Covington Day

Welcome to Shire's Georgia Manufacturing Facility

November 7, 2018

Shire

“Safe Harbor” Statement Under The Private Securities Litigation Reform Act Of 1995

Statements included herein that are not historical facts, including without limitation statements concerning future strategy, plans, objectives, expectations and intentions, projected revenues, the anticipated timing of clinical trials and approvals for, and the commercial potential of, inline or pipeline products, are forward-looking statements. Such forward-looking statements involve a number of risks and uncertainties and are subject to change at any time. In the event such risks or uncertainties materialize, Shire’s results could be materially adversely affected. The risks and uncertainties include, but are not limited to, the following:

- Shire’s products may not be a commercial success;
- increased pricing pressures and limits on patient access as a result of governmental regulations and market developments may affect Shire’s future revenues, financial condition and results of operations;
- Shire depends on third parties to supply certain inputs and services critical to its operations including certain inputs, services and ingredients critical to its manufacturing processes. Any disruption to the supply chain for any of Shire’s products may result in Shire being unable to continue marketing or developing a product or may result in Shire being unable to do so on a commercially viable basis for some period of time;
- the manufacture of Shire’s products is subject to extensive oversight by various regulatory agencies. Regulatory approvals or interventions associated with changes to manufacturing sites, ingredients or manufacturing processes could lead to, among other things, significant delays, an increase in operating costs, lost product sales, an interruption of research activities or the delay of new product launches;
- the nature of producing plasma-based therapies may prevent Shire from timely responding to market forces and effectively managing its production capacity;
- Shire has a portfolio of products in various stages of research and development. The successful development of these products is highly uncertain and requires significant expenditures and time, and there is no guarantee that these products will receive regulatory approval;
- the actions of certain customers could affect Shire’s ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such customers can adversely affect Shire’s revenues, financial conditions or results of operations;
- failure to comply with laws and regulations governing the sales and marketing of its products could materially impact Shire’s revenues and profitability;
- Shire’s products and product candidates face substantial competition in the product markets in which it operates, including competition from generics;
- Shire’s patented products are subject to significant competition from generics;
- adverse outcomes in legal matters, tax audits and other disputes, including Shire’s ability to enforce and defend patents and other intellectual property rights required for its business, could have a material adverse effect on Shire’s revenues, financial condition or results of operations;
- Shire may fail to obtain, maintain, enforce or defend the intellectual property rights required to conduct its business;
- Shire faces intense competition for highly qualified personnel from other companies and organizations;
- failure to successfully execute or attain strategic objectives from Shire’s acquisitions and growth strategy may adversely affect Shire’s financial condition and results of operations;
- Shire’s growth strategy depends in part upon its ability to expand its product portfolio through external collaborations, which, if unsuccessful, may adversely affect the development and sale of its products;
- a slowdown of global economic growth, or economic instability of countries in which Shire does business, could have negative consequences for Shire’s business and increase the risk of non-payment by Shire’s customers;
- changes in foreign currency exchange rates and interest rates could have a material adverse effect on Shire’s operating results and liquidity;
- Shire is subject to evolving and complex tax laws, which may result in additional liabilities that may adversely affect Shire’s financial condition or results of operations;
- if a marketed product fails to work effectively or causes adverse side effects, this could result in damage to Shire’s reputation, the withdrawal of the product and legal action against Shire;
- Shire is dependent on information technology and its systems and infrastructure face certain risks, including from service disruptions, the loss of sensitive or confidential information, cyber-attacks and other security breaches or data leakages that could have a material adverse effect on Shire’s revenues, financial condition or results of operations;
- Shire faces risks relating to the expected exit of the United Kingdom from the European Union;
- Shire incurred substantial additional indebtedness to finance the Baxalta acquisition, which has increased its borrowing costs and may decrease its business flexibility;
- the potential uncertainty among our employees, customers, suppliers, and other business partners resulting from the announcement by Takeda Pharmaceutical Company Limited on May 8, 2018 of a recommended offer for Shire under the U.K. Takeover Code; and

A further list and description of risks, uncertainties and other matters can be found in Shire’s most recent Annual Report on Form 10-K and in Shire’s subsequent Quarterly Reports on Form 10-Q, in each case including those risks outlined in “ITEM1A: Risk Factors”, and in Shire’s subsequent reports on Form 8-K and other Securities and Exchange Commission filings, all of which are available on Shire’s website.

All forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by this cautionary statement. Readers are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof. Except to the extent otherwise required by applicable law, we do not undertake any obligation to update or revise forward-looking statements, whether as a result of new information, future events or otherwise.

Agenda

Welcome	**Carlos Soto** *Covington Site Head*
Plasma-Derived Therapies Business Overview	**Kasha Witkos** *Immunology Franchise Head* **Paul Blanchfield** *US Immunology Head*
Plasma Technical Operations Overview	**Matt Walker** *Technical Operations Head* **Susan Brown** *BioLife Head* **Adrian Murphy** *Plasma Operating Unit Head*
Q&A	
Small Group Rotation	

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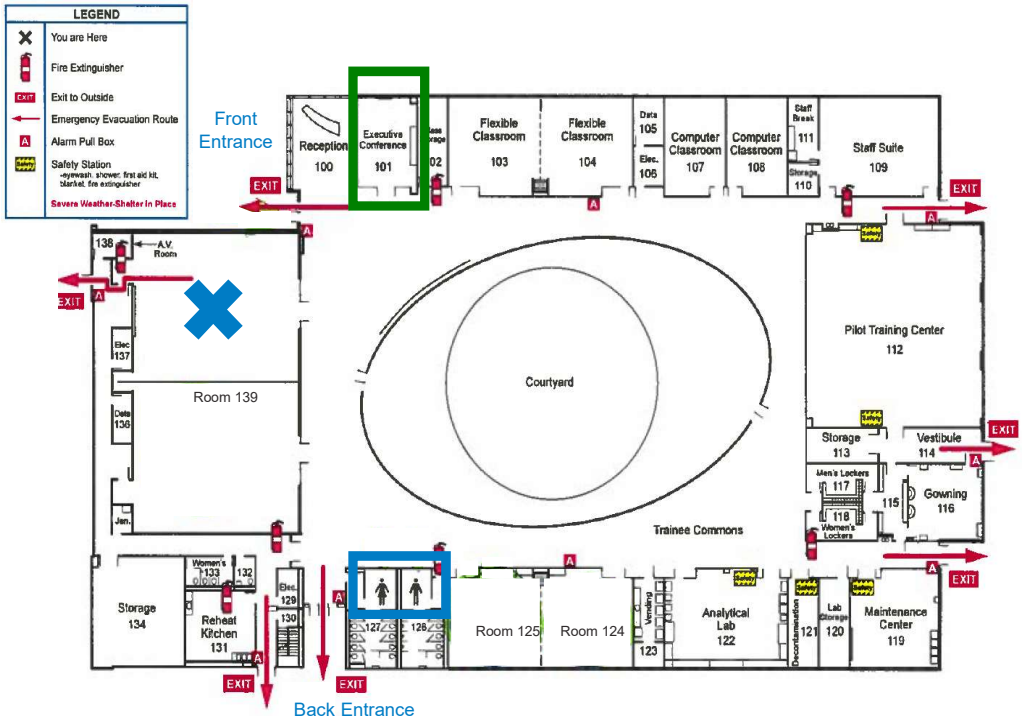
Georgia BioScience Training Center



QUICKSTART®
TECHNICAL COLLEGE SYSTEM OF GEORGIA

- Strong Public-Private Partnership with the state of Georgia

Shire

October 2012

Georgia Manufacturing Facility

Increases Shire's capacity for **PLASMA-DERIVED THERAPIES**

Investment of **$1 BILLION+**

Manufacturing campus covers **1 MILLION+ FT²**

Georgia site will employ **~1,500 EMPLOYEES** at full ramp up

Schedule

Shire

June 2018

Magnitude of scale

8,775,000
Hours worked on site

2,600
Peak workforce (p/per day)

42 FOOTBALL FIELDS
of building area

63,000
Cubic yards of concrete

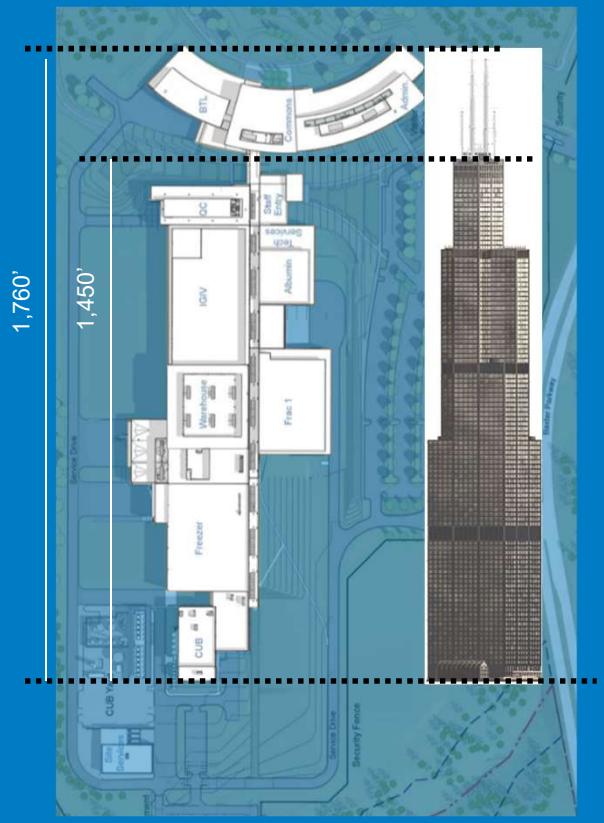
9,000
Tons of steel

2,000,000
Pounds of ductwork

86 miles
of piping

1,400
Pieces of equipment

30,000
Instruments



Shire's Georgia Manufacturing Facility

Willis (Sears) Tower Chicago, Illinois

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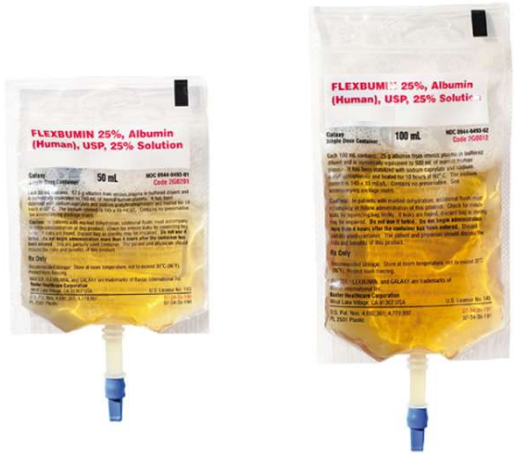
What we will manufacture – Therapies from proteins

GAMMAGARD

Immunoglobulin product (antibodies)

Treats primary immune deficiency disorders

FDA APPROVED *



FLEXBUMIN

Treats burns and trauma victims; plasma volume replacement therapy

FDA Submitted *

Shire

* FDA Submissions and approval related Georgia manufacture of products

Shire Georgia is vertically integrated

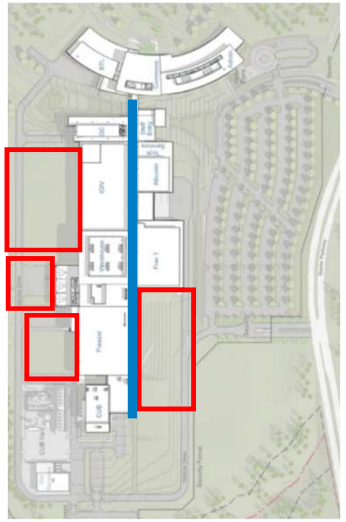
Fully integrated end-to-end production site

Plasma testing	Fractionation	Purification	Filling	Packaging
BioLife PLASMA SERVICES				

- ~900 employees today / ramp up plan in place
- Site includes already approved BioLife testing and storage facility

Flexible design for future expansion

Fractionation capacity, million liters



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Georgia site video

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Q&A	
Small Group Rotation	

Shire

Our personalized approach to supporting patients

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Intelligent Care for Life Patient Pledge

Your lifelong journey with immunodeficiency is unique and personal. We think your treatment should be too.

As life moves on, you need support that can grow and change with you. From newborn diagnosis screening to services and treatments from childhood to old age: at Shire, we believe your journey is our journey. Working in partnership with patients and their caregivers, we offer a personalised, human approach to therapies, services and devices.

That's why we do what we do: Intelligent Care for Life.

Shire

Clinical uses of plasma products span four primary categories

	Description	Uses
Immune globulin (IG)	• Aids in the destruction of foreign molecules • Main function of the humoral immune system	• **IV/SCIG** — congenital antibody deficiencies, neurologic, hematology — 350+ diseases • **Hyperimmune** — target antigens of specific conditions
Albumin	• Maintains intravascular colloid osmotic pressure • Can compete with non-protein based volume replacement solutions such as starches, Ringer's Lactate, or saline	• **Albumin** — Fluid loss, sepsis/septic shock, plasma exchange, burn therapy, renal dialysis
Coagulation	• Replaces missing factors in the clotting cascade due to deficiencies or dysfunctions	• **Factor VIII/IX** – Hemophilia A/B • **vWF** — Von Willebrand Disease • **AT-111** — excessive clotting • **Factor II, V, VII, X, XI, XIII & fibrogen** — deficiencies for blood loss or congenital
Other replace-ment therapies	• Plasma proteins used to treat extremely rare diseases • Orphan drug designation with additional therapies expected	• **AAT/AIPI** — COPD, cirrhosis, jaundice • **CI-INH** — Hereditary Angioedema

Today's focus

Most plasma-derived therapies (e.g., polyvalent IG) **cannot be made in a lab**. These therapies can only be created from donated human plasma from healthy volunteers

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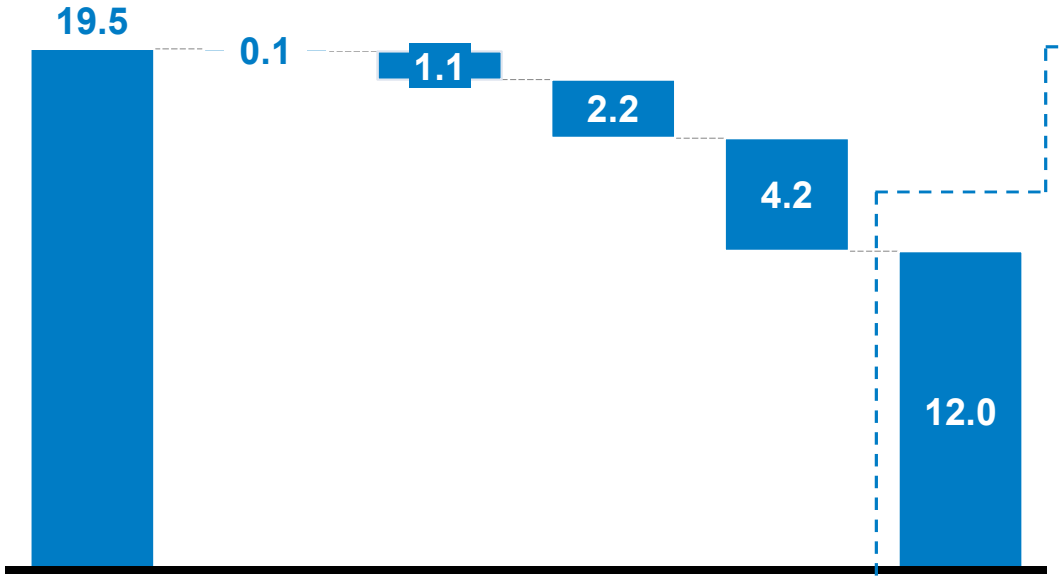
Note: Indications vary by country; see local product labeling

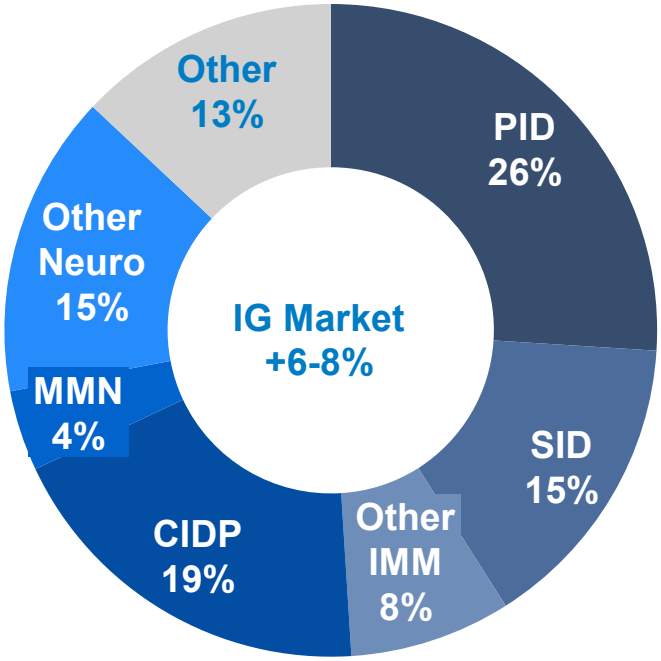
Global Immunology Market: Opportunity for growth

Immunology market size
2018e, USD billion



	Total	Protein C	Alpha-1	HAE	Albumin	IG
Y/Y growth	~7%	n/a	6%	7%	6%	8%

IG market by TA (US & EU)
2018e forecast, percentage



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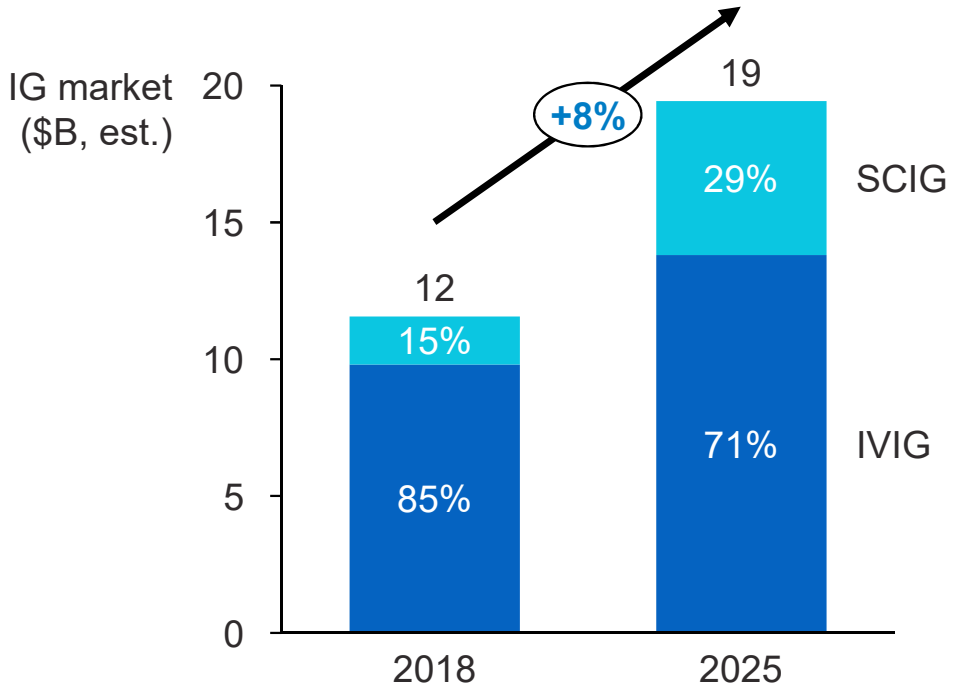
SOURCE: 2016 WW MRB Report, 2017 US MRB Report, & Internal estimates

IG market is expected continue to grow ~8% per year

Total IG Market Overview



SCIG Market

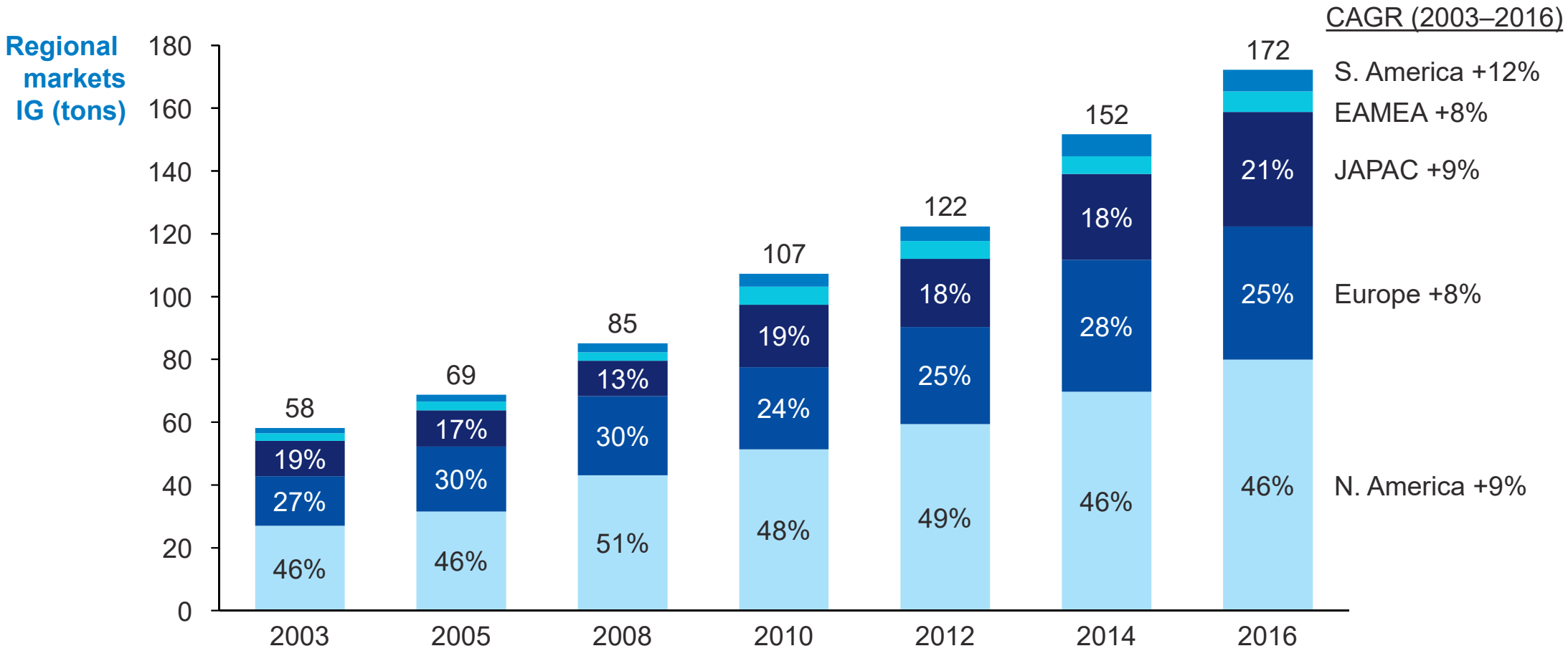
- 15% of the current IG market but growing faster than IVIG
- Today SCIGs are currently approved for PID and SID (INT)
- Key marketed products: Hizentra™ (2010), HyQvia* (2013), Cuvitru* (2016/ 2017)

IVIG Market

- 85% of current market and expected to remain largest segment in 2025
- Market with stable growth
- Top 4 players 75% of global market share, with many smaller, regional players

SOURCE: 2016 WW MRB Report, 2017 US MRB Report, & Internal estimates
Hizentra is a CSL product
*Indications vary by country; see local product labeling

Consistently strong growth globally



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SOURCE: MRB_WW_History 2016, Internal estimates; EAMEA = Eurasia, MEA

Immunoglobulin uses

	Immunoglobulin			
Indication	**PI** Primary immunodeficiency	**CIDP** Chronic inflammatory demyelinating polyneuropathy	**MMN** Multifocal motor neuropathy	**Other** Other Approved & Evidence based
Therapeutic area	Immunology	Neurology	Neurology	Multiple
Primary physician	Immunologist	Neurologist	Neurologist	Multiple
Age groups	Various	Middle age to older adults	Middle age to older adults	Various
2017 Growth	9%	9%	17%	6%

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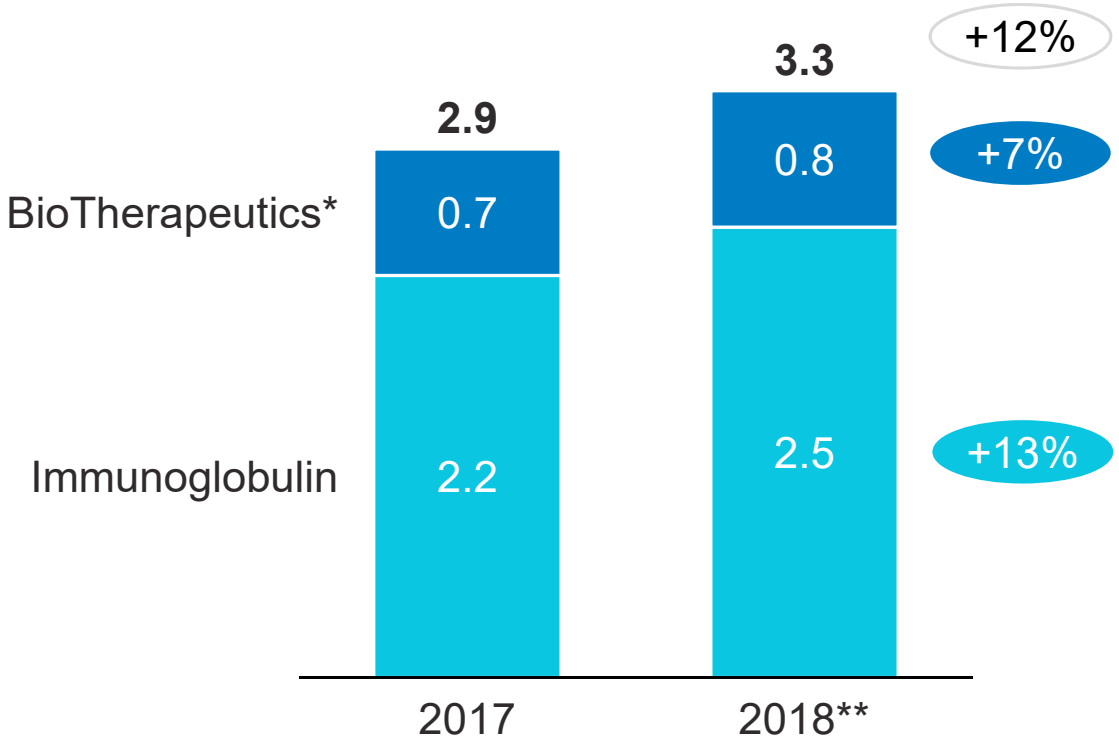
Note: Indications vary by country; see local product labeling

Double-digit growth

Immunoglobulin (IG) and Bio Therapeutics

$MM



Key growth drivers

- Strong demand for **subcutaneous IG portfolio**
- Increasing **focus on execution** (e.g., market penetration, geographic expansion)
- Improving **patient experiences** (e.g., patient services, delivery systems)
- Approval of new **Covington**, Georgia manufacturing facility adds supply

* Bio Therapeutics excludes Prothromplex, Prothromplex T and Bebulin
** Bloomberg consensus, as of Oct 31, 2018

Broadest subcutaneous portfolio

Self infusion available

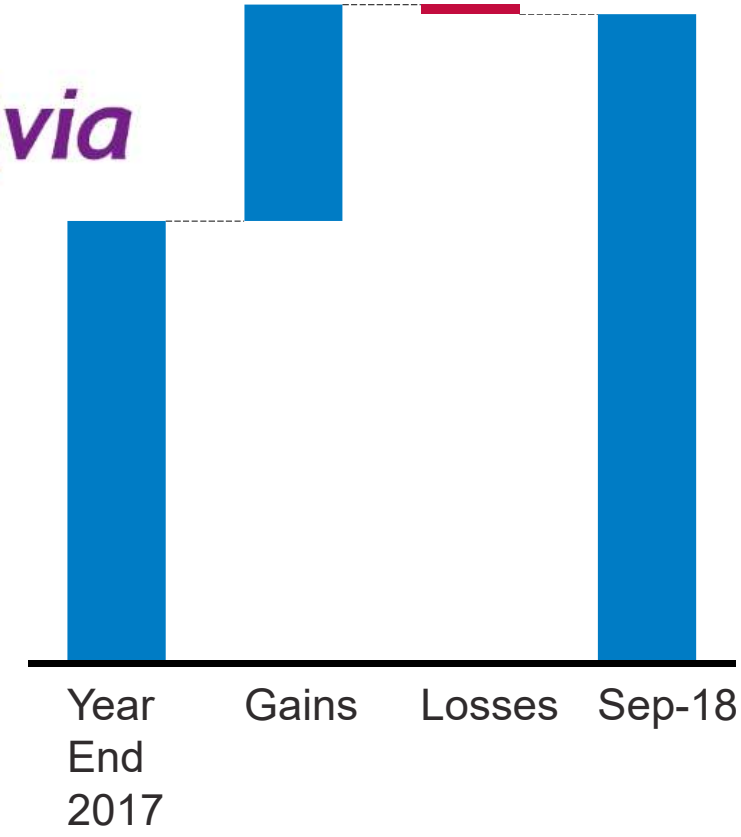
	IGIV	SCIG Weekly	SCIG Monthly	A-1 IV	A-1 IV	Other fractions*
Shire	GAMMAGARD LIQUID	Cuvitru	HyQvia	Glassia	Aralast NP	Ceprotin Protein C Concentrate (Human)
	Gammagard S/D	GAMMAGARD LIQUID				Flexbumin
	Kiovig					
CSL	✓	✓		✓	✓	✓
GRIFOLS	✓	✓			✓	✓
Other	✓	✓			✓	✓

* Includes Albumin, Protein C, pdFVIII, Hyperimmunes, other bleeding disorders, etc.
Note: Indications vary by country; see local product labeling

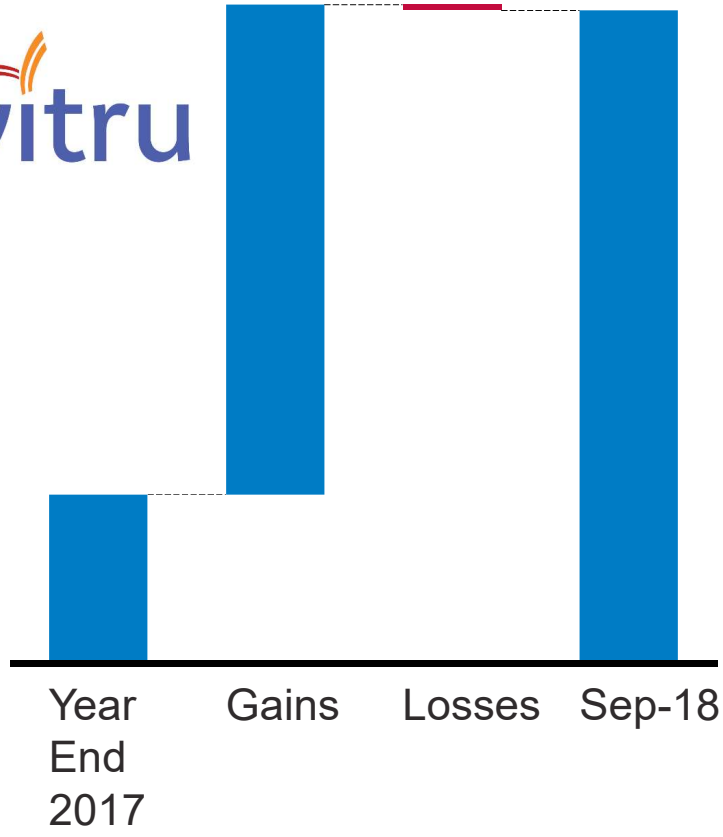
High patient retention

INTL

HyQvia



Cuvitru



Note: CW39 data, weekly pt tracker

Impact of FcRN technology

FcRn technology

- IgG auto-antibodies are directed against the patients' own tissues for IgG mediated autoimmune diseases
- Blocking FcRn induces IgG clearance in diseases driven by IgG auto-antibodies
- Anti-FcRn could play a role in the treatment of IgG autoimmune conditions (immune modulatory)

Opportunity for Shire	• Shire has invested in PRIM technology* which is well-positioned thanks to broader specificity than anti-FcRn
Durability of IG market	• While the anti-FcRn class has shown promise, questions remain about long-term safety vs IG • Immunodeficiency cannot be addressed by anti-FcRn • Continued demand growth expected in all indications
Strategic flexibility	• Any potential impact on the IG market could partially be compensated by selling the relevant IG elsewhere in other markets

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* Press release Jan 2018 regarding partnership with AB Biosciences
SOURCE: Shire competitive intelligence, R&D, BD

Our pledge to patients

Shire

Intelligent Care for Life Patient Pledge

Your lifelong journey with immunodeficiency is unique and personal. We think your treatment should be too.

As life moves on, you need support that can grow and change with you. From newborn diagnosis screening to services and treatments from childhood to old age: at Shire, we believe your journey is our journey. Working in partnership with patients and their caregivers, we offer a personalised, human approach to therapies, services and devices.

That's why we do what we do: Intelligent Care for Life.

Shire Plasma Derived Therapies are well positioned for continued success

Robust demand growth expected to continue

Shire has a **broad**, differentiated **portfolio**

Strong execution globally is driving competitive success

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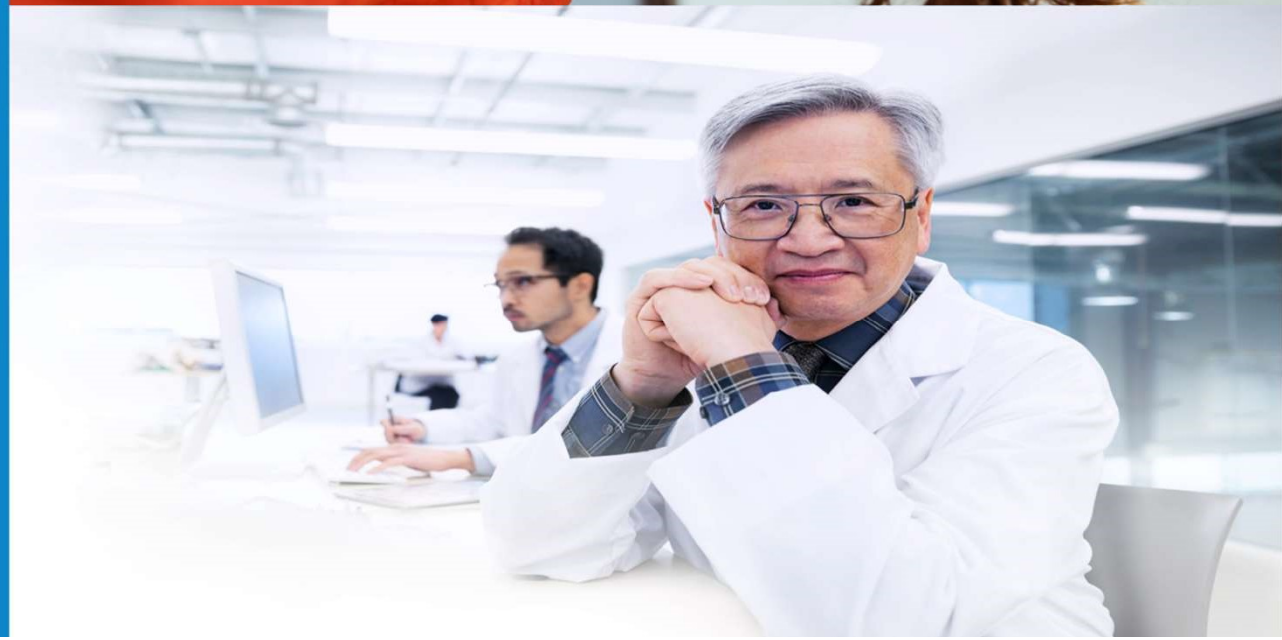
US Plasma Business Review

IG and Bio Therapeutics



US Business Overview

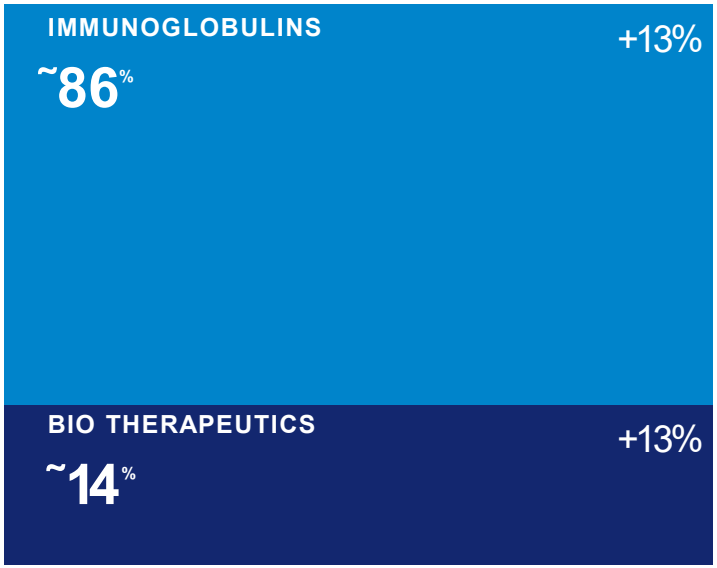
Business Dynamics

Competitive Dynamics

Shire Strategic Priorities

Majority of US Plasma Derived Therapies: IG and Bio Therapeutics

Net Product Sales
Millions, Percentages, YOY Revenue Growth



TTM Ending 2Q18

SHIRE US PLASMA DERIVED BRANDS

- Cuvitru (Immune Globulin Subcutaneous (Human)) 20%
- HyQvia
- GAMMAGARD LIQUID (Immune Globulin Infusion (Human)) 10%
- GAMMAGARD S/D
- Glassia (Alpha1-Proteinase Inhibitor (Human))
- Aralast NP (Alpha1-Proteinase Inhibitor (Human))
- Flexbumin (Albumin (Human))
- Ceprotin (Protein C Concentrate (Human))

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US Immunoglobulin (IG) market overview

US IG Usage by Indication
Percent of Total Volume

~32% Neuro

~31% PI

~37% Other inc. SID*

Site of Care Options

HOME

CLINIC

HOSPITAL

Route of Administration

IV
INTRAVENOUS

SC
SUBCUTANEOUS

FSC
FACILITATED SUBCUTANEOUS

Concentration

5%

20%

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Shire US IG Portfolio

	Cuvitru [Immune Globulin Subcutaneous (Human)] 20%	HyQvia	GAMMAGARD LIQUID [Immune Globulin Infusion (Human)] 10%	GAMMAGARD S/D
Concentration	20%	10% with Hyaluronidase	10%	↑↓
Approved indications	Primary Immunodeficiency	Primary Immunodeficiency	Primary Immunodeficiency Multifocal Motor Neuropathy	PI, CLL, ITP, Kawasaki Syndrome
Route of administration	SC	FSC	SC IV	IV
Frequency	Daily to Every 2 Weeks	3-4 Weeks	Customizable	Customizable
Primary site of care				
Key differentiator	Customize without Compromise	SC Treatment Frequency	Proven Efficacious / Safe IV	Only Low IGA

These differences are important to patients / HCPs

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IG strategic priorities

Hospital Portfolio

PI In The Home

Patient Services

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Alpha-1 product overview & opportunities

	Glassia [Alpha$_1$-Proteinase Inhibitor (Human)]	Aralast NP [Alpha$_1$-Proteinase Inhibitor (Human)]
Approved indications	Alpha1-Antitrypsin Deficiency	Alpha1-Antitrypsin Deficiency
Route of administration	IV	IV
Frequency	Weekly	Weekly
Primary site of care		
Product medium	Liquid	Lyophilized
Key differentiator	1st Liquid / Self-Infused	

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Business conclusion

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Q&A	
Small Group Rotation	

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Plasma Technical Operations Overview: *Positioning Shire's Supply Chain for Future Growth*

Matt Walker, Head of Technical Operations

Shire


ARM in ARM

Manufacturing network assessment announced in 2017

Goals

- Effectively and efficiently meet future patient demand while improving quality and compliance
- Increase utilization and improve working capital
- Accelerate speed to market

Drivers

1 *Modernize*

- 3 biologics sites to be divested based on utilization
- New site builds continue, invest in remaining sites

2 *Position for Growth*

- Continue with plasma production expansion at Covington - site adds ~30% capacity
- New BioLife plasma collection sites opening to meet demand

3 *Enhance Capabilities*

- Focus sites on clear roles to further enhance core capabilities and improve efficiencies

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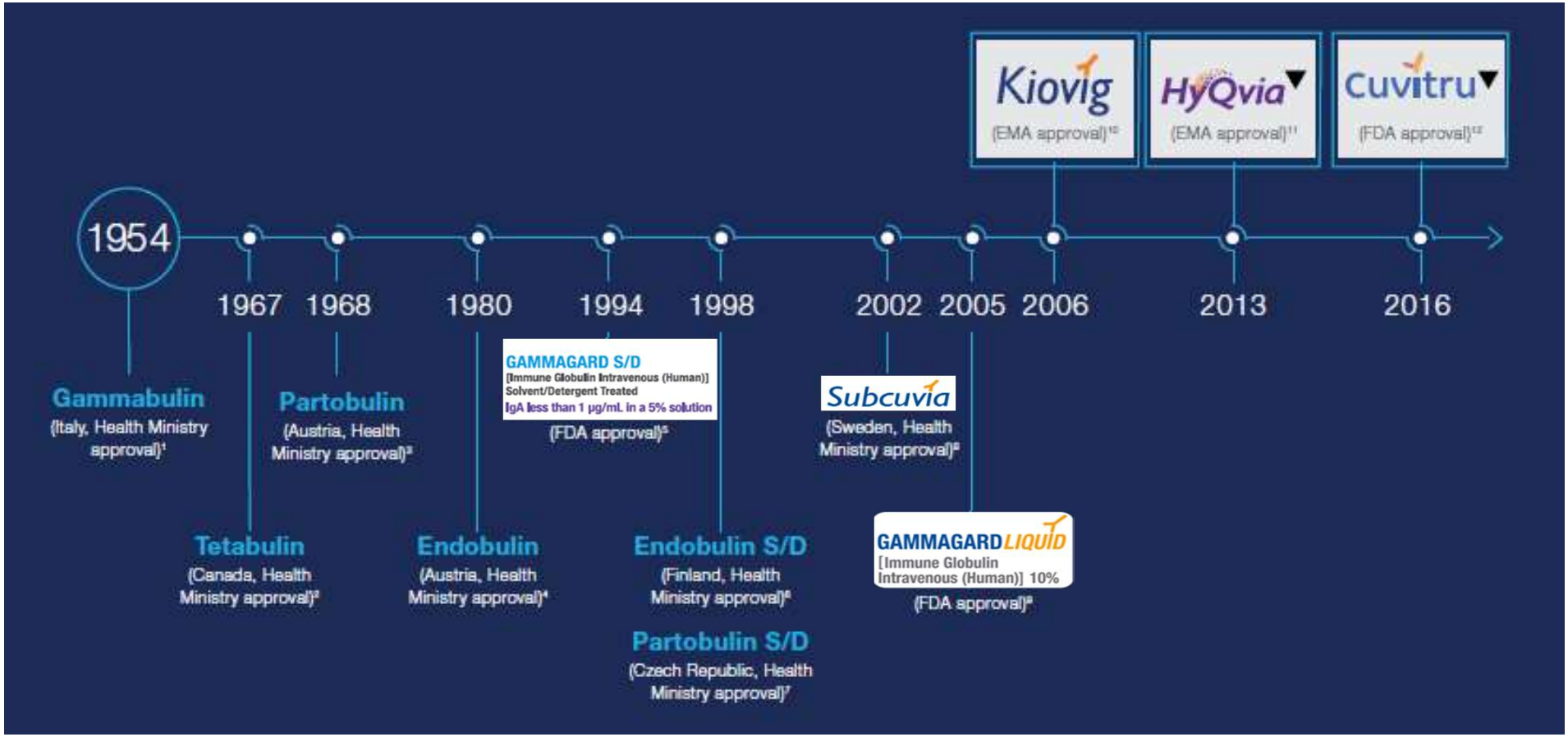
A long heritage in Plasma-Derived Therapies



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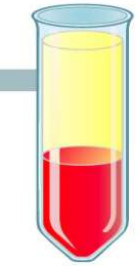
Shire Plasma Manufacturing video

What is Plasma?

Plasma proteins are important in the treatment of a variety of serious medical conditions

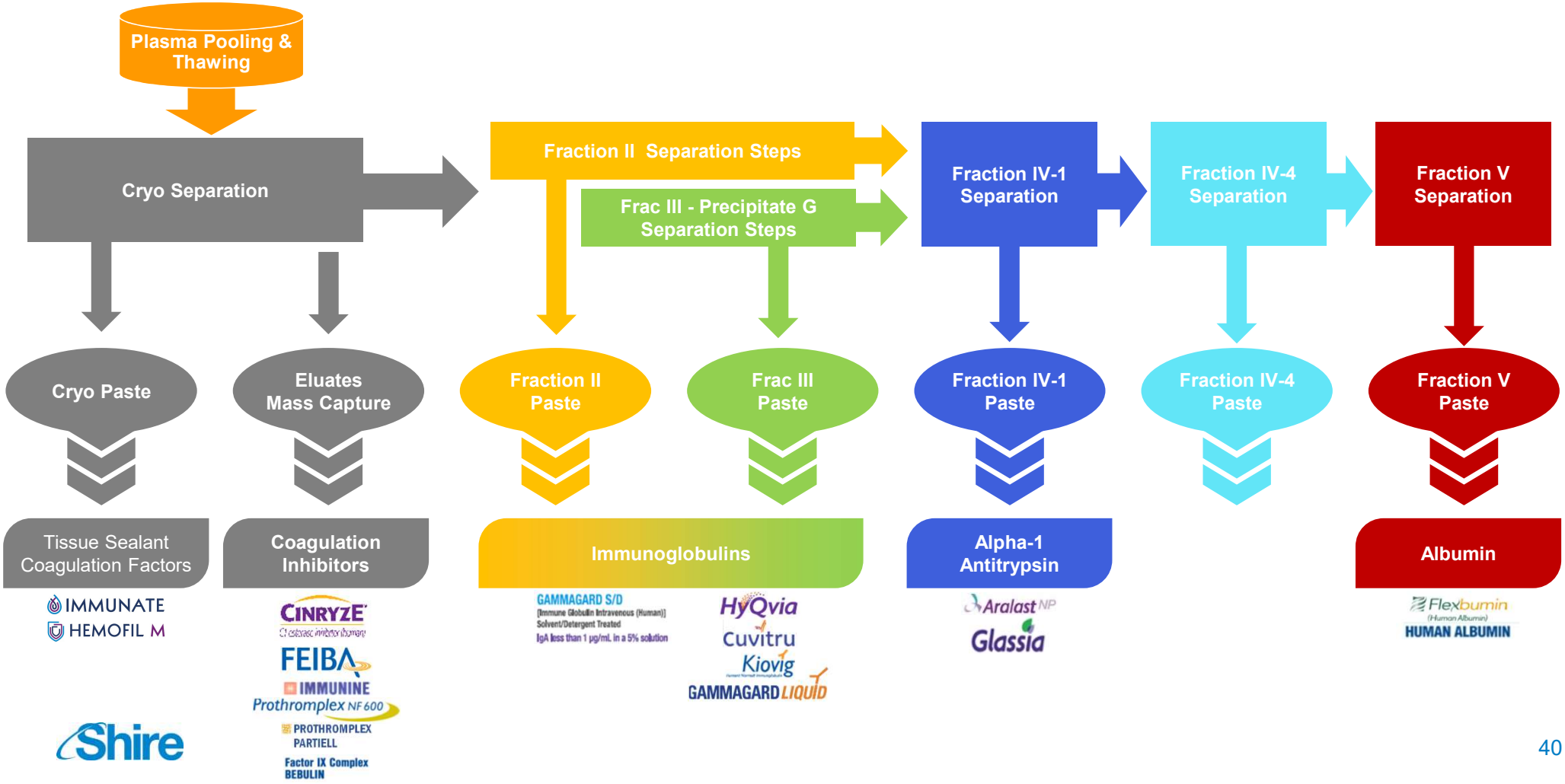
Plasma (55%)	
Constituent	**Major functions**
Water	Solvent for carrying other substances
Salts (ions) Sodium Potassium Calcium Magnesium Chloride Bicarbonate	Osmotic balance, pH buffering, and nerve and muscle function
Plasma proteins	Osmotic balance and pH buffering
Fibrinogen	Clotting
Immunoglobulins (antibodies)	Immunity
Substances transported by blood Nutrients (e.g., glucose, fatty acids, vitamins) Waste products of metabolism Respiratory gases (O_2 and CO_2) Hormones	



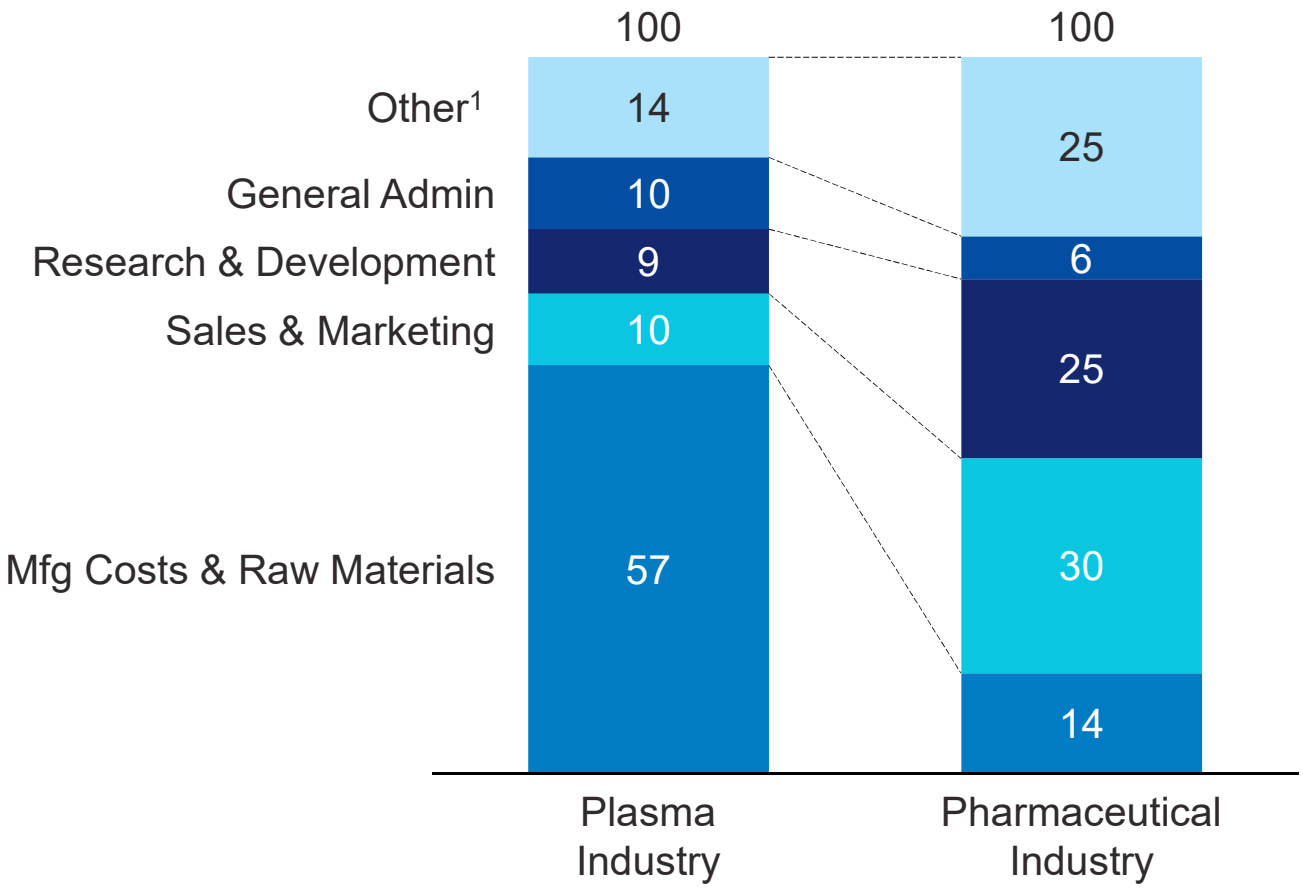
Centrifuged blood sample

Key Take Away: Plasma is critical for production of our product lines.

Multiple products can be derived from each liter of plasma



Manufacturing cost structures of plasma-based protein therapies and of chemical-based pharmaceuticals – 2011 Industry Avg



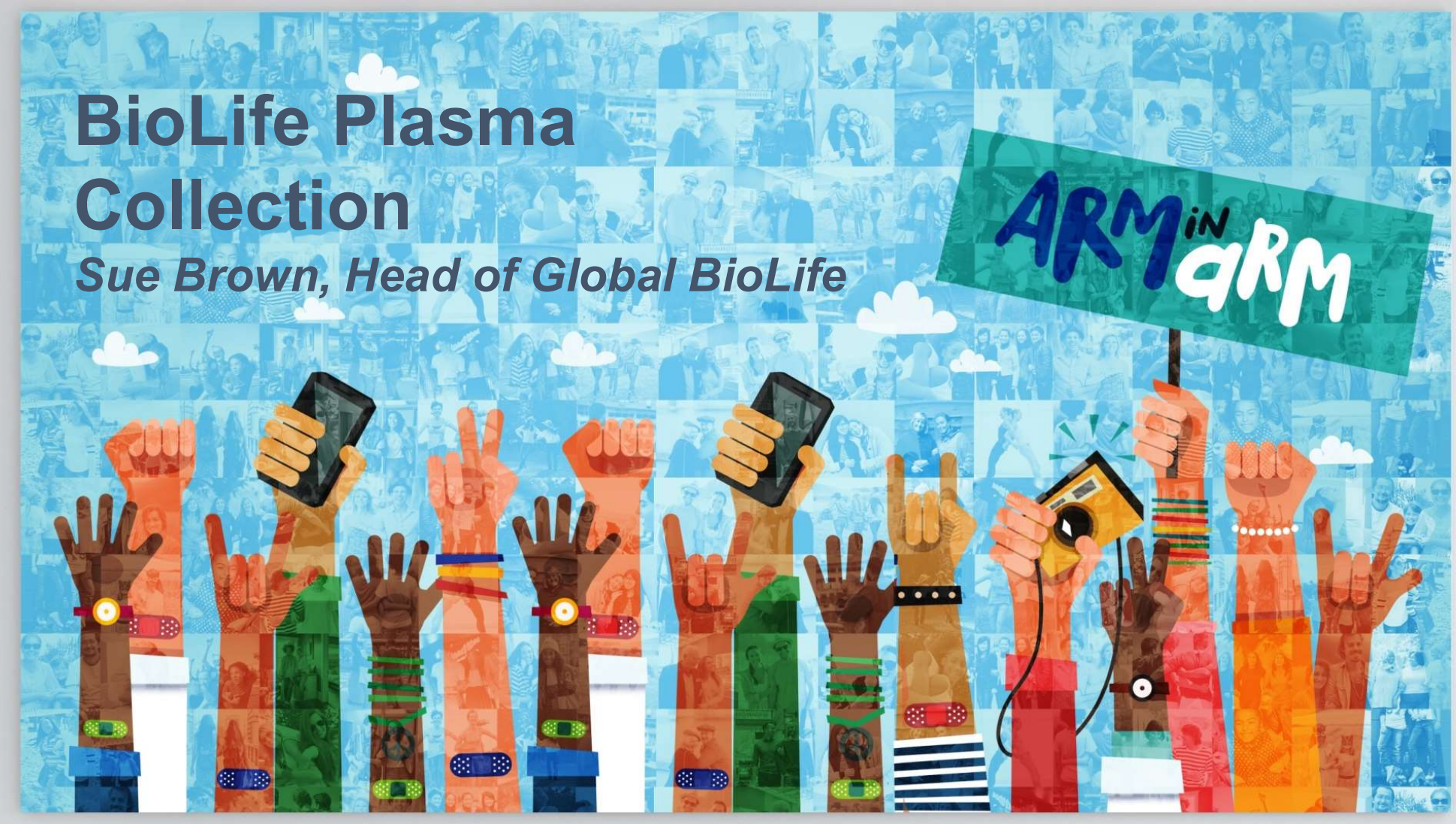
1 Includes General Administration in the Pharma Industry

SOURCE: Industry Reports & Estimations 2011

Collaboration and execution excellence is required

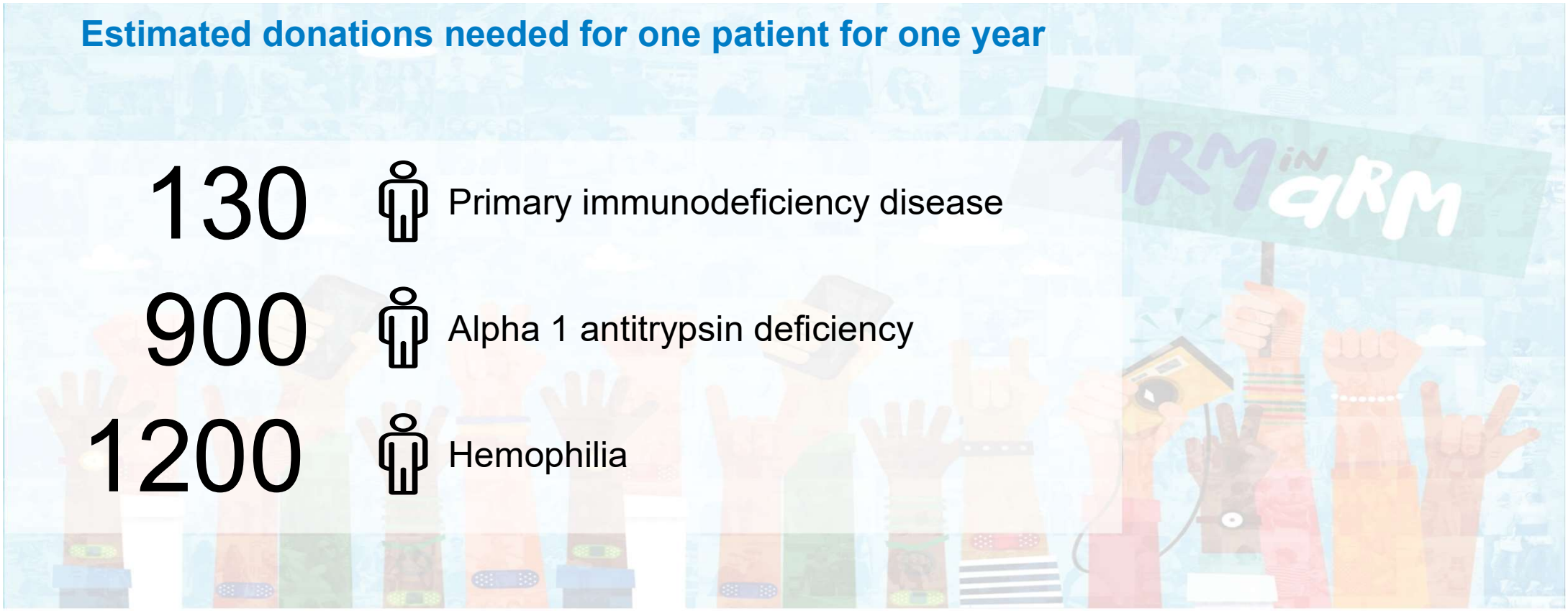
BioLife Plasma Collection

Sue Brown, Head of Global BioLife



It can take 1000+ donations to derive a one-year therapy for 1 patient

Estimated donations needed for one patient for one year



130 Primary immunodeficiency disease

900 Alpha 1 antitrypsin deficiency

1200 Hemophilia

BioLife Plasma Services

Our Mission:

To provide the highest-quality plasma to meet the expectations of our customers, ensuring the availability of life-saving therapies for patients.

Our Vision:

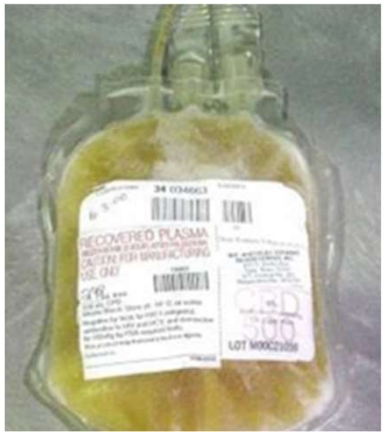
To be the leading plasma supply company in the world by continuously improving, to ensure:

- Every employee is valued and a fully engaged member of our team
- Every donor is recognized for his or her contribution and given exceptional service
- Every process is innovative and efficient
- Every customer is delighted with our performance

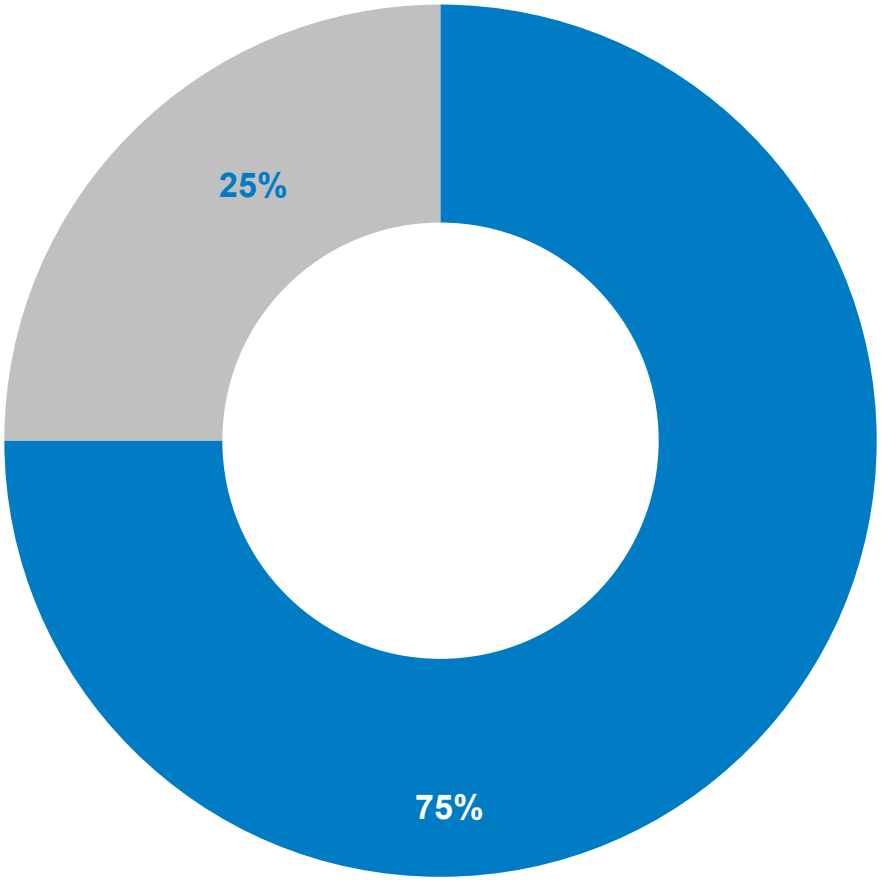
Plasma sourced through BioLife centers and third parties

Recovered Plasma

Small Bags (280 mL)



Recovered plasma is “recovered” from a whole blood donation (with donation allowed every 56 days)

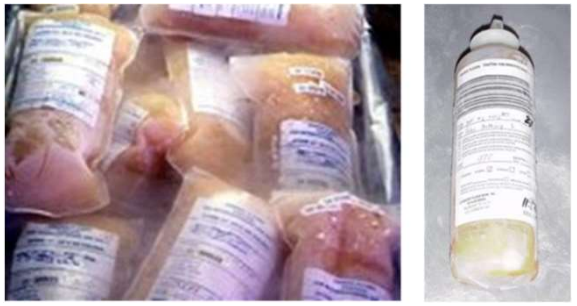


BioLife Centers

Third Parties

Source Plasma

Large Bags or Bottles (810 mL)



Source plasma is plasma collected by plasmapheresis, returning non-plasma components back to the donor (with donations allowed twice/week in U.S.)

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BioLife global operations 2018 snapshot

Global BioLife Plasma Operations

5,000 +

Global Employees

101

U.S. Centers across 27 states

7

Centers in Austria

3

Screening Labs

3rd Party Plasma Supplies

5 US suppliers

~50 locations

~50 EU suppliers

~130 locations across 7 countries

Shire

BioLife screening laboratories

- A sample from every plasma donation is sent to a BioLife Screening Laboratory to screen for a variety of diseases prior to being approved for use in manufacturing
- Tests are run for HIV, Hepatitis A, B & C, Parvo B19, Syphilis, atypical antibodies, proteins
- U.S. labs located in Alabama and Georgia

Organic and inorganic growth strategies

- Met target for new collection facilities in 2018 and planning to grow by double digits in 2019
- sanaplasma AG acquisition announced Sept 5
  - 14 centers in Czech Republic & Hungary
  - Entry point into owning more plasma centers outside the US to support high sales growth international markets

SOURCE: TechOps / Press Releases / Publicly available images

BioLife Productivity

Not every plasma center is created equal

- BioLife gets more plasma on average from our centers versus competitors*, which is more cost effective than opening new centers
- Our labor productivity has improved over 15% since 2015 – a result of our relentless drive for effectiveness and efficiency in centers, as well as volume leverage
- Our donor processing time of less than 70 minutes for repeat donors is a competitive advantage
- We have ramped over 70% of our new centers opened in the last 3 years to 1000 donations per week in their first year of operation

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* PPTA 2017 and May YTD 2018 data and internal Shire data

Plasma Manufacturing

Adrian Murphy, Head of Plasma Operating Unit

A long heritage in both Europe & US

Los Angeles site history: 65 years
"Sister Site" to this Georgia facility

Early Years

1935 Dr. Clarence M. Hyland leaves the Los Angeles Children's Hospital to start the Convalescent Serum Center

1940 The Convalescent Serum Center becomes **Hyland Labs**

1952 Baxter acquires Hyland

1953 Hyland moves into **present site**

Liquid Gamma Globulin

Building 5 licensed to begin manufacturing

Shire Acquisition

Building 6 QC Labs licensed

2000 2004 2005 2006 2015 2016 2017 2018

Van Nuys Warehouse built

Flexbumin

Baxalta split

Building 8 licensed to begin manufacturing

Building 8 and **QC Labs** receive FOYA awards

FOYA 2018 Facility of the Year Awards

Building 1 demolition

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Manufacturing overview

1. Plasma Collection

2. Receipt and Use

3. Fractionation

4. Purification

5. Filling

6. Packaging and Distribution

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Manufacturing facility overview

Cryo Precipitation, Absorption and Fractionation


Los Angeles, USA


Rieti, Italy

Vienna, Austria


Sanquin, NL


Covington, USA

Downstream Processing


Lessines, Belgium


Covington, USA

Worldwide Distribution

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Productivity levers unlock hidden capacity and value in existing sites

- Reducing Lost Time Incident Rate
- Reducing water consumption
- Successful quality inspections

EHS, Quality & Compliance

- Improving conversion costs
- Reducing cost & supply risk through selective internalization
- Targeted capacity expansion projects at sites

Value

Supply Assurance

- Maximizing yield at each stage of manufacturing
- Reducing lead time, cycle time
- Optimizing supply performance

People

- Developing capabilities and talent
- Accelerating continuous improvement, reducing discards
- Increasing colleague engagement

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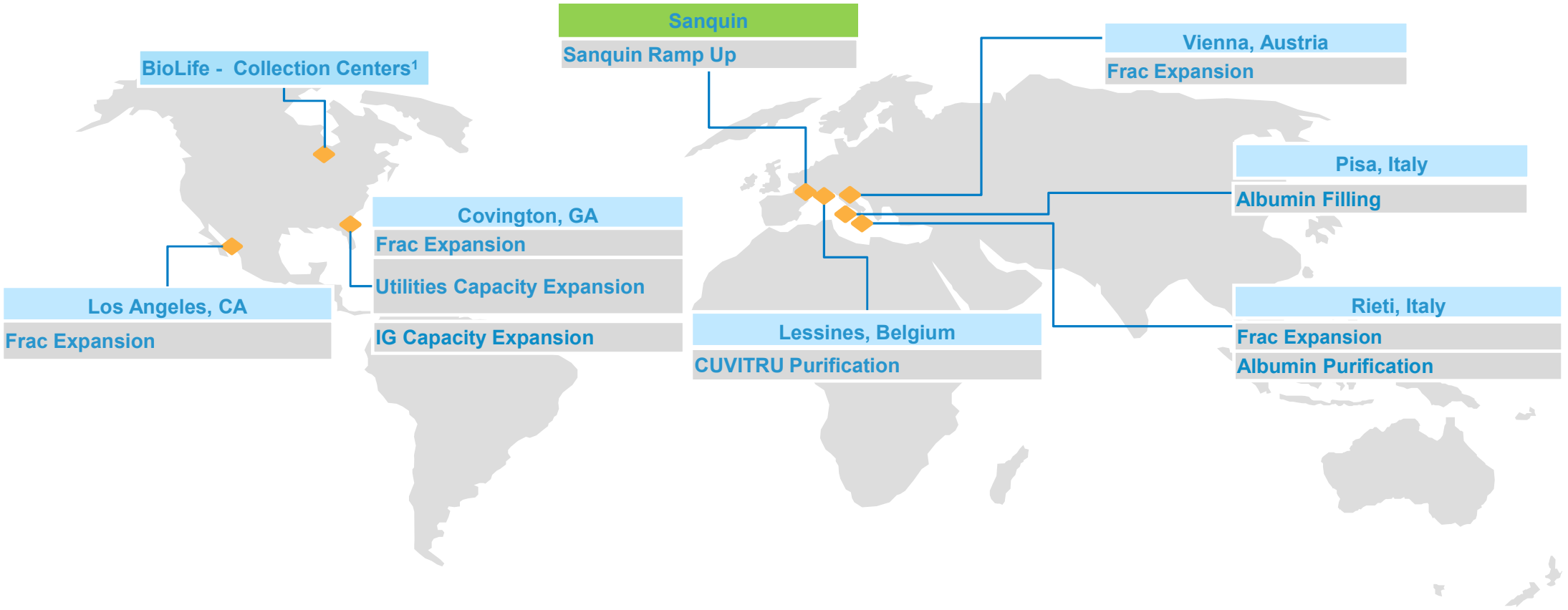
Modernization and capacity expansion across the network



1 Multiple New US Based Locations

Patient-centered and multi-generation innovation in medical devices

Our Why – Understand Patient Needs

Inputs

Patient Needs:

- Patient Needs: Patient Journey
- Patient Feedback: Field & Complaints Process
- Market Research
- Brand Plans

Medical Device Strategy Planning:

- R&D Pipeline Planning
- Device Strategy Planning & Delivery

Our Vision – Serial Innovative Solutions

Diagnostics & Advanced Delivery Systems

- **At Home Diagnostics**
- **Advanced Delivery Systems**

Connected & Software Devices

- **HCP Portal & Patient App**
- **Connected Device & App**

- **More than 30 device programs in development**
- **A significant amount of Shire revenue is supported by devices**
- **Approved medical device in diagnostics, advanced delivery system and eHealth in major global markets**

Shire

Agenda

Welcome	**Carlos Soto** *Covington Site Head*
Plasma-Derived Therapies Business Overview	**Kasha Witkos** *Immunology Franchise Head* **Paul Blanchfield** *US Immunology Head*
Plasma Technical Operations Overview	**Matt Walker** *Technical Operations Head* **Susan Brown** *BioLife Head* **Adrian Murphy** *Plasma Operating Unit Head*
Q&A	
Small Group Rotation	

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Q & A

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Small group rotations

	Group 1	Group 2
Rotation 1 1pm - 1:40pm	Life of a Batch	Lunch
Rotation 2 1:40pm - 2:20pm	Lunch	Life of a Batch
Rotation 3 2:20pm - 3:00pm	Site Tour	

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