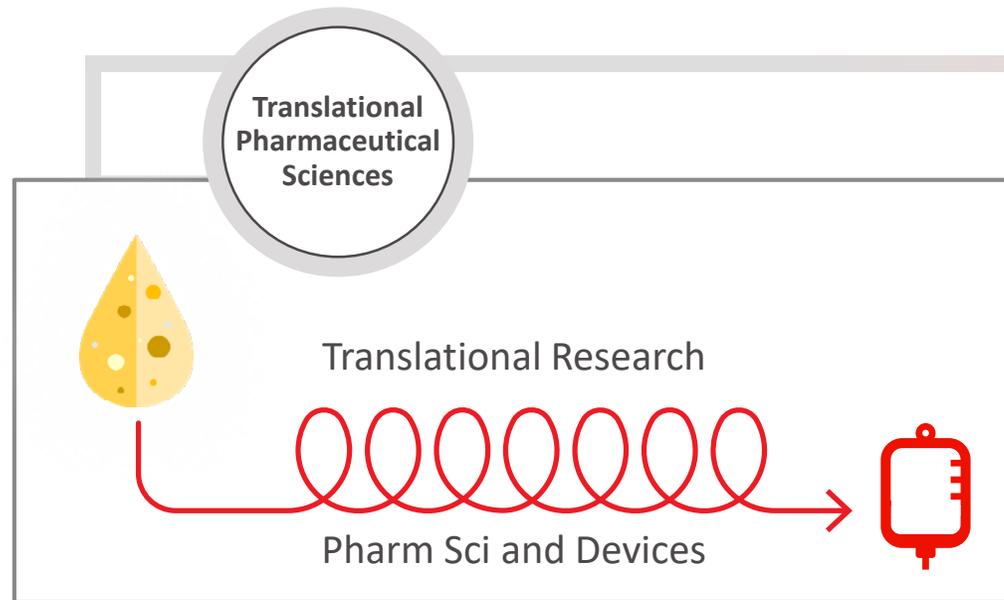


**Pritesh Patel**  
Finance  
Boston, MA

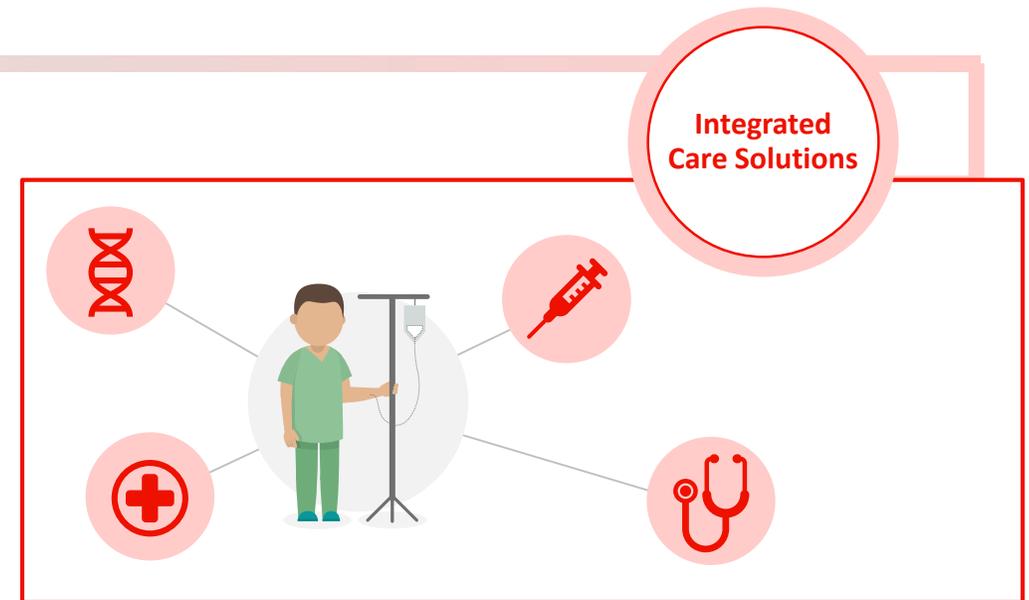


**Julia Ellwanger**  
Communications  
Bannockburn, IL

# We are driving a culture of innovation through two R&D engines



**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*



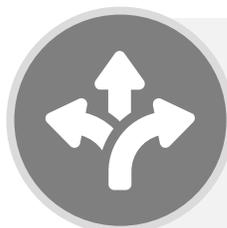
## **Realize full potential of in-line First and Last Litter products**

- 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		<p><b>CUVITRU</b> Wearable Device</p>	<p><b>HYQVIA</b> <i>Halozyme</i> US - Pediatric PID</p>
			<p><b>HYQVIA</b> <i>Halozyme</i> Chronic inflammatory demyelinating polyneuropathy (CIDP)</p>
			<p><b>HYQVIA</b> Geographic expansion</p>
			<p><b>CUVITRU</b> Geographic expansion</p>
HEMATOLOGY			<p><b>HYQVIA - HyHub</b> <i>Flextronics</i> Delivery Device</p>
			<p><b>CINRYZE</b> Geographic expansion</p>
			<p><b>GLASSIA</b> <i>Kamada</i> Immunogenicity/ bronchioalveolar lavage</p>
			<p><b>FEIBA</b> Volume reduction</p>

# ... while enabling discovery of next generation therapeutics



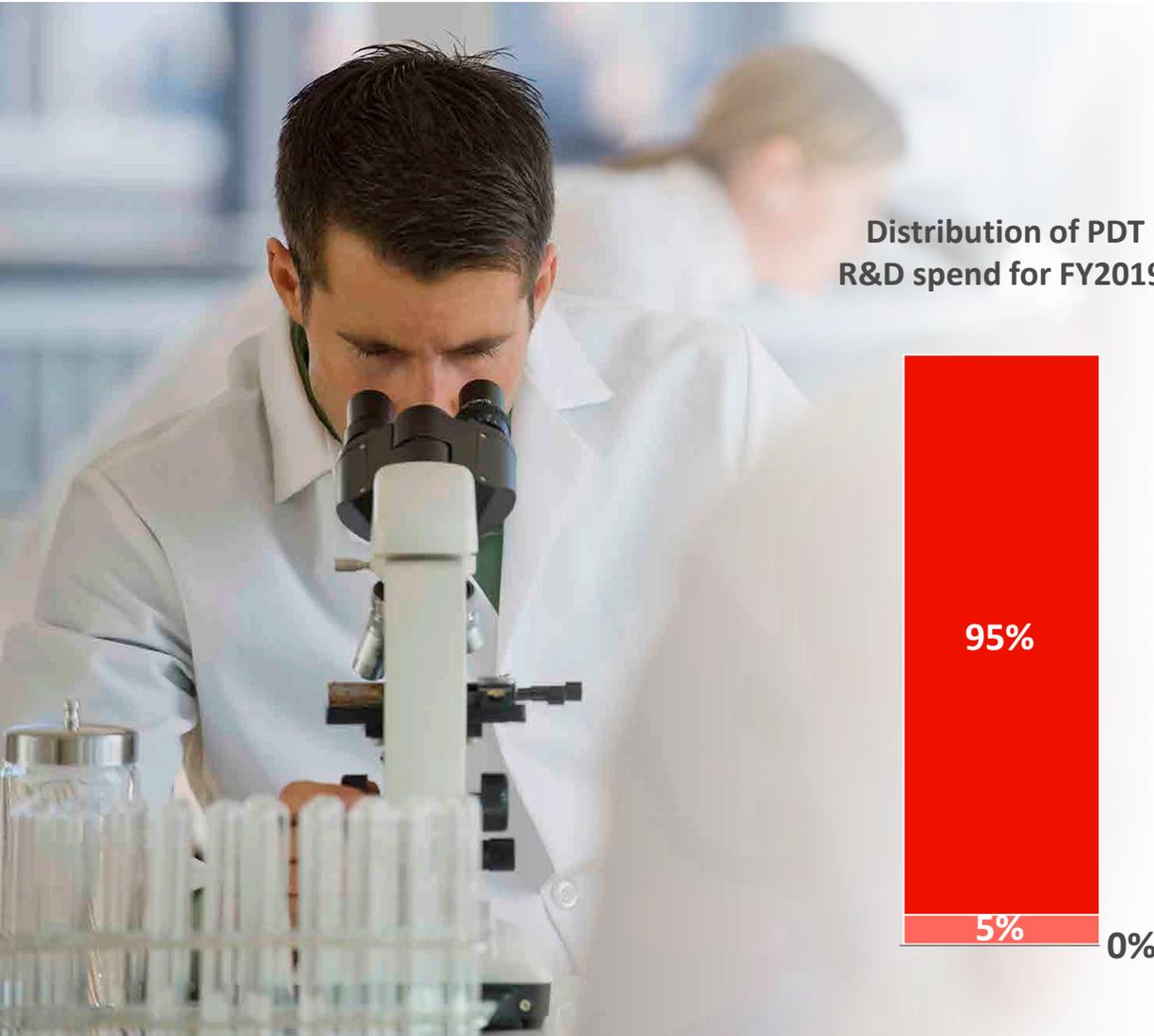
		RESEARCH / NON-CLINICAL DEVELOPMENT		LATE DEVELOPMENT	
IMMUNOLOGY		<b>CUVITRU</b> Wearable Device	<b>TAK 881</b> Facilitated 20% SC IgG <i>Halozyme</i> Primary Immunodeficiency (PID)	<b>HYQVIA</b> <i>Halozyme</i> US - Pediatric PID	<b>HYQVIA</b> <i>Halozyme</i> EU - Pediatric PID
		<b>TAK 880</b> Low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

\*Subject to regulatory approval

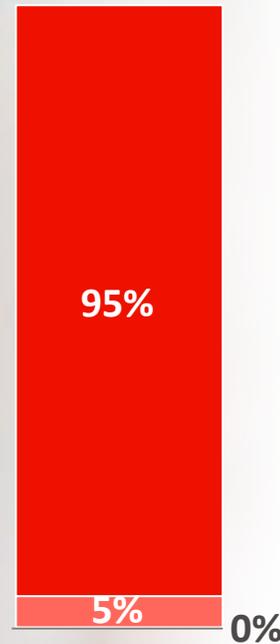
\*\*Pending FDA Pre-IND consultation and future acceptance of an IND

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